Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

69451 Weinheim, Germany

Highly Diastereoselective Sulfonium Ylide Rearrangements to Quaternary Substituted Indolines

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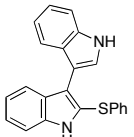
Experimental protocols and spectroscopic data and copies of spectra for all new compounds:

General

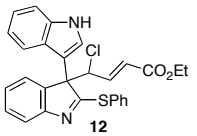
NMR spectra were recorded on either Varian Inova-500 MHz or Varian VXR-500 MHz spectrometers. Chemical shifts were reported in δ, parts per million (ppm), relative to benzene (7.16), chloroform (7.26), or dichloromethane (5.32) as internal standards. Coupling constants, *J*, were reported in Hertz (Hz) and refer to apparent peak multiplicities and not true coupling constants. Mass spectra were recorded at the Mass Spectrometry Facility at the Department of Chemistry of the University of Utah at Salt Lake City on a Finnigan MAT 95 mass spectrometer and at the Mass Spectrometry Facility at the Department of Chemistry of the University of California at Riverside on a Agilent LCTOF mass spectrometer. IR spectra were recorded on a Bruker Tensor 27 FT-IR spectrometer. Solvents were purified according to the guidelines in *Purification of Common Laboratory Chemicals* (Perrin, Armarego, and Perrin: Oxford, 1966). (*i*-Pr)$_2$NEt, 2,6-lutidine, TMEDA, chlorobenzene, and pyridine were distilled from CaH_2. Spectroscopic grade DMF was stored over activated 4Å molecular sieves and used without purification. Zn dust (<10 mm, Aldrich) was activated by sequentially washing with HCl, H_2O, ether, and acetone and then drying under vacuum overnight. All other reagents were used without purification. Unless otherwise stated, all reactions were run under an atmosphere of dried nitrogen in flame-dried glassware. Concentration refers to removal of solvent under reduced pressure (house vacuum at ca. 20 mm Hg).



11

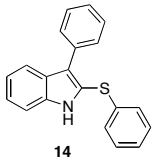
2-Phenylsulfanyl-1*H*,1'*H*-[3,3']bisindolyl (**11**). Synthesized according to the general procedure for the preparation of **17** using bis-indole (0.785 g, 3.380 mmol)[1] CH_2Cl_2 (10 mL), and phenyl sulfonyl chloride (0.487 g, 3.38 mmol). Flash chromatography (2:1 hexanes/ethyl acetate) gave 827 mg (72%) of **11** as a white solid. mp = 127 ° C; R_f 0.54 (3:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, CD_2Cl_2) δ 8.38 (s, 2 H), 7.64 (d, *J* = 8.3 Hz, 1 H), 7.61 (d, *J* = 7.8 Hz, 1 H), 7.45 (d, *J* = 7.8 Hz, 1 H), 7.40 (d, *J* = 8 Hz, 1 H), 7.27 (t, *J* = 7.8 Hz, 2 H), 7.21 (m, 3 H), 7.12 (m, 5 H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 137.9, 137.7, 136.7, 129.7, 128.7, 127.8, 127.3, 126.4, 124.3, 124.1, 122.6, 121.3, 121.0, 120.5, 120.1, 118.6, 111.8, 111.8, 111.5, 109.5. IR 3396, 3054, 1580, 1477 cm^{-1}. LRMS (ESI) calc'd for $C_{22}H_{17}N_2S$ (MH^+) 341.1 found 341.1 (10), 207.9 (10), 151.2 (15), 143.2 (100).

[1]. Berens, U.; Brown, J. M.; Long, J.; Selke, R. *Tetrahedron: Asymm.* **1996**, *7*, 285.



12

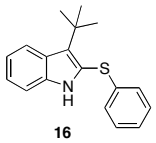
4-Chloro-4-(2-phenylsulfanyl-1'*H*-[3,3']biindolyl-3-yl)-but-2-enoic acid ethyl ester (**12**). To a solution of **11** (0.210 g, 0.620 mmol) and CH_2Cl_2 (3 mL) was added $Rh_2(OAc)_4$ (0.014 g 0.031 mmol). To the mixture was added a solution of vinyl diazoacetate **2** (0.324 g, 1.89 mmol) and CH_2Cl_2 (0.5 mL) over 3 h. After the addition, the mixture was concentrated. Flash chromatography (3:1, hexanes/ethyl acetate) afforded 196 mg (78%) of **12** as a 10:1 mixture of diastereomers. mp = 102 °C; R_f 0.18 (3:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, CD_2Cl_2) δ 8.60 (s, 1 H), 7.57 (d, *J* = 7.3 Hz, 1 H), 7.53-7.43 (m, 5 H), 7.41-7.35 (m, 4 H), 7.19 (t, *J* = 7.8 Hz, 1 H), 7.13 (t, *J* = 8.3 Hz, 1 H), 6.87 (t, *J* = 7.3 Hz, 1 H), 6.53 (d, *J* = 7.8 Hz, 1 H), 6.30 (d, *J* = 15.1 Hz, 1 H), 6.20 (dd, *J* = 15.1, 8.7 Hz, 1 H), 5.69 (d, *J* = 8.7 Hz, 1 H), 4.20-4.09 (m, 2 H), 1.24 (t, *J* = 7.3 Hz, 3 H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 165.5, 156.2, 140.5, 139.7, 137.0, 135.0, 130.1, 130.0, 129.8, 128.3, 126.3, 126.2, 125.5, 125.4, 125.0, 122.9, 120.5, 120.0, 119.8, 112.1, 71.6, 67.0, 62.9, 61.3, 14.5. IR (neat) 3407, 3061, 2981, 1720, 1516 cm^{-1}. LRMS (ESI) calc'd for $C_{28}H_{24}ClN_2O_2S$ (MH^+) 487.1 found 488.0 (40), 485.9 (95).



14

3-Phenyl-2-phenylsulfanyl-1*H*-indole (**14**). Synthesized according to the general procedure for the preparation of **17** using 3-phenylindole[2] (0.500 g, 2.59 mmol), CH_2Cl_2 (8 mL), and phenyl sulfonyl chloride (0.373 g, 2.59 mmol). Flash chromatography (10:1 hexanes/ethyl acetate) gave 622 mg (80%) of **14** as a viscous oil. R_f 0.35 (10:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, CD_2Cl_2) δ 8.33 (broad s, 1 H), 7.80 (m, 1 H), 7.66 (m, 2 H), 7.48 (m, 2 H), 7.37 (m, 2 H), 7.31 (m, 1 H), 7.25 (t, *J* = 7.3 Hz, 1 H), 7.30-7.13 (m 5 H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 137.5, 137.4, 134.5, 134.4, 130.3, 129.8, 128.9, 127.7, 127.6, 127.4, 126.6, 124.8, 124.3, 122.4, 121.1, 120.5, 111.6, 111.6; IR (neat) 3404, 3055, 1602, 1581 cm^{-1}. MS (CI) calc'd for $C_{20}H_{16}NS$ (MH^+) 302.1, found 302.2 (MH^+).

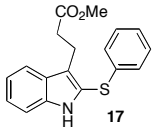
[2]. Gonzalo, J.; Lafuente, A.; Garcia-Almaraz, P. *J. Het. Chem.* **2000**, *37*, 1281.



16

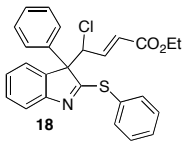
3-*tert*-Butyl-2-phenylsulfanyl-1*H*-indole (**16**). Synthesized according to the general procedure for the preparation of **17** using 3-*t*-butylindole[3] (0.107 g, 0.660 mmol), CH_2Cl_2 (4 mL), and phenyl sulfonyl chloride (0.095 g, 0.66 mmol). Flash chromatography (8:1 hexanes/ethyl acetate) gave 156 mg (85%) of **16** as a viscous oil. R_f 0.50 (8:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, CD_2Cl_2) d 8.04 (broad s, 1 H), 7.96 (d, *J* = 7.8 Hz, 1 H), 7.27 (t, *J* = 8.3 Hz, 1 H), 7.23 (t, *J* = 7.3 Hz, 2 H), 7.18 (t, *J* = 7.3 Hz, 1 H), 7.13 (t, *J* = 6.8 Hz, 1 H), 7.08 (t, *J* = 8.3 Hz, 1 H), 7.04 (d, *J* = 7.81 Hz, 2 H), 1.62 (s, 9 H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 138.8, 137.8, 135.5, 130.8, 129.9, 129.6, 127.6, 126.7, 126.0, 123.2, 123.0, 119.9, 119.5, 111.3, 32.1; IR (neat) 3390, 3052, 1590 cm^{-1};LRMS (ESI) calc'd for $C_{18}H_{20}NS$ (MH^+) 282.1 found 283.0 (10), 242.0 (20), 188.1 (100).

General procedure for the preparation of 2-thioindoles.



17

3-(2- Phenylsulfanyl -1H-indol-3-yl)-propionic acid methyl ester (**17**). To a solution of 3-indolepropionic acid methyl ester[4] (0.943g, 4.65 mmol) in CH_2Cl_2 (10 mL) at rt was added phenylsulfonyl chloride (1.01 g, 6.97 mmol) dropwise over 0.5 h. After stirring for an additional 0.5 h, the reaction was quenched with aq. $NaHCO_3$ (sat., 21 mL). After extraction of the aqueous phase with EtOAc (3 x 70 mL), the combined organic extracts were washed with brine (1 x 70 mL), dried (Na_2SO_4), and concentrated. The crude material was purified by flash chromatography (ethyl acetate/hexanes 1:10) to give 1.19 g (82%) of **17** as a white solid. mp = 85-86 °C; R_f 0.50 (2:1 hexanes:ethyl acetate); ^{1}H NMR (300 MHz, CD_2Cl_2) δ 8.07 (broad s, 1 H), 7.64 (d, *J* = 8.1 Hz, 1H), 7.33-7.04 (m, 8 H), 3.64 (s, 3 H), 3.22 (ddd, *J* = 7.8, 7.8, 0 Hz, 2 H), 2.64 (ddd, *J* = 8.1, 8.1, 0 Hz, 2 H); ^{13}C NMR (75 MHz, CD_2Cl_2) δ 173.7, 137.2, 137.1, 129.4, 127.6, 126.9, 126.1, 123.8, 122.3, 120.1, 119.5, 111.2, 51.8, 35.2, 20.6; IR (neat) 3336, 2920, 1708, 1447, 1297, 743 cm^{-1}. LRMS (ESI) calc'd for $C_{18}H_{18}NO_2S$ (MH^+) 312.1 found 312.0 (50), 334.0 (MNa^+, 100), 350 (MK^+, 55).

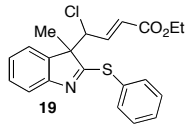


18

[3]. Zhu, X.; Ganesan, A. *J. Org. Chem.* **2002**, *67*, 2705.
[4]. Yato, M.; Homma, K.; Ishida, A. *Tetrahedron* **2001**, *57*, 5353.

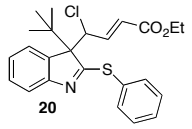
4-Chloro-4-(3-phenyl-2-phenylsulfanyl-3*H*-indol-3-yl)-but-2-enoic acid ethyl ester (**18**). Synthesized according to the general procedure for the preparation of **21** using **12** (0.014 g, 0.047 mmol), CH_2Cl_2 (1 mL), $Rh_2(OAc)_4$ (0.001 g 0.002 mmol), and vinyl diazoacetate **2** (0.016 g, 0.093 mmol) in CH_2Cl_2 (0.5 mL). Flash chromatography (8:1, hexanes/ethyl acetate) afforded 18 mg (88%) of **18** as a 8:1 mixture of diastereomers. R_f 0.32 (5:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.63 (d, *J* = 7.3 Hz, 1 H), 7.48-7.36 (m, 9 H), 7.28-7.20 (m, 4 H), 7.26 (d, *J* = 15.2 Hz, 1 H), 6.10 (dd, *J* = 15.1, 8.8 Hz, 1 H), 5.68 (d, *J* = 8.8 Hz, 1 H), 4.17-4.03 (m, 2 H), 1.21 (t, *J* = 6.8 Hz, 3 H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 181.4, 165.4, 156.7, 140.5, 139.6, 136.7, 135.1, 130.2, 130.1, 129.9, 129.5, 128.9, 128.1, 127.9, 126.4, 126.3, 125.6, 120.1, 71.5, 62.7, 61.3, 14.5; IR (neat) 3060, 2981, 1721, 1517, 1451 cm^{-1}. MS (CI) 448.2 (MH^+).

COSY Summary. The following cross peaks were observed: H(1) and H(2); H(2) and H(3).



19

Synthesized according to the general procedure for the preparation of **21** using **15** (0.015 g, 0.053 mmol),[5] CH_2Cl_2 (1 mL), $Rh_2(OAc)_4$ (0.001 g 0.003 mmol), and vinyl diazoacetate **2** (0.022 g, 0.13 mmol) in CH_2Cl_2 (0.5 mL). Flash chromatography (8:1, hexanes/ethyl acetate) afforded 15 mg (75%) of **19** as a 7:1 mixture of diastereomers. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62-7.59 (m, 3H), 7.44-7.43 (m, 3H), 7.38 (d, *J* = 7.8 Hz, 1H), 7.31 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.16 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.18 (dd, *J* = 8.7, 15.5 Hz, 1H), 6.09 (d, *J* = 15.4 Hz, 1H), 4.87 (d, *J* = 8.5 Hz, 1H), 4.14-4.06 (m, 2H), 1.66 (s, 3H), 1.21 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 182.2, 165.3, 155.0, 140.9, 140.0, 135.2, 130.0, 129.7, 129.4, 127.7, 125.6, 125.0, 124.1, 119.6, 65.7, 62.9, 61.1, 22.4, 14.3; IR (neat) 3062, 2980, 1723, 1517, 1442, 1267, 1173, 1023, 756 cm^{-1}. LRMS (ESI) calc'd for $C_{22}H_{23}ClNO_2S$ (MH^+) 386.1 found 386.0 (100).



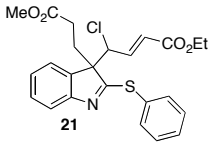
20

4-(3-*tert*-Butyl-2-phenylsulfanyl-3*H*-indol-3-yl)-4-chloro-but-2-enoic acid ethyl ester (**20**). Synthesized according to the general procedure fort he preparation of **21** using **16** (0.015 g, 0.56 mmol) and CH_2Cl_2 (1 mL), $Rh_2(OAc)_4$ (0.0012 g 0.0030 mmol), and vinyl diazoacetate **3.52** (0.019 g, 0.111 mmol) in CH_2Cl_2 (0.5 mL). Flash chromatography (10:1, hexanes/ethyl acetate) afforded 21 mg (91%) of **20** as a 15:1 mixture of diastereomers. R_f 0.22 (10:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.75 (d, *J* = 7.31 Hz, 1 H), 7.50 (d, *J* = 6.83 Hz, 2 H), 7.45-7.39 (m, 3 H), 7.33 (t, *J* = 7.81 Hz, 1 H), 7.30 (d, *J* = 7.80 Hz, 1 H), 7.17 (t, *J* = 7.32 Hz, 1 H), 6.10 (d, *J* = 15.62 Hz, 1 H), 5.90 (dd, *J* = 15.2, 9.27 Hz, 1 H), 5.19 (d, *J* = 9.27 Hz, 1 H), 4.11-4.01 (m, 2 H), 1.26 (s, 9 H), 1.18 (t, *J* = 7.31 Hz, 3 H); ^{13}C NMR

[5]. Maeda, Y.; Koyabu, M.; Nishimura, T.; Uemura, S. *J. Org. Chem.* **2004**, *69*, 7688.

(125 MHz, CD_2Cl_2) δ 181.6, 165.7, 156.2, 142.0, 137.6, 135.4, 130.1, 129.8, 129.4, 128.8, 127.7, 125.2, 124.4, 119.7, 72.7, 62.9, 61.2, 36.4, 28.2, 14.5; IR (neat) 2976, 1723, 1517, 1451 cm^{-1}. LRMS (CI) calc'd for $C_{24}H_{26}ClNO_2S$ (MH^+) 427.1 found 428.3 (100).

General procedure for coupling reaction.

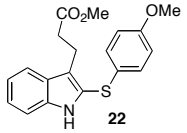


21

(E)-4-Chloro-4-[3-(2-methoxycarbonyl-ethyl)-2-phenylsulfanyl-3H-indol-3-yl]-but-2-enoic acid ethyl ester (**21**). To a solution of **17** (0.010 g, 0.035 mmol) and $Rh_2(OAc)_4$ (0.39 mg, $8.7x10^{-4}$ mmol) in CH_2Cl_2 (0.3 mL) at rt was slowly added a solution of vinyl diazoacetate **2** (0.014 g, 0.081 mmol) in CH_2Cl_2 (0.2 ml) via syringe pump over 3 h. Following the addition the solvent was removed in vacuo and the resulting residue was purified by column chromatography (1:2 ethyl acetate:hexanes) to give 13 mg (88%) of **21** as a pale yellow oil and as an 8:1 mixture of diastereomers (HPLC). Pure diastereomers were isolated by preparative TLC using ethyl acetate: hexanes, 1:10 as the eluting solvent.

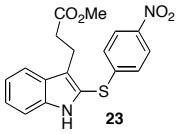
Major diastereomer: colorless oil; R_f 0.46 (2:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.60-7.56 (m, 3 H), 7.47-7.46 (m, 3 H), 7.37-7.32 (m, 2 H), 7.22-7.19 (m, 1 H), 6.13-6.12 (m, 1 H), 4.91 (d, *J* = 7.5, 2 H), 4.09 (q, *J* = 6.5 Hz, 2 H), 3.55 (s, 3 H), 2.90-2.84 (m, 1 H), 2.29-2.23 (m, 1 H), 2.08-2.02 (m, 1 H), 1.57-1.51 (m, 1 H), 1.21 (t, *J* = 7 Hz, 3 H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 180.2, 172.9, 165.2, 155.9, 140.4, 136.9, 135.2, 130.2, 129.8, 127.2, 125.8, 125.2, 124.5, 119.7, 66.5, 65.2, 61.1, 51.9, 30.6, 28.6, 14.3; IR (neat) 2953, 2361, 1725, 1519, 1173 cm^{-1}LRMS (ESI) calc'd for $C_{24}H_{25}ClNO_4S$ (MH+) 458.1 found 458.0 (100), 424.1 (5).

Minor diastereomer: colorless oil; R_f 0.42 (2:1 hexanes:ethyl acetate); ^{1}H NMR (300 MHz, CD_2Cl_2) δ 7.68-7.66 (m, 2H), 7.49-7.47 (m, 3H), 7.36-7.34 (m, 2H), 7.26 (d, *J* = 7.4 Hz, 1H), 7.22-7.17 (m, 1H), 6.94 (dd, *J* = 8.8, 15.3 Hz, 1H), 6.12 (d, *J* = 15.3 Hz, 1H), 4.85 (d, *J* = 8.8 Hz, 1H), 4.21 (q, *J* = 7.2 Hz, 2H), 3.53 (s, 3H), 2.35-2.30 (m, 2H), 2.05 (ddd, *J* = 5.2, 11.3, 16.4 Hz, 1H), 1.56 (ddd, *J* = 4.9, 11.7, 16.3 Hz, 1H), 1.30 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 180.3, 172.7, 165.1, 155.8, 140.6, 136.1, 134.4, 129.5, 129.4, 129.4, 127.3, 125.9, 124.9, 122.6, 120.0, 66.3, 63.0, 61.0, 51.7, 30.2, 28.6, 14.2; IR (neat) 3062, 2981, 2951, 1725, 1522, 1441, 1174, 1024, 745; LRMS (ESI) calc'd for $C_{24}H_{25}ClNO_4S$ (MH+) 458.1 found 458.1 (100), 454.1 (10).



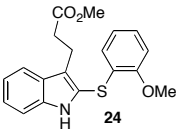
22

3-[2-(4-Methoxy-phenylsulfanyl)-1H-indol-3-yl]-propionic acid methyl ester (**22**). Synthesized according to the general procedure for the preparation of **17** using 3-indolepropionic acid methyl ester (0.203 g, 1 mmol), CH_2Cl_2 (2 mL) and 0.244 g (1.5 mmol) of 4-methoxybenzenesulfonyl chloride. Flash chromatography (ethyl acetate/hexanes 1:10) afforded 0.310 g (91%) of **22** as a colorless oil. R_f 0.42 (2:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, CD_2Cl_2) δ 8.13 (broad s, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.29 (d, *J* = 8.2 Hz, 1H), 7.20 (partially obscured dd, *J* = 7.5, 7.5 Hz, 1H), 7.16 (d, *J* = 8.8 Hz, 2 H), 7.11 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.81 (d, *J* = 8.8 Hz, 2H), 3.75 (s, 3H), 3.63 (s, 3H), 3.21 (broad dd, *J* = 8.0, 8.0 Hz, 2H), 2.62 (broad dd, *J* = 7.9, 7.9 Hz, 2H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 175.6, 161.3, 139.2, 132.8, 129.9, 128.8, 126.7, 125.5, 122.8, 122.1, 121.4, 117.2, 113.2, 57.7, 53.8, 37.3, 22.8; IR (neat) 3352, 3058, 3001, 2949, 2837, 1722, 1492, 1442, 1288, 1244, 1175, 1030; LRMS (ESI) calc'd. for $C_{19}H_{20}NO_3S$ 342.4 (MH^+); found 342.0 (75), 479.9 (100), 260.0 (15).



23

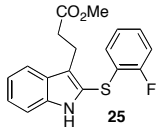
3-[2-(4-Nitro-phenylsulfanyl)-1H-indol-3-yl]-propionic acid methyl ester (**23**). Synthesized according to the general procedure fort he preparation of **17** using 3-indolepropionic acid methyl ester (0.203 g, 1.00 mmol), CH_2Cl_2 (2 mL), and 0.244 g (1.5 mmol) of 4-nitrobenzenesulfonyl chloride. Flash chromatography (ethyl acetate/hexanes 1:10) afforded 0.338 g (95%) of **23** as a yellow solid. m.p. = 109-110°C; R_f 0.46 (2:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, CD_2Cl_2) δ 8.32 (broad s, 1H), 8.05-8.02 (m, 2H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.40 (d, *J* = 8.2 Hz, 1H), 7.30 (ddd, *J* = 7.1, 7.1, 1.0 Hz, 1H), 7.18 (ddd, 7.1, 7.1, 0.9 Hz, 1H), 7.12-7.09 (m, 2H), 3.58 (s, 3H), 3.18 (broad dd, *J* = 7.8, 7.8 Hz, 2H), 2.63 (broad dd, *J* = 7.9, 7.9 Hz, 2H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 175.4, 149.7, 148.0, 139.8, 129.7, 128.0, 126.6, 126.5, 126.1, 122.6, 122.0, 121.2, 113.7, 53.8, 37.2, 22.7; IR (neat) 3380, 2949, 1730, 1574, 1513, 1445, 1295, 1177, 1083; LRMS (ESI) calc'd for $C_{18}H_{17}N_2O_4S$ (MH^+) 357.4 found 356.9 (100), 342.0 (65), 282.9 (25).



24

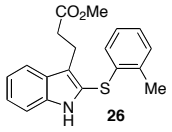
3-[2-(2-Methoxy-phenylsulfanyl)-1H-indol-3-yl]-propionic acid methyl ester (**24**). Synthesized according to the general procedure for the preparation of **17** using 3-indolepropionic acid methyl ester (0.020 g, 0.10 mmol), CH_2Cl_2 (0.2 mL) and 0.026 g (0.15 mmol) of 2-methoxybenzenesulfonyl chloride. Flash chromatography (ethyl acetate/hexanes 1:10) afforded 0.031 g (92%) of **22** as a white solid. m.p. = 101-102°C; R_f 0.42 (2:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, CD_2Cl_2) δ 8.27 (broad s, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.34 (d, *J* = 8.2 Hz, 1H), 7.23 (dd, *J* = 7.1, 7.1 Hz, 1H), 7.18 (d, *J* = 7.4 Hz, 1H), 7.14 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.90 (d, *J* = 8.1 Hz, 1H), 6.76 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.65 (d,

J = 7.8 Hz, 1H), 3.93 (s, 3H), 3.60 (s, 3H), 3.16 (broad t, *J* = 8.0 Hz, 2H), 2.62 (broad t, *J* = 8.0 Hz, 2H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 175.6, 139.5, 138.3, 137.9, 132.6, 129.9, 129.1, 129.0, 128.2, 125.7, 124.3, 124.2, 122.1, 121.5, 113.3, 53.7, 37.2, 22.8, 22.1; IR (neat) 3389, 3057, 3001, 2947, 2835, 1718, 1577, 1475, 1446, 1434, 1339, 1272; LRMS (ES) calc'd for $C_{19}H_{20}NO_3S$ (MH^+) 342.4 found 342.0 (100), 267.9 (20).



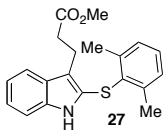
25

3-[2-(2-Fluoro-phenylsulfanyl)-1H-indol-3-yl]-propionic acid methyl ester (**25**). Synthesized according to the general procedure for the preparation of **17** using 3-indolepropionic acid methyl ester (0.203 g, 1.00 mmol), CH_2Cl_2 (2 mL), and 0.24 g (1.5 mmol) of 2-fluorobenzenesulfonyl chloride. Flash chromatography (ethyl acetate/hexanes 1:10) afforded 0.242 g (74%) of **25** as a white solid. m.p. = 82-83 °C; R_f 0.52 (2:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, CD_2Cl_2) δ 8.25 (broad s, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.35 (d, *J* = 8.2 Hz, 1H), 7.24 (dd, *J* = 7.2, 7.2 Hz, 1H), 7.18-7.12 (m, 2H), 7.07 (dd, *J* = 8.2, 8.2 Hz, 1H), 6.98 (dd, *J* = 7.5, 7.5 Hz, 1H), 6.84 (dd, *J* = 7.8, 7.8 Hz, 1H), 3.61 (s, 3H), 3.20 (broad t, *J* = 8.0 Hz, 2H), 2.62 (broad t, *J* = 8.0 Hz, 2H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 175.6, 162.8, 160.9, 139.6, 131.7, 130.4, 130.3, 127.3, 127.2, 126.0, 125.1, 122.2, 121.6, 118.0, 117.8, 113.5, 53.8, 37.2, 22.7; IR (neat) 3336, 3055, 2948, 1716, 1470, 1446, 1418, 1338, 1259, 1219; LRMS (ESI) calc'd for $C_{18}H_{17}FNO_2S$ (MH^+) 330.4 found 329.9 (100), 255.9 (30).

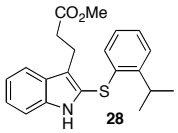


26

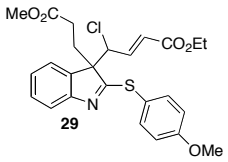
3-(2-o-Tolylsulfanyl-1H-indol-3-yl)-propionic acid methyl ester (**26**). Synthesized according to the general procedure fort he preparation of **17** using 3-indolepropionic acid methyl ester (0.203 g, 1.00 mmol), CH_2Cl_2 (2 mL), and 0.24 g (1.5 mmol) of 2-methylbenzenesulfonyl chloride. Flash chromatography (ethyl acetate/hexanes 1:10) afforded 0.295 g (91%) of **26** as a white solid. m.p. = 131-132°C; R_f 0.54 (2:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, CD_2Cl_2) δ 8.16 (broad s, 1H), 7.53 (d, *J* = 7.9 Hz, 1H), 7.33 (d, *J* = 8.2 Hz, 1H), 7.23 (dd, *J* = 7.1, 7.1 Hz, 1H), 7.18 (d, *J* = 7.3 Hz, 1H), 7.13 (dd, *J* = 7.5, 7.5 Hz, 1H), 7.06 (dd, *J* = 7.4, 7.4 Hz, 1H), 6.99 (dd, *J* = 7.4, 7.4 Hz, 1H), 6.70 (d, *J* = 7.9 Hz, 1H), 3.60 (s, 3H), 3.18 (broad t, *J* = 8.0 Hz, 2H), 2.61 (broad t, *J* = 7.5 Hz, 2H), 2.43 (s, 3H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 175.6, 139.5, 138.3, 137.9, 132.6, 129.9, 129.1, 129.0, 128.2, 125.7, 124.3, 124.2, 122.1, 121.5, 113.3, 53.7, 37.2, 22.8, 22.1;; IR (neat) 3341, 3055, 2946, 1717, 1465, 1446, 1338, 1294, 1270, 1197; LRMS (ESI) calc'd for $C_{19}H_{20}NO_2S$ (MH^+) 326.4 found 326.0 (100), 260.0 (35).



3-[2-(2,6-Dimethyl-phenylsulfanyl)-1H-indol-3-yl]-propionic acid methyl ester (**27**). Synthesized according to the general procedure for **17** using 3-indolepropionic acid methyl ester (0.203 g, 1.00 mmol), CH_2Cl_2 (2 mL), and 0.260 g (1.5 mmol) of 2,6-dimethylbenzenesulfonyl chloride. Flash chromatography (ethyl acetate/hexanes 1:10) afforded 0.292 g (86%) of **27** as a colorless oil. R_f 0.55 (2:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.63 (broad s, 1H), 7.49 (d, *J* = 7.5 Hz, 1H), 7.21 (dd, *J* = 8.3, 6.5 Hz, 1H), 7.16-7.15 (m, 3H), 7.10-7.04 (m, 2H), 3.66 (s, 3H), 3.15 (dd, *J* = 7.9 Hz, 2H), 2.59 (dd, *J* = 7.8 Hz, 2H), 2.46 (s, 6H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 175.7, 145.1, 138.8, 132.8, 131.4, 131.1, 130.4, 128.5, 124.2, 121.9, 120.3, 117.6, 112.6, 53.8, 36.8, 24.1, 22.6; IR (neat) 3384, 3053, 2948, 2920, 2850, 1721, 1484, 1339, 1269, 1196, 1173; LRMS (ESI) $C_{20}H_{22}NO_2S$ (MH^+) 340.4 found 340.0 (100).



3-[2-(2-Isopropyl-phenylsulfanyl)-1H-indol-3-yl]-propionic acid methyl ester (**28**). Synthesized according to the general procedure for **17** using 3-indolepropionic acid methyl ester (0.203 g, 1.00 mmol), CH_2Cl_2 (2 mL), and 0.28 g (1.5 mmol) of 2-isopropylbenzenesulfonyl chloride. Flash chromatography (ethyl acetate/hexanes 1:10) afforded 0.268 g (76%) of **28** as a colorless oil. R_f 0.59 (2:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, CD_2Cl_2) δ 8.23 (broad s., 1H), 7.64 (d, *J* = 7.9 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.23 (dd, *J* = 7.2, 7.2 Hz, 1H), 7.15 (d, *J* = 7.8 Hz, 1H), 7.14 (d, *J* = 7.0 Hz, 1H), 6.96 (dd, *J* = 8.2, 8.2 Hz, 1H), 6.84 (d, *J* = 7.9 Hz, 1H), 3.61 (s, 3H), 3.51 (septet, *J* = 7.0 Hz, 1H), 3.20 (broad t, *J* = 7.9 Hz, 2H), 2.63 (broad t, *J* = 8.0 Hz, 2H), 1.32 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 175.6, 148.4, 139.5, 137.2, 129.9, 129.5, 128.9, 128.6, 127.9, 125.7, 124.7, 124.3, 122.1, 121.4, 113.4, 53.7, 37.2, 32.7, 25.2, 22.8; IR (neat) 3347, 3055, 2959, 2866, 1719, 1444, 1338, 1271, 1198; LRMS (ESI) calc'd for $C_{21}H_{24}NO_2S$ (MH^+) 354.5 found 354.0 (100), 342.0 (25).

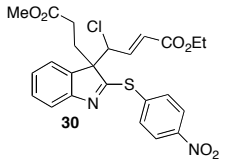


(E)-4-Chloro-4-[3-(2-methoxycarbonyl-ethyl)-2-(4-methoxy-phenylsulfanyl)-3H-indol-3-yl]-but-2-enoic acid ethyl ester (**29**).

Synthesized according to the general procedure for the preparation of **21** using **22** (0.020 g, 0.059 mmol) in CH_2Cl_2

(0.6 mL), Rh_2[(S)-TBSP]$_4$ (2.1 mg, 1.5x10^{-3} mmol) and diazoacetate **2** (0.031 g, 0.18 mmol) in CH_2Cl_2 (0.4 mL). Column chromatography (1:2 ethyl acetate: hexanes) provided 27 mg (94%) of **29** as a 7:1 mixture of diastereomers based on ^{1}H NMR integration of the allylic protons. Minor diastereomer could not be isolated from the major isomer.

Major diastereomer: white crystals; mp=148-149 °C ; R$_f$ 0.31 (1:2 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) 7.57 (d, *J* = 7.4 Hz, 1H), 7.48 (d, *J* = 8.7 Hz, 2H), 7.37 (d, *J* = 7.7 Hz, 1H), 7.31 (dd, *J* = 7.5, 7.5 Hz, 1H), 7.16 (dd, *J* = 7.4, 7.4 Hz, 1H), 6.96 (d, *J* = 8.5 Hz, 2H), 6.17-6.09 (m, 2H), 4.86 (d, *J* = 7.3 Hz, 1H), 4.14-4.07 (m, 2H), 3.84 (s, 3H), 3.58 (s, 3H), 2.88 (ddd, *J* = 4.7, 13.4, 13.4 Hz, 1H), 2.24 (ddd, *J* = 4.9, 13.7, 13.7 Hz, 1H), 2.06 (ddd, *J* = 4.6, 11.8, 16.5 Hz, 1H), 1.55 (ddd, *J* = 4.6, 11.6, 16.2 Hz, 1H), 1.21 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 180.2, 172.8, 165.0, 160.9, 155.5, 140.4, 136.4, 136.2, 129.3, 125.3, 124.8, 124.0, 119.8, 116.8, 115.2, 65.9, 64.9, 60.7, 55.4, 51.7, 30.4, 28.3, 14.1; IR (neat) 2952, 2841, 1727, 1494, 1450, 1252, 1110, 1030, 767; LRMS (ESI) calcd for $C_{25}H_{27}ClNO_5S$ (MH+) 488.1 found 488.1 (100), 510.1 (MNa$^+$, 5).



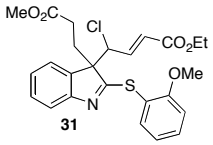
30

(E)-4-Chloro-4-[3-(2-methoxycarbonyl-ethyl)-2-phenylsulfanyl-3H-indol-3-yl]-but-2-enoic acid ethyl ester (**30**). Synthesized according to the general procedure for the preparation of **21** using **23** (0.013 g, 0.036 mmol) in CH_2Cl_2 (0.3 mL), $Rh_2(OAc)_4$ (0.40 mg, 9.0 x 10^{-4} mmol), and diazoacetate **2** (0.019 g, 0.11 mmol) in CH_2Cl_2 (0.2 mL). Column chromatography (1:2 ethyl acetate: hexanes) provided 14 mg (74%) of **30** as a 7:1 mixture of diastereomers based on ^{1}H NMR integration of the allylic protons. The diastereomers were separated using preparative TLC using ethyl acetate/hexanes, 1:10 as the eluting solvent.

Major diastereomer: yellow oil; R$_f$ 0.40 (2:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, *J* = 8.8 Hz, 2H), 7.84 (d, *J* = 8.8 Hz, 2H), 7.60 (d, *J* = 7.4, 1H), 7.36-7.42 (m, 2H), 7.24 (dd, *J* = 7.4, 7.4 Hz, 1H), 6.18 (dd, *J* = 15.4, 8.9 Hz, 1H), 6.07 (d, *J* = 15.5 Hz, 1H), 4.84 (d, *J* = 8.8 Hz, 1H), 4.11 (q, *J* = 7.1 Hz, 2H), 3.57 (s, 3H), 2.91 (ddd, *J* = 14.0, 12.0, 5.0 Hz, 1H), 2.26 (ddd, *J* = 14.5, 12.0, 5.0 Hz, 1H), 2.00 (ddd, *J* = 16.4, 11.5, 4.5 Hz, 1H), 1.58 (ddd, *J* = 16.4, 11.4, 5.0 Hz, 1H), 1.21 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.0, 172.5, 164.9, 154.9, 140.0, 136.1, 135.8, 134.0, 129.7, 125.7, 125.5, 124.2, 124.1, 120.1, 66.5, 64.3, 60.9, 51.8, 30.1, 28.2, 14.1; IR (neat) 3101, 3070, 2981, 2952, 1733, 1726, 1520, 1448, 1343, 1174 cm^{-1}; LRMS (ES) calcd for $C_{24}H_{24}ClN_2O_6S$ (MH+) 503.1 found 502.8 (100).

Minor diastereomer: yellow oil; R$_f$ 0.30 (2:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (d, *J* = 8.7 Hz, 2H), 7.92 (d, *J* = 8.6 Hz, 2H), 7.44 (d, *J* = 7.7 Hz, 1H), 7.38 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.25-7.22 (m, 2H), 6.93 (dd, *J* =

15.3, 8.5 Hz, 1H), 6.12 (d, *J* = 15.4 Hz, 1H), 4.81 (d, *J* = 8.5 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.56 (s, 3H), 2.29-2.42 (m, 2H), 1.98-2.05 (m, 1H), 1.59 (ddd, *J* = 16.4, 9.0, 5.2 Hz, 1H), 1.32 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.1, 172.4, 165.0, 155.3, 140.1, 136.4, 135.9, 134.2, 129.7, 126.2, 125.6, 124.2, 122.7, 120.2, 66.8, 62.7, 61.1, 51.8, 30.0, 28.6, 14.2; IR (neat) 2919, 2849, 1733, 1720, 1520, 1343, 1174 cm^{-1}; LRMS (ESI) calcd for $C_{24}H_{24}ClN_2O_6S$ (MH+) 503.1 found 502.8 (100).



31

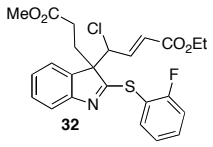
(E)-4-Chloro-4-[3-(2-methoxycarbonyl-ethyl)-2-(2-methoxy-phenylsulfanyl)-3H-indol-3-yl]-but-2-enoic acid ethyl ester (**31**).

Synthesized according to the general procedure for the preparation of **21** using **24** (0.010 g, 0.029 mmol) in CH_2Cl_2 (0.3 mL), $Rh_2(OAc)_4$ (0.32 mg, 7.3 x 10^{-4} mmol), and vinyl diazoacetate **2** (0.015 g, 0.088 mmol) in CH_2Cl_2 (0.2 mL). Column chromatography (1:2 ethyl acetate: hexanes) provided 11 mg (74%) of **23** as a 9:1 mixture of diastereomers based ^{1}H NMR integration. The diastereomers were separated by preparative TLC using ethyl acetate:hexanes (1:10) as the eluting solvent.

Major diastereomer: yellow oil; R*f* 0.33 (2:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 7.5 Hz, 1H), 7.56 (d, *J* = 7.0 Hz, 1H), 7.46 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.33 (d, *J* = 7.4 Hz, 1H), 7.28 (dd, *J* = 7.4, 7.4 Hz, 1 H), 7.14 (dd, *J* = 7.0, 7.0 Hz, 1H), 7.05-7.00 (m, 2H), 6.24 (dd, *J* = 15.5, 8.5 Hz, 1H), 6.10 (d, *J* = 15.5, 1H), 4.93 (d, *J* = 8.0 Hz, 1H), 4.11-4.04 (m, 2H), 3.84 (s, 3H), 3.58 (s, 3H), 2.94-2.87 (m, 1H), 2.32-2.22 (m, 2H), 1.52 (ddd, *J* = 16.8, 12.1, 5.6 Hz, 1H), 1.19 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.7, 173.0, 165.1, 159.5, 155.6, 140.6, 136.6, 136.4, 131.9, 129.2, 125.2, 124.6, 123.8, 121.3, 119.6, 111.8, 66.0, 64.9, 60.6, 55.9, 51.6, 30.9, 28.0, 14.1; IR (neat) 3068, 2952, 2841, 1727, 1518, 1478, 1452, 1277, 1252, 1175, 1025; LRMS (ESI) calc'd for $C_{25}H_{27}ClNO_5S$ (MH+) 488.1 found 488.0 (100), 391.2 (5).

Minor diastereomer: yellow oil; R*f* 0.31 (2:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.4 Hz, 1H), 7.46 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.36 (d, *J* = 7.6 Hz, 1H), 7.30 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.21 (d, *J* = 7.2 Hz, 1H), 7.14 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.05 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.02 (d, *J* = 8.2 Hz, 1 H), 6.94 (dd, *J* = 15.5, 8.5 Hz, 1H), 6.06 (d, *J* = 15.5 Hz, 1H), 4.81 (d, *J* = 8.7 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.85 (s, 3H), 3.57 (s, 3H), 2.23-2.41 (m, 2H), 1.57-1.50 (m, 2H), 1.30 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.6, 173.0, 165.2, 159.4, 155.8, 140.8, 136.6, 136.5, 131.7, 129.2, 125.7, 124.6, 122.4, 121.4, 119.7, 111.8, 66.2, 62.8, 60.9, 55.9, 51.7, 30.7, 28.3,

14.2; IR (neat) 3066, 2950, 2847, 1732, 1725, 1478, 1464, 1277, 1251, 1174, 1024 cm^{-1}; LRMS (ESI) calcd for $C_{25}H_{27}ClNO_5S$ (MH+) 488.1 found 488.0 (100), 391.2 (15).

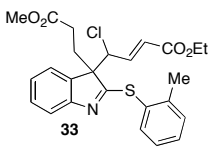


32

Ethyl (2*E*)-4-chloro-4-[2-[(2-fluorophenyl)thio]-3-(3-methoxy-3-oxopropyl)-3*H*-indol-3-yl]but-2-enoate (**32**). Prepared according to the general procedure for the preparation of **21** using **25** (0.010 g, 0.030 mmol) in CH_2Cl_2 (0.3 mL), $Rh_2(OAc)_4$ (0.033 g, 7.6 x 10^{-4} mmol) and a solution of diazoacetate **2** (0.016 mg, 0.091 mmol) in CH_2Cl_2 (0.2 mL). Column chromatography provided 0.012 g (81%) of the diastereomeric mixture (d.r. 7:1 based on NMR integration). Diastereomers were separated by preparative TLC eluting with ethyl acetate/hexanes (1:10).

Major diastereomer: colorless oil; R_f 0.33 (2:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59-7.62 (m, 1H), 7.57 (d, *J* = 7.4 Hz, 1H), 7.47-7.51 (m, 1H), 7.35 (d, *J* = 7.6 Hz, 1H), 7.31 (t, *J* = 7.2 Hz, 1H), 7.20-7.25 (m, 2H), 7.17 (t, *J* =7.4 Hz, 1H), 6.18 (dd, *J* = 8.4, 15.3 Hz, 1H), 6.10 (d, *J* = 15.4 Hz, 1H), 4.88 (d, *J* = 8.4 Hz, 1H), 4.06-4.15 (m, 2H), 3.58 (s, 3H), 2.91 (ddd, *J* = 4.9, 12.0, 13.8 Hz, 1H), 2.29 (ddd, *J* = 4.9, 11.6, 13.9 Hz, 1H), 2.12 (ddd, *J* = 4.9, 11.8, 16.5 Hz, 1H), 1.54 (ddd, *J* = 4.8, 11.6, 16.4 Hz, 1H), 1.21 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.7, 172.8, 165.0, 163.4, 161.4, 155.3, 140.0, 136.7, 136.4, 132.5, 132.5, 129.4, 125.5, 125.0, 124.0, 119.9, 116.6, 116.4, 66.2, 64.7, 60.7, 51.7, 30.5, 28.1, 14.1; IR (neat) 2952, 1725, 1521, 1476, 1448, 1263, 1227, 1173, 1027, 976; LRMS (ESI) calc'd for $C_{24}H_{24}ClFNO_4S$ (MH+) 476.1 found 475.8 (100).

Minor diastereomer: colorless oil; R_f 0.31 (2:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (ddd, *J* = 1.3, 7.1, 7.1 Hz, 1H), 7.51-7.47 (m, 1H), 7.37 (d, *J* = 7.7 Hz, 1H), 7.31 (t, *J* = 7.3 Hz, 1H), 7.25-7.21 (m, 3H), 7.17 (t, *J* = 7.3 Hz, 1H), 6.89 (dd, *J* = 8.5, 15.3 Hz, 1H), 6.07 (d, *J* = 15.4 Hz, 1H), 4.81 (d, *J* = 8.6 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.57 (s, 3H), 2.45-2.34 (m, 2H), 2.16 (ddd, *J* = 5.6, 10.9, 16.5 Hz, 1H), 1.58-1.52 (ddd, *J* = 5.3, 11.0, 16.5 Hz, 1H), 1.30 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.6, 172.8, 165.1, 164.0, 155.4, 140.4, 136.7, 136.5, 132.3, 132.2, 129.4, 125.9, 125.0, 124.9, 122.4, 120.0, 116.6, 116.3, 66.3, 62.7, 60.9, 51.8, 30.5, 28.4, 14.1; IR (neat) 2952, 1725, 1521, 1476, 1448, 1263, 1227, 1173, 1027, 976; LRMS (ESI) calcd for $C_{24}H_{24}ClFNO_4S$ (MH+) 476.1 found 476.0 (50), 498.0 (MNa^+, 100), 513.9 (MK^+, 30).

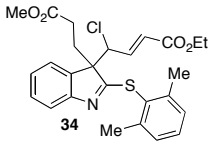


33

(E)-4-Chloro-4-[3-(2-methoxycarbonyl-ethyl)-2-o-tolylsulfanyl-3H-indol-3-yl]-but-2-enoic acid ethyl ester (**33**). Prepared according to the general procedure for the preparation of **21** using **26** (0.010 g, 0.031 mmol) in CH_2Cl_2 (0.3 mL), $Rh_2(OAc)_4$ (0.34 mg, 7.7 x 10^{-4} mmol) and vinyl diazoacetate **2** (0.016 g, 0.092 mmol) in CH_2Cl_2 (0.2 mL). Column chromatography (1:2 ethyl acetate:hexanes) provided 11 mg (76%) of **33** as a 11:1 mixture of diastereomers based on ^{1}H NMR integration. The diastereomers were separated by preparative TLC using ethyl acetate:hexanes (1:10) as the eluting solvent.

Major diastereomer: colorless oil; R_f 0.42 (2:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.4 Hz, 1H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.35-7.40 (m, 3H), 7.30 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.27-7.24 (m, 1H), 7.16 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.17 (dd, *J* = 15.5, 8.0 Hz, 1H), 6.12 (d, *J* = 15.5 Hz, 1H), 4.89 (d, *J* = 8.1 Hz, 1H), 4.14-4.06 (m, 2H), 3.58 (s, 3H), 2.91 (ddd, *J* = 14.0, 12.0, 5.0 Hz, 1H), 2.43 (s, 3H), 2.29 (ddd, *J* = 14.0, 11.5, 5.0 Hz, 1H), 2.07 (ddd, *J* = 16.5, 11.5, 5.0 Hz, 1H), 1.56 (ddd, *J* = 16.0, 11.5, 4.5 Hz, 1H), 1.21 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.7, 172.8, 165.0, 155.5, 142.7, 140.4, 136.2, 136.0, 131.0, 130.5, 129.4, 126.9, 125.6, 124.8, 124.0, 119.8, 66.0, 64.8, 60.7, 51.7, 30.8, 28.3, 21.1, 14.1; IR (neat) 2981, 1728, 1516, 1452, 1370, 1263, 1225, 1174, 1030; LRMS (ESI) calc'd for $C_{25}H_{26}NO_4S$ (MH^+) 472.0 found 472.0 (100), 325.0 (15).

Minor diastereomer: colorless oil; R_f 0.37 (2:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, *J* = 7.6 Hz, 1H), 7.40-7.37 (m, 3H), 7.31-7.28 (m, 2H), 7.22 (d, *J* = 7.5 Hz, 1H), 7.16 (dd, *J* = 7.4, 7.4 Hz, 1H), 6.97 (dd, *J* =15.5, 8.5 Hz, 1H), 6.13 (d, *J* = 15.3 Hz, 1H), 4.83 (d, *J* = 8.5 Hz, 1H), 4.23 (q, *J* = 7.2 Hz, 2H), 3.57 (s, 3H), 2.50 (s, 3H), 2.40-2.31 (m, 2H), 2.10 (ddd, *J* = 6.0, 11.0, 16.5 Hz, 1H), 1.56 (ddd, *J* = 16.4, 11.0, 5.5 Hz, 1H), 1.32 (t, *J* = 7.1 Hz); ^{3}C NMR (75 MHz, $CDCl_3$) δ 179.8, 172.7, 165.1, 155.7, 142.8, 140.7, 136.2, 131.0, 130.4, 129.3, 126.9, 125.8, 124.7, 122.5, 119.8, 66.2, 63.0, 61.0, 51.8, 30.6, 28.6, 21.1, 14.2; IR (neat) 2982, 1727, 1520, 1458, 1370, 1306, 1262, 1174, 1032; LRMS (ESI) calc'd for $C_{25}H_{26}NO_4SCl$ (MH^+) 472.0 found 472.0 (100), 325.0 (15).



34

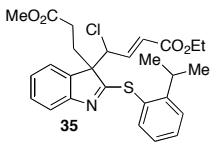
Prepared according to the general procedure for the preparation of **21** using **27** (0.020 g, 0.059 mmol) in 0.6 mL of CH_2Cl_2, $Rh_2[(S)\text{-}TBSP]_4$ (2.1 mg, 1.47 x 10^{-3} mmol) and vinyl diazoacetate **2** (0.031 g, 0.18 mmol) in of CH_2Cl_2 (0.4 mL). Column chromatography (1:2 ethyl acetate: hexanes) provided 26 mg (91%) of diastereomerically pure **34** (minor diastereomer was not present in crude ^{1}H NMR spectrum). The minor diastereomer was accessed by running the reaction in refluxing benzene.

Major diastereomer: yellow oil; R_f 0.32 (2:1 hexanes:ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.4 Hz, 1H), 7.34 (d, *J* = 7.7 Hz, 1H), 7.31-7.28 (m, 2H), 7.20 (d, *J* = 7.6 Hz, 2H), 7.15 (t, *J* = 7.4 Hz, 1H), 6.26 (dd, *J* = 8.6,

15.2 Hz, 1H), 6.12 (d, *J* = 15.4 Hz, 1H), 4.94 (d, *J* = 8.6 Hz, 1H), 4.14-4.07 (m, 2H), 3.57 (s, 3H), 2.93 (ddd, *J* = 5.1, 11.9, 13.6 Hz, 1H), 2.43 (s, 6H), 2.35 (ddd, *J* = 4.7, 11.6, 13.7 Hz, 1H), 2.07 (ddd, *J* = 4.5, 11.7, 16.3 Hz, 1H), 1.58 (ddd, *J* = 5.1, 11.3, 16.3 Hz, 1H), 1.21 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.9, 173.0, 172.8, 165.0, 155.6, 140.5, 136.3, 130.3, 129.3, 128.6, 125.9, 124.6, 123.9, 119.7, 66.2, 64.6, 60.7, 51.7, 31.3, 29.7, 28.4, 22.1, 14.1; IR (neat): 2979, 2953, 1732, 1516, 1463, 1369, 1263, 1225, 1174, 1031, 769 ; LRMS (ESI) calc'd for $C_{26}H_{29}ClNO_4S$ (MH+) 486.1 found 486.0 (100), 508.0 (MNa^+, 20), 339.0 (10).

Minor diastereomer: yellow oil; R_f 0.28 (2:1 hexanes:ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 7.6 Hz, 1H), 7.31-7.27 (m, 2H), 7.22-7.20 (m, 3H), 7.14 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.96 (dd, *J* = 8.4, 15.4 Hz, 1H), 6.11 (d, *J* = 15.4 Hz, 1H), 4.86 (d, *J* = 8.5 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.56 (s, 3H), 2.50 (s, 6H), 2.41-2.37 (m, 1H), 2.08 (ddd, *J* = 7.0, 9.2, 16.3 Hz, 1H), 1.63-1.55 (m, 1H), 1.32 (q, *J* = 7.2 Hz, 3H), 1.21-1.30 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.9, 172.8, 165.1, 155.9, 140.8, 130.2, 129.3, 128.5, 128.4, 125.8, 125.7, 124.5, 122.4, 119.8, 66.3, 63.2, 60.9, 51.7, 30.9, 28.8, 22.0, 14.2; IR (neat): 2979, 2952, 1735, 1520, 1462, 1174, 1031, 769 ; LRMS (ESI) calc'd for $C_{26}H_{29}ClNO_4S$ (MH+) 486.1 found 486.0 (100), 508.0 (MNa^+, 5), 339.0 (10).

$Rh_2(OAc)_4$ procedure: Synthesized according to the general procedure for the preparation of **21** using **27** (0.010 g, 0.029 mmol) in CH_2Cl_2 (0.5 mL), $Rh_2(OAc)_4$ (0.32 mg, $7.3x10^{-4}$ mmol) in CH_2Cl_2 (0.25 mL); vinyl diazoacetate **2** (0.015 g, 0.088 mmol) in 0.2 ml of CH_2Cl_2 to give 13.8 mg (96%) of **34** as a 15:1 mixture of diastereomers.



35

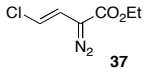
(E)-4-Chloro-4-[2-(2-isopropyl-phenylsulfanyl)-3-(2-methoxycarbonyl-ethyl)-3H-indol-3-yl]-but-2-enoic acid ethyl ester (**35**).

According to the general procedure for preparation of **21** using **28** (0.012 g, 0.035 mmol) in CH_2Cl_2 (0.3 mL), $Rh_2(OAc)_4$ (0.39 mg, $8.7x10^{-4}$ mmol) and diazoacetate **2** (0.018 g, 0.10 mmol) in CH_2Cl_2 (0.2 mL). Column chromatography (1:2 ethyl acetate:hexanes) provided 14 mg (91%) of **35** as an 18:1 mixture of diastereomers. The minor diastereomer was accessed by carrying out the reaction in refluxing benzene.

Major diastereomer: colorless oil; R_f 0.46 (2:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.3 Hz, 1H), 7.53 (d, *J* = 7.7 Hz, 1H), 7.46-7.42 (m, 2H), 7.35-7.29 (m, 2H), 7.24-7.23 (m, 1H), 7.16 (dd, *J* = 7.2, 7.2 Hz, 1H), 6.18-6.10 (m, 2H), 4.90 (d, *J* = 7.2 Hz, 1H), 4.11 (q, *J* = 7.1 Hz, 2H), 3.59 (s, 3H), 3.37-3.31 (m, 1H), 2.92 (ddd, *J* = 12.8, 12.8, 4.7 Hz, 1H), 2.29 (ddd, *J* = 12.7, 12.7, 5.0 Hz, 1H), 2.06 (ddd, *J* = 16.3, 11.7, 6.3 Hz, 1H), 1.58-1.52 (m, 1H), 1.23-1.20 (m, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.2, 172.9, 165.0, 155.6, 152.6, 140.6, 136.3, 136.3, 130.8,

129.4, 126.7, 126.6, 125.3, 124.8, 124.7, 124.0, 119.8, 66.0, 64.8, 60.7, 51.7, 31.6, 30.9, 28.2, 23.9, 23.4, 14.1; IR (neat) 3062, 2962, 1724, 1517, 1446, 1367, 1263, 1173, 1112, 1027; LRMS (ESI) calc'd for $C_{27}H_{30}NO_4SCl$ (MH^+) 500.1 found 499.9 (100).

Minor diastereomer: colorless oil; R_f 0.40 (2:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.7 Hz, 1H), 7.47-7.44 (m, 2H), 7.36 (d, *J* = 7.7 Hz, 1H), 7.28-7.32 (m, 2H), 7.22 (d, *J* = 7.3 Hz, 1H), 7.15 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.97 (dd, *J* = 15.3, 8.5 Hz, 1H), 6.14 (d, *J* = 15.4 Hz, 1H), 4.84 (d, *J* = 8.5 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.57 (s, 3H), 3.55-3.49 (m, 1H), 2.38-2.33 (m, 2H), 2.08 (ddd, *J* = 16.5, 10.0, 6.0 Hz, 1H), 1.59-1.50 (m, 1H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.25 (d, *J* = 6.7 Hz, 6H); ^{3}C NMR (125 MHz, $CDCl_3$) δ 180.3, 172.8, 165.2, 155.9, 152.6, 140.7, 136.6, 136.2, 130.7, 129.4, 126.7, 126.6, 125.8, 125.2, 124.7, 122.5, 119.8, 66.2, 63.0, 61.0, 51.8, 31.4, 30.5, 28.6, 23.9, 23.7, 14.2; IR (neat) 2962, 1724, 1517, 1446, 1367, 1263, 1173, 1027; LRMS (ESI) calc'd for $C_{27}H_{30}NO_4SCl$ (MH^+) 500.1 found 499.9 (100).

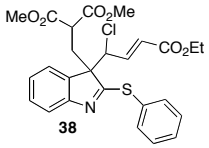


37

4-(E)-Chloro-2-diazo ethyl but-3-eneoate (**37**). To a solution of 4-chloro ethyl acetoacetate (0.500 g, 3.04 mmol) in CH_3CN (10 mL) was added acetamidobenzenesulfonyl azide (ABSA) (0.700 g 3.04 mmol). The mixture was cooled to 0 °C and triethyl amine (1.27 mL, 9.11 mmol) was added dropwise. After stirring for 24 h, the mixture was concentrated and then diluted with a 1:1 mixture of pentane/ether (10 mL). The slurry was passed through a plug of silica gel (1:1, pentane/ether) to yield 266 mg (56%) of 4-chloro-2-diazo ethyl acetoacetate.

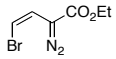
To a solution of 4-chloro-2-diazo ethyl acetoacetate (0.275 g, 1.44 mmol) in MeOH (6 mL) at 0 °C was added $NaBH_4$ (0.82 g, 2.2 mmol) in 4 small portions at 3 minutes intervals. After stirring for 1 h at 0 °C, the reaction was quenched with H_2O (2 mL) and extracted with methylene chloride (2 x 5 mL). The extracts were washed with brine (1 x 3 mL), dried (Na_2SO_4), and carefully concentrated to a volume of 1 mL.

To the solution from above was added CH_2Cl_2 (5 mL) and NEt_3 (0.780 mL, 5.60 mmol). The mixture was cooled to 0 °C and $POCl_3$ (0.192 g, 2.10 mmol) was added dropwise. After stirring at 0 °C for 2 h, the reaction mixture was warmed to rt and stirred an additional 20 h. The reaction was quenched with H_2O (2 mL), extracted with CH_2Cl_2 (2 x 5 mL), dried (Na_2SO_4) and concentrated to 2 mL. The resulting slurry was passed through a plug of silica gel (1:1, pentane/ether) to yield (*E*)-chloro vinyl diazoacetate **37** as the major isomer of a 2:1 mixture of stereoisomers. Flash chromatography (100:1, hexanes/ethyl acetate) yielded 97 mg (40%) of **37** as a single olefin isomer. R_f 0.37 (10:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, CD_2Cl_2) δ 6.21 (d, *J* = 13.7 Hz 1 H), 6.13 (d, *J* = 13.2 Hz 1 H), 4.25 (q, *J* = 7.3 Hz, 2 H), 1.28 (t, *J* = 7.3 Hz, 3 H); IR (neat) 2984, 2095, 1703, 1371 cm^{-1}.



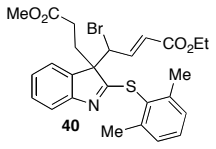
38

2-[3-(1-Chloro-3-ethoxycarbonyl-allyl)-2-phenylsulfanyl-3*H*-indol-3-ylmethyl]-malonic acid dimethyl ester (**38**). Synthesized according to the general procedure for the preparation of **21** using **36** (0.015 g, 0.041 mmol) and CH_2Cl_2 (1 mL), $Rh_2(OAc)_4$ (0.001 g 0.002 mmol), and vinyl diazoacetate **37** (0.014 g, 0.081 mmol) in CH_2Cl_2 (0.5 mL). Flash chromatography (5:1, hexanes/ethyl acetate) afforded 19 mg (88%) of **38** as an 8:1 mixture of diastereomers. R_f 0.34 (3:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, CD2Cl2) δ 7.68 (m, 2 H), 7.49 (m, 3 H), 7.34 (m, 2 H), 7.17 (m, 2 H), 6.90 (dd, J = 15.61, 8.78 Hz 1 H), 6.12 (d, J = 15.13 Hz 1 H), 4.86 (d, J = 8.78 Hz 1 H), 4.21 (q, J = 6.83 Hz 1 H), 3.68 (s, 3 H), 3.18 (s, 3 H), 2.83-2.75 (m, 3 H), 2.73-2.68 (m, 1 H), 1.30 (t, J = 6.83 Hz 3 H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 180.9, 169.2, 169.1, 165.4, 156.5, 140.4, 135.6, 135.5, 130.3, 130.2, 129.9, 128.0, 126.8, 125.0, 124.8, 120.1, 66.5, 63.6, 61.5, 48.2, 33.8, 14.5. IR (neat) 2983, 2955, 1750, 1735, 1728, 1516 cm^{-1}. LRMS (ESI) calc'd for $C_{26}H_{27}ClNO_6S$ (MH^+) 516.1 found 516.2 (10), 538.1 (MNa^+, 100), 554.1 (MK^+, 10).



39

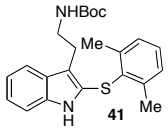
Ethyl (3*Z*)-4-bromo-2-(1l^5-diazynylidene)but-3-enoate (**39**). To a solution of ethyl 4-bromocrotonate (1.805 g, 9.35 mmol) in CH_3CN (32 mL) was added 4-acetamidobenzenesulfonyl azide (ABSA) (2.47 g, 10.28 mmol). The mixture was cooled to 0 °C and 1,8-diazobicyclo[5.4.0]undec-7-ene (DBU) (1.708 g, 11.22 mmol) was added dropwise. After stirring for 3 h at rt, the mixture was concentrated and then diluted with a 1:1 mixture of pentane/ether (30 mL). The resulting slurry was passed through a plug of silica gel and the solvent was removed to yield 1.173 g (57%) of **39** as a yellow oil. **39** was used in the subsequent coupling reaction without additional purification. R_f 0.40 (10:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, CD_2Cl_2) δ 6.33 (d, *J* = 7.9 Hz, 1H), 6.22 (d, *J* = 7.8 Hz, 1H), 4.25 (q, *J* = 7.2 Hz, 2H), 1.28 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 165.3, 130.2, 116.8, 103.0, 62.0, 14.6; IR (neat) 3092, 2983, 2909, 2092, 1706, 1369, 1329, 1308, 1274, 1106, 788.



40

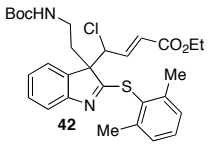
Ethyl (2*E*)-4-bromo-4-[2-[(2,6-dimethylphenyl)thio]-3-(3-methoxy-3-oxopropyl)-3*H*-indol-3-yl]but-2-enoate (**40**). Synthesized according to the general procedure for the preparation of **21** using **27** (40.0 mg, 0.118 mmol) in CH_2Cl_2 (0.5 mL), Rh_2[(S)-TBSP]$_4$ (8.5 mg, 5.9x10^{-3} mmol) and a solution of diazoacetate **39** (61.6 mg, 0.354 mmol) in CH_2Cl_2 (0.5 mL). Column chromatography provided 54.0 mg (86%) of indoline **40** as yellow oil and as a single diastereomer (according to ^{1}H NMR of the crude reaction mixture). R_f 0.42 (2:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$)

δ 7.63 (d, *J* = 7.4 Hz, 1H), 7.25-7.28 (m, 3H), 7.20-7.15 (m, 3H), 6.33-6.28 (m, 1H), 6.10 (d, *J* = 15.3 Hz, 1H), 5.02 (d, *J* = 10.2 Hz, 1H), 4.17-4.06 (m, 2H), 3.57 (s, 3H), 2.89 (ddd, *J* = 5.1, 13.4, 13.4 Hz, 1H), 2.41 (broad s, 6H), 2.33 (ddd, *J* = 4.8, 12.0, 13.4 Hz, 1H), 2.07 (ddd, *J* = 4.8, 11.7, 16.4 Hz, 1H), 1.58 (ddd, *J* = 5.1, 11.5, 16.5 Hz, 1H), 1.22 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 177.9, 172.8, 165.0, 155.7, 141.1, 136.6, 130.3, 129.4, 128.6, 128.5, 125.5, 125.1, 124.5, 123.8, 119.7, 65.5, 60.7, 56.1, 51.7, 32.7, 28.6, 22.1, 14.1; IR (neat) 2953, 1737, 1724, 1516, 1463, 1258, 1172, 765.6; LRMS (ESI) calc'd for $C_{26}H_{29}BrNO_4S$ (MH+) 530.1 found 530.0 (90), 531.9 (100), 553.9 (MNa^+, 20), 567.9 (MK^+, 10), 482.1 (20).



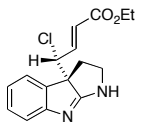
41

tert-Butyl (2-{2-[(2,6-dimethylphenyl)thio]-1*H*-indol-3-yl}ethyl)carbamate (**41**). Synthesized according to the general procedure for the preparation of **17** using *tert*-butyl [2-(1*H*-indol-3-yl)ethyl]carbamate (0.520 g, 2 mmol), CH_2Cl_2 (4 mL), and 0.380 g (2.2 mmol) of 2,6-dimethylbenzenesulfenyl chloride. Flash chromatography (ethyl acetate/hexanes 1:10) afforded 0.588 g of **41** as a white solid. m.p. = 158-160 ° C (dec.); R_f 0.56 (2:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.56 (broad s, 1H), 7.49 (d, *J* = 7.2 Hz, 1H), 7.21 (dd, *J* = 6.5, 8.2 Hz, 1H), 7.17-7.14 (m, 3H), 7.09-7.03 (m, 2H), 4.63 (broad s, 1H), 3.34-3.33 (m, 2H), 3.00 (t, *J* = 6.8 Hz, 2H), 2.44 (s, 6H), 1.43 (s, 9H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 156.0, 143.2, 136.8, 130.3, 129.4, 129.1, 128.7, 127.1, 122.2, 120.0, 118.4, 113.9, 110.6, 41.2, 28.5, 28.4, 25.6, 22.1; IR (neat) 3419, 3243, 3056, 2976, 2927, 1689, 1504, 1459, 1166, 743; LRMS (ESI) calc'd for $C_{23}H_{28}N_2O_2S$ (MH^+) 397.2 found 397.1 (100), 341.1 (8).



42

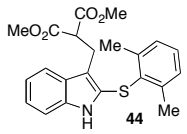
Ethyl (2*E*)-4-{3-{2-[(*tert*-butoxycarbonyl)amino]ethyl}-2-[(2,6-dimethylphenyl)thio]-3*H*-indol-3-yl}-4-chlorobut-2-enoate (**42**). According to the general procedure for preparation of **21** using **41** (40.0 mg, 0.101 mmol) in CH_2Cl_2 (0.5 mL), Rh_2[(S)-TBSP]$_4$ (7.3 mg, 5.0x10^{-3} mmol) and a solution of diazoacetate **2** (52.7 mg, 0.303 mmol) in CH_2Cl_2 (0.5 mL). Column chromatography provided 49.0 mg (89%) of the product as yellow oil; R_f 0.40 (2:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.61 (d, *J* = 7.4 Hz, 1H), 7.36-7.29 (m, 3H), 7.24-7.19 (m, 3H), 6.31-6.22 (m, 1H), 4.95 (d, *J* = 8.8 Hz, 1H), 4.34 (br. s, 1H), 4.12-4.05 (m, 2H), 2.92 (ddd, *J* = 4.6, 10.2, 14.4 Hz, 1H), 2.76-2.70 (m, 1H), 2.43 (br. s, 6H), 2.27-2.21 (m, 1H), 1.37 (br. s, 9H), 1.20 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 166.9, 157.5, 145.9, 142.2, 132.4, 132.2, 131.4, 130.6, 130.5, 128.3, 126.8, 125.9, 121.4, 66.9, 63.0, 62.8, 60.6, 38.6, 38.1, 32.9, 30.2, 24.0, 16.0; IR (neat) 3380, 3056, 2978, 1716, 1514, 1463, 1267, 1171, 1042, 768; LRMS (ESI) calc'd for $C_{29}H_{36}ClN_2O_4S$ (MH+) 543.2 found 543.1 (100), 565.2 (MNa^+, 85), 581.2 (MK^+, 35), 480.1 (25).



43

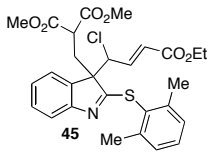
4-Chloro-4-(2,3-dihydro-1H-pyrrolo[2,3-b]indol-3a-yl)-but-2-enoic acid ethyl ester (**43**). To a solution of **42** (0.010 g, 0.018 mmol) and CH_2Cl_2 (2 mL) was added TFA (2 mL) at 0°C. After stirring at rt for 4 h, the reaction was diluted with CH_2Cl_2 (2 mL) and quenched with aq. $NaHCO_3$ (1.5 mL). Following separation, the organic phase was washed with brine (1 mL) and the aqueous phase was back extracted with CH_2Cl_2 (3 x 2 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated. Preparative TLC (0:1, hexanes/ethyl acetate) afforded 5.2 mg (95%) of **43**. R_f 0.10 (ethyl acetate); ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.45 (d, J = 7.81 Hz 1 H), 7.21 (m, 2 H), 7.08 (d, J = 7.81Hz 1 H), 6.20 (dd, J = 15.14, 8.3 Hz 1 H), 5.90 (d, J = 15.63 Hz 1 H), 4.83 (d, J = 8.3 Hz 1 H), 4.27-4.21 (m, 1 H), 4.10-4.04 (m, 3 H), 2.86 (dd, J = 12.7, 4.4 Hz 1 H), 2.44-2.37 (m, 1 H), 1.19 (t, J = 7.33 Hz 3 H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 166.3, 140.9, 134.8, 131.8, 130.5, 128.0, 127.3, 127.2, 124.5, 115.5, 66.7, 62.6, 62.4, 35.2, 31.2, 15.4. IR (neat) 3278 (broad), 3060, 2984, 1720, 1673 cm^{-1}. LRMS (ESI) calc'd for $C_{16}H_{18}ClN_2O_2$ (MH^+) 305.8 found 305.0 (30), 157.8 (100).

COSY Summary. The following cross peaks were observed: H(1) and H(2); H(2) and H(3), H(4) and H(5).



44

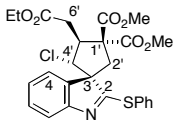
Dimethyl ({2-[(2,6-dimethylphenyl)thio]-1*H*-indol-3-yl}methyl)malonate (**44**). Synthesized according to the general procedure for the preparation of **17** using dimethyl (1*H*-indol-3-methyl)malonate (0.102 g, 0.295 mmol), CH_2Cl_2 (0.5 mL), and 0.082 g (0.473 mmol) of 2,6-dimethylbenzenesulfenyl chloride. Flash chromatography (ethyl acetate/hexanes 1:10) afforded 0.109 g (76%) of **44** as a colorless oil. R_f 0.46 (2:1 hexanes:ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (broad s, 1H), 7.53-7.56 (m, 1H), 7.22-7.35 (m, 3H), 7.12-7.19 (m, 2H), 5.41 (br. s, 1H), 3.76 (s, 6H), 3.52 (d, *J* = 7.8 Hz, 2H), 2.52 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.7, 145.2, 138.6, 132.3, 131.5, 131.1, 130.3, 129.6, 124.2, 122.1, 120.2, 114.3, 112.6, 54.8, 54.3, 26.7, 24.1; IR (neat) 3381, 3055, 2952, 1732, 1436, 1341, 1249, 1157, 1033, 743.8 cm^{-1}; LRMS (ESI) calc'd for C22H23NNaO4S (MNa+) 420.5 found 420.0 (100), 435.9 (MK^+, 50), 398.0 (MH^+, 10).



45

Dimethyl ({3-[(2*E*)-1-chloro-4-ethoxy-4-oxobut-2-en-1-yl]-2-[(2,6-dimethylphenyl)thio]-3*H*-indol-3 yl}methyl)malonate (**45**). Prepared according to the general procedure for the preparation of **21** using **44** (0.067 g, 0.169 mmol) in CH_2Cl_2 (1 mL), Rh_2[(S)-TBSP]$_4$ (0.012 g, 8.4 x 10^{-3} mmol), and vinyl diazoacetate **2** (0.088 g, 0.507

mmol) in CH_2Cl_2 (0.4 mL). Column chromatography (1:2 ethyl acetate/hexane) provided 0.114 g (82%) of **45** as a single diastereomer (d.r. > 95:5) as a yellow oil. R_f 0.30 (2:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.3 Hz, 1H), 7.33 (d, *J* = 7.8, 1H), 7.27-7.30 (m, 2H), 7.19-7.22 (m, 2H), 7.10 (t, *J* = 7.3 Hz, 1H), 6.19 (dd, *J* = 8.4, 15.3 Hz, 1H), 6.11 (d, *J* = 15.4 Hz, 1H), 4.95 (d, *J* = 8.3 Hz, 1H), 4.06-4.13 (m, 2 H), 3.71 (s, 3H), 3.44 (dd, *J* = 11.0, 14.2 Hz, 1H), 3.14 (s, 3H), 2.84 (d, *J* = 10.3 Hz, 1H), 2.71 (d, *J* = 13.7, 1H), 2.41 (br. s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.5, 168.9, 168.7, 164.9, 155.8, 140.2, 135.0, 130.3, 128.6, 126.0, 125.5, 124.2, 119.8, 65.9, 64.6, 60.7, 52.9, 52.3, 47.4, 34.7, 31.0, 21.9, 14.1; IR (neat) 2969, 2954, 1754, 1735, 1514, 1463, 1436, 1266, 1166, 1034, 770, 588; LRMS (ESI) calc'd for C28H31ClNO6S (MH+) 544.1 found 544.1 (100), 510.1 (10).



46

Dimethyl 5-chloro-2'-[(2,6-dimethylphenyl)thio]-4-(2-ethoxy-2-oxoethyl)-3*H*-spiro[cyclopentane-1,3'-indole]-3,3-dicarboxylate (**46**). To a solution of **45** (0.021 g, 0.0380 mmol) and THF (0.5 ml) was added potassium *tert*-butoxide at room temperature. After stirring for 15 min the reaction was quenched with aq. NH_4Cl (sat., 0.5 ml) and extracted with EtOAc (3 x 1 mL). The combined organic extracts were washed with brine, filtered through a short plug of silica gel and dried (Na_2SO_4). Concentration gave 0.015 g (73%, d.r. 10:1) of spirocycle **46** as yellow oil. R_f 0.39 (2:1 hexanes:ethyl acetate); ^{1}H NMR (500 MHz, C_6D_6) δ 7.55-7.53 (m, 1H), 7.27-7.25 (m, 1H), 7.03-7.00 (m, 1H), 6.96-6.93 (m, 4H), 4.97 (d, *J* = 12.7 Hz, 1H), 4.52 (ddd, *J* = 5.9, 12.2, 12.2 Hz, 1H), 4.03-3.94 (m, 2H), 3.42 (s, 3H), 3.26 (s, 3H), 3.22 (d, *J* = 15.4 Hz, 1H), 3.07 (dd, *J* = 5.1, 16.1 Hz, 1H), 3.01 (d, *J* = 15.4 Hz, 1H), 2.81 (dd, *J* = 6.3, 16.4 Hz, 1H), 2.51 (broad s, 6H), 0.99 (t, *J* = 7.1 Hz, 3 H); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.4 Hz, 1H), 7.30 (d, *J* = 7.9 Hz, 1H), 7.24-7.31 (m, 2H), 7.14-7.21 (m, 3H), 4.69 (d, *J* = 12.8 Hz, 1H), 4.17-4.23 (m, 2H), 4.14 (ddd, *J* = 5.5, 11.8, 11.8 Hz, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.07 (d, *J* = 15.5 Hz, 1H), 2.98 (d, *J* = 15.4 Hz, 1H), 2.94 (dd, *J* = 4.9, 16.4 Hz, 1H), 2.66 (dd, *J* = 6.4, 16.1 Hz, 1H), 2.47 (broad s, 6H), 1.30 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.4, 171.7, 171.0, 170.5, 154.6, 140.7, 130.0, 128.8, 128.4, 128.3, 126.8, 125.9, 121.2, 119.1, 66.6, 65.7, 60.8, 59.4, 53.2, 48.3, 41.4, 33.8, 21.9, 14.2; IR (neat) 3054, 2953, 2852, 1736, 1512, 1462, 1436, 1274, 1206, 1048, 769 cm^{-1}; LRMS (ESI) calcd for $C_{28}H_{31}ClNO_6S$ (MH+) 544.2 found 544.1 (100), 486.1 (10).

COSY summary: Cross peaks were observed between H(4') and H(5'); H(5') and H(6').

NOE summary: Enhancements were observed between H(4) and H(4'); H(4') and H(6'); H(4) and H(2' ax.); H(5') and H(2' eq.).