Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Electronic Supplementary Information

Practical Synthesis of β-oxo benzo[*d*]thiazol sulfones: Scope and Limitations

Jiří Pospíšil,* Raphaël Robiette, Hitoshi Sato and Kevin Debrus

Institute of Condensed Matter and Nanosciences – Molecules, Solids and Reactivity (IMCN/MOST), Université catholique de Louvain, Bâtiment Lavoisier, Place Louis Pasteur 1, B-1348 Louvain-la-Neuve, Belgium

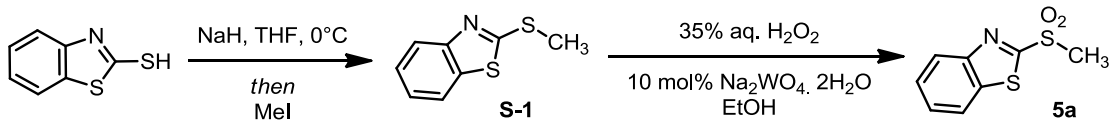
jiri.pospisil@uclouvain.be

Table of Contents

Experimental procedures

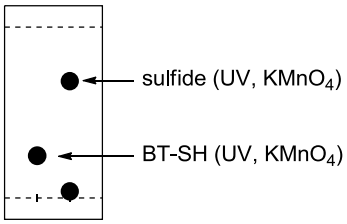
Sulfone synthesis (5)

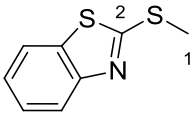
2-(methylthio)benzo[*d*]thiazole (5a)



Sulfide S-1 synthesis: A solution of BTSH (10.0 g, 59.8 mmol, 1.0 equiv) in THF (240 mL, 0.25M) was cooled to 0°C and NaH (60% in min. oil) (2.63 g, 65.8 mmol, 1.1 equiv) was added portionwise within 10 min. The resulting solution was stirred at 0°C for 30 min, before methyl iodide (4.5 mL, 71.8 mmol, 1.2 equiv) was added dropwise. The cooling bath was removed and the resulting mixture was allowed to warm to rt and stirred for a further 8h. Saturated aqueous NH_4Cl (100 mL) was added and resulting layers were separated. The aqueous layer was extracted with EtOAc (3x250 mL) and the combined organic layers were washed with brine (50 mL), dried over $MgSO_4$, filtered and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (petroleum ether:EtOAc = 10:1->4:1) yielding the desired sulfide as a white solid (10.5 g, 99 % yield).

TLC (petroleum ether:EtOAc = 4:1)

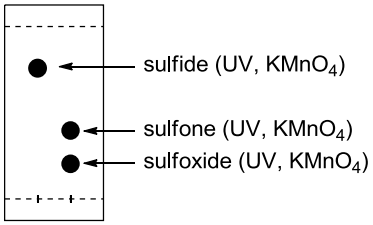


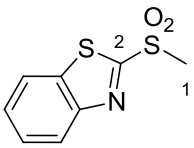


Mp = 48-49°C, lit.[1] 48-49°C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 2.81 (s, 3H, H-1), 7.30 (td, *J* = 7.6, 1.2 Hz, 1 H), 7.43 (td, *J* = 8.3, 1.2 Hz, 1H), 7.77 (d, *J* = 7.9 Hz, 1H), 7.90 (d, *J* = 8.2 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 16.1 (C-1), 121.1, 121.5, 124.2, 126.2, 135.3, 153.5, 168.2 (C-2); IR (film): ν^{-1} = 3062, 2925, 2851, 1462, 1429, 1311, 1240, 1082, 1007, 964, 908, 756, 727, 675.

Sulfone 5a: A solution of sulfide (10.0 g, 55.2 mmol, 1.0 equiv) in EtOH (276 mL, 0.20M) was cooled to 0°C and $Na_2WO_4.2\ H_2O$ (1.82 g, 5.51 mmol, 0.1 equiv) was added. After 5 min at 0°C, 35% aqueous solution of H_2O_2 (21.4 mL, 221 mmol, 4.0 equiv) was added dropwise. The resulting mixture was stirred at 0°C for 30 min, before the cooling bath was removed and the stirring continued at rt for a further 10h. Saturated aqueous $Na_2S_2O_3$ (100 mL) was added and resulting layers were separated. The aqueous layer was extracted with EtOAc (3x250 mL) and the combined organic layers were washed with brine (50 mL), dried over $MgSO_4$, filtered and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (petroleum ether:EtOAc = 4:1->2:1->1:1) yielding the desired sulfone as yellowish crystals (9.88 g, 84 % yield). In some cases, if the reaction was stopped before a full sulfide and/or sulfoxide conversion, sulfoxide **S-2** was isolated as a byproduct).

TLC (petroleum ether:EtOAc = 2:1)

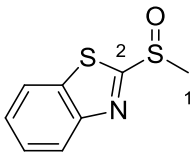




Sulfone (5a)

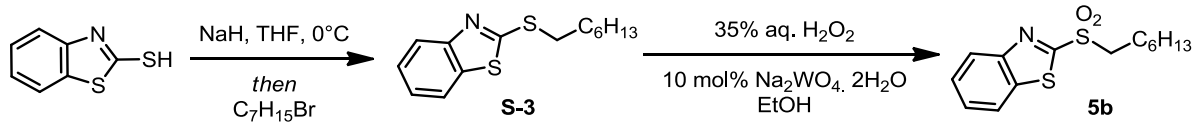
Mp = 91-92°C, lit.[2] = 92-93°C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 3.40 (s, 3H, H-1), 7.60 (pd, *J* = 7.2, 1.4 Hz, 2H), 8.00 (dd, *J* = 7.2, 1.8 Hz, 1H), 8.19 (dd, *J* = 7.3, 1.7 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 42.6 (C-1), 122.5, 125.5, 127.8, 128.2, 136.7, 152.5, 166.5 (C-3); IR (film): ν^{-1} = 3181, 3023, 3009, 2927, 1699, 1683, 1473, 1425, 1317, 1309, 1151, 1028, 956, 756, 690; MS (APCI), *m/z* (%): 214 (100) [M^++H], 183 (7), 251 (12), 136 (17); El. an. for $C_8H_7NO_2S_2$, calc. C 45.23, H 3.31, N 6.57, S 30.07; found C 45.23, H 3.24, N 6.82, S 29.88.

Sulfoxide (S-2)



Mp = 69-70°C, lit.[3] = 70.5-71.5°C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 3.08 (d, *J* = 7.5 Hz, 1H, H-1), 7.48 (td, *J* = 7.9, 1.9 Hz, 1H), 7.55 (td, *J* = 8.1, 1.8 Hz, 1H), 7.99 (dd, *J* = 7.9, 1.4 Hz, 1H), 8.05 (dd, *J* = 8.1, 1.0 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 43.3 (C-1), 122.5, 124.1, 126.4, 127.1, 136.1, 153.9, 178.5 (C-2); IR (film): ν^{-1} = 3062, 3000, 2915, 1649, 1558, 1475, 1427, 1338, 1315, 1236, 1153, 1086, 1059, 1003, 953, 758, 725; MS (APCI), *m/z* (%): 198 (100) [M^+], 183 (34), 180 (40), 151 (17), 136 (21); El. an. for $C_8H_7NOS_2$, calc. C 48.71, H 3.58, N 7.10; found C 49.03, H 3.68, N 7.02.

2-(heptylsulfonyl)benzo[d]thiazole (5b)

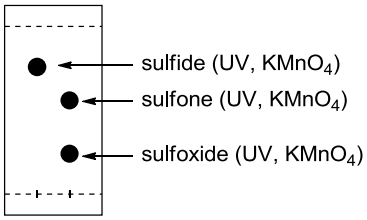


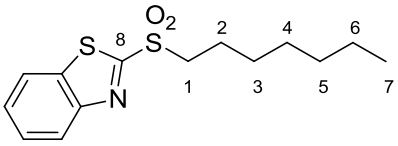
Sulfide S-3 synthesis: A solution of BTSH (8.0 g, 47.8 mmol, 1.0 equiv) in THF (191 mL, 0.25M) was cooled to 0°C and NaH (60% in min. oil) (2.30 g, 57.4 mmol, 1.2 equiv) was added portionwise within 10 min. The resulting solution was stirred at 0°C for 30 min, before heptyl bromide (8.27 mL, 52.6 mmol, 1.1 equiv) was added dropwise. The cooling bath was removed and the resulting mixture was allowed to warm to rt and stirred for a further 8h. Saturated aqueous NH_4Cl (100 mL) was added and resulting layers were separated. The aqueous layer was extracted with EtOAc (3x250 mL) and the combined organic layers were washed with brine (50 mL), dried over $MgSO_4$, filtered and the solvents were removed under reduced pressure. The crude sulfide was used in the next step without additional purification

Sulfone 5b: A solution of crude sulfide **S-3** in EtOH (214 mL, 0.20M) was cooled to 0°C and $Na_2WO_4.2\ H_2O$ (1.82 g, 5.51 mmol) was added. After 5 min at 0°C, 35% aqueous solution of H_2O_2 (21.4 mL, 221 mmol) was added dropwise. The resulting mixture was stirred at 0°C for 30 min, before the cooling bath was removed and the stirring continued at rt for a further 10h. Saturated aqueous $Na_2S_2O_3$ (100 mL) was

added and resulting layers were separated. The aqueous layer was extracted with EtOAc (3x250 mL) and the combined organic layers were washed with brine (50 mL), dried over $MgSO_4$, filtered and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (petroleum ether:EtOAc = 20:1->10:1) yielding the desired sulfone **5b** (13.4 g, 94 % yield).

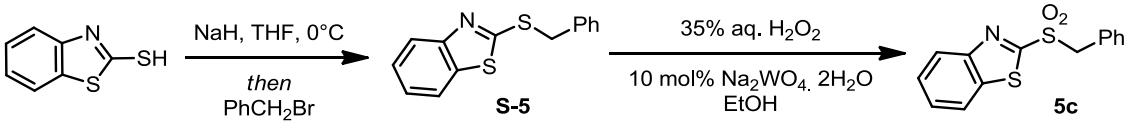
TLC (petroleum ether:EtOAc = 10:1)



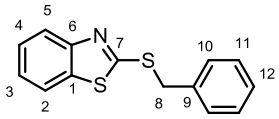


Mp = 38-39°C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.85 (t, *J* = 6.8 Hz, 3H, H-7), 1.16 – 1.37 (m, 6H), 1.44 (dt, *J* = 14.6, 6.7 Hz, 2H, H-3), 1.88 (dt, *J* = 12.1, 7.6 Hz, 2H, H-2), 3.51 (dd, *J* = 9.1, 7.0 Hz, 2H, H-1), 7.63 (pd, *J* = 7.2, 1.8 Hz, 2H), 8.03 (dd, *J* = 7.2, 1.7 Hz, 1H), 8.23 (dd, *J* = 7.3, 1.5 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 14.16 (C-7), 22.43, 22.64, 28.37, 28.75, 31.53 (C-2), 54.90 (C-1), 122.54, 125.63, 127.83, 128.18, 136.95, 152.93, 166.11 (C-8); IR (film): ν^{-1} = 3064, 2951, 2924, 2854, 1555, 1472, 1458, 1329, 1317, 1143, 1126, 1024, 912, 853, 762; MS (CI), *m/z* (%): 298 (100) [M^+], 299 (19), 250 (14), 234 (17), 183 (17), 136 (14); HRMS (CI), *m/z*: calc. 298.0936 for $C_{14}H_{20}NO_2S_2$, found 298.0938.

2-(benzylsulfonyl)benzo[*d*]thiazole (5c)



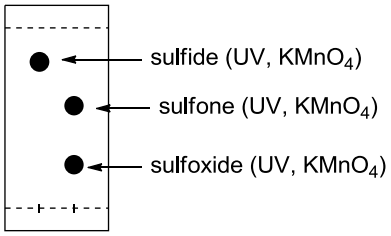
Sulfide S-5 synthesis: A solution of BTSH (6.51 g, 39 mmol, 1.0 equiv) in THF (195 mL, 0.20M) was cooled to 0°C and NaH (60% in min. oil) (1.86 g, 46.6 mmol, 1.2 equiv) was added portionwise within 10 min. The resulting solution was stirred at 0°C for 30 min, before benzyl bromide (5.33 mL, 46.6 mmol, 1.2 equiv) was added dropwise. The cooling bath was removed and the resulting mixture was allowed to warm to rt and stirred for a further 8h. Saturated aqueous NH_4Cl (100 mL) was added and resulting layers were separated. The aqueous layer was extracted with EtOAc (3x250 mL) and the combined organic layers were washed with brine (50 mL), dried over $MgSO_4$, filtered and the solvents were removed under reduced pressure. The crude sulfide **S-5** was used in the next step without further purification.

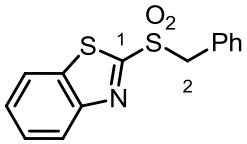


Mp = 39-40°C, lit.[4] = 39°C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 4.61 (s, 2H, H-8), 7.30(m, 5H), 7,41 – 7.49 (m, 2H), 7.76 (d, *J* = 8.0 Hz, 1H),7.92 (d, *J* = 8.1 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 37.9 (C-8), 121.2, 121.8, 124.5, 126.3, 128.0, 128.9, 129.3, 135.5, 136.4, 153.4, 166.6 (C-7); IR (film): ν^{-1} = 3060, 3028, 2922, 1600, 1560, 1495, 1454, 1425, 1310, 1275, 1238, 1126, 1074, 993, 916, 852, 754, 725, 698, 667.

Sulfone 5c: A solution of crude sulfide **S-5** in EtOH (200 mL, 0.20M) was cooled to 0°C and $Na_2WO_4.2\ H_2O$ (1.82 g, 5.51 mmol, 0.1 equiv) was added. After 5 min at 0°C, 35% aqueous solution of H_2O_2 (15.2 mL, 156 mmol, 4.0 equiv) was added dropwise. The resulting mixture was stirred at 0°C for 30 min, before the cooling bath was removed. The reaction was stirred at rt for a further 10h. Saturated aqueous $Na_2S_2O_3$ (100 mL) was added and resulting layers were separated. The aqueous layer was extracted with EtOAc (3x250 mL) and the combined organic layers were washed with brine (50 mL), dried over $MgSO_4$, filtered and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (petroleum ether:EtOAc = 10:1->2:1) yielding the desired sulfone **5c** (8.94 g, 79 % yield).

TLC (petroleum ether:EtOAc = 4:1)





Mp = 112-113°C, lit.[5] = 112°C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 4.78 (s, 1H, H-2), 7.23-7.38 (m, 5H), 7.56-7.75 (m, 2H), 7.96 (d, *J* = 8.0 Hz, 1H), 8.28 (d, *J* = 7.8 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 61.2 (C-2), 122.5, 125.7, 126.5, 127.9, 128.2, 129.1, 129.4, 131.3, 137.3, 152.8, 165.4 (C-1); IR (film): ν^{-1} = 3063, 2982, 2922, 1553, 1470, 1456, 1331, 1198, 1153, 1071, 1026, 914, 874, 853, 762, 729, 696; MS (CI), *m/z* (%):290 (43) [M^+], 291 (9) [M^++1], 289 (23), 274 (22), 225 (37), 224 (100), 91 (97); HRMS (CI), *m/z*: calc. 290.0309 for $C_{14}H_{12}NO_2S_2$, found 290.0313.

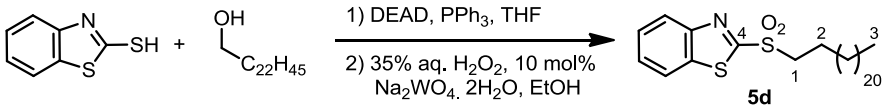
Starting from alcohol and BT-SH or PT-SH

General procedure: A solution of BT-SH or PT-SH (1.2 mmol, 1.2 equiv), PPh_3 (1.2 mmol, 1.2 equiv) and alcohol (1.0 mmol, 1.0 equiv) in THF (10 mL, 0.1M) was cooled to 0°C and DEAD (1.2 mmol, 1.2 equiv) was added. The resulting solution was allowed to warm to rt and stirred for 5-8 h.

The resulting solution was diluted with EtOH (25 mL), cooled to 0°C and $Na_2WO_4.2H_2O$ (0.1 mmol, 0.1 equiv) in one portion. After 5 min at 0°C, an aqueous 35% solution of H_2O_2 (10.0 mmol, 10 equiv) was added dropwise with a use of pipette Pasteur. The resulting yellowish solution was allowed to warm to rt and stirred at rt for 10h.

Water (50 mL) was added and the whole mixture was extracted with EtOAc (3x100 mL). The combined organic layers were washed with brine (50 mL), dried over $MgSO_4$, filtered and the solvents were evaporated under reduced pressure. The residue was purified by flash chromatography on SiO_2 using the appropriate eluting system.

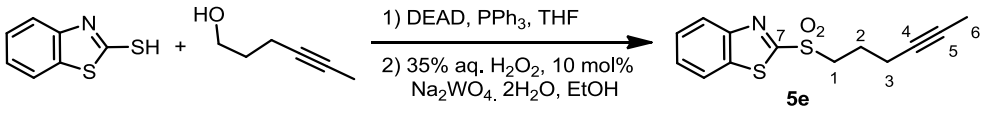
2-(tricosanylsulfonyl)benzo[*d*]thiazole (5d)



Purification by flash chromatography (petroleum ether:EtOAc = 50:1 -> 10:1) gave sulfone **5d** (459 mg, 89%).

Mp = 35-36°C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.85 (t, *J* = 6.8 Hz, 3H, H-3), 1.05 – 1.79 (m, 40H), 1.88 (dt, *J* = 12.1, 7.6 Hz, 2H, H-2), 3.51 (dd, *J* = 9.1, 7.0 Hz, 2H, H-1), 7.62 (pd, *J* = 7.2, 1.4 Hz, 2H), 8.03 (dd, *J* = 7.2, 1.7 Hz, 1H), 8.23 (dd, *J* = 7.3, 1.5 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 14.3 (C-6), 22.9, 26.4, 27.1, 29.2, 29.3, 29.6, 29.8, 29.9, 31.5, 54.8 (C-1), 122.4, 125.6, 127.8, 128.2, 136.9, 152.9, 166.1 (C-4); IR (film): ν^{-1} = 3063, 2982, 2922, 1553, 1470, 1456, 1331, 1198, 1153, 1071, 1026, 914, 874, 853, 762, 729, 696; MS (APCI), *m/z* (%): 522 (100) [M^+], 324 (25), 134 (27); HRMS (CI), *m/z*: calc. 521.3361 for $C_{30}H_{51}NO_2S_2$, found 521.3359.

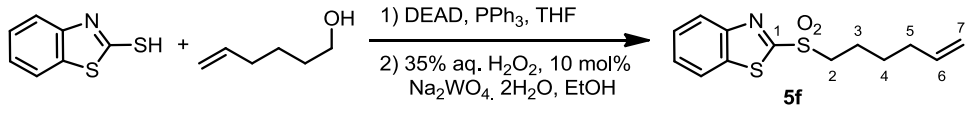
2-(hex-3-yn-1-ylsulfonyl)benzo[*d*]thiazole (5e)



Purification by flash chromatography (petroleum ether:EtOAc = 10:1 -> 4:1) gave sulfone **5e** (228 mg, 86%).

Mp = 40-41°C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.80 (t, *J* = 2.3 Hz, 3H, H-6), 2.03 – 2.23 (m, 2H, H-2), 2.38 – 2.52 (m, 2H, H-3), 3.25 (t, *J* = 8.2 Hz, 2H, H-2), 7.64 (pd, *J* = 7.2, 1.5 Hz, 2H), 8.03 (dd, *J* = 7.2, 2.1 Hz, 1H), 8.26 (dd, *J* = 7.4, 2.0 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 14.4, 21.2, 25.8, 60.6, 75.9, 78.2, 122.5, 125.9, 128.0, 128.5, 137.4, 152.8, 164.2 (C-1); IR (film): ν^{-1} = 3062, 2983, 2921, 1555, 1468, 1335, 1197, 1152, 1026, 914, 874, 762, 729; MS (APCI), *m/z* (%): 280 (100) [M^+], 281 (29), 199 (31), 145 (24); HRMS (APCI), *m/z*: calc. 279.0388 for $C_{13}H_{13}NO_2S_2$, found 279.0389.

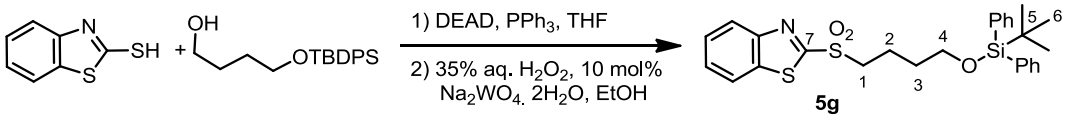
2-(hex-5-en-1-ylsulfonyl)benzo[*d*]thiazole (5f)



Purification by flash chromatography (petroleum ether:EtOAc = 10:1 -> 4:1) gave sulfone **5f** (250 mg, 89%).

Mp = 42-43°C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.18 – 1.36 (m, 2H), 1.67 (dt, *J* = 14.6, 6.7 Hz, 2H), 2.34 (dt, *J* = 12.1, 7.6 Hz, 2H, H-5), 3.48 (dd, *J* = 9.3, 7.0 Hz, 2H, H-2), 4.92 – 5.08 (m, 2H, H-7), 5.65 (ddt, *J* = 16.1, 11.2, 6.4 Hz, 1H, H-6), 7.63 (pd, *J* = 7.2, 1.3 Hz, 2H), 8.01 (dd, *J* = 7.2, 1.7 Hz, 1H), 8.22 (dd, *J* = 7.3, 1.5 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 23.2, 28.7, 31.5 (C-5), 55.6 (C-2), 115.8, 122.54, 125.63, 127.83, 128.18, 133.8, 136.95, 152.93, 166.1 (C-1); IR (film): ν^{-1} = 3063, 2951, 2924, 2853, 1557, 1471, 1458, 1317, 1144, 1122, 853, 762; MS (APCI), *m/z* (%): 282 (100) [M^+], 283 (38), 195 (19), 137 (19); HRMS (APCI), *m/z*: calc. 281.0544 for $C_{13}H_{15}NO_2S_2$, found 281.0549.

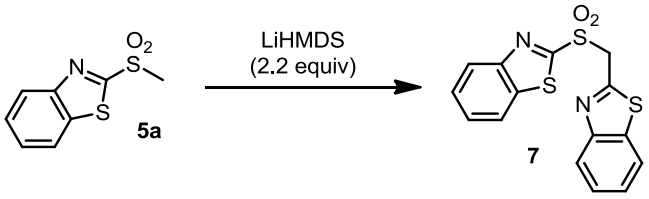
2-((4-((tert-butyldiphenylsilyl)oxy)butyl)sulfonyl)benzo[*d*]thiazole (5g)



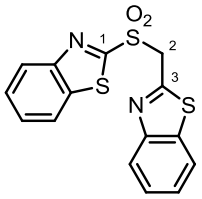
Purification by flash chromatography (petroleum ether:EtOAc = 20:1 -> 10:1) gave sulfone **5g** (449 mg, 88%). Obtained characterization data were in agreement with those published in the literature.[6]

Self-condensation of sulfone 5a

2-((benzo[*d*]thiazol-2-ylmethyl)sulfonyl)benzo[*d*]thiazole (7)



A solution of sulfone **5a** (200 mg, 0.94 mmol, 1.0 equiv) in THF (9.4 mL, 0.10 M) was cooled to -78°C and stirred for 10 min at this temperature. A solution of $LiN(TMS)_2$ in THF (10.3 mL, 1.03 mmol, 1.1 equiv, 1.0M solution in THF) was added dropwise and the resulting mixture was stirred at -78°C for 2h. A 10% solution of HCl in MeOH (10 mL) was added and the resulting mixture was allowed to warm to rt. The whole mixture was extracted with EtOAc (3x20 mL) and the resulting organic layers were combined, washed with brine (15 mL), dried over $MgSO_4$, filtered and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography on SiO_2 (petroleum ether/EtOAc = 10:1 -> 4:1 -> 2:1) yielding compound **7** (99 mg, 30.5% (61% after recalculation)) as yellow crystals.



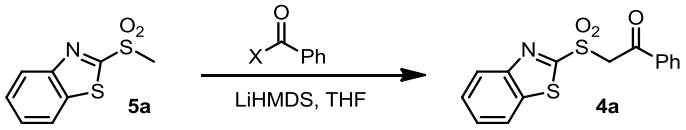
Mp 182-183°C (lit.[5] 181-182°C); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 5.32 (s, 2H, H-2), 7.39 – 7.53 (m, 2H), 7.57 – 7.74 (m, 2H), 7.86 (dd, *J* = 7.7, 1.0 Hz, 1H), 7.97 (dd, *J* = 13.0, 4.8 Hz, 2H), 8.27 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (75 MHz, CDCl3): δ = 59.0 (C-2), 121.9, 122.6, 124.0, 126.0, 126.3, 126.8, 128.0, 128.5, 136.5, 137.4, 152.7, 153.0, 155.2 (C-3), 164.3 (C-1); IR (film): ν_{max}/cm^{-1} = 2986 (w), 2923 (w), 2911 (w), 1556 (w), 1504 (m), 1469 (s), 1434 (m), 1421 (w), 1394 (w), 1338 (s), 1317 (s), 1280 (w), 1240 (m), 1201 (m), 1155 (s), 1128 (m), 1097 (m), 1088 (m), 1064 (w), 1028 (m), 1014 (w), 910 (m), 856 (m), 762 (s), 731 (s); MS (CI), *m/z* (%): 347 (M^+, 13), 311 (5), 283 (29), 178 (36), 164 (33), 150 (100), 136 (100), 104 (65); HRMS (CI), *m/z*: calc. 346.9983 for $C_{15}H_{11}N_2O_2S_3$, found 346.9986; El. an. for $C_{15}H_{10}N_2O_2S_3$, calc. C 52.00, H 2.91, N 8.09; found C 52.06, H 3.09, N 8.16.

α-Heterosulfonyl ketones (4) and esters (11)

General procedure

A solution of sulfone (1.0 mmol, 1.0 equiv) in THF (5 mL, 0.20M) was cooled to -78°C and LiHMDS (1.0M sol. in THF) (2.2 mL, 2.2 mmol, 2.2 equiv) was added dropwise. A color of the reaction mixture turned from colorless or slightly yellow to orange/red. Immediately after, a solution of acylating agent (acyl halide, carboxylic acid anhydride or acyl imidazole[7]) or alkoxy carbonylating agent (alkoxy chloroformate, alkoxy imidazoylformate[8] or Boc_2O) (1.1 mmol, 1.1 equiv) in THF (0.5 mL)[9] was added. The color of the reaction mixture faded within few minutes. The resulting mixture was stirred at -78°C for 30 min, allowed to warm to 0°C within 1h and stirred at 0°C for a further 30 min before sat. aq. sol. of NH_4Cl (15 mL) was added. The whole mixture was extracted with EtOAc (3x75 mL) and the combined organic layers were washed with brine (50 mL), dried over $MgSO_4$, filtered and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography on SiO_2.

2-(benzo[*d*]thiazol-2-ylsulfonyl)-1-phenylethanone (4a)

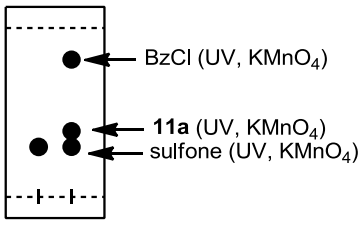


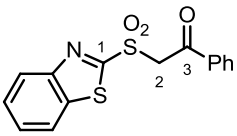
Starting from sulfone **5a** (100 mg, 0.47 mmol), the crude material was purified by flash chromatography (petroleum ether:EtOAc = 4:1->2:1->1:1):

- Using BzCl as acylating agent (Table 1, entry 4), the reaction yielded 143 mg (96%) of **4a**.
- Using Bz_2O as acylating agent (Table 1, entry 16), the reaction yielded 137 mg (92%) of **4a**.
- Using Bz-Im as acylating agent (Table 1, entry 17), the reaction yielded 137 mg (92%) of **4a**.
- Using Bz-CN as acylating agent (Table 1, entry 18), the reaction yielded 135 mg (92%) of **4a**.

The reaction performed with 2.0 g (9.4 mmol) of sulfone **5a** and 1.31 mL (11.4 mmol) of BzCl[10] gave 2.89 g (97%) of **4a**.

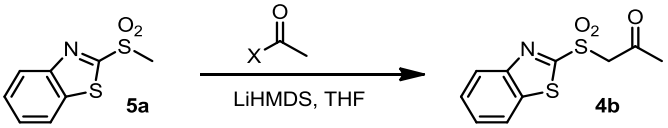
TLC (petroleum ether:EtOAc = 2:1)





Mp = 123-124°C, lit.[11] 122°C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 5.22 (s, 2H, H-2), 7.43 – 7.53 (m, 2H), 7.55 – 7.69 (m, 3H), 7.94 (dd, *J* = 8.4, 1.2 Hz, 2H), 8.01 (dd, *J* = 7.0, 2.2 Hz, 1H), 8.20 (dd, *J* = 7.2, 2.1 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 61.4 (C-2), 122.6, 125.7, 127.9, 128.4, 129.17, 129.19, 134.9, 135.6, 137.3, 152.6, 165.5 (C-1), 187.3 (C-3); IR (film): ν^{-1} = 3063 (w), 2959 (w), 2925 (w), 2921 (w), 2919 (w), 1683 (s), 1598 (m), 1471 (m), 1338 (s), 1155 (s), 991 (m), 760 (s), 731 (s), 688 (s); MS (APCI), *m/z* (%): 318 (100) [M^++1], 319 (20), 236 (9), 105 (11); El. an. for $C_{15}H_{11}NO_3S_2$, calc. C 56.76, H 3.49, N 4.41; found C 56.78, H 3.11, N 4.67.

1-(benzo[d]thiazol-2-ylsulfonyl)propan-2-one (4b)

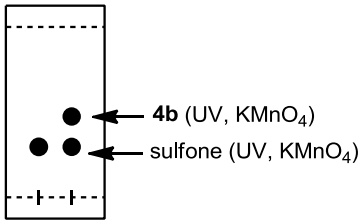


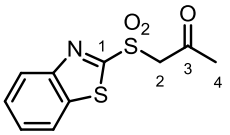
Starting from sulfone **5a** (100 mg, 0.47 mmol), the crude material was purified by flash chromatography (petroleum ether:EtOAc = 4:1->2:1->1:1):

- Using AcCl as acylating agent (Table 5, entry 1), the reaction yielded 108 mg (90%) of **4b**.
- Using Ac_2O as acylating agent (Table 5, entry 2), the reaction yielded 110 mg (92%) of **4b**.
- Using Ac-Im as acylating agent (Table 5, entry 3), the reaction yielded 107 mg (89%) of **4b**.

The reaction performed with 2.0 g (9.4 mmol) of sulfone **5a** and 0.8 mL (11.4 mmol) of AcCl[12] gave 2.15 g (90%) of **4b**.

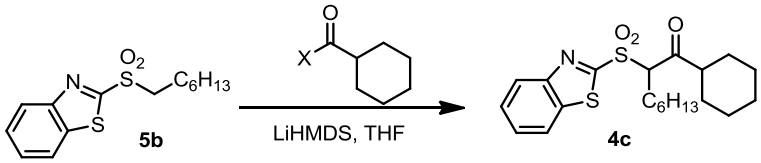
TLC (petroleum ether:EtOAc = 2:1)





Mp = 126-127°C, lit.[13] 125-127°C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 2.46 (s, 3H, H-4), 4.60 (s, 2H, H-2), 7.57 – 7.71 (m, 2H), 8.03 (dd, *J* = 8.0, 1.4 Hz, 1H), 8.22 (dd, *J* = 6.7, 1.5 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 31.7 (C-4), 65.6 (C-2), 122.6, 125.8, 128.0, 128.5, 137.1, 152.6, 165.0 (C-1), 194.8 (C-3); IR (film): ν^{-1} = 2990 (w), 2952 (w), 2925 (w), 2853 (w), 1726 (s), 1556 (w), 1471 (m), 1334 (s), 1159 (s), 1028 (m), 854 (m), 762 (s); MS (APCI), *m/z* (%): 256 (100) [M^++1], 258 (15), 214 (27), 136 (13); El. an. for $C_{10}H_9NO_3S_2$, calc. C 46.82, H 3.35, N 5.49; found C 46.82, H 3.35, N 5.12.

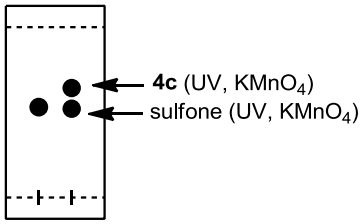
2-(benzo[*d*]thiazol-2-ylsulfonyl)-1-cyclohexyloctan-1-one (4c)

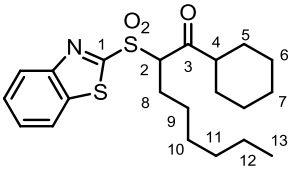


Starting from sulfone **5b** (100 mg, 0.34 mmol), the crude material was purified by flash chromatography (petroleum ether:EtOAc = 10:1):

- Using AcCl as acylating agent (Table 5, entry 4), the reaction yielded 114 mg (83%) of **4c**.
- Using Ac-Im as acylating agent (Table 5, entry 5), the reaction yielded 126 mg (92%) of **4c**.

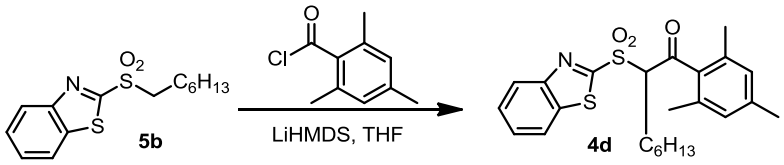
TLC (petroleum ether:EtOAc = 4:1)





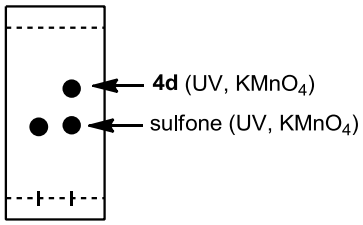
Mp = 132-133°C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.82 (t, *J* = 6.7 Hz, 3H, H-13), 1.06 – 1.56 (m, 13H), 1.59 – 2.09 (m, 6H), 2. 12 – 2.33 (m, 1H), 2.78 (tt, *J* = 11.3, 3.3 Hz, 1H, H-4), 4.73 (dd, *J* = 10.7, 3.5 Hz, 1H, H-2), 7.64 (pd, *J* = 7.2, 1.6 Hz, 1H), 7.65 (p, *J* = 7.2 Hz, 1H), 8.01 (dd, *J* = 7.2, 1.8 Hz, 1H), 8.25 (dd, *J* = 7.4, 1.9 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 14.1 (C-13), 22.6, 25.2, 25.8, 26.0, 27.1, 27.3, 27.6, 28.5, 29.0, 31.4, 52.8 (C-4), 72.7 (C-2), 122.5, 125.9, 127.9, 128.4, 137.4, 152.8, 164.2 (C-1), 204.1 (C-3); IR (film): ν^{-1} = 2991 (w), 2952 (w), 2927 (w), 2852 (w), 1728 (s), 1554 (w), 1475 (m), 1161 (s), 1029 (m), 853 (m), 761 (s); MS (APCI), *m/z* (%): 408 (100) [M^+], 409 (21), 105 (40); El. an. for $C_{21}H_{29}NO_3S_2$, calc. C 61.88, H 7.17, N 3.44; found C 62.03, H 7.29, N 3.13.

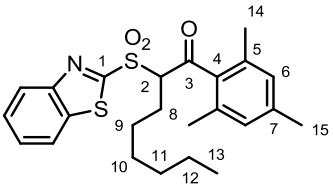
2-(benzo[d]thiazol-2-ylsulfonyl)-1-mesityloctan-1-one (4d)



Starting from sulfone **5b** (100 mg, 0.34 mmol), the crude material was purified by flash chromatography (petroleum ether:EtOAc = 10:1) yielding 112 mg (89%) of **4d** (Table 5, entry 6).

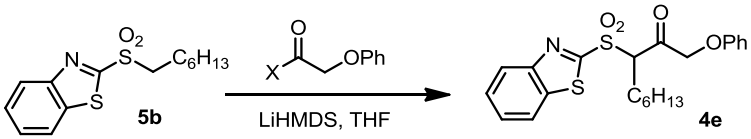
TLC (petroleum ether:EtOAc = 4:1)





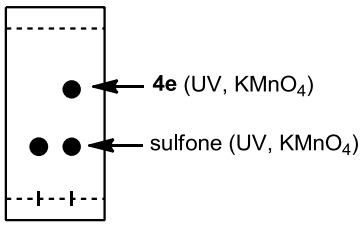
Mp = 145-146°C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 6.7 Hz, 3H, H-13), 1.20 – 1.31 (m, 4H), 1.36 (dt, *J* = 14.6, 7.3 Hz, 2H, H-10), 1.51 (tt, *J* = 12.1, 6.2 Hz, 2H, H-9), 1.98 (s, 3H, H-15), 2.29 (s, 6H, H-14, partial overlap), 2.31 – 2.43 (m, 2H, H-8), 5.38 (t, *J* = 6.5 Hz, 1H, H-2), 6.55 (s, 2H, H-6), 7.50 – 7.64 (m, 2H), 7.92 (d, *J* = 7.7 Hz, 1H), 8.12 (dd, *J* = 7.6, 0.8 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 14.16 (C-13), 20.6 (C-14), 21.0 (C-15), 22.6, 24.9, 27.6, 29.3, 31.4, 74.2 (C-2), 122.2, 125.3, 127.6, 128.0, 129.4, 135.5, 136.0, 137.2, 140.6, 152.4, 165.9 (C-1), 197.3 (C-3); IR (film): ν^{-1} = 3063 (w), 3059 (w), 2958 (w), 2925 (w), 2920 (w), 2920 (w), 1681 (s), 1597 (m), 1471 (m), 1331 (s), 1156 (s), 990 (m), 761 (s), 730 (s), 689 (s); MS (APCI), *m/z* (%): 444 (100) [M^+], 445 (26), 324 (51); El. an. for $C_{24}H_{29}NO_3S_2$, calc. C 64.98, H 6.59, N 3.16; found C 65.21, H 6.23, N 3.19.

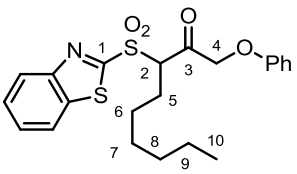
3-(benzo[*d*]thiazol-2-ylsulfonyl)-1-phenoxynonan-2-one (4e)



Starting from sulfone **5b** (100 mg, 0.34 mmol), the crude material was purified by flash chromatography (petroleum ether:EtOAc = 10:1->4:1) yielding 125 mg (86%) of **4e** as yellowish oil (Table 5, entry 7).

TLC (petroleum ether:EtOAc = 4:1)

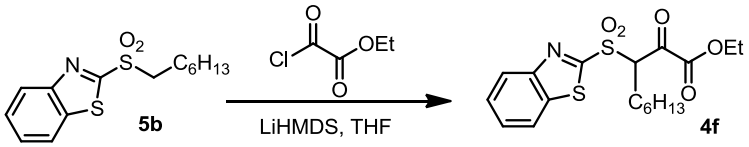




^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.83 (t, *J* = 6.8 Hz, 3H, H-10), 1.07 – 1.48 (m, 8H), 2.09 – 2.37 (m, 2H, H-5), 4.89 (dd, *J* = 17.1 Hz, 2H, H-4), 5.02 (dd, *J* = 10.4, 4.0 Hz, 1H, H-2), 6.90 (d, *J* = 8.0 Hz, 2H), 7.00 (t, *J* = 7.3 Hz, 1H), 7.22 – 7.37 (m, 2H), 7.55 – 7.71 (m, 2H), 7.99 (dd, *J* = 7.1, 2.2 Hz, 1H), 8.21 (dd, *J* = 7.2, 2.1 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 14.1 (C-10), 22.5, 26.7, 26.9, 28.8, 31.4, 70.1 (C-4), 73.6 (C-2), 114.8,

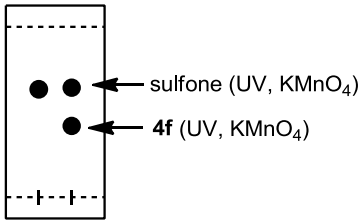
122.25, 122.47, 125.9, 128.0, 128.5, 129.8, 137.3, 152.7, 157.4, 163.8 (C-1), 197.9 (C-3); IR (film): ν^{-1} = 3062 (w), 2928 (s), 1739 (s), 1589 (m), 1494 (m), 1467 (m), 1334 (s), 1149 (s), 758 (m); MS (APCI), *m/z* (%): 432 (100) [M^+], 433 (24), 368 (15), 298 (74), 233 (11); El. an. for $C_{22}H_{25}NO_4S_2$, calc. C 61.23, H 5.84, N 3.25; found C 60.83, H 5.78, N 3.16.

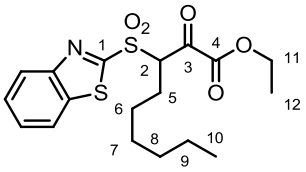
ethyl 3-(benzo[*d*]thiazol-2-ylsulfonyl)-2-oxononanoate (4f)



Starting from sulfone **5b** (100 mg, 0.34 mmol), the crude material was purified by flash chromatography (petroleum ether:EtOAc = 4:1->2:1) yielding 104 mg (78%) of **4f** as yellow oil (Table 5, entry 8).

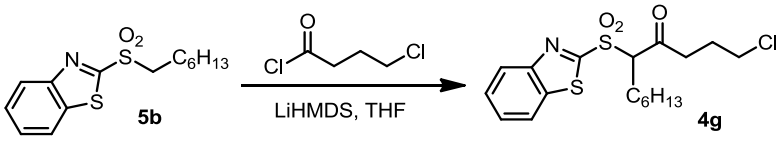
TLC (petroleum ether:EtOAc = 2:1)





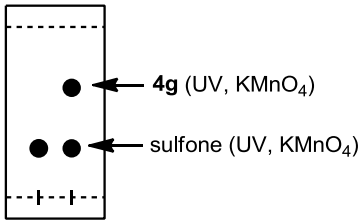
Keto/enol forms of **11f** = ~1:1. Peaks belonging to enol form are marked with*.
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.84 (t, *J* = 6.7 Hz, 3H, H-10). 0.98 – 1.57 (m, 8H), 2.08 – 2.38 (m, 2H), 4.12 (q, *J* = 7.2 Hz, 2H, H-11*), 4.30 (q, *J* = 7.2 Hz, 2H, H-11), 5.55 (t, *J* = 7.2 Hz, 1H, H-2), 7.51 – 7.72 (m, 2H), 7.93 – 8.07 (m, 1H), 8.14 – 8.27 (m, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 14.1 (C-10*), 14.4 (C-10), 21.23, 22.56, 26.18, 26.87, 28.06, 28.91, 31.24, 31.37, 60.6 (C-11), 63.8 (C-11*), 68.6 (C-2*), 122.6, 125.7, 128.0, 127.8, 128.6, 137.2, 152.3, 160.3, 164.3, 171.3 (C-4), 185.1 (C-3); IR (film): ν^{-1} = 3320 (w), 2955 (m), 2928 (s), 2856 (m), 1731 (s), 1705 (s), 1674 (s), 1470 (s), 1330 (m), 1150 (s), 1020 (m), 852 (m), 762 (m), 729 (s); MS (APCI), *m/z* (%): 398 (100) [M^+], 399 (22), 370 (48), 334 (31), 298 (30), 281 (58), 199 (14), 136 (11); El. an. for $C_{18}H_{23}NO_5S_2$, calc. C 54.39, H 5.83, N 3.52; found C 54.42, H 5.89, N 3.58.

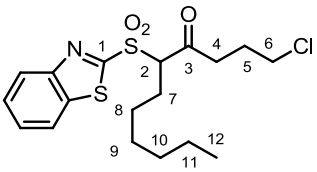
5-(benzo[*d*]thiazol-2-ylsulfonyl)-1-chloroundecan-4-one (4g)



Starting from sulfone **5b** (100 mg, 0.34 mmol), the crude material was purified by flash chromatography (petroleum ether:EtOAc = 10:1->4:1) yielding 110 mg (81%) of **4g** as yellow oil (Table 5, entry 9).

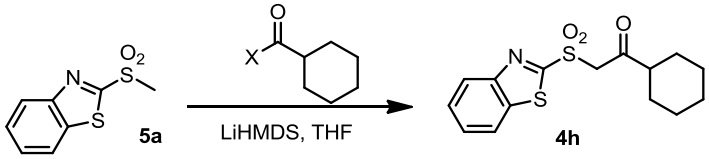
TLC (petroleum ether:EtOAc = 4:1)





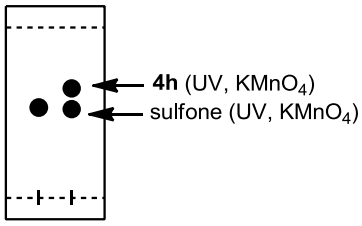
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.83 (t, *J* = 6.7 Hz, 3H, H-12), 1.12 – 1.37 (m, 8H), 2.31 – 1.99 (m, 4H, H-5 and H-7), 2.89 (dt, *J* = 19.1, 6.8 Hz, 1H, one of H-4), 3.13 (dt, *J* = 19.1, 6.8 Hz, 1H, one of H-4), 3.58 (pd, *J* = 6.5, 2.6 Hz, 2H, H-6), 4.55 (dd, *J* = 10.7, 3.9 Hz, 1H, H-2), 7.63 (pd, *J* = 7.2, 1.4 Hz, 2H), 8.02 (dd, *J* = 7.1, 1.9 Hz, 1H), 8.24 (dd, *J* = 7.3, 1.9 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 14.10 (C-12), 22.6, 26.2, 26.8, 27.0, 28.9, 31.4, 41.6, 44.0, 74.6 (C-2), 122.5, 125.9, 128.0, 128.5, 137.3, 152.7, 164.0 (C-1), 200.3 (C-3); IR (film): ν^{-1} = 2955 (m), 2928 (s), 2856 (m), 1720 (s), 1467 (s), 1330 (s), 1315 (s), 1144 (m), 1022 (m), 852 (m), 762 (m), 729 (s); MS (APCI), *m/z* (%): 402 (11) [M^+], 404 (7), 366 (100), 302 (40); El. an. for $C_{18}H_{24}ClNO_3S_2$, calc. C 53.78, H 6.02, N 3.48; found C 53.92, H 5.91, N 3.69.

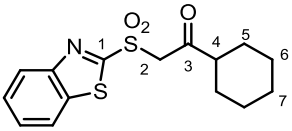
2-(benzo[*d*]thiazol-2-ylsulfonyl)-1-cyclohexylethanoe (4h)



Starting from sulfone **5a** (200 mg, 0.94 mmol), the crude material was purified by flash chromatography (petroleum ether:EtOAc = 4:1->2:1) yielding sulfone **4h** (252 mg, 83%) as slightly yellow crystals (Table 4, entry 3).

TLC (petroleum ether:EtOAc = 2:1)

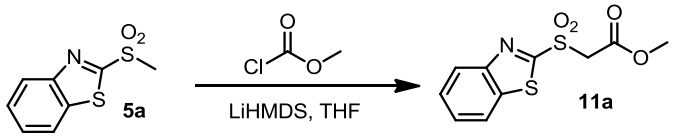




Keto/enol forms of **4h** = ~9:1. Peaks belonging to enol form are marked with*.

Mp = 87-88°C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.12 – 1.42 (m, 6H), 1.61 – 2.01 (m, 4H), 2.55 – 2.70 (ddd, *J* = 14.0, 7.5, 3.4 Hz, 1H, H-4), 4.68 (s, 2H, H-2), 5.30 (s, 1H, H-2*), 7.41 – 7.54 (m, 2H), 8.01 (dd, *J* = 7.8, 1.5 Hz, 1H), 8.19 (dd, *J* = 7.5, 1.3 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 25.4, 25.7, 27.9, 51.8 (C-4), 62.7 (C-2), 122.6, 125.6, 127.9, 128.3, 137.1, 152.5, 165.5 (C-1), 200.5 (C-3); IR (film): ν^{-1} = 2940 (m), 2932 (m), 2925 (m), 2909 (w), 2894 (w), 2857 (m), 1716 (m), 1706 (s), 1473 (s), 1450 (m), 1336 (s), 1317 (s), 1294 (m), 1278 (m), 1157 (s), 1147 (s), 1128 (s), 1088 (m), 1062 (m), 1028 (m), 999 (s), 902 (m), 856 (s), 760 (s), 731 (s), 708 (s), 692 (s); MS (APCI), *m/z* (%): 324 (100) [M^+], 198 (60), 134 (29); El. an. for $C_{15}H_{17}NO_3S_2$, calc. C 55.70, H 5.30, N 4.33; found C 55.79, H 5.18, N 4.11.

methyl 2-(benzo[d]thiazol-2-ylsulfonyl)acetate (11a)

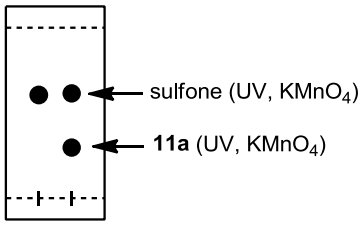


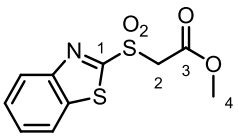
Starting from sulfone **5a** (100 mg, 0.34 mmol), the crude material was purified by flash chromatography (petroleum ether:EtOAc = 4:1->2:1->1:1):

- Using ClCOOMe as alkoxycarbonylating agent (Table 6, entry 1), the reaction yielded 120 mg (94%) of **11a**.
- Using Im-COOMe as alkoxycarbonylating agent (Table 6, entry 2), the reaction yielded 113 mg (89%) of **11a**.
- Using NC-COOMe as alkoxycarbonylating agent (Table 6, entry 3), the reaction yielded 116 mg (91%) of **11a**.

The reaction performed with 3.0 g (14.1 mmol) of sulfone **5a** and 1.3 mL (16.9 mmol) of ClCOOMe[14] gave 3.74 g (98%) of **11a**.

TLC (petroleum ether:EtOAc = 2:1)

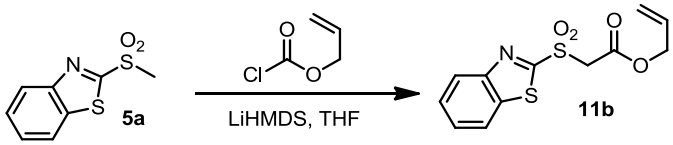




Keto/enol forms of **11a** = ~7:1. Peaks belonging to enol form are marked with*.

Mp = 69-70°C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 3.66 (s, 3H, H-4), 3.73 (s, 3H, H-4*), 4.59 (s, 2H, H-2), 5.31 (s, 1H, H-2*), 7.54 – 7.71 (m, 2H), 8.02 (dd, *J* = 7.1, 2.1 Hz, 1H), 8.21 (dd, *J* = 7.3, 2.2 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 52.4 (C-4*), 53.5 (C-4), 58.7 (C-2), 122.6, 125.7, 127.9, 128.4, 137.1, 152.6, 162.3 (C-1), 165.0 (C-3); IR (film): ν^{-1} = 2992 (w), 2984 (w), 2938 (w), 1803 (m), 1741 (s), 1471 (s), 1342 (s), 1155 (s), 1122 (s), 762 (s), 729 (s); MS (APCI), *m/z* (%): 272 (100) [M^+], 240 (35), 214 (7); El. an. for $C_{10}H_9NO_4S_2$, calc. C 44.27, H 3.34, N 5.16; found C 44.67, H 3.12, N 4.97.

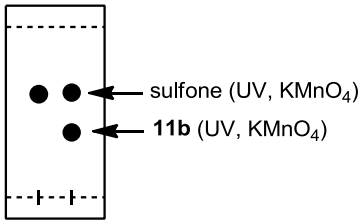
allyl 2-(benzo[d]thiazol-2-ylsulfonyl)acetate (11b)

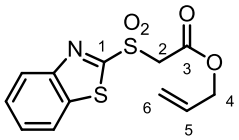


Starting from sulfone **5a** (100 mg, 0.47 mmol), the crude material was purified by flash chromatography (petroleum ether:EtOAc = 4:1->1:1) yielding 132 mg (95%) of **11b** (Table 6, entry 34).

The reaction performed with 1.0 g (4.69 mmol) of sulfone **13a** and 0.598 mL (5.63 mmol) of $ClCOOCH_2CH{=}CH_2$[15] gave 1.31 g (94%) of **11b**.

TLC (petroleum ether:EtOAc = 2:1)

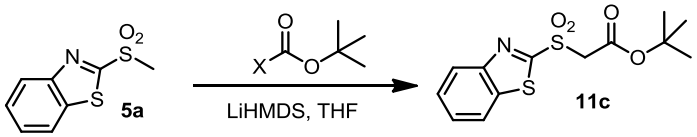




Keto/enol forms of **11b** = ~7:1. Peaks belonging to enol form are marked with*.

Mp = 72-73°C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 4.60 (td, *J* = 2.7, 1.3 Hz, 2H, H-4), 4.61 (s, 2H, H-2), 4.65 – 4.70 (m, 1H, H-2*), 5.18 (ddd, *J* = 10.5, 2.2, 1.1 Hz, 1H, H-6), 5.24 (ddd, *J* = 17.3, 2.8, 1.4 Hz, 1H, H-6), 5.31 – 5.42 (m, 2H, H-6*), 5.77 (ddt, *J* = 22.2, 10.4, 5.9 Hz, 1H, H-5), 5.85 – 6.00 (m, 1H, H-5*), 7.58 – 7.69 (m, 2H), 8.02 (dd, *J* = 7.0, 1.9 Hz, 1H), 8.22 (dd, *J* = 7.4, 2.1 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 58.8 (C-4), 67.3 (C-2), 119.8, 122.6, 125.7, 128.0, 128.5, 130.6, 137.2, 152.6, 161.5 (C-1), 165.0 (C-3); IR (film): ν^{-1} = 3089 (w), 3073 (w), 2992 (w), 2984 (w), 2938 (w), 1803 (m), 1741 (s), 1650 (w), 1554 (w), 1519 (m), 1471 (s), 1423 (m), 1342 (s), 1317 (s), 1300 (s), 1276 (s), 1240 (s), 1195 (s), 1155 (s), 1122 (s), 1088 (s), 1028 (s), 987 (s), 935 (s), 854 (s), 796 (s), 762 (s), 729 (s), 710 (s), 694 (s), 652 (m), 644 (s), 633 (s), 625 (s), 617 (s), 609 (m); MS (APCI), *m/z* (%): 298 (100) [M^+], 240 (24); El. an. for $C_{12}H_{11}NO_4S_2$, calc. C 48.47, H 3.73, N 4.71; found C 48.82, H 3.65, N 4.38.

***tert*-butyl 2-(benzo[*d*]thiazol-2-ylsulfonyl)acetate (11c)**

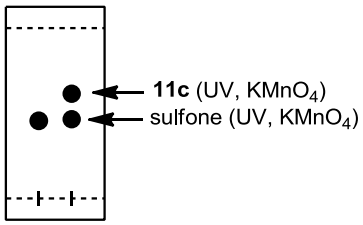


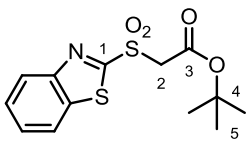
Starting from sulfone **5a** (100 mg, 0.47 mmol), the crude material was purified by flash chromatography (petroleum ether:EtOAc = 4:1):

- Using Boc_2O as alkoxycarbonylating agent (Table 6, entry 5), the reaction yielded 138 mg (94%) of **11c**.
- Using Im-COO*t*Bu as alkoxycarbonylating agent (Table 6, entry 6), the reaction yielded 144 mg (89%) of **11c**.

The reaction performed with 2.0 g (9.38 mmol) of sulfone **5a** and 2.46 g (11.3 mmol) of Boc_2O[16] gave 2.88 g (98%) of **11c**.

TLC (petroleum ether:EtOAc = 4:1)



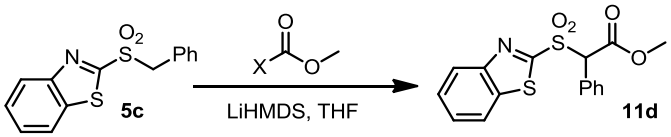


Keto/enol forms of **11c** = ~6:1. Peaks belonging to enol form are marked with*.

Mp = 75-76°C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.34 (s, 9H, H-5), 1.48 (s, 9H, H5*), 4.49 (s, 2H, H-2), 7.63 (p, *J* = 7.2, 1.5 Hz, 2H), 8.03 (dd, *J* = 7.1, 1.8 Hz, 1H), 8.23 (dd, *J* = 7.2, 1.7 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 27.8 (C-5), 28.2 (C-5*), 60.1 (C-2), 84.6 (C-4), 122.6, 125.7, 127.9, 128.4, 137.0, 152.7, 160.6 (C-1), 165.4

(C-3); IR (film): ν^{-1} = 2977 (w), 2935 (w), 1794 (m), 1732 (s), 1471 (m), 1339 (s), 1144 (s), 1088 (s), 761 (s), 629 (s); MS (ESI), *m/z* (%): 336 (33) [M+Na$^+$], 258 (100), 240 (19); El. an. for $C_{13}H_{15}NO_4S_2$, calc. C 49.82, H 4.82, N 4.47; found C 50.13, H 4.98, N 4.75.

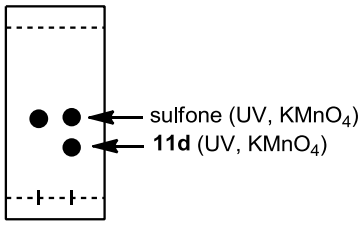
methyl 2-(benzo[*d*]thiazol-2-ylsulfonyl)-2-phenylacetate (11d)

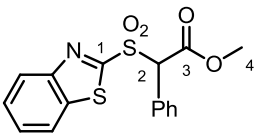


Starting from sulfone **5c** (100 mg, 0.35 mmol), the crude material was purified by flash chromatography (petroleum ether:EtOAc = 4:1->1:1):

- Using ClCOOMe as alkoxycarbonylating agent (Table 6, entry 7), the reaction yielded 106 mg (88%) of **11d**.
- Using Im-COOMe as alkoxycarbonylating agent (Table 6, entry 8), the reaction yielded 113 mg (94%) of **11d**.
- Using NC-COOMe as alkoxycarbonylating agent (Table 6, entry 9), the reaction yielded 110 mg (92%) of **11d**.

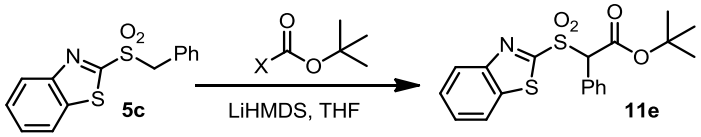
TLC (petroleum ether:EtOAc = 2:1)





Mp = 115-116°C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 3.78 (s, 3H, H-4), 5.77 (s, 1H, H-2), 7.30 – 7.42 (m, 3H), 7.50 – 7.55 (m, 2H), 7.55 – 7.62 (m, 1H), 7.62 – 7.68 (m, 1H), 7.95 (d, *J* = 8.4 Hz, 1H), 8.24 (d, *J* = 7.6 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 53.7 (C-4), 73.6 (C-2), 122.5, 125.7, 126.4, 127.9, 128.4, 129.2, 130.3, 130.9, 137.4, 152.5, 164.5, 164.7; IR (film): ν^{-1} = 3072 (s), 3063 (m), 2993 (w), 2937 (w), 1740 (s), 1472 (s), 1341 (s), 1144 (s), 1121 (s), 762 (s), 729 (s); MS (APCI), *m/z* (%): 348 (100) [M$^+$], 284 (26), 224 (12), 149 (7); El. an. for $C_{16}H_{13}NO_4S_2$, calc. C 55.32, H 3.77, N 4.03; found C 55.67, H 3.60, N 3.99.

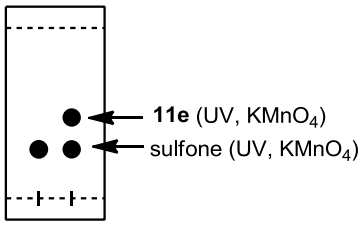
***tert*-butyl 2-(benzo[*d*]thiazol-2-ylsulfonyl)-2-phenylacetate (11e)**

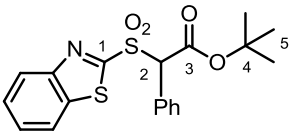


Starting from sulfone **5c** (100 mg, 0.35 mmol), the crude material was purified by flash chromatography (petroleum ether:EtOAc = 4:1->2:1):

- Using Boc_2O as alkoxycarbonylating agent (Table 6, entry 10), the reaction yielded 124 mg (91%) of **11**.
- Using Im-COO*t*Bu as alkoxycarbonylating agent (Table 6, entry 11), the reaction yielded 134 mg (98%) of **11e**.

TLC (petroleum ether:EtOAc = 4:1)

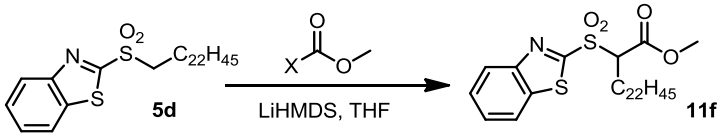




Keto/enol forms of **11e** = ~5:1. Peaks belonging to enol form are marked with*.

Mp = 121-122°C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.38 (s, 9H, H-5), 1.49 (s, *J* = 5.5 Hz, 9H, H-5*), 5.71 (s, 1H, H-2), 7.33 – 7.43 (m, 3H), 7.51 – 7.69 (m, 4H), 7.96 (d, *J* = 7.7 Hz, 1H), 8.24 (d, *J* = 8.3 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 27.7 (C-5), 28.04 (C-5*), 74.2 (C-2), 84.6 (C-4), 122.3, 125.5, 126.6, 127.7, 128.1, 128.9, 130.0, 130.8, 137.1, 152.4, 162.6 (C-2), 165.1 (C-3); 53.7 (C-4), 73.6 (C-2), 122.5, 125.7, 126.4, 127.9, 128.4, 129.2, 130.3, 130.9, 137.4, 152.5, 164.5 (C-3); IR (film): ν^{-1} = 3071 (s), 3062 (m), 2995 (w), 2938 (w), 1805 (w), 1742 (s), 1471 (s), 1332 (s), 1143 (s), 1112 (s), 761 (s), 728 (s); MS (APCI), *m/z* (%): 390 (100) [M^+], 200 (31); El. an. for $C_{19}H_{19}NO_4S_2$, calc. C 58.59, H 4.92, N 3.60; found C 58.21, H 5.02, N 3.83.

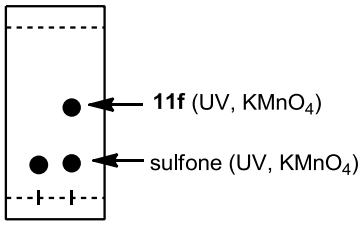
methyl 2-(benzo[*d*]thiazol-2-ylsulfonyl)-2-lignocerate (11f)

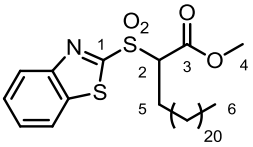


Starting from sulfone **5d** (100 mg, 0.19 mmol), the crude material was purified by flash chromatography (petroleum ether:EtOAc = 20:1->10:1):

- Using ClCOOMe as alkoxycarbonylating agent (Table 6, entry 12), the reaction yielded 98 mg (88%) of **11f**.
- Using Im-COOMe as alkoxycarbonylating agent (Table 6, entry 13), the reaction yielded 104 mg (94%) of **11f**.
- Using NC-COOMe as alkoxycarbonylating agent (Table 6, entry 14), the reaction yielded 103 mg (93%) of **11f**.

TLC (petroleum ether:EtOAc = 10:1)



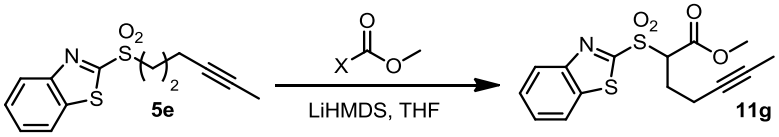


Keto/enol forms of **11f** = ~8:1. Peaks belonging to enol form are marked with*.

Mp = 111-112°C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 6.7 Hz, 3H, H-6), 1.05 – 1.71 (m, 40H), 2.14 – 2.34 (m, 2H, H-5), 3.64 (t, *J* = 6.7 Hz, 2H, H-5*), 3.74 (s, 3H, H-4), 4.44 (dd, *J* = 8.8, 6.0 Hz, 1H, H-2), 5.30 (s, 1H*), 7.58 – 7.71 (m, 2H), 8.03 (dd, *J* = 7.1, 1.9 Hz, 1H), 8.26 (dd, *J* = 7.2, 1.8 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 14.3 (C-6), 22.9, 26.4, 27.1, 29.2, 29.3, 29.6, 29.8, 29.9, 32.1, 53.5 (C-4), 70.0 (C-2), 122.5, 125.9, 127.9, 128.4, 137.4, 152.8, 164.5 (C-1), 165.6 (C-3); IR (film): ν^{-1} = 3061 (w), 2996 (s), 2929 (s),

1801 (w), 1744 (s), 1472 (m), 1331 (s), 1143 (s), 1122 (s), 761 (s), 727 (s); MS (APCI), *m/z* (%): 580 (100) [M^+], 581 (37); El. an. for $C_{32}H_{53}NO_4S_2$, calc. C 66.28, H 9.21, N 2.42; found C 66.49, H 9.17, N 2.57.

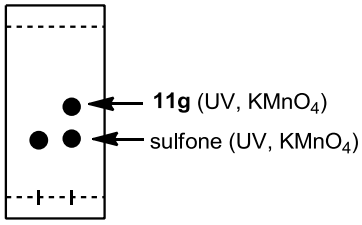
methyl 2-(benzo[*d*]thiazol-2-ylsulfonyl)hept-5-ynoate (11g)

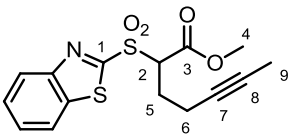


Starting from sulfone **5e** (100 mg, 0.19 mmol), the crude material was purified by flash chromatography (petroleum ether:EtOAc = 10:1->4:1->2:1->1:1):

- Using ClCOOMe as alkoxycarbonylating agent (Table 6, entry 15), the reaction yielded 112 mg (88%) of **11g** as yellowish oil.
- Using Im-COOMe as alkoxycarbonylating agent (Table 6, entry 16), the reaction yielded 118 mg (93%) of **11g** as yellowish oil.
- Using NC-COOMe as alkoxycarbonylating agent (Table 6, entry 17), the reaction yielded 119 mg (94%) of **11g** as yellowish oil.

TLC (petroleum ether:EtOAc = 2:1)

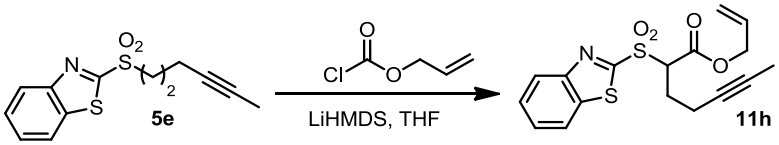




Keto/enol forms of **11g** = ~8:1. Peaks belonging to enol form are marked with*.

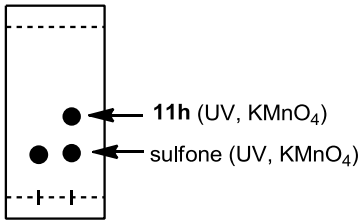
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.73 (t, *J* = 2.3 Hz, 3H, H-9), 2.13 – 2.33 (m, 1H), 2.34 – 2.49 (m, 3H), 2.67 – 2.87 (m, 2H, H-6*), 3.74 (s, 3H, H-4), 4.70 (dd, *J* = 7.8, 6.1 Hz, 1H, H-2), 5.31 (s, 1H*), 5.39 – 5.55 (m, 1H), 7.49 – 7.37 (m, 1H*), 7.63 (p, *J* = 7.2 Hz, 1H), 7.65 (p, *J* = 7.2 Hz, 1H), 7.94 – 7.80 (m, 2H*), 8.03 (dd, *J* = 7.2, 2.1 Hz, 1H), 8.26 (dd, *J* = 7.4, 2.0 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 3.6, 14.4, 16.7, 21.2, 25.8, 53.6, 60.6, 68.9, 75.8, 78.6, 122.5, 125.9, 128.0, 128.5, 137.4, 152.8, 164.2 (C-1), 165.2 (C-3); IR (film): ν^{-1} = 2954 (w), 2917 (w), 1739 (s), 1471 (m), 1436 (m), 1336 (s), 1149 (s), 1024 (m), 854 (m), 764 (s), 731 (s), 694 (m), 640 (m); MS (APCI), *m/z* (%): 338 (100) [M^+], 339 (12), 306 (16); El. an. for $C_{15}H_{15}NO_4S_2$, calc. C 53.40, H 4.48, N 4.15; found C 53.71, H 4.63, N 4.25.

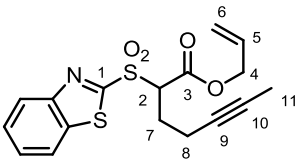
allyl 2-(benzo[*d*]thiazol-2-ylsulfonyl)hept-5-ynoate (11h)



Starting from sulfone **5e** (100 mg, 0.36 mmol), the crude material was purified by flash chromatography (petroleum ether:EtOAc = 10:1->4:1); the reaction yielded 116 mg (89%) of **11h** as yellow oil (Table 6, entry 18).

TLC (petroleum ether:EtOAc = 4:1)

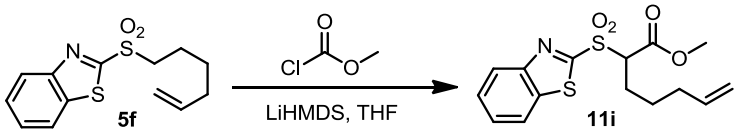




Keto/enol forms of **11h** = ~7:1. Peaks belonging to enol form are marked with*.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.75 (t, *J* = 2.3 Hz, 3H, H-11), 2.17 – 2.67 (m, 4H), 3.95 – 4.23 (m, 2H*), 4.61 (dd, *J* = 5.8, 1.2 Hz, 2H, H-4), 4.72 (dd, *J* = 7.6, 6.3 Hz, 1H, H-2), 5.14 (dd, *J* = 10.4, 1.1 Hz, 1H, H-6), 5.22 (dd, *J* = 17.2, 1.3 Hz, 1H, H-6), 5.29 – 5.41 (m, 2H, H-6*), 5.73 (ddt, *J* = 16.2, 10.5, 5.8 Hz, 1H, H-5), 7.37 (t, *J* = 8.1 Hz, 1H*), 7.47 (t, *J* = 7.7 Hz, 1H*), 7.63 (p, *J* = 7.2 Hz, 1H), 7.65 (p, *J* = 7.2 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H*), 7.98 (d, *J* = 8.3 Hz, 1H*), 8.02 (dd, *J* = 7.0, 1.8 Hz, 1H), 8.26 (dd, *J* = 7.2, 1.8 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 3.7, 16.7, 25.8, 67.3, 68.9, 75.9, 78.6, 119.6, 122.5, 126.0, 127.9, 128.5, 130.8, 137.4, 152.9, 164.2, 164.5; IR (film): ν^{-1} = 3071 (w), 3063 (w), 2934 (w), 2919 (w), 2855 (w), 1739 (s), 1677 (w), 1650 (w), 1554 (w), 1471 (s), 1149 (s), 1024 (s), 941 (s), 854 (s), 764 (s), 731 (s); MS (APCI), *m/z* (%): 364 (100) [M^+], 365 (17), 306 (7); El. an. for $C_{17}H_{17}NO_4S_2$, calc. C 56.18, H 4.71, N 3.85; found C 55.82, H 4.83, N 3.95.

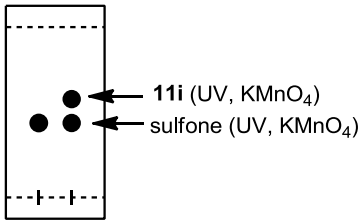
methyl 2-(benzo[*d*]thiazol-2-ylsulfonyl)hept-6-enoate (11i)

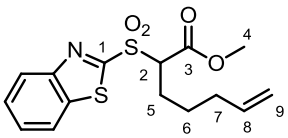


Starting from sulfone **5f** (100 mg, 0.36 mmol), the crude material was purified by flash chromatography (petroleum ether:EtOAc = 10:1->4:1):

- Using ClCOOMe as alkoxycarbonylating agent (Table 6, entry 19), the reaction yielded 105 mg (87%) of **11i** (yellow oil).
- Using Im-COOMe as alkoxycarbonylating agent (Table 6, entry 20), the reaction yielded 115 mg (95%) of **11i** (yellow oil).
- Using NC-COOMe as alkoxycarbonylating agent (Table 6, entry 21), the reaction yielded 113 mg (94%) of **11i** (yellow oil).

TLC (petroleum ether:EtOAc = 2:1)



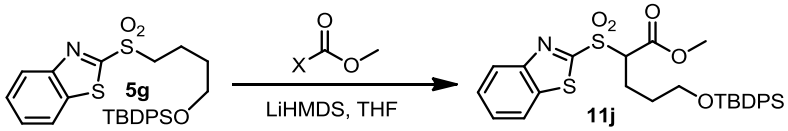


Keto/enol forms of **11i** = ~11:1. Peaks belonging to enol form are marked with*.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.58 – 1.45 (m, 2H), 2.11 (dt, *J* = 14.2, 4.7 Hz, 2H), 2.20 – 2.32 (m, 2H), 3.73 (s, 3H, H-4), 4.47 (td, *J* = 7.9, 5.4 Hz, 1H, H-2), 4.95 (dd, *J* = 10.5, 1.3 Hz, 1H, H-9), 5.05 (dt, *J* = 3.0, 1.5 Hz, 1H, H-9), 5.73 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H, H-8), 7.64 (pd, *J* = 7.2, 1.5 Hz, 2H), 8.03 (dd, *J* = 7.2, 2.1 Hz,

1H), 8.25 (dd, *J* = 7.4, 1.9 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 25.8, 26.3, 33.1, 53.5 (C-4), 69.8 (C-2), 115.9, 122.5, 125.9, 127.9, 128.5, 137.2, 137.3, 152.8, 164.4 (C-1), 165.5 (C-3); IR (film): ν^{-1} = 2940 (w), 2932 (w), 2923 (w), 2911 (w), 2903 (w), 1739 (s), 1641 (w), 1554 (w), 1471 (m), 1338 (s), 1149 (s), 1024 (m), 854 (m), 764 (s), 731 (s), 619 (m); MS (APCI), *m/z* (%): 340 (100) [M^+], 341 (21), 308 (7); El. an. for $C_{15}H_{17}NO_4S_2$, calc. C 53.08, H 5.05, N 4.13; found C 52.95, H 5.17, N 4.16.

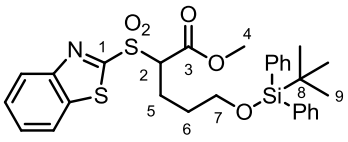
methyl 2-(benzo[d]thiazol-2-ylsulfonyl)-5-((tert-butyldiphenylsilyl)oxy)pentanoate (11j)



Starting from sulfone **5g** (100 mg, 0.20 mmol), the crude material was purified by flash chromatography (petroleum ether:EtOAc = 10:1->4:1):

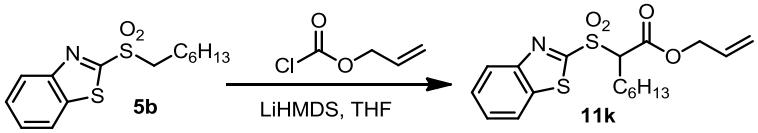
- Using ClCOOMe as alkoxycarbonylating agent (Table 6, entry 22), the reaction yielded 99 mg (89%) of **11j** (yellow oil).
- Using Im-COOMe as alkoxycarbonylating agent (Table 6, entry 23), the reaction yielded 104 mg (93%) of **11j** (yellow oil).
- Using Im-COOMe as alkoxycarbonylating agent (Table 6, entry 24), the reaction yielded 102 mg (91%) of **11j** (yellow oil).

Keto/enol forms of **11j** = ~6:1. Peaks belonging to enol form are marked with*.



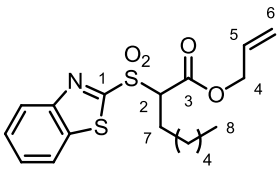
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.99 (s, 9H, H-9), 1.58 – 1.77 (m, 2H), 2.33 – 2.48 (m, 2H), 3.68 (t, *J* = 5.9 Hz, 2H, H-7), 3.73 (s, 3H, H-4), 4.62 (dd, *J* = 9.6, 5.4 Hz, 1H, H-2), 5.30 (s, 1H*), 7.30 – 7.47 (m, 6H), 7.57 – 7.69 (m, 6H), 7.85 – 7.94 (m, 2H*), 8.02 (dd, *J* = 6.7, 2.1 Hz, 1H), 8.24 (dd, *J* = 7.2, 2.3 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 19.3, 23.6, 26.9, 29.7, 53.5 (C-4), 63.0, 69.7, 122.5, 126.0, 127.9, 128.4, 129.9, 133.6, 135.7, 137.4, 152.9, 164.5 (C-1), 165.5 (C-3); IR (film): ν^{-1} = 2957 (w), 2938 (w), 2929 (w), 2855 (w), 1747 (s), 1471 (m), 1429 (m), 1340 (s), 1317 (m), 1151 (s), 1111 (s), 910 (s), 764 (s), 704 (s), 600 (w); MS (APCI), *m/z* (%): 568 (100) [M^+], 569 (36), 490 (96), 432 (36), 312 (47); El. an. for $C_{29}H_{33}NO_5S_2Si$, calc. C 61.34, H 5.86, N 2.78; found C 60.94, H 5.91, N 2.78.

allyl 2-(benzo[*d*]thiazol-2-ylsulfonyl)octanoate (11k)



Starting from sulfone **5b** (100 mg, 0.34 mmol), the crude material was purified by flash chromatography (petroleum ether:EtOAc = 10:1->4:1); the reaction yielded 118 mg (92%) of **11k** as yellow oil (Table 6, entry 25).

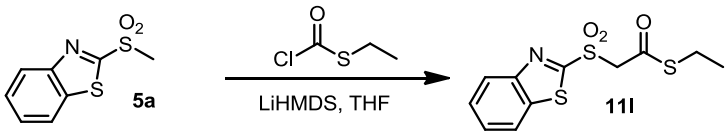
Keto/enol forms of **11k** = >20:1. Peaks belonging to enol form are marked with*.



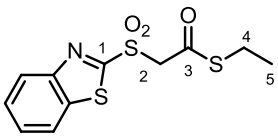
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 6.8 Hz, 1H, H-8), 1.13 – 1.52 (m, 8H), 2.15 – 2.45 (m, 2H, H-7), 4.46 (dd, *J* = 9.0, 5.8 Hz, 1H, H-2), 4.59 (d, *J* = 5.7 Hz, 2H, H-4), 5.12 (dd, *J* = 10.4, 1.1 Hz, 1H, H-6), 5.20 (dd, *J* = 17.2, 1.4 Hz, 1H, H-6),

5.71 (ddt, *J* = 16.3, 10.4, 5.9 Hz, 1H, H-5), 7.63 (pd, *J* = 7.2, 1.5 Hz, 2H), 8.01 (dd, *J* = 7.0, 1.9 Hz, 1H), 8.24 (dd, *J* = 7.2, 1.8 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 14.1, 22.6, 26.2, 27.0, 28.8, 31.4, 67.1, 69.9, 119.6, 122.4, 125.8, 127.9, 128.4, 130.8, 137.4, 152.8, 164.4 (C-1), 164.8 (C-3); IR (film): ν^{-1} = 2930 (w), 2923 (w), 2861 (w), 1741 (s), 1471 (m), 1340 (s), 1319 (m), 1149 (s), 1126 (m), 854 (m), 764 (s), 731 (m), 694 (w), 636 (m); MS (APCI), *m/z* (%): 382 (100) [M^+], 383 (19), 324 (29), 149 (5); El. an. for $C_{18}H_{23}NO_4S_2$, calc. C 56.67, H 6.08, N 3.67; found C 56.92, H 5.79, N 3.84.

S-ethyl 2-(benzo[*d*]thiazol-2-ylsulfonyl)ethanethioate (11l)

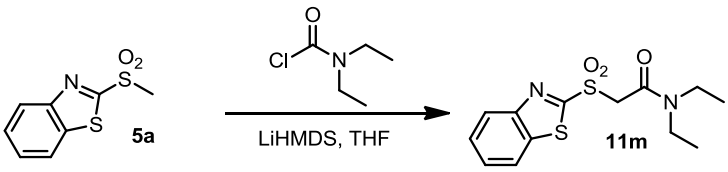


Starting from sulfone **5a** (200 mg, 0.94 mmol), the crude material was purified by flash chromatography (petroleum ether:EtOAc = 10:1->4:1); the reaction yielded 266 mg (94%) of **11l** as yellow oil (Table 7, entry 2).

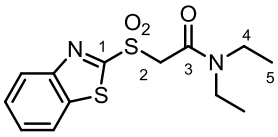


Keto/enol forms of **11l** = 8:1. Peaks belonging to enol form are marked with*. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.20 (t, *J* = 7.5 Hz, 3H, H-5), 2.89 (q, *J* = 7.4 Hz, 2H, H-4), 4.11 (q, *J* = 7.1 Hz, 2H, H-4*), 4.71 (s, 2H, H-2), 7.62 (pd, *J* = 7.2, 3.6 Hz, 2H), 7.95 – 8.06 (m, 1H), 8.14 – 8.28 (m, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 14.3 (C-5), 15.7 (C-5*), 21.2 (C-4*), 24.9 (C-4), 60.5 (C-2*), 65.2 (C-2), 122.6, 125.7, 127.9, 128.5, 137.2, 152.6, 164.8 (C-1), 186.3 (C-3); IR (film): ν^{-1} = 2978 (w), 2930 (w), 1675 (s), 1471 (s), 1340 (s), 1317 (s), 1240 (m), 1159 (s), 1140 (s), 1005 (s), 974 (m), 764 (s), 731 (s), 692 (m); MS (ES), *m/z* (%): 302 (M^++H, 100), 253 (11), 240 (100), 216 (9), 175 (41), 170 (12), 134 (18); HRMS (ES), *m/z*: calc. 301.9979 for $C_{11}H_{12}NO_3S_3$, found 301.9977;El. an. for $C_{11}H_{11}NO_3S_3$, calc. C 43.83, H 3.68, N 4.65; found C 43.92, H 3.86, N 6.84.

2-(benzo[*d*]thiazol-2-ylsulfonyl)-*N*,*N*-diethylacetamide (11m)



Starting from sulfone **5a** (200 mg, 0.94 mmol), the crude material was purified by flash chromatography (petroleum ether:EtOAc = 2:1->1:1); the reaction yielded 185 mg (63%) of **11m** as white solid (Table 7, entry 3).

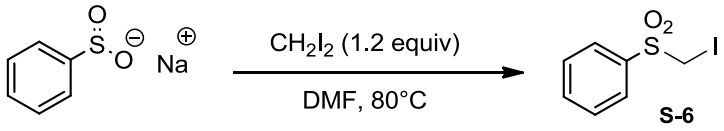


Keto/enol forms of **11l** = 8:1. Peaks belonging to enol form are marked with*. Mp 125-126°C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.07 (t, *J* = 7.1 Hz, 3H, H-5), 1.25 (t, *J* = 7.2 Hz, 3H, H-5), 3.34 (q, *J* = 7.1 Hz, 2H, H-4), 3.45 (q, *J* = 7.2 Hz, 2H, H-4), 4.64 (s, 2H, H-2), 7.59 (pd, *J* = 7.2, 1.5 Hz, 2H), 7.99 (dd, *J* = 7.1, 1.9 Hz, 1H), 8.21 (dd, *J* = 7.4, 1.9 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 12.9 and 14.6 (C-5), 41.1 and 43.3 (C-4), 58.0 (C-2), 122.6, 125.6, 127.7, 128.1, 137.4, 152.6, 160.0 (C-1), 165.6 (C-3);
IR (film): ν^{-1} = 2969 (w), 2919 (w), 2901 (w), 1647 (s), 1461 (s), 1330 (s), 1153 (s), 1126 (s), 1086 (m), 1028 (m), 893 (m), 762 (s), 733 (s); MS (ES), *m/z* (%): 335 (M^++Na, 100), 313 (M^++H, 61), 240 (65), 175 (12), 170

(7); HRMS (ES), *m/z*: calc. 335.0500 for $C_{13}H_{16}N_2O_3S_2Na$, found 335.0483;El. an. for $C_{13}H_{16}N_2O_3S_2$, calc. C 49.98, H 5.16, N 8.97; found C 50.03, H 5.15, N 8.94.

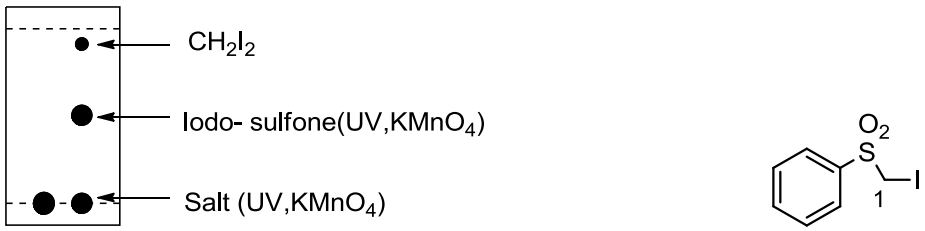
Synthesis of 2-(((phenylsulfonyl)methyl)sulfonyl)benzo[*d*]thiazole (12b) [17]

((Iodomethyl)sulfonyl)benzene (*S*-6)



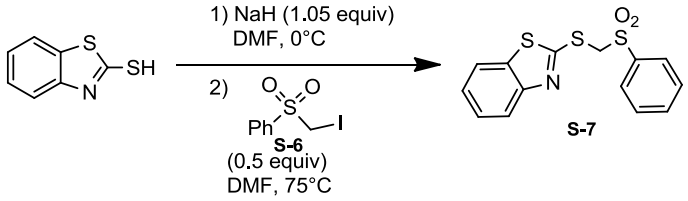
A solution of sodium benzenesulfinate (10.0 g, 60.92 mmol, 1.0 equiv) in DMF (250 mL, 0.25M) was stirred at RT for 15 min. Diiodidemethane (6.0 mL, 75.06 mmol, 1.2 equiv) was added dropwise and the solution was stirred for a further 17h at RT. H_2O (100 mL) was added and resulting layers were separated. The aqueous layer was extracted with EtOAc (3x250 mL) and the combined organic layers were washed with brine (50 mL), dried over $MgSO_4$, filtered and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (Petroleum Ether:EtOAc = 10:1->4:1->2:1) yielding the desired iodo-sulfone **S-6** as a yellow oil (12.0 g, 70 % yield).

TLC (Petroleum Ether:EtOAc = 2:1)



^{1}H-NMR (300 MHz, $CDCl_3$): δ = 2.47 (s, 2H, H-1), 7.59 (t, *J* = 7.5 Hz, 2 H), 7.43 (t, *J* = 7.2 Hz, 1H), 7.98 (d, *J* = 7.5 Hz, 2H) ; ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 16.9 (C-1), 129.0, 129.4, 134.6, 135.9; IR (film): ν^{-1} = 3016, 2948, 1583, 1477, 1446, 1369, 1307, 1211, 1157, 1134, 1080, 1024, 999, 931, 906, 844, 790, 769, 736, 707, 684, 671, 617; MS (APCI), *m/z* (%): 283 (100) [M^++H], 141 (7), 125 (12).

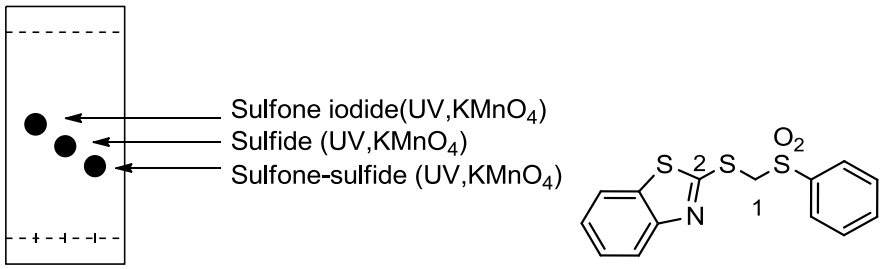
2-(((phenylsulfonyl)methyl)thio)benzo[*d*]thiazole (*S*-7)



A solution of BT-SH (14.23 g, 85.08 mmol, 1.0 equiv) in DMF (450 mL, 0.20M) was cooled to 0°C and NaH (60% in min. oil) (3.6 g, 89.33 mmol, 1.05 equiv) was added portionwise within 10 min. The resulting solution was stirred at 0°C for 30 min, before ((iodomethyl)sulfonyl)benzene (**S-6**) (12.0 g, 42.5 mmol, 0.5 equiv) was added dropwise. The cooling bath was removed and the resulting mixture was stirred at 75°C for a further 18h.

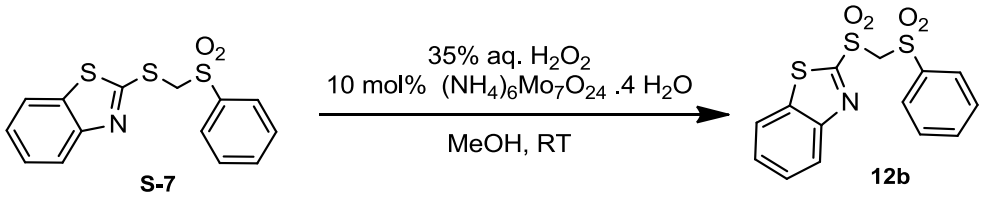
The resulting mixture was cooled to rt and saturated aqueous NH_4Cl (200 mL) was added. Resulting layers were separated and the aqueous layer was extracted with EtOAc (3x400 mL). The combined organic layers were washed with brine (100 mL), dried over $MgSO_4$, filtered and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (Petroleum Ether:EtOAc = 10:1->4:1->2:1) yielding the desired sulfide-sulfone **S-7** (8.3 g, 82 % yield) as yellowish crystals.

TLC (Petroleum Ether:EtOAc = 2:1)



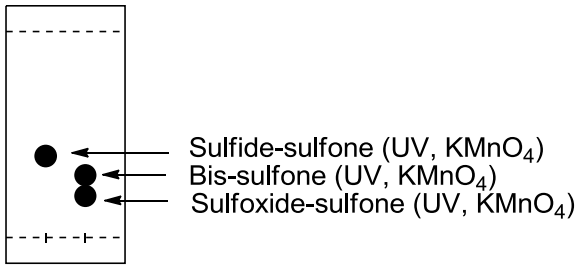
Mp = 142-143°C, lit.[17] = 144°C ; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 5.05 (s, 2H, H-1), 7.34-7.40 (m, 5 H), 7.71 (t, *J* = 7.5 Hz, 2H), 7.97 (dd, *J* = 7.7 Hz, 1.6 Hz, 2H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 54.9 (C-1), 121.1, 121.8, 124.9, 126.2, 128.7, 129.2, 134.0, 135.5, 137.0, 151.9, 161.5 (C-2); IR (film): ν^{-1} = 3060, 2995, 2916, 1583, 1446, 1427, 1307, 1238, 1207, 1149, 1124, 1081, 999, 829, 756, 727, 715, 688; MS (APCI), *m/z* (%): 322 (86) [M^++H], 292 (70), 167.(100)

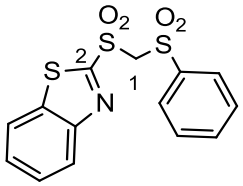
2-(((phenylsulfonyl)methyl)sulfonyl)benzo[*d*]thiazole (12b)



A solution of sulfone-sulfide **S-7** (12.0 g, 37.3 mmol, 1.0 equiv) in EtOH (200 mL, 0.19M) was cooled to 0°C and $(NH_4)_6Mo_7O_{24}.4H_2O$ (4.6 g, 3.7 mmol, 0.1 equiv) was added. After 5 min at 0°C, 35% aqueous solution of H_2O_2 (36.2 mL, 373.0 mmol, 10.0 equiv) was added. The resulting mixture was stirred at 0°C for 30 min, before the cooling bath was removed and the stirring continued at RT for a further 18h. Saturated aqueous $Na_2S_2O_3$ (200 mL) was added and resulting layers were separated. The aqueous layer was extracted with EtOAc (3x250 mL) and the combined organic layers were washed with brine (150 mL), dried over $MgSO_4$, filtered and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (Petroleum Ether:EtOAc = 4:1->2:1->1:1) yielding the desired bis-sulfone as yellowish crystals (10.26 g, 78 % yield)[18].

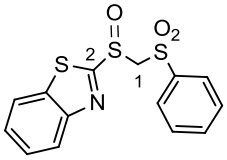
TLC (Petroleum Ether:EtOAc = 2:1)





Mp = 144°C[19]; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 5.25 (s, 2H, H-1), 7.50-7.58 (m, 2H), 7.60-7.73 (m, 3H), 7.94-8.10 (m, 3H), 8.21 (dd, *J* = 7.5, 1.6 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 72.5 (C-1), 122.6, 125.9, 128.1, 128.7, 129.3, 129.6, 135.2, 138.1, 152.5 (C-2); IR (film): ν^{-1} = 2952, 2896, 2844, 1583, 1552, 1467, 1448, 1419, 1330, 1315, 1217, 1164, 1145, 1080, 1026, 999, 854, 827, 759, 827, 759, 748, 729, 648, 617 ; MS (APCI), *m/z* (%): 322 (86) [M^++H], 292 (70), 167 (100).

Characteristic peaks that belongs to sulfoxide-sulfone (**S-8**) by-product:



^{1}H-NMR (300 MHz, $CDCl_3$): □ = 4.71 (d, *J* = 13.9 Hz, 1H, H-1), 4.98 (d, *J* = 13.9 Hz, 1H, H-1').

Computations

Computational details

Geometry optimisation has been carried out using the Jaguar 7.5 pseudospectral program package.[20] These calculations used density functional theory (DFT) with the B3LYP functional[21] and the 6-31+G* basis set[22] on all atoms. All the optimization calculations were carried out using the Poisson-Boltzmann polarizable continuum method as incorporated in Jaguar,[23,] and parameters for tetrahedron solvent (THF), *i.e.* a dielectric constant of 7.43, and a solvent probe radius of 2.5221 Å.

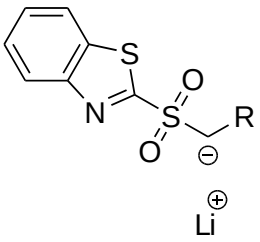
Gas phase electronic energies were obtained by single point calculations at the SCS-MP2 level of theory[24] using ORCA program.[25] The ' aug-cc-pVTZ' basis used is the standard aug-cc-pVTZ basis[26] on all C, N, O and S atoms, the cc-(p)VTZ basis on H atoms, and the 6-311+G** basis[27] on lithium atom.

Solvation energies were obtained by single point calculations using the Poisson-Boltzmann polarisable continuum method as implemented in Jaguar 7.5 program package, at the B3LYP/cc-pVTZ level, using the parameters appropriate for THF.

NBO analysis[28] has been performed at the B3LYP/cc-pVTZ level of theory using the Jaguar 7.5 program package. Reported charges are NPA charges.

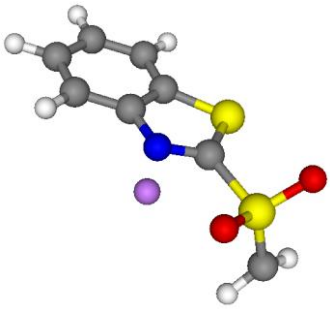
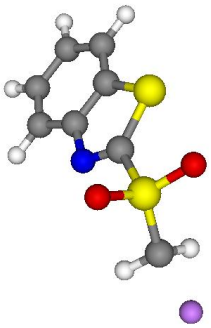
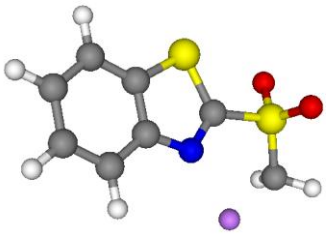
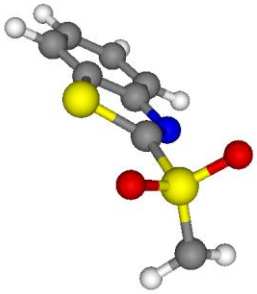
Conformational analysis

Energies are given in kcal/mol relative to the most stable isomer.

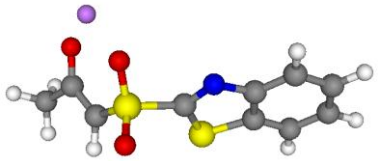
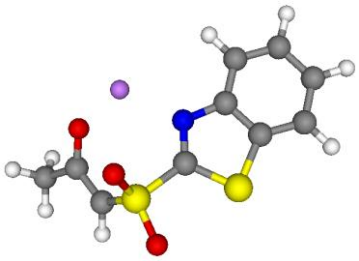
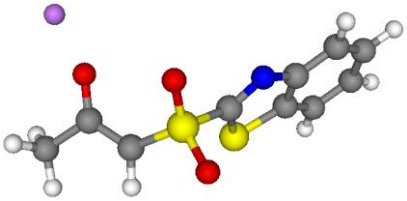
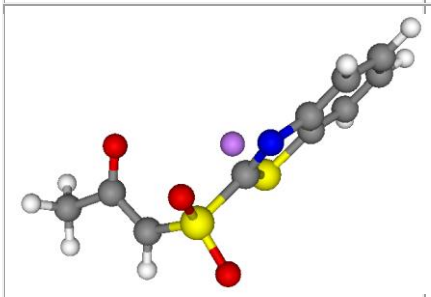
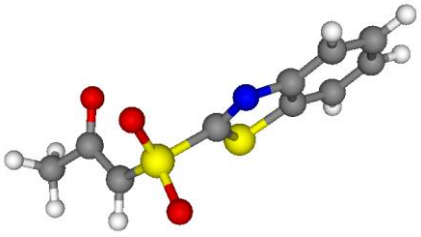


R = H, COMe, SO_2Ph

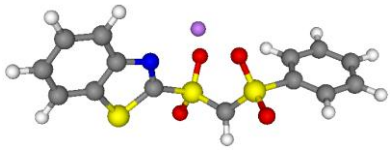
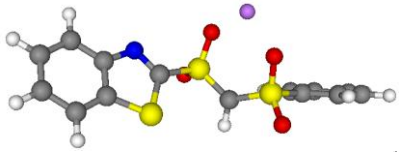
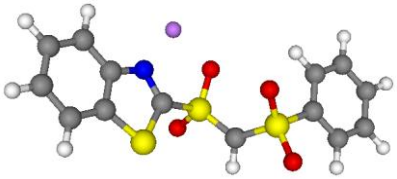
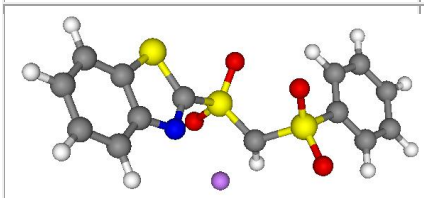
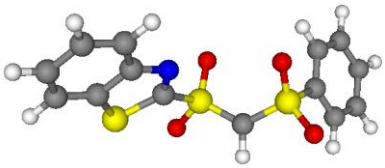
R = H

		
0.0	**0.3**	**2.9**
Charge C1 = -0.191 Charge C2 = -1.061	Charge C1 = -0.184 Charge C2 = -1.217	Charge C1 = -0.178 Charge C2 = -1.233
Without Li^+		
		
Charge C1 = -0.176 Charge C2 = -1.102		

R = COMe

		
0.0	**2.5**	**6.3**
Charge C1 = -0.184 Charge C2 = -0.802	Charge C1 = -0.188 Charge C2 = -0.775	Charge C1 = -0.176 Charge C2 = -0.789
		Without Li^+
		
6.5		
Charge C1 = -0.178 Charge C2 = -0.831		Charge C1 = -0.176 Charge C2 = -1.102

R = SO_2Ph

		
0.0	**3.0**	**4.1**
Charge C1 = -0.194 Charge C2 = -1.140	Charge C1 = -0.187 Charge C2 = -1.184	Charge C1 = -0.179 Charge C2 = -1.156
		Without Li^+
		
6.2		
Charge C1 = -0.180 Charge C2 = -1.234		Charge C1 = -0.168 Charge C2 = -1.153

Litterature

[1] Halasa, A.F.; Smith,G.E.P. *J. Org. Chem.* **1971**, *36*, 636.
[2] Bourdais, J.; Abenhaim, D.; Sabourault, B.; Lorre, A. *J. Het. Chem.* **1976**, *3*, 491.
[3] Rabai, J.; Kapovits, I.; Tanacs, B.; Tamas, J. *Synthesis* **1990**, 847.
[4] Fei, X.; Gu, Y.; Ban, Y.; Liu, Z.; Zhang, B. *Bioorg. Med. Chem.* **2009**, *17*, 585.
[5] Baudin, J. B.; Hareau, G.; Julia, S. A.; Lorne, R.; Ruel, O. *Bull. Soc. Chim. Fr.* **1993**, *130*, 856.
[6] Pattenden, G.; Stoker, D. A.; Thomson, N. M. *Org. Biomol.Chem.* **2007**, *5*, 1776.
[7] Prepared *in situ* from the corresponding carboxylic acid and used as a THF solution: Ibarra, C. A.; Rodriguez, R. C.; Fernandez Monreal, M. C.; Garcia Navarro, F. J.; Martin Tesorero, J. *J. Org. Chem.* **1989**, *54*, 5620.
[8] Prepared according to the literature procedure: (a) Rannard, S. P.; Davis, N. J. *Org. Lett.* **1999**, *1*, 933. (b) Rannard, S. P.; Davis, N. J. *Org. Lett.* **2000**, *2*, 2117.
[9] If the reaction was performed on 2 mmol scale of sulfone (or bigger), acylating or alkoxy carbonylating agents in THF were pre-cooled to -78°C prior to their addition.
[10] A solution of BzCl in THF (5 mL) was cooled to -78°C prior to its addition.
[11] Nielsen, M.; Jacobsen, C. B.; Paixão, M. W.; Holub, N.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2009**, *131*, 10581.
[12] A solution of AcCl in THF (5 mL) was cooled to -78°C prior to its addition.
[13]. Prueger, B.; Hofmeister, G. E.; Jacobsen, C. B.; Alberg, D. G.; Nielsen, M.; Jørgensen, K. A. *Chem. Eur. J.* **2010**, *16*, 3783.
[14] A solution of ClCOOMe in THF (10 mL) was cooled to -78°C prior to its addition.
[15] A solution of ClCOOallyl in THF (2 mL) was cooled to -78°C prior to its addition.
[16] A solution of Boc_2O in THF (10 mL) was cooled to -78°C prior to its addition.
[17] Prepared according to published procedure, see: He, M.; Ghosh, A. K.; Zacj, B. *Synlett*, 7, 999.
[18] Product obtained as 99:1 mixture of $(PhO_2S)CH_2$ and $PhO_2S\text{-}CH_2\text{-}S(O)Ph$.
[19] At 144°C product sublimates.
[20] Jaguar, version 7.5, Schrödinger, LLC, New York, NY, 2008.
[21] Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648-5652.
[22] (a) Ditchfield, R.; Hehre, W. J.; Pople, J. A. *J. Chem. Phys.* **1971**, *54*, 724. (b) Hehre, W. J.; Pople, J. A. *J. Chem. Phys.* **1972**, *56*, 4233. (c) Binkley, J. S. Pople, J. A. *J. Chem. Phys.* **1977**, *66*, 879. (d) Hariharan, P. C.; Pople, J. A. *Theor. Chim. Acta* **1973**, *28*, 213. (e) Hehre, W. J.; Ditchfield, R.; Pople, J. A. *J. Chem. Phys.* **1972**, *56*, 2257-2261. (f) Francl, M. M.; Pietro, W. J.; Hehre, W. J.; Binkley, J. S.; Gordon, M. S. DeFrees, D. J.; Pople, J. A. *J. Chem. Phys.* **1982**, *77*, 3654.
[23] (a) Tannor, D. J.; Marten, B.; Murphy, R.; Friesner, R. A.; Sitkoff, D.; Nicholls, A.; Ringnalda, M.; Goddard, W. A., III; Honing, B. *J. Am. Chem. Soc.* **1994**, *116*, 11875-11882. (b) Marten, B.; Kim, K.; Cortis, C.; Friesner, R. A.; Murphy, R. B.; Ringnalda, M. N.; Sitkoff, D.; Honing, B. *J. Phys. Chem.* **1996**, *100*, 11775-11788.
[24] Grimme, S. *J. Chem. Phys.* **2003**, *118*, 9095-9102.
[25] F. Neese, ORCA, *An Ab Inition, DFT, and Semiempirical Electronic Structure Package*, version, 2.7.0, Universität Bonn, Germany, 2010
[26] (a) Dunning Jr. T. H. *J. Chem. Phys.* **1989**, *90*, 1007-1023. (b) Kendall, R. A.; Dunning Jr, T. H.; Harrison, R. J. *J. Chem. Phys.* **1992**, *96*, 6796-6806.
[27] Krishnan, R.; Binkley, J. S.; Seeger, R.; Pople, J. A. *J. Chem. Phys.* **1980**, *72*, 650.
[28] Glendening, E. D.; Badenhoop, J. K.; Reed, A. E.; Carpentier, J. E.; Bohmann, J. A.; Morales, C. M.; Weinhold, F. *NBO 5.0*, Madison, WJ, 2001.