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Regioselective aerobic oxidation of bis-sulfides into monosulfoxides

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Abstract

The cobalt(II) acetylacetonate/aldehyde-promoted aerobic oxidation of three bis-sulfides of general formula R^1-SCH_2CH_2S-R^2, where R^1 is a heterocycle and R^2 is *p*-tolyl, provides a method to functionalise selectively the sulfur atom bonded to the *p*-tolyl moiety leading to the corresponding monosulfoxides. The same chemoselectivity and little diastereoisomeric excess (10%) was achieved by submitting to oxidative conditions the chiral bis-sulfide (*S*)-R^3-$SCH_2CH(CH_3)CH_2$-SR^4 (R^3 = benzothiazolyl, R^4 = *p*-tolyl).

Keywords: Oxidation; Sulfides; Sulfoxides; Catalysis

1. Introduction

Sulfoxides are important reaction intermediates in organic synthesis [1] and recently much effort has been devoted in accomplishing new selective methods of sulfides oxidation.

Among the most recent examples of selective sulfoxidation [2] we reckon those based on microwave thermolysis of wet silica-supported sodium periodates [3], hydroxy-(tosyloxy)iodobenzene [4], 4,4-dibromo-3-methylpyrazol-5-one [5], urea-hydrogen peroxide [6,7], $BiBr_3$-$Bi(NO_3)_3$ [8] 2,6dichloropyridine *N*-oxide/ruthenium porphyrins [9], calcium hypochlorite/moist alumina [10], 1,1,1-trifluoroacetone/H_2O_2 [11], clay-supported iodosylbenzene [12], oxochromium(V) ion [13] and dinitrogen tetroxide complexes of copper(II) nitrate [14].

Pursuing our studies on the oxyfunctionalization of sulfides using the catalytic system based on cobalt(II) acetylacetonate, a sacrificial aldehyde and oxygen or air [15,16], we decided to test the chemo- and possibly the stereo-selectivity of the aforementioned system by submitting to oxidative conditions polyfunctional substrates

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containing two sulfanyl moieties linked by a short alkyl chain.

2. Results and discussion

The bis-sulfides **1a–c** have been synthesised following the general Scheme 1, via a Mitsunobu's reaction of 2-*p*-tolylsulfanyl ethanol **6** and the relevant 2-mercaptoheterocycle (Het-SH).

These substrates were exposed to air at room temperature in dichloromethane solution, in the presence of catalytic amount of cobalt(II)acetylacetonate and excess 3-methylbutanal (three equivalents in total).

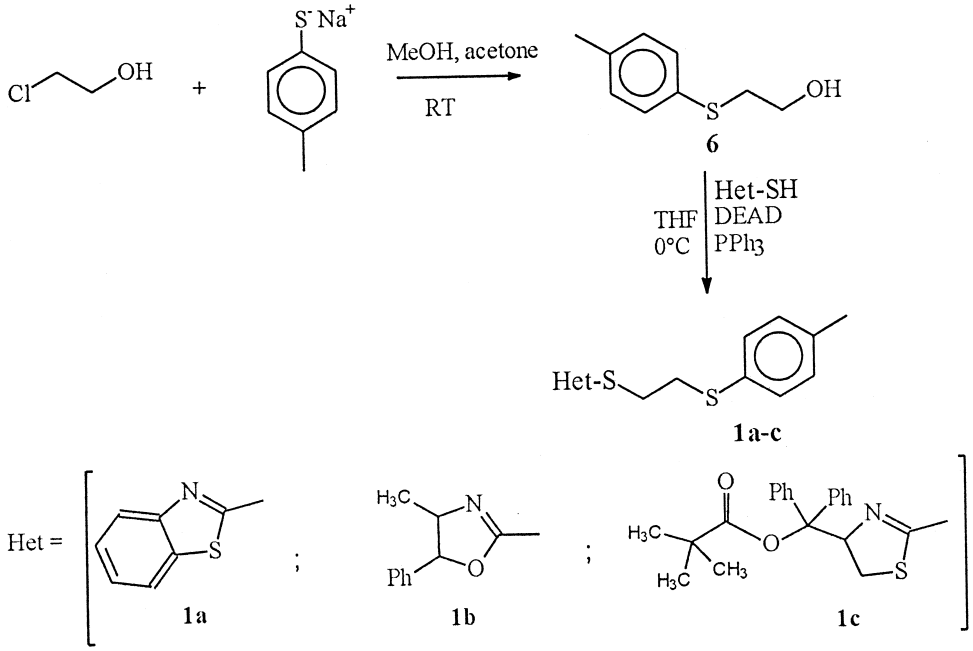
In all three cases, after suitable times (ranging from 8 to 23 h) the selective formation of the corresponding *p*-tolylmonosulfoxides **2a–c** was achieved in high yield (entries 1–3 of Table 1).

The high selectivity exhibited by the system catalyst/aldehyde/air toward the *p*-tolylmonosulfoxides can be explained by invoking the different inductive effects of the *p*-tolyl and of the heterocycle groups, the latter being more electron withdrawing and, consequently, rendering the vicinal sulfur atom less oxidisable.

Table 1
Oxidation of bis-sulfides **1a–d** to *p*-tolylmonosulfoxides **2a–d**

Entry	Substrate	Catalyst	Time (h)	Yield in monosulfoxide (%)
1	**1a**	$Co(acac)_2$	8	95
2	**1b**	$Co(acac)_2$	7	90
3	**1c**	$Co(acac)_2$	23	90
4	**1a**	Co-polymer	20	93
5	**1d**	$Co(acac)_2$	36	92
6	**1d**	$Co(tfac)_2$	36	85

In order to gain insight into the kinetic of overoxidation of this kind of substrates, compound **1a** was submitted to stronger oxidative conditions by adding 1.5 equivalents of fresh aldehyde every 8 h and prolonging the reaction up to 32 h. Time course of the reaction is reported in Fig. 1.



Scheme 1.

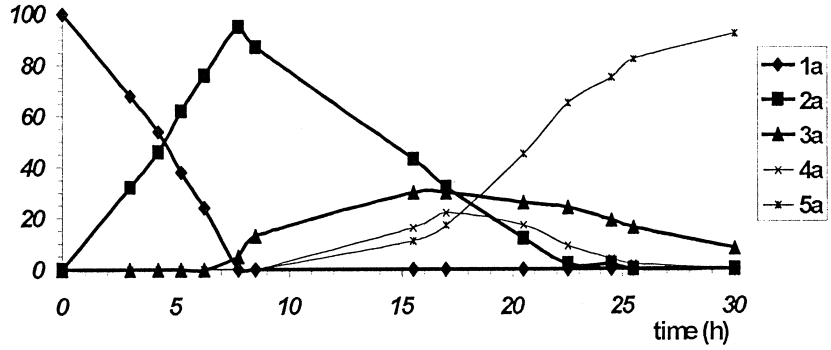


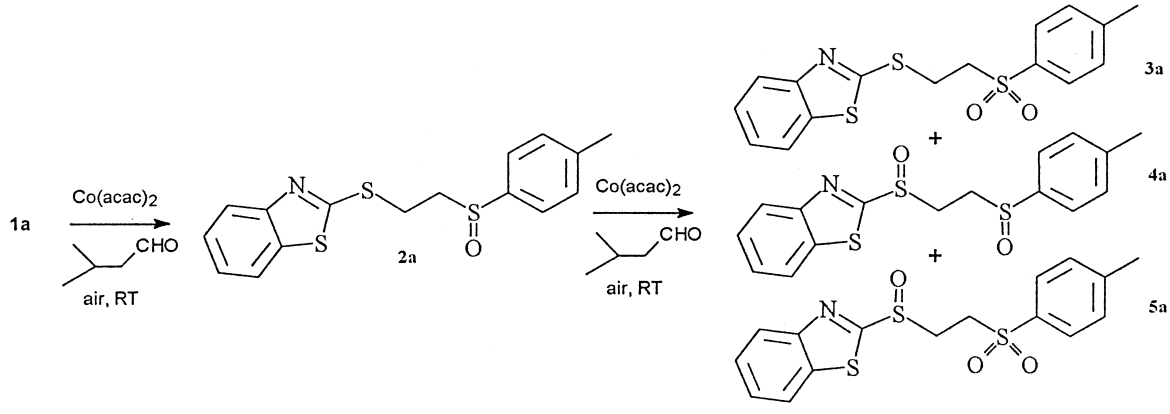
Fig. 1. Kinetic of overoxidation of substrate **1a** (1.2 mmol) in presence of $Co(acac)_2$ (0.02 mmol) and 3-methylbutanal in DCE (4 ml); 1.8 mmol of fresh aldehyde were added every 8 h.

It is apparent that after the first stage of oxidation (e.g., transformation of bis-sulfide into mono(*p*-tolyl)sulfoxide) the reaction proceeds towards the contemporaneous formation of **3a**, **4a** and **5a**, and stops when most of the substrate is converted into **5a** (Scheme 2). Even after prolonged reaction times and successive additions of aldehyde, compound **5a**, which is insoluble in the reaction medium, is not oxidised to bis-sulfone.

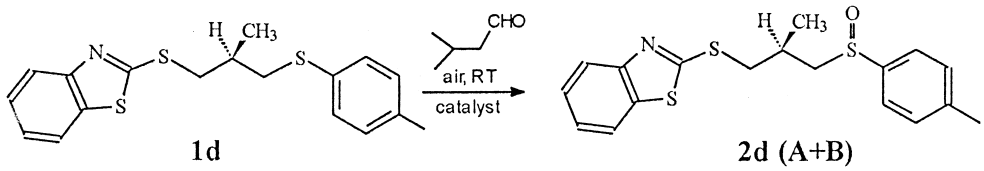
In order to transfer on a heterogeneous scale the results obtained with the system $Co(acac)_2$/aldehyde/air, we carried out the oxidation of **1a** with a supported cobalt polymer already described by us [17], that revealed itself active and reusable in converting simple sulfides into sulfoxides and sulfones [16].

After 20 h reaction, it was possible to isolate in high yield the desired *p*-tolylsulfoxide **2a** (entry 4 of Table 1).

In order to test the possible stereoselectivity of the catalytic system we have submitted to oxidative conditions the chiral bis-sulfide **1d**, obtaining the two expected diastereoisomeric sulfoxides **2d** (A + B) with 92% overall yield after 36 h reaction (entry 5 of Table 1, Scheme 3). The diastereoisomeric excess assessed by HPLC and ^1H NMR analysis was as high as 10% and did not increase when the complex $Co(tfac)_2$ containing the optically active 3-(tri-



Scheme 2.



Scheme 3.

fluoroacetyl)-*d*-camphorate ligand was used in the place of $Co(acac)_2$.

3. Experimental

3.1. Materials and apparatus

R(−)-3-Bromo-2-methyl-1-propanol and 2-mercaptobenzothiazole were purchased by Fluka and used as received. Cobalt(II) acetylacetonate and 3-methylbutanal were purchased by Aldrich. 2-*p*-Tolylsulfanyl-ethanol [18] (**6**) and (4*R*,5*S*)-4-methyl-5-phenyl-2-thioxo-1,3-oxazolidine [19] (the heterocyclic compound used for the synthesis of **1b**) were synthesised as reported in the literature. 4-[(Trimethylacetoxy)diphenylmethyl]-2-thioxothiazolidine (the heterocyclic compound used for the synthesis of **1c**) was prepared by reacting 4-carboxyethyl-2-thioxothiazolidine [20] with excess PhMgBr and subsequent esterification of the tertiary alcohol intermediate with pivaloyl chloride [^{1}H NMR: $\delta = 1.20$ (9 H, s, *t*-bu), 3.44 (1 H, dd, $J = 11.5$, 9.1 SHCH), 3.54 (1 H, dd, $J = 11.5$, 6.7 SHCH), 5.78 (1 H, t-like, $J = 7.9$ C*H*NH), 7.24–7.39 (10 H, m, Ph), 7.79 (1 H, br s, NH); ^{13}C NMR: $\delta = 26.9$, 34.8, 39.7, 67.2, 86.1, 127.0, 127.3, 128.4, 129.6, 139.3, 176.5, 201.7; IR (KBr): 1735 (s), 1481 (s), 1448 (s), 1278 (s), 1201 (m), 1137 (s), 1062 (m), 1033 (m), 977 (m), 756 (m), 702 (s) cm^{-1}]. IR spectra were recorded on a Perkin Elmer 681 instrument. NMR spectra were recorded on a Bruker AM 500 spectrometer using $CDCl_3$ as solvent. Chemical shifts are reported relative to solvent resonance and are given in ppm.

Chromatographic analyses were carried out on a Hewlett Packard 6890 instrument using a HP-1 methyl-siloxane capillary column (60.0 m × 250 μm × 1.00 μm). GCMS data (EI, 70 eV) were acquired on a HP 5973 instrument. HPLC analyses were carried out by a LC-10AD Shimadzu instrument using a 25 cm × 4.6 mm Spherisorb 5-C8 column and CH_3CN/H_2O mixtures as mobile phase (flow rate = 0.8 ml/min). Optical rotations were measured on a Perkin Elmer 241 polarimeter at 25°C.

Conversions and yields were calculated by HPLC analyses as moles of oxidised product per mole of starting substrate by using the internal standard method. Isolated yields were 4–8% lower than chromatographic ones.

3.2. Synthesis of bis[3-(trifluoroacetyl)-D-camphorate]cobalt (II) Co(tfac)$_2$

The whole synthesis was carried out under nitrogen.

The solution obtained by mixing up 1.19 g (4.8 mmol) of 3-(trifluoroacetyl)-D-camphor with 5 ml of a 0.96 M solution of NaOH was added slowly to a solution obtained by dissolving 0.6 g of $Co(OAc)_2 \cdot 4H_2O$ (2.4 mmol) in 20 ml of H_2O causing the immediate formation of a pink solid, which was filtered, washed with water and H_2O/EtOH 1:1 and dried in vacuo for 24 h. This solid, characterised by IR and elemental analysis was identified as the desired complex. Yield = 1.0 g, 75%.

IR (KBr): 1638 (s) and 1525 (s) [$\nu_{C=O} + \nu_{C=C}$] and [$\nu_{C=C} + \nu_{C=O}$]; 2964 (s) ν_{C-H}; 1419 (w); 1383 (s); 1327 (m); 1296 (w); 1269 (s); 1224(s); 1201 (s); 1133 (s); 1105 (m); 1080 (m); 1056 (m); 1006 (w); 921 (w); 807 (m); 739

(w); 715 (w); 687 (w); 646 (w); 561 (w); 497 (w) cm^{-1}.

(Found: Co% = 10.68%, C% = 51.89%, H% = 5.05%; calculated for $C_{24}H_{28}F_6O_4Co$: Co% = 10.65%, C% = 52.09%, H% = 5.10%).

3.3. General procedure for the synthesis of the bis-sulfides (**1a-c**)

To a stirred solution of 11 mmol of 2-mercaptobenzothiazole (or 2-thioxo-oxazolidine or 2-thioxo-thiazolidine) in 70 ml of anhydrous toluene, was added, at room temperature, 11 mmol of **6** and 21 mmol of triphenylphosphine. The suspension was cooled to 0°C and a toluene solution of diethyl azodicarboxylate (DEAD, 19 mmol in 5 ml) was added dropwise. After 4 h, GCMS analysis of the reaction mixture showed the complete consumption of the starting heterocycle. Evaporation of the solvent followed by silica gel chromatography (eluant petroleum ether–ethyl acetate 10:1) gave the following compounds.

2-(2-p-Tolylsulfanyl-ethylsulfanyl)-benzothiazole (**1a**) obtained as pale yellow solid (88% yield): M.p.: 52–54°C; ^{1}H NMR: $\delta = 2.35$ (3 H, s, CH_3), 3.33 (2 H, m, *p*-tol-SCH_2), 3.51 (2 H, m, Het-SCH_2), 7.12–7.16 (2 H, m, *p*-tol), 7.26–7.32 (1 H, m, Het), 7.37–7.44 (3 H, m, 1 Het + 2 *p*-tol), 7.71–7.76 (1 H, m, Het), 7.82–7.86 (1 H, m, Het); ^{13}C NMR: $\delta = 20.9$ (CH_3-*p*-tol), 32.7 (CH_2-S-*p*-tol), 33.7 (Het-S-CH_2), 120.9, 121.4, 124.1, 125.7, 129.7, 130.5, 130.9, 135.2, 136.6, 153.0, 165.7 (S(S)C=N); IR (KBr): 1491 (m), 1452 (m), 1426 (s), 1308 (m), 1280 (m), 1240 (m), 1203 (m), 1088 (m), 1078 (m), 1016 (m), 1001 (s), 804 (s), 752 (s), 723 (s), 698 (s) cm^{-1}; *m/z* (%): 317 (1.5, M^+), 194 (7), 180 (1), 167 (46), 150 (100), 135 (39), 123 (39), 108 (12), 91 (9), 79 (7), 77 (6).

(4R,5S)-Methyl-phenyl-2-(2-p-tolylsulfanyl-ethylsulfanyl)-4,5-dihydro-oxazole (**1b**) obtained as yellow powder (yield 45%): M.p.: 36–38°C; ^{1}H NMR: $\delta = 0.78$ (3 H, d, $J = 6.9$, CH_3-Het), 2.29 (3H, s, CH_3), 3.29–3.15 (4 H, m, S-CH_2CH_2-S), 4.45 [1 H, dq, $J = 9.4$, 6.9, $HC(CH_3)$], 5.64 (1 H, d, $J = 9.4$, HC(Ph)), 7.04–7.09 (2 H, m, *p*-tol), 7.17–7.21 (2 H, m, *p*-tol), 7.27–7.39 (5 H, m, Ph); ^{13}C NMR: $\delta = 17.8$ (CH_3-Het), 21.0 (CH_3-*p*-tol), 31.3 (CH_2-S-*p*-tol), 34.1 (Het-S-CH_2), 65.5 ($HC(CH_3)$), 85.7 HC(Ph)), 126.1, 128.0, 128.3, 129.8, 130.5, 131.3, 136.4, 136.6, 163.9 (O(S)C=N); IR (KBr): 1613 (s), 1492 (s), 1426 (m), 1284 (s), 1276 (s), 1153 (s), 1112 (s), 964 (s), 806 (s), 746 (s), 699 (s); *m/z* (%): 343 (0.2, M^+), 160 (1), 150 (100), 135 (26), 123 (27), 105 (5), 91 (14), 77 (8).

2,2-Dimethylpropionic acid diphenyl-[2-(2-p-tolylsulfanylethylsulfanyl)-4,5-dihydrothiazol-4-yl]methyl ester (**1c**) obtained as a white powder (yield 62%): ^{1}H NMR: $\delta = 1.31$ (9 H, s, t-But), 2.32 (3 H, s, CH_3), 3.09–3.29 (4 H, m, S-CH_2CH_2-S), 3.44 (2 H, m, CH_2(CH)S), 6.41 (1 H, t-like, $J = 9.0$, $CH_2(CH)$S), 7.05–7.09 (2 H, m, *p*-tol), 7.21–7.40 (10 H, m, Ar), 7.61–7.66 (2 H, m, Ar); IR (neat): 1732 (s, $\nu_{C=O}$), 1566 (s, $\nu_{C=N-}$), 1279 (s), 1140 (s, C–O), 963 (s), 807 (s), 754 (s), 700 (s) cm^{-1}; *m/z* (%): 283 (100), 191 (8), 151 (7), 123 (22).

3.4. Synthesis of (R)-2-methyl-3-p-tolylsulfanyl propanol (**7**)

The whole synthesis was carried out under nitrogen. 10 mmol of *p*-thiocresol was added to a stirred solution of sodium methoxide (13 mmol in 8 ml of methanol). Then, a solution of 1.48 g of (*R*)-(−)-3-bromo-2-methyl-1-propanol in 28 ml of acetone, was added dropwise. After 2.5 h and complete consumption of the chiral alcohol the mixture was concentrated in vacuo, washed with NaOH 1 M and extracted with ethyl acetate. The organic phase was washed with water until neutrality and dried on sodium sulphate. The solvent was evaporated and the crude product was chromatographed on silica gel (eluant petroleum ether–ethyl ether 2:1) affording 1.83 g of **7** as pale yellow oil (yield 96%).

^{1}H NMR: $\delta = 1.06$ [3 H, d, $J = 6.8$, CH_3(CH)], 1.76 (1 H, br s, OH), 1.95 [1 H, m, $CH_3(CH)$], 2.34 (3 H, s, CH_3), 2.83 (1 H, dd,

J = 13.0, 6.8, SHCH), 3.04 (1 H, dd, J = 13.0, 6.5, SHCH), 3.58–3.67 (2 H, m, CH_2OH), 7.10–7.15 (2 H, m, *p*-tol), 7.28-7.32 (2 H, m, *p*-tol); ^{13}C NMR: δ = 16.4, 20.9, 35.5, 38.2, 66.8, 129.7, 129.9, 132.9, 136.1; IR (neat): 3700-3100 (ν_{OH}), 1896 (w), 1598 (w), 1564 (w), 1490 (s), 1451 (s), 1377 (m), 1244 (m), 1091 (m), 1030 (s), 985 (s), 940 (w), 801 (s) cm^{-1}; m/z (%): 196 (61, M$^+$), 137 (35), 124 (100), 91 (41), 77 (10); $[\alpha]_D = -10.7°$ (c = 1.8 in $CHCl_3$).

3.5. Synthesis of (S)-2-(2-methyl-3-p-tolyl-sulfanyl-propylsulfanyl)-benzothiazole (**1d**)

To 1.0 g (5 mmol) of (*R*)-3-(4-methylphenylthio)-2-methyl propanol **7** dissolved in 12 ml of anhydrous tetrahydrofuran, was added, under stirring and nitrogen atmosphere at room temperature, 0.81 g (5 mmol) of 2-mercaptobenzothiazole and 1.33 g (5 mmol) of triphenylphosphine. The mixture was cooled at 0°C and a solution of 0.89 g (3 mmol) of DEAD in 7 ml of THF was added dropwise. After 4 h GCMS analysis of the reaction mixture showed complete disappearance of **7**. Evaporation of the solvent followed by silica gel chromatography (eluant petroleum ether-ethyl ether 4:1) gave pure **1d** as white oil.

^{1}H NMR: δ = 1.18 [3 H, d, J = 6.7, CH_3(CH)], 2.18–2.27 [1 H, m, CH$_3$(CH)], 2.26 (3 H, s, CH$_3$), 2.86 (1 H, dd, J = 13.3, 7.3, *p*-tol-SHCH), 3.09 (1 H, dd, J = 13.3, 5.9, *p*-tol-SHCH), 3.32 (1 H, dd, J = 13.2, 7.0, Het-SHCH), 3.52 (1 H, dd, J = 13.2, 6.0, Het-SHCH), 7.01–7.05 (2 H, m, *p*-tol), 7.27–7.31 (3 H, m, 2 H *p*-tol + 1 H Het); 7.32–7.43 (1 H, m, Het), 7.70–7.75 (1 H, m, Het), 7.81-7.85 (1 H, m, Het); ^{13}C NMR: δ = 18.9, 21.0, 33.3, 39.2, 40.5, 120.9, 121.5, 124.2, 126.0, 129.7, 130.2, 132.5, 135.2, 136.2, 153.2, 166.9; IR (neat): 1490 (m), 1455 (s), 1424 (s), 1374 (m), 1308 (m), 1238 (m), 994 (s), 802 (s), 754 (s), 726 (s) cm^{-1}; m/z (%): 345 (49, M$^+$), 298 (100), 271 (13), 222 (76), 176 (39), 163 (26), 124 (31), 108 (13), 91 (22), 77 (8), 55(9), 45(10); $[\alpha]_D = +45.2°$ (c = 1.9 in $CHCl_3$).

3.6. Catalytic runs

A round flask equipped with a dropping funnel and a Torion™ stopcock (0.25 mm diameter, left open during the runs in order to allow air to get into the reaction medium but to limit solvent evaporation) was charged with the substrate and cobalt(II) complex [Co(acac)$_2$ or Co(tfac)$_2$ or supported cobalt polymer, in all cases Co/substrate = 1/60 mol/mol] in dichloromethane (DCM, 2 ml). To the resultant solution, 3-methylpropanal (1.5 equivalents in 2 ml DCM) was added dropwise under stirring. The mixture was kept under vigorous stirring under air (p = 1 atm), at room temperature (21°C), and monitored by GC, TLC and HPLC. When GC analyses showed the almost complete consumption of the aldehyde (6–18 h), 1.5 equivalents of fresh aldehyde dissolved in 2 ml DCM was added dropwise to the reaction mixture and the reaction stopped when TLC and HPLC analyses showed the disappearance of the starting bissulfide. Purification of the *p*-tolylmonosulfoxides **2a–d** was achieved by silica gel column chromatography (Merck, Silica Gel 60 230–400 mesh) using petroleum ether–acetone 4:1 as eluant and afforded little amount of the corresponding *p*-tolylsulfones **3a–d** characterised by ^{1}H NMR and IR. Sulfoxides **2b** and **2c** were isolated as mixture of diastereoisomers (1:1) whereas it was possible to separate the two diastereoisomers **2d** (A + B) by column chromatography.

2-[2-(Toluene-4-sulfinyl)-ethylsulfanyl]-benzothiazole (**2a**) ^{1}H NMR: δ = 2.40 (3 H, s, CH$_3$), 3.25 (1 H, ddd, J = 13.2, 9.4, 4.7, Het-S-HCH), 3.39 (1 H, ddd, J = 13.2, 9.3, 6.3, Het-S-HCH), 3.52 (1 H, ddd, J = 13.9, 9.3, 4.7, S(O)HCH), 3.62 (1 H, ddd, J = 13.9, 9.4, 6.3, S(O)HCH), 7.25–7.41 (4 H, m, 2 *p*-tol + 2 Het), 7.50–7.55 (2 H, m, *p*-tol), 7.68–7.73 (1 H, m, Het), 7.76–7.80 (1 H, m, Het); ^{13}C NMR: δ = 21.4 (CH$_3$), 25.5 (S-CH_2), 55.7

($S(O)CH_2$), 121.0, 121.5, 124.1, 124.4, 126.0, 130.0, 135.2, 139.3, 141.7, 152.9, 165.0; IR (KBr): 1702 (m), 1494 (m), 1461 (s), 1310 (m), 1239 (m), 1085 (s), 1046 (s), 1017 (s), 998 (s), 811 (s), 758 (s), 728 (s) cm^{-1}.

(4R,5S)-Methylphenyl-2-[2-(toluene-4-sulfinyl)-ethylsulfanyl]-4,5-dihydro-oxazole (**2b**) *(mixture of diastereoisomers 1:1)* ^{1}H NMR: δ = 0.71–0.75 (3 H, two doublets partially overlapped, J = 6.9, CH_3-Het), 2.38 and 2.39 (3H, two singlets, CH_3), 3.14–3.39 [4 H, m, S-CH_2CH_2-S(O)], 4.37–4.46 [1 H, m, $HC(CH_3)$], 5.62 and 5.63 [1 H, two partially overlapped doublets, J = 9.3, HC(Ph)], 7.10–7.55 (9 H, m, Ar); IR (KBr): 1769 (s), 1609(s), 1491(w), 1452(w), 1149(s), 1114 (m), 1083(m), 1041(s, $\nu_{S=O}$), 957(s), 810(m), 748(m), 701(m) cm^{-1}.

2,2-Dimethyl-propionic acid diphenyl-{2-[2-(toluene-4-sulfinyl)-ethylsulfanyl]-4,5-dihydro-thiazol-4-yl]}-methyl ester (**2c**) *(mixture of diastereoisomers 1:1)* ^{1}H NMR: δ = 1.21 and 1.23 (9 H, two singlets, *t*-But), 2.30 and 2.39 (3 H, two singlets, CH_3), 2.95-3.44 (6 H, m, S-CH_2CH_2-S + CH_2(CH)S), 6.26 and 6.31 (1 H, two dd, J = 9.6, 8.7 $CH_2(CH)$S), 7.01-7.55 (14 H, m, Ar); ^{13}C NMR: δ = 21.3, 21.4, 24.5, 25.3, 27.1, 35.9, 36.1, 39.5, 39.6, 55.4, 56.6, 78.4, 78.6, 86.8, 86.9, 124.0, 124.1, 127.0, 127.2, 127.5, 127.7, 127.8, 127.9, 128.0, 128.1, 130.0, 130.1, 139.7, 140.3, 141.5, 141.8, 143.6, 164.5, 176.1; IR (neat): 1731 (s, $\nu_{C=O}$), 1570 (s), 1230 (m), 1147(s), 1049 (m, $\nu_{S=O}$), 961 (s), 811 (s), 758 (m), 704 (m) cm^{-1}.

(R)-2-[2-Methyl-3-(toluene-4-sulfinyl)-propylsulfanyl]-benzothiazole (**2d**) *(diastereoisomer* **A***)* ^{1}H NMR: δ = 1.33 [3 H, d, J = 6.3, CH_3(CH)], 2.34 (3 H, s, CH_3), 2.53–2.68 [2 H, m, $CH_3(CH)$ + Het-SHCH], 2.99–3.05 (1 H, m, Het-SHCH), 3.39 [1 H, dd, J = 13.3, 6.0, *p*-tol-S(O)HCH], 3.48 (1 H, dd, J = 13.3, 6.0, *p*-tol-S(O)HCH), 7.21–7.33 (3 H, m, 2 *p*-tol + 1 Het), 7.35–7.43 (1 H, m, Het), 7.47–7.55 (2 H, m, 2 *p*-tol), 7.69–7.75 (1 H, m, Het), 7.79–7.85 (1 H, m, Het); ^{13}C NMR: δ = 19.5, 21.3, 29.3, 39.7, 63.8, 121.0, 121.5, 124.0, 124.3, 126.1, 130.0, 135.2, 140.8, 142.0, 153.0, 166.1; IR (neat): 1490 (m), 1458 (s), 1427 (s), 1400 (m), 1379 (w), 1085 (m), 1055 (m, $\nu_{S=O}$), 1029 (s), 1014 (m), 993 (s), 803 (m), 759 (m), 729 (m), 506 (m), 477 (m) cm^{-1}; $[\alpha]_D$ = −132.1° (c = 0.5 in $CHCl_3$).

(R)-2-[2-Methyl-3-(toluene-4-sulfinyl)-propylsulfanyl]-benzothiazole (**2d**) *(diastereoisomer* **B***)* ^{1}H NMR: δ = 1.23 [3 H, d, J = 6.8, CH_3(CH)], 2.30 (3 H, s, CH_3), 2.49-2.58 [1 H, m, $CH_3(CH)$], 2.84 (1 H, dd, J = 13.2, 6.3, Het-SHCH), 2.92 (1 H, dd, J = 13.2, 7.0, Het-SHCH), 3.44–3.58 [2 H, m, *p*-tol-S(O)CH_2], 7.17–7.22 (2 H, m, *p*-tol), 7.24–7.29 (1 H, m, Het), 7.36–7.41 (1 H, m, Het), 7.42–7.47 (2 H, m, *p*-tol), 7.69–7.73 (1 H, m, Het), 7.78-7.82 (1 H, m, Het); ^{13}C NMR: δ = 19.7, 21.3, 29.3, 39.0, 63.7, 120.9, 121.5, 124.0, 124.3, 126.0, 129.9, 135.2, 140.7, 141.6, 152.9, 166.1; IR (neat): 1491 (m), 1455 (s), 1426 (s), 1377 (m), 1308 (m), 1264 (m), 1238 (m), 1124 (m), 1084 (s), 1034 (s, $\nu_{S=O}$), 1015 (s), 996 (s), 807 (m), 756 (s), 728 (s), 507 (m); $[\alpha]_D$ = +2.8° (c = 0.4 in $CHCl_3$).

2-[2-(Toluene-4-sulfonyl)-ethylsulfanyl]-benzothiazole (**3a**) ^{1}H NMR: δ = 2.46 (3 H, s, CH_3), 3.52–3.58 (2 H, m, Het-S-CH_2), 3.65–3.71 (2 H, m, SO_2CH_2), 7.25–7.31 (1 H, m, Het), 7.28–7.39 (3 H, m, 2 *p*-tol + 1 Het), 7.68–7.73 (2 H, m, Het), 7.81–7.86 (2 H, m, *p*-tol); ^{13}C NMR: δ = 21.6 (CH_3), 25.8 (S-CH_2), 55.6 (SO_2CH_2), 121.0, 121.5, 124.5, 126.1, 128.2, 130.0, 135.2, 135.6, 145.1, 152.8, 169.3; IR (KBr): 1598 (m), 1494 (w), 1471 (s), 1454 (m), 1428 (s), 1411 (s), 1314 (s, ν_{SO2}), 1302 (s), 1262 (s), 1228 (m), 1218 (m), 1145 (s, ν_{SO2}), 1086 (s), 1017 (s), 991 (s), 817 (s), 801 (s), 764 (s), 744 (m), 729 (s) cm^{-1}.

(4R,5S)-Methylphenyl-2[2-(toluene-4-sulfonyl)-ethylsulfanyl]-4,5-dihydro-oxazole (**3b**) ^{1}H NMR: δ = 0.69 (3 H, d, J = 6.9, CH_3-Het), 2.41 (3 H, s, CH_3), 3.20–3.28 [2 H, m, Het-S-CH_2], 3.60–3.68 (2 H, m, CH_2SO_2), 4.35–4.45 [1 H, m, $HC(CH_3)$], 5.60 [1 H, d, J = 9.3, HC(Ph)], 7.10–7.15 (2 H, m, Ar), 7.26–7.37 (5 H, m, Ar), 7.76–7.80 (2 H, m, Ar); ^{13}C NMR: 17.6, 21.6, 24.5, 29.7, 55.8, 65.4, 86.0, 126.0,

128.1, 128.2, 128.3, 130.6, 135.8, 136.1, 145.0, 163.0. IR(neat): 1740(s), 1460(s), 1377(m), 1318(m, ν_{SO2}), 1146(m, ν_{SO2}), 1085(w), 813(s), 702(w), 555(m).

2,2-Dimethylpropionic acid diphenyl-{2-[2-(toluene-4-sulfonyl)ethylsulfanyl]-4,5-dihydro-thiazol-4-yl]}-methyl ester (**3c**) ^{1}H NMR: $\delta =$ 1.21 (9 H, s, *t*-But), 2.47 (3 H, s, CH_3), 3.08–3.16 (1 H, m, Het-S-HCH), 3.19–3.27 (1H, m, Het-S-HCH), 3.33 (1 H, dd, $J = 10.7$, 8.4, HCH(CH)S), 3.39 (1 H, t like, $J = 10.5$, HCH(CH)S), 3.41–3.55 (2 H, m, CH_2SO_2), 6.26 (1 H, dd, $J = 10.2$, 8.4 $CH_2(CH)S$), 7.04–7.13 (4 H, m, Ar), 7.16–7.23 (3 H, m, Ar), 7.32–7.39 (3 H, m, Ar), 7.49–7.55 (2 H, m, Ar), 7.65–7.70 (2 H, m, Ar); ^{13}C NMR: $\delta =$ 21.6, 25.4, 27.0, 36.1, 39.5, 55.9, 78.5, 86.7, 127.1, 127.5, 127.6, 127.7, 128.0, 128.1, 130.0, 135.6, 140.3, 143.6, 144.9, 163.9, 176.1; IR (neat): 1728 (s, $\nu_{C=O}$), 1596 (m), 1565 (s), 1491 (s), 1477 (m), 1445 (m), 1412 (m), 1319 (s, ν_{SO2}), 1288 (s), 1231 (s), 1148 (s, ν_{SO2}), 1086 (s), 1033 (m), 965 (s), 808 (m), 756 (m), 699 (s), 554 (s) cm^{-1}.

2-[2-(Toluene-4-sulfinyl)-ethanesulfinyl]-benzothiazole (**4a**) *(mixture of diastereoisomers 1:1 ca.)* ^{1}H NMR: $\delta = 2.35$ and 2.38 (3 H, two singlets, CH_3), 2.78-2.84 (0.5 H, m, *p*-tol-S(O)CH_2), 3.08–3.24 (1.5 H, m, *p*-tol-S(O)CH_2), 3.32–3.40 (0.5 H, m, Het-S(O)CH_2), 3.46–3.58 (1 H, m, Het-S(O)CH_2), 3.68–3.76 (0.5 H, m, Het-S(O)CH_2), 7.20-7.30 (2 H, m, *p*-tol), 7.34–7.43 (2 H, m, *p*-tol), 7.45–7.51 (1 H, m, Het), 7.53–7.59 (1 H, m, Het), 7.93–8.06 (2 H, m, Het); ^{13}C NMR: $\delta = 21.4$, 29.6, 46.3, 46.6, 46.9, 47.1, 122.2, 123.9, 124.0, 124.1, 124.2, 126.3, 126.4, 1270, 127.1, 130.0, 130.1, 135.9, 136.0, 141.9, 142.0, 153.7, 153.8, 175.5; IR (KBr): 1598 (m), 1619 (w), 1557 (w), 1494 (m), 1428 (s), 1471 (s), 1455 (m), 1419 (s), 1313 (m), 1209 (m), 1086 (s), 1045 (s), 1017 (m), 1003 (s), 817 (s), 810 (s), 758 (s), 727 (m) cm^{-1}.

2-[2-(Toluene-4-sulfonyl)-ethanesulfinyl]-benzothiazole (**5a**) ^{1}H NMR: $\delta = 2.42$ (3 H, s, CH_3), 3.11–3.20 (1 H, m, Het-S(O)HCH), 3.44–3.53 (1 H, m, Het-S(O)HCH), 3.61–3.72 (2 H, m, *p*-tol-SO_2CH_2), 7.27–7.33 (2 H, m, *p*-tol), 7.48–7.53 (1 H, m, Het), 7.56–7.60 (1 H, m, Het), 7.69-7.73 (2 H, m, *p*-tol), 7.95–7.99 (1 H, m, Het), 8.01-8.05 (1 H, m, Het); ^{13}C NMR: $\delta = 21.5$, 47.4, 122.1, 124.1, 126.4, 127.0, 127.7, 130.0, 135.0, 135.8, 145.3, 153.6, 174.7 (–S–C=N–); IR (KBr): 1599 (m), 1561 (m), 1461 (s), 1398 (m), 1318 (s, ν_{SO2}), 1216 (s), 1143 (s, ν_{SO2}), 1086 (s), 1057 (s, $\nu_{S=O}$), 778 (m), 759 (s), 743 (s).

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