Concise Synthesis of 6-Sulfonylated 3,4-Dihydro-2*H*-thiopyrans and 7-Sulfonylated 3,4,5,6-Tetrahydrothiepines from Lactols

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A concise method for the synthesis of the title compounds has been developed, which involves condensation of lactols with methylthiomethyl *p*-tolyl sulfone, followed by mesylation and further cyclisation of the elimination products by refluxing with excess of sodium iodide in dimethyl formamide (DMF).

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In connection with our ongoing program[1] for the synthesis of carbocycles from carbohydrates we were interested in an efficient method for converting carbohydrates **1** to chiral polyhydroxy sulfonylated thiopyrane and thiepin derivatives **3** (Figure 1). Compounds of this type could be very useful for a number of further synthetic transformations [2]. For example, Michael addition to the double bond, either radical [3] or ionic [2], followed by alkylation at the 2-position could result in products **4**. Conversion of the last to bis-sulfones **5** and employing the well-established Ramberg-Bäcklund reaction conditions [4], chiral hydroxylated cyclopentene and cyclohexene derivatives **6** could be obtained. In addition, polyhydroxylated compounds **3**-**5** themselves are expected to be of potential biological interest. Thiosugars and their derivatives (nucleosides, glycosides, *etc*.) have gained increasing attention in recent years, because they exhibit interesting biological activities [5]. Several 1,5-dithiopyranoxylosides and 1,5-dithipyranoarabosides are valuable therapeutic agents, possessing antithrombotic and anticoagulant properties[6].

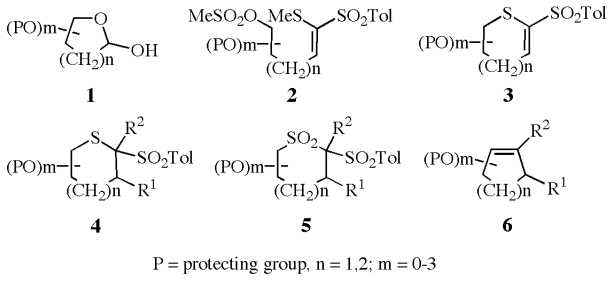
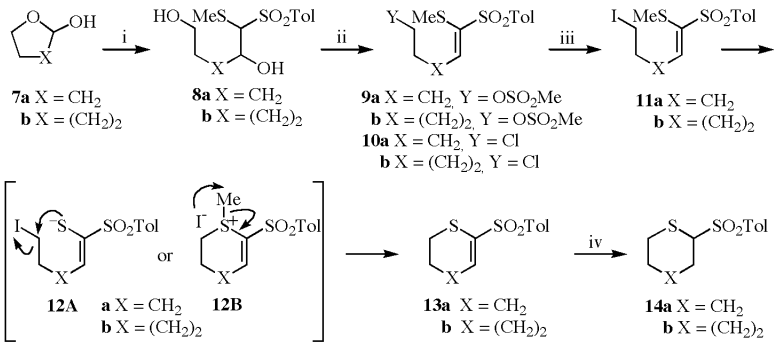


Figure 1

Apart from the well-known 1,5-dithiopyranosides, to the best of our knowledge, there is no general synthetic method for polyhydroxylated compounds of the type **3**-**5** and no examples of these compounds were found in the literature [7]. In the non-hydroxylated series, a method for the synthesis of compounds of the type **3**-**5** (m=0) has been reported by Fuchs, which involves fluoride ion mediated intramolecular sulfenylation of α-silyl sulfones [4a]. Further Ramberg-Bäcklund ring contraction led to cyclic olefins. Our approach towards compounds **3** involves condensation of methylthiomethyl *p*-tolyl sulfone with a pyranose or furanose having the hemiacetal moiety free and protected all the other hydroxyl groups. The resulting compounds **2** could be further cyclised to **3** with the sulfide group acting as nucleophile [8].

2-Hydroxytetrahydrofuran **7a** and 2-hydroxy-2*H*-tetrahydropyran **7b** (Scheme 1) were used as model compounds, since they can be considered as naked sugars in the furanose and pyranose forms, respectively. Condensation of methylthiomethyl *p*-tolyl sulfone with **7a,b** using *n*-butyl lithium (*n*-BuLi) yielded **8a,b** and further treatment with methanesulfonyl chloride/pyridine gave mixtures of **9a,b** and **10a,b**. The yield in the conversion of 2-hydroxytetrahydrofuran to **8a** was moderate evidently due to its instability [9b].

Scheme 1



Reagents and conditions: i, $MeSCH_2SO_2Tol$ (3.25 equiv.), 12-crown-4, *n*-BuLi 1.6 *M* in hexanes, THF, -60 °C, 12 h, 32-62%; ii, $MeSO_2Cl$ (2.2 equiv.), pyridine, 0 °C, 12 h; iii, see text; iv, 10% Pd/C, H_2, ethyl acetate, 20 °C, 2 h, 80-87%.

When a solution of **9a** or **10a** was refluxed in acetonitrile for 4 hours in the presence of 10 equivalents of sodium iodide, these compounds were completely converted to the cyclic product **13a** in good yield [8]. Compounds **9b** or **10b** under the same reaction conditions gave traces of the cyclic product **13b**, the known iodide **11b** [3a] being formed as the main product. Reflux, however, of **11b** in dimethyl formamide (DMF) in the presence of 10 equivalents of sodium iodide gave the heterocyclic product **13b** in good yield. The same product was formed directly from **9b** and **10b** by refluxing their solution in DMF in the presence of 10 equivalents of sodium iodide. It is apparent that the cyclisation of **9a** or **10a** proceeds *via* the respective iodide **11a**, which spontaneously cyclised to **13a** in a reaction favored by the six-membered ring formed, compared to the seven-membered ring of **13b**. The double bond in compounds **13a,b** was easily hydrogenated to give **14a,b** in high yields.

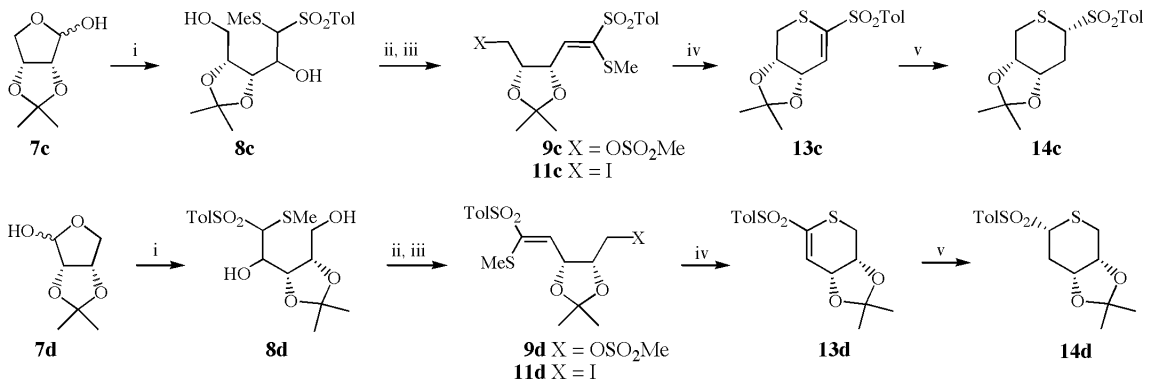
A cyclic sulfonium ion similar to **12B** has been suggested as intermediate in analogous cyclisations towards sulfur heterocycles [8], which undergoes further cleavage of the S-Me bond, by the iodide. The fact, however, that the presence of sodium iodide is necessary for the cyclisation of compounds **11**, makes the formation of intermidiate **12B** not likely and this is due to the lessened nucleophilicity of sulfur, caused by the conjugated double bond. The formation of the intermediate **12A** is more possible in the present case, generated from abstraction of the methyl group in **11** by the iodide, which is then readily cyclised to **13**.

Compounds **8a,b** were isolated as inseparable mixtures of diastereoisomers in *ca*. 3:1 ratios, as shown by ^{1}H nmr. For the major isomer of **8a**, the 5-H appeared at δ 3.74 as a singlet and the 4-H at δ 4.48 (dd, J = 8.7 and 2.4 Hz), while for the minor isomer of **8a** the respective resonances were δ 3.90 (d, J = 6.3 Hz) and δ 4.19 (ddd, J = 8.9, 6.3 and 2.4 Hz). The C-5 and C-4 signals in the ^{13}C nmr spectrum appeared at δ 68.9 and 77.2 for the major isomer and δ 69.6 and 76.0 for the minor isomer of **8a**, respectively. Analogous data were obtained for **8b**. Regarding compounds **9a,b**, **10a,b** and **11a,b**, the geometry of the double bond was assigned by comparison with similar examples found in the literature[3]. The fact also that upon treatment with sodium iodide they undergo facile cyclisation supports the assignment given. It is, finally, worth mentioning that compound **14a** in its preferred conformation has the sulfonyl group axial, as deduced from the coupling constants of 2-H (δ 3.83, dd, J = 4.4 and 3.6 Hz), which unequivocally show that this proton is equatorial.

Protected *D*- and *L*-erythrose (**7c,d**) (Scheme 2), are sugars in the furanose form, readily available [10] from the naturally abundant *D*- and *L*-arabinose, respectively, with the free hemiacetal group. Upon their condensation with methylthiomethyl *p*-tolyl sulfone, using *n*-BuLi they afforded **8c,d** in 6% yield, isolated as single enantiomers. We did not try to determine the absolute configuration of the newly formed stereocenters in **8c,d**, which were further mesylated (both hydroxyl groups) to give, after elimination, compounds **9c,d** in 80% yield; the respective chlorides were not formed this time. Reflux of **9c,d** in acetonitrile in the presence of 10 equivalents of sodium iodide gave the respective iodides **11c,d** as the main products and **13c,d** in low yields (<10%). However, in refluxing DMF, the desired cyclic compounds **13c,d** were obtained in good yield. These products were eventually converted to saturated **14c,d** by conventional hydrogenation.

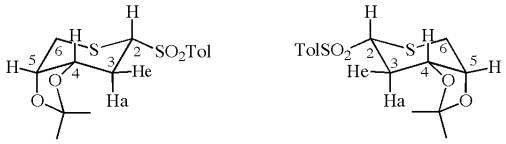
The absolute configuration of the newly formed chiral center in compounds **14c,d** and their preferred conformation were deduced by the ^{1}H nmr spectra (Figure 2). The proton spectral assignment was made by successive proton decouplings, starting from the unequivocally assigned 2-H signal, which appeared at δ 4.11 as a doublet of doublets with J = 12.4 and 6.0 Hz, indicative for an axial position of this proton. The neighboring axial 3-Ha resonated at δ 1.83 as a quartet with J = 12.4 Hz, which implies that this proton has three equal (one geminal and two axial-axial)

Scheme 2



Reagents and conditions: i, $MeSCH_2SO_2Tol$ (3.25 equiv.), 12-crown-4, *n*-BuLi 1.6 *M* in hexanes, THF, -60 °C, 12 h, 61%; ii, $MeSO_2Cl$ (2.2 equiv.), pyridine, 0 °C, 12 h, 80%; iii, see text; iv, NaI, DMF, reflux, 6 h, 66%; iv, 10% Pd/C, H_2, ethyl acetate, 20 °C, 5 h, 44%.

coupling constants, confirming that 4-H is also axial. The all-*cis* geometry of **14c,d** is the expected one, since the hydrogen can be added to the double bond of **13c,d** from the less hindered face. It is interesting to note the different conformation preferred by compounds **14a** and **14c,d**: as shown in the first case the sulfonyl group is axial (stabilized by the anomeric effect), whereas in compounds **14c,d** it is equatorial, apparently because this conformation minimizes the steric interactions of all-*cis* substituents.



14c **14d**

Figure 2

In conclusion, we have developed an efficient method for converting lactols to sulfonylated thiopyrane and thiepin derivatives, which are all new compounds. These products are expected to be valuable intermediates for further ring contraction to five and six-membered carbocycles. Work to this direction is in progress.

EXPERIMENTAL

Melting points were determined on a Kofler hot-stage microscope and are uncorrected. All commercially available reagents were used without further purification. Solvents were dried by standard methods. 2-Hydroxytetrahydrofuran [9a], 2-hydroxy-2*H*-tetrahydropyran [11] and protected *D*- and *L*-erythrose[10] were prepared according to literature methods. Reaction progress was monitered by thin layer chromatography (TLC) on Merck silica gel $60F_{254}$ glass plates (0.25 mm). Column chromatography was performed with Merck silica gel 60 (0.063-0.200 mm). Optical rotations were determined at room temperature on an A. Krüss P3000 Automatic Digital Polarimeter. The ^1H and ^{13}C nmr spectra were recorded at 300 and 75 MHz, respectively, on a Bruker AM 300 spectrometer, with tetramethylsilane (TMS) as internal standard. Electron impact mass spectra were recorded at 70 eV on a VG TS-250 spectrometer and microanalyses were performed on a Perkin-Elmer 2400-II Element analyser.

General Procedure for the Condensation of Methylthiomethyl *p*-Tolyl Sulfone with Lactols (**7**).

All of these reactions were carried out under an argon atmosphere. A solution of methylthiomethyl *p*-tolyl sulfone (2.111 g, 9.76 mmol) and 12-crown-4 (0.229 g, 1.3 mmol) in dry tetrahydrofuran (THF) (20 ml) was cooled at -78 °C. The methylthiomethyl *p*-tolyl sulfone was lithiated by slowly adding 6.7 ml of 1.6 *M* of *n*-butyllithium in hexane. After the addition was complete, the solution was allowed to warm to 0 °C and was then cooled again at -78 °C. A solution of lactol **7a-d** (3.25 mmol) in dry THF (5 ml) was added at the same temperature and the resulting solution was allowed to warm to room temperature. After stirring for 12 hours at this temperature, the mixture was decanted into a10% aqueous Na_2CO_3 (100 ml) solution and extracted with CH_2Cl_2 (3x100 ml). The organic layer was dried over Na_2SO_4, the solvent was evaporated and the residue was chromatographed on silica gel with hexane/ethyl acetate (10:1 v/v) as the eluent to give the desired addition products **8a-d**.

5-(Methylthio)-5-[(*p*-tolyl)sulfonyl]-1,4-pentanediol (**8a**).

This compound was obtained as colorless crystals in 32% yield, mp 70-80 °C; ^1H nmr (deuteriochloroform): δ 1.65 (m, 3H, 2-H, 3-Ha), 1.93 (m, 1H, 3-Hb), 2.03 (s, 3H, MeS), 2.46 (s, 3H, MeC_6H_4), 3.24 (br s, 2H, two OH), 3.62 (dd, 2H, 1-H, J = 5.6, 4.9 Hz), 3.74 (s, 5-H of the major diastereoisomer), 3.90 (d, 5-H of the minor diastereoisomer, J = 6.3 Hz), 4.19 (ddd, 4-H of the minor diastereoisomer, J = 8.9, 6.3, 2.4 Hz), 4.48 (dd, 4-H of the major diastereoisomer, J = 8.7, 2.4 Hz), 7. 37 (d, 2H, J = 8.2 Hz), 7.86 ppm (d, 2H, J = 8.2 Hz); ^{13}C nmr (deuteriochloroform): δ 17.0, 21.6, 28.7, 31.7, 62.1, 68.9, 77.1, 129.5, 129.6, 133.9, 145.3 ppm for the major diastereoisomer and 16.8, 21.6, 28.4, 30.8, 62.3, 69.6, 76.0, 129.4, 129.6, 134.2, 145.2 ppm for the minor diastereoisomer.

Anal. Calcd. for $C_{13}H_{20}O_4S_2$: C, 51.29; H, 6.62. Found: C, 51.28; H, 6.43.

6-(Methylthio)-6-[(*p*-tolyl)sulfonyl]- 1,5-hexanediol (**8b**).

This compound was obtained as a colorless oil in 62% yield. ^1H nmr (deuteriochloroform): δ 1.55 (m, 5H, 2-H, 3-H, 4-Ha), 1.88 (m, 1H, 4-Hb), 2.03 (s, MeS of the major diastereoisomer), 2.11 (s, MeS of the minor diastereoisomer), 2.43 (br s, 2H, two OH), 2.46 (s, 3H, MeC_6H_4), 3.62 (t, 2H, 1-H, J = 6.1 Hz), 3.70 (s, 6-H of the major diastereoisomer), 3.83 (d, 6-H of the minor diastereoisomer, J = 6.5 Hz), 4.19 (ddd, 5-H of the minor diastereoisomer, J = 8.7, 6.5, 2.9 Hz), 4.48 (dd, 5-H of the major diastereoisomer, J = 8.3, 2.9 Hz), 7. 38 (d, 2H, J = 8.2 Hz), 7.86 ppm (d, 2H, J = 8.2 Hz); ^{13}C nmr (deuteriochloroform): δ 62.3 (C-1), 68.9 (C-5), 77.0 (C-6) ppm for the major diastereoisomer and 62.4 (C-1), 69.6 (C-5), 76.0 (C-6) ppm for the minor diastereoisomer and other peaks at the aliphatic and aromatic region; ms: m/z 271 (M^+-CH_3S), 253 (M^+-CH_3S-H_2O), 216 ($TolSO_2CH_2SCH_3^+$).

Anal. Calcd. for $C_{14}H_{22}O_4S_2$: C, 52.80; H, 6.96. Found: C, 53.15; H, 7.33.

1-[(4*S*,5*R*)-5-(Hydroxymethyl)-2,2-dimethyl-1,3-dioxolan-4-yl]-2-[(*p*-tolyl)sulfonyl]-2-(methylthio)-1-ethanol (**8c**) and 1-[(4*R*,5*S*)-5-(Hydroxymethyl)-2,2-dimethyl-1,3-dioxolan-4-yl]-2-[(*p*-tolyl)sulfonyl]-2-(methylthio)-1-ethanol (**8d**).

These enantiomers were isolated in enantiomerically pure form as colorless oils in 61% yield each one. For **8c** $[\alpha]_D$ -38.7 (c = 2.7, chloroform); for **8d** $[\alpha]_D$ +39.2 (c = 0.8, chloroform); ^1H nmr (deuteriochloroform): δ 1.17 (s, 3H), 1.30 (s, 3H), 2.11 (s, 3H, CH_3S), 2.44 (s, 3H, $CH_3C_6H_4$), 3.19 (br s, 2H, two OH), 3.81 (dd, 1H, 1-Ha, J = 11.8, 4.7 Hz) 3.88 (dd, 1H, 1-Hb, J = 11.8, 6.7 Hz), 4.14 (s, 1H, 5-H), 4.32 (m, 2H, one s [4-H] and one ddd [2-H] overlapping), 5.57, 1H, 3-H, J = 8.8 Hz), 7. 37 (d, 2H, J = 8.2 Hz), 7.87 ppm (d, 2H, J = 8.2 Hz); ^{13}C nmr (deuteriochloroform): δ 16.9, 21.2, 25.0, 27.1, 59.7, 66.8, 73.7, 75.4, 76.7, 108.4, 129.1, 129.4, 133.6, 145.0 ppm.

Anal. Calcd. for $C_{16}H_{24}O_6S_2$: C, 51.05; H, 6.43. Found: C, 51.40; H, 6.36.

General Procedure for Conversion of Compounds **8a-d** to Compounds **9a-d** and **10a,b**.

All of these reactions were carried out under an argon atmosphere. To a stirred solution of **8a-d** (3 mmol) in dry pyridine (20 ml), methanesulfonyl chloride (0.7 g, 9 mmol) was added at 0 °C, the mixture was allowed to warm at room temperature and stirred for 12 hours CH_2Cl_2 (100 ml) and aqueous 5% HCl (80 ml) were then added, the organic layer was washed with aqueous 5% HCl (2x80 ml) and H_2O (80 ml) and dried over Na_2SO_4. The solvent was then evaporated and the residue chromatographed on silica gel with hexane/ethyl acetate (4:1 v/v) as the eluent to give firstly compounds **10a,b**, followed by compounds **9a-d**.

(*E*)-5-(Methylthio)-5-[(*p*-tolyl)sulfonyl]-4-pentenylmethanesulfonate (**9a**).

This compound was isolated as a colorless oil in 15% yield. ^{1}H nmr (deuteriochloroform): δ 1.97 (m, 2H, central CH_2), 2.22 (s, 3H, MeS), 2.43 (s, 3H, MeC_6H_4), 2.65 (q, 2H, CH_2, J = 7.3 Hz), 3.01 (s, 3H, $MeSO_2$), 4.25 (t, 2H, CH_2O, J = 6.0 Hz), 7. 37 (d, 2H, J = 8.1 Hz), 7.48 (t, 1H, =C-H, J = 7.3 Hz), 7.80 ppm (d, 2H, J = 8.1 Hz); ^{13}C nmr (deuteriochloroform): δ 19.0, 21.4, 26.2, 27.5, 37.2, 68.6, 128.5, 129.4, 139.8, 144.4, 149.9, 152.0 ppm.

Anal. Calcd. for $C_{14}H_{20}O_5S_3$: C, 46.13; H, 5.53. Found: C, 46.25; H, 5.27.

[(*E*)-5-Chloro-1-(methylthio)-1-pentenyl](*p*-tolyl)dioxo-λ^6-sulfane (**10a**).

This compound was isolated as a colorless oil in 50% yield. ^{1}H nmr (deuteriochloroform): δ 1.94 (m, 2H, central CH_2), 2.21 (s, 3H, MeS), 2.41 (s, 3H, MeC_6H_4), 2.66 (q, 2H, CH_2, J = 7.4 Hz), 3.55 (t, 2H, CH_2O, J = 6.1 Hz), 7. 32 (d, 2H, J = 8.1 Hz), 7.49 (t, 1H, =C-H, J = 7.3 Hz), 7.80 ppm (d, 2H, J = 8.1 Hz); ^{13}C nmr (deuteriochloroform): δ 19.0, 21.2, 27.2, 30.5, 43.7, 128.3, 129.2, 135.4, 139.5, 144.1, 150.1 ppm; ms: m/z 306 (M^++2), 304 (M^+).

Anal. Calcd. for $C_{13}H_{17}ClO_2S_2$: C, 51.22; H, 5.62. Found: C, 51.35; H, 5.44.

(*E*)-6-(Methylthio)-6-[(*p*-tolyl)sulfonyl]-5-hexenylmethanesulfonate (**9b**).

This compound was isolated as a colorless oil in 41% yield. ^{1}H nmr (deuteriochloroform): δ 1.65 (m, 2H, CH_2), 1.79 (m, 2H, CH_2), 2.22 (s, 3H, MeS), 2.43 (s, 3H, MeC_6H_4), 2.55 (q, 2H, CH_2, J = 7.3 Hz), 3.01 (s, 3H, $MeSO_2$), 4.24 (t, 2H, CH_2O, J = 6.4 Hz), 7. 33 (d, 2H, J = 8.0 Hz), 7.48 (t, 1H, =C-H, J = 7.3 Hz), 7.80 ppm (d, 2H, J = 8.0 Hz); ^{13}C nmr (deuteriochloroform): δ 19.3, 21.5, 24.0, 28.5, 29.2, 37.3, 69.1, 128.6, 129.5, 135.6, 139.4, 144.3, 151.0 ppm; ms: m/z 378 (M^+), 283 (M^+-CH_3SO_3), 268 (M^+-$CH_3SO_3CH_3$).

Anal. Calcd. for $C_{15}H_{22}O_5S_3$: C, 47.60; H, 5.86. Found: C, 47.53; H, 5.89.

[(*E*)-6-Chloro-1-(methylthio)-1-hexenyl](*p*-tolyl)dioxo-λ^6-sulfane (**10b**).

This compound was isolated as a colorless oil in 26% yield. ^{1}H nmr (deuteriochloroform): δ 1.69 (m, 2H, CH_2), 1.79 (m, 2H, CH_2), 2.24 (s, 3H, MeS), 2.44 (s, 3H, MeC_6H_4), 2.55 (q, 2H, CH_2, J = 7.3 Hz), 3.55 (t, 2H, CH_2O, J = 6.3 Hz), 7. 33 (d, 2H, J = 8.0 Hz), 7.50 (t, 1H, =C-H, J = 7.3 Hz), 7.81 ppm (d, 2H, J = 8.0 Hz); ^{13}C nmr (deuteriochloroform): δ 19.3, 21.6, 25.2, 29.2, 31.8, 44.3, 128.6, 129.5, 135.6, 139.2, 144.3, 151.4 ppm; ms: m/z 320 (M^++2), 318 (M^+), 268 (M^+-CH_3Cl).

Anal. Calcd. for $C_{14}H_{19}ClO_2S_2$: C, 52.73; H, 6.01. Found: C, 52.94; H, 5.80.

{(4*R*,5*S*)-2,2-Dimethyl-5-[(*E*)-2-[(*p*-tolyl)sulfonyl]-2-(methylthio)-ethenyl]-1,3-dioxolan-4-yl}methyl methanesulfonate (**9c**) and {(4*S*,5*R*)-2,2-Dimethyl-5-[(*E*)-2-[(*p*-tolyl)sulfonyl]-2-(methylthio)ethenyl]-1,3-dioxolan-4-yl}methyl methanesulfonate (**9d**).

These enantiomers were isolated in enantiomerically pure form as colorless crystals in 80% yield each one, mp 126-128 °C. For **9c** $[\alpha]_D$ +19.4 (c = 0.78, chloroform); for **9d** $[\alpha]_D$ –18.9 (c = 4.2, chloroform); ^{1}H nmr (deuteriochloroform): δ 1.41 (s, 3H, CH_3), 1.55 (s, 3H, CH_3), 2.40 (s, 3H, MeS), 2.44 (s, 3H, MeC_6H_4), 3.02 (s, 3H, $MeSO_2$), 4.01 (dd, 1H, CH_2O, J = 12.1, 5.1 Hz),), 4.03 (dd, 1H, CH_2O, J = 12.1, 5.4 Hz), 4.53 (ddd, 1H, J = 7.3, 5.4, 5.1 Hz), 5.29 (t, 1H, J = 7.3 Hz), 7. 35 (d, 2H, J = 8.3 Hz), 7.38 (t, 1H, =C-H, J = 7.3 Hz), 7.82 ppm (d, 2H, J = 8.3 Hz); ^{13}C nmr (deuteriochloroform): δ 19.2, 21.6, 25.1, 27.4, 37.7, 66.6, 74.5, 76.0, 110.8, 128.7, 129.8, 134.8, 142.2, 144.9, 145.0 ppm; ms: m/z 358 (M^++H-CH_3SO_2).

Anal. Calcd. for $C_{17}H_{24}O_7S_3$: C, 46.77; H, 5.54. Found: C, 47.03; H, 5.36.

3,4-Dihydro-2*H*-thiopyran-6-yl-*p*-tolylsulfone (**13a**) by Cyclisation of Sulfonate **9a** and Chloride **10a**.

To a solution of sulfonate **9a** or chloride **10a** (2 mmol) in dry acetonitrile (20 ml), NaI (3.0 g, 20 mmol) was added and the mixture was refluxed with stirring for 5 hours CH_2Cl_2 (30 ml) and saturated aqueous $Na_2S_2O_3$ (30 ml) were then added and the organic layer was washed with H_2O and dried over Na_2SO_4. The solvent was then evaporated *in vacuo* and the residue was chromatographed on silica gel with hexane/ethyl acetate (12:1 v/v) as the eluent to give the cyclisation product **13a** in 87% yield from **9a** and 82% yield from **10a**. M.p. 138-140 °C. ^{1}H nmr (deuteriochloroform): δ 1.96 (quint., 2H, central CH_2, J = 5.5 Hz), 2.31 (dt 2H, J = 5.5, 4.4 Hz), 2.45 (s, 3H), 2.84 (t, 2H, J = 5.5 Hz), 7.02 (t, 1H, J = 4.4 Hz), 7.35 (d, 2H, J = 8.0 Hz), 7.82 ppm (d, 2H, J = 8.0 Hz); ^{13}C nmr (deuteriochloroform): δ 20.7, 21.2, 24.2, 27.0, 127.3, 129.2, 130.9, 136.1, 137.3, 144.1 ppm; ms: m/z 254 (M^+), 189, 175.

Anal. Calcd. for $C_{12}H_{14}O_2S_2$: C, 56.66; H, 5.55. Found: C, 57.02; H, 5.59.

General Procedure for Conversion of Sulfonates **9b-d** or Chloride **10b** into Iodides **11b-d**.

To a solution of sulfonates **9b-d** or chloride **10b** (2 mmol) in dry acetonitrile (20 ml), NaI (3.0 g, 20 mmol) was added and the mixture was refluxed with stirring for 4 hours CH_2Cl_2 (30 ml) and saturated aqueous $Na_2S_2O_3$ (30 ml) were then added and the organic layer was washed with H_2O and dried over Na_2SO_4. The solvent was then evaporated *in vacuo* and the residue was chromatographed on silica gel with hexane/ethyl acetate (12:1 v/v) as the eluent to give iodides **11b-d**, followed by the cyclisation products in yields less than 10%.

[(*E*)-6-Iodo-1-(methylthio)-1-hexenyl](*p*-tolyl)dioxo-λ^6-sulfane (**11b**).

This compound was isolated as colorless crystals in 74% yield from **9b** and 77% yield from **10b**, mp 104-106 °C. ^{1}H nmr (deuteriochloroform): δ 1.63 (quintet., 2H, J = 7.5 Hz), 1.82 (quintet., 2H, J = 7.4 Hz), 2.24 (s, 3H, MeS), 2.43 (s, 3H, MeC_6H_4), 3.19 (t, 2H,

J = 7.3 Hz), 7.35 (d, 2H, J = 7.9 Hz), 7.49 (t, 1H, J = 7.3 Hz), 7.81 (d, 2H, J = 7.9 Hz); ^{13}C nmr (deuteriochloroform): δ 5.9, 19.2, 21.4, 28.5, 28.6, 32.4, 128.3, 129.3, 135.5, 138.9, 144.0, 151.1 ppm.

Anal. Calcd. for $C_{14}H_{19}IO_2S_2$: C, 40.98; H, 4.67. Found: C, 41.08; H, 4.78.

(4*S*,5*S*)-4-(Iodomethyl)-2,2-dimethyl-5-[(*E*)-2-[(*p*-tolyl)sulfonyl]-2-(methylthio)ethenyl]-1,3-dioxolane (**11c**) and (4*R*,5*R*)-4-(Iodomethyl)-2,2-dimethyl-5-[(*E*)-2-[(*p*-tolyl)sulfonyl]-2-(methylthio)ethenyl]-1,3-dioxolane (**11d**).

These enantiomers were isolated as colorless crystals in enantiomerically pure form in 80% yield each one, mp 82-84 °C. For **11c** $[\alpha]_D$ +53.4 (c = 0.46, chloroform); for **11d** $[\alpha]_D$ -53.2 (c = 1.2, chloroform); ^{1}H nmr (deuteriochloroform): δ 1.40 (s, 3H), 1.55 (s, 3H), 2.42 (s, 3H), 2.46 (s, 3H), 2.91 (dd, 1H, J = 9.8, 6.6 Hz), 3.06 (dd, 1H, J = 9.8, 6.6 Hz), 4.52 (q, 1H, J = 6.6 Hz), 5.25 (dd, 1H, J = 8.7, 6.2 Hz), 7.33 (d, 2H, J = 8.2 Hz), 7.34 (d, 1H, J = 8.7 Hz), 7.81 ppm (d, 2H, J = 8.2 Hz); ^{13}C nmr (deuteriochloroform): δ 1.2, 19.4, 21.6, 25.5, 28.0, 75.6, 78.7, 110.5, 128.9, 129.7, 135.2, 142.6, 144.4, 144.9 ppm.

Anal. Calcd. for $C_{16}H_{21}IO_4S_2$: C, 41.03; H, 4.52. Found: C, 41.42; H, 4.56.

General Procedure for Cyclisation of Sulfonates **9b-d** or Halides **10b** and **11b-d**.

To a solution of sulfonates **9b-d** or halides **10b** and **11b-d** (2 mmol) in dry DMF (20 ml), NaI (3.0 g, 20 mmol) was added, the mixture was refluxed with stirring for 4 hours and then partitioned between CH_2Cl_2 (30 ml) and saturated aqueous $Na_2S_2O_3$ (30 ml). The organic layer was washed with H_2O and dried over Na_2SO_4. The volatiles were evaporated *in vacuo* and the residue was chromatographed on silica gel with hexane/ethyl acetate (5:1 v/v) as the eluent to give products **13a-d**.

p-Tolyl 4,5,6,7-tetrahydro-2-thiepinylsulfone **(13b)**.

This compound was isolated as colorless crystals in 59% yield from **9b**, 62% yield from **10b** and 55% yield from **11b**, mp 104-106 °C; ^{1}H nmr (deuteriochloroform): δ 1.55 (m, 2H), 1.98 (m, 2H), 2.38 (m, 2H), 2.44 (s, 3H), 2.58 (m, 2H), 7.33 (d, 2H, J = 8.2 Hz), 7.61 (t, 1H, J = 7.2 Hz), 7.82 ppm (d, 2H, J = 8.2 Hz); ^{13}C nmr (deuteriochloroform): δ 21.6, 22.5, 28.9, 32.1, 34.1, 128.5, 129.4, 136.0, 143.3, 144.1, 147.2 ppm; ms: m/z 268 (M^+).

Anal. Calcd. for $C_{13}H_{16}O_2S_2$: C, 58.17; H, 6.01. Found: C, 58.06; H, 6.04.

(3a*S*,7a*S*)-2,2-Dimethyl-6-[(*p*-tolyl)sulfonyl]-3a,7a-dihydro-4*H*-thiopyrano[3,4-*d*][1,3]dioxole (**13c**) and (3a*R*,7a*R*)-2,2-Dimethyl-6-[(*p*-tolyl)sulfonyl]-3a,7a-dihydro-4*H*-thiopyrano[3,4-*d*][1,3]dioxole (**13d**).

These enantiomers were isolated as colorless crystals in enantiomerically pure form in 66% yield each one from **9c,d** and 55% yield from **11c,d**, mp 121-123 °C. For **13c** $[\alpha]_D$ +181.0 (c = 0.62, chloroform); for **13d** $[\alpha]_D$ –179.9 (c = 4.62, chloroform); ^{1}H nmr (deuteriochloroform): δ 1.39 (s, 3H), 1.40 (s, 3H), 2.36 (dd ,1H, 6-H_{axial}, J = 12.4, 10.5 Hz), 2.45 (s, 3H), 2.86 (dd, 1H, 6-$H_{equatorial}$, J = 12.4, 3.9 Hz), 4.30 (ddd, 1H, 5-H, J = 12.4, 3.9, 3.5 Hz), 4.62 (dd, 1H, 4-H, J = 4.6, 3.5 Hz), 7.17 (d, 1H, 3-H, J = 4.6 Hz), 7.35 (d, 2H, J = 8.2 Hz), 7.83 ppm (d, 2H, J = 8.2 Hz); ^{13}C nmr (deuteriochloroform): δ 21.6, 25.3, 27.8, 30.7, 70.4, 73.0, 108.5, 128.6, 129.7, 129.8, 135.5, 143.9, 145.0 ppm; ms: m/z 326 (M^+), 311, 269, 251.

Anal. Calcd. for $C_{15}H_{18}O_4S_2$: C, 55.19; H, 5.56. Found: C, 55.51; H, 5.59.

General Procedure for the Hydrogenation of Compounds **13a-d**.

To a solution of compounds **13a-d** (0.5 mmol) in ethyl acetate (10 ml) catalytic ammount of 10% Pd/C was added and the solution was degassed. Hydrogen was added through an adjusted balloon and the mixture was stirred at room temperature for 2 hours (**13a,b**) or 5 hours (**13c,d**). The catalyst was filtered off and the solution concentrated and chromatographed on silica gel with hexane/ethyl acetate 3:1 as the eluent to give compounds **14a-d**.

2-[(*p*-Tolyl)sulfonyl]tetrahydro-2*H*-thiopyran (**14a**).

This compound was isolated as colorless crystals in 87% yield, mp 83-84 °C; ^{1}H nmr (deuteriochloroform): δ 1.55-1.83 (m, 2H), 1.95 (m, 1H), 2.03-2.17 (m, 2H), 2.38-2.54 (m, 2H) overlapping with 2.45 (s, 3H, CH_3), 3.26 (ddd, 1H, J = 10.8, 7.4, 3.0 Hz, 6-Ha), 3.83 (dd, 1H, J = 4.4, 3.6 Hz, 1-H) 7.35 (d,2H, J = 8.0 Hz), 7.83 ppm (d, 2H, J = 8.0 Hz); ^{13}C nmr (deuteriochloroform): δ 21.3, 21.6, 25.4, 25.5, 26.1, 61.2, 129.1, 129.4, 134.4, 144.6 ppm.

Anal. Calcd. for $C_{12}H_{16}O_2S_2$: C, 56.22; H, 6.29. Found: C, 56.48; H, 6.26.

2-[(*p*-Tolyl)sulfonyl]thiepane (**14b**).

This compound was isolated as colorless crystals in 80% yield, mp 104-106 °C; ^{1}H nmr (deuteriochloroform): δ 1.5-2.1 (m, 7H), 2.45 (s, 3H, CH_3) overlapping with 2.5 (m, 2H), 2.80 (ddd, 1H, J = 11.3, 10.4, 2.3 Hz, 7-Ha), 4.06 (dd 1H, 2-H, J = 11.5, 6.1 Hz), 7.35 (d,2H, J = 7.8 Hz), 7.82 ppm (d, 2H, J = 7.8 Hz); ^{13}C nmr (deuteriochloroform): δ 21.6, 24.5, 28.4, 28.6, 30.3, 32.4, 68.2, 129.4, 129.6, 134.1, 144.6 ppm.

Anal. Calcd. for $C_{13}H_{18}O_2S_2$: C, 57.74; H, 6.71. Found: C, 57.88; H, 6.57.

(3a*S*,6*R*,7a*S*)-2,2-Dimethyl-6-[(*p*-tolyl)sulfonyl]tetrahydro-4*H*-thiopyrano[3,4-*d*][1,3]dioxole (**14c**) and (3a*R*,6*S*,7a*R*)-2,2-Dimethyl-6-[(*p*-tolyl)sulfonyl]tetrahydro-4*H*-thiopyrano[3,4-*d*]-[1,3]dioxole (**14d**).

These enantiomers were isolated as colorless crystals in enantiomerically pure form in 44% yield each one, mp 154-156 °C. For **14c** $[\alpha]_D$ +83.2 (c = 0.48, chloroform); for **14d** $[\alpha]_D$ -83.5 (c = 0.5, chloroform); ^{1}H nmr (deuteriochloroform): δ 1.32 (s, 3H), 1.43 (s, 3H), 1.83 (q, 1H, J = 12.4 Hz, 3-H_{axial}), 2.44 (ddd, 1H, J = 12.4, 6.1, 5.0 Hz, 3-$H_{equatorial}$) overapping with 2.47 (s, 3H, CH_3), 2.68 (dd, 1H, J = 13.7, 7.2, 6-Ha), 2.72 (dd, 1H, J = 13.7, 10.1, 6-Hb), 4.09 (dd, 1H, J = 12.4, 6.1 Hz, 2-H), 4.16 (ddd, 1H, J = 12.4, 7.2, 5.0 Hz, 4-H), 4.41 (dt, 1H, J = 10.1, 7.2 Hz, 5-H), 7.37 (d, 2H, J = 8.0 Hz), 7.84 ppm (d, 2H, J = 8.0 Hz); ^{13}C nmr (deuteriochloroform): δ 21.6, 24.5, 26.0, 26.2, 27.0, 60.7, 72.8, 73.5, 108.8, 129.6, 129.7, 132.8, 145.3 ppm.

Anal. Calcd. for $C_{15}H_{20}O_4S_2$: C, 54.85; H, 6.14. Found: C, 54.91; H, 6.09.

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