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Hetero-Diels-Alder reactions of new sulfonylsulfines generated from α-substituted methylsulfones

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Dedicated to Professor Heinz Heimgartner on the occasion of his 70th birthday

Abstract
Hetero-Diels-Alder reaction with sulfines generated in situ from methylsulfones 5a-e substituted in α-position with a phosphonyl, carboxyl, carboxyoxazolidinyl, pyridyl, or a quinolyl substituent, respectively, led to new highly functionalized thiopyrans cycloadducts. When in the substrates (i.e. 5a-c) the sulfonyl group and the second substituent on the methylene carbon have comparable electronwithdrawing effect, a mixture of cis and trans isomers of the corresponding cycloadducts is obtained with low to moderate selectivities. In the case of substrates 5d and 5e, due to the strong electronwithdrawing effect of the sulfonyl compared to the pyridyl or quinolyl groups, a single isomer is obtained for cycloadducts 7d and 7e. The stereochemical arrangements in the two cycloadducts resulting from 5b and 5d (carboxylate and pyridine derivatives) have been determined by single-crystal X-ray analysis and showed that the trans isomer was favored in both cases.

Keywords: thia-Diels-Alder reaction, sulfones, sulfines, thiopyran S-oxide

Introduction

Although less explored than the oxa and aza hetero-Diels-Alder (HDA) reactions, the thia-Diels–Alder version represents an efficient and atom-economical synthetic method to obtain dihydrothiopyrans, which were then used as precursors for the synthesis of some bioactive molecules,1 in particular thiosugars.2 In the main reported cases, the functionalities required in the target molecule (obtained via a thia-HDA step) were introduced directly in the cycloaddition step, as they belong to the thiocarbonyl heterodienophile or to the diene, or they were introduced by subsequent reactions in particular on the cycloadduct double bond.
In some recent publications, in order to introduce new functionalities in the thiopyran structure, the cycloadduct was oxidized into the corresponding sulfoxide and a nucleophile was introduced via a Pummerer reaction. For this purpose, in our laboratory, three substrates have been selected, namely sulfoxides 3a-c, which can be obtained by HDA reaction between dithioesters 1a-c and 1,3-butadiene, and subsequent S-oxidation of the resulting cycloadducts 2a-c (Scheme 1). This required a selective oxidation of the endocyclic sulfur atom of 2 versus the exocyclic one. The oxidation of 2a and 2b by m-CPBA at -78 °C afforded sulfoxides 3a and 3b, respectively, as the major products (> 80% in the crude reaction mixture), however together with a little amount of the isomer 3'. In the case of the pyridine derivative 2c, the oxidation by m-CPBA led to a complex mixture. To avoid these problems, a solution is to access directly compound 3 by using as heterodienophile the sulfine 4, which could be obtained by S-oxidation of dithioester 1c (Scheme 1). However, it was described that oxidation by m-CPBA of dithioester 1c led to the corresponding sulfine, which was unstable and easily rearranged and decomposed into S-methyl 2-pyridylthiocarboxylate [2-PyC(O)SMe]. Indeed, similar results were obtained also with the phosphonate and carboxylate derivatives, and the corresponding thiocarboxylates ZC(O)SMe have been detected in the mixture of the reaction products.

Scheme 1

Therefore, the use as heterodienophiles of sulfonylsulfines 6 was envisaged (Scheme 2). This type of sulfines bearing two electron-withdrawing groups cannot be isolated because of their high reactivity, but they can be generated as already described in the literature, from the corresponding α-substituted methylsulfones 5 (as doubly activated methylene compounds) and thionyl chloride (SOCl2), in the presence of a base, then trapped in situ by a HDA reaction with a diene.

Scheme 2
This paper describes our results obtained in the thia-Diels-Alder reaction of sulfonylsulfines generated from α-substituted methylsulfones. The newly obtained cycloadducts represent highly functionalized thiopyrans and interesting substrates for Pummerer reactions.

Results and Discussion

For this study we selected five structures of methylsulfones 5 (ZCH₂SO₂Ph) in which the substituent Z is a phosphonyl, carboxylate, carboxyoxazolidinone, 2-pyridyl, or a 2-quinolyl group (Figure 1). The corresponding dithioesters (ZCS₂Me) having the same Z substituents have already been used in our laboratory in HDA reaction.¹⁻⁴ Sulfonyl methylphosphonate 5a was obtained by oxidation with m-CPBA of the corresponding sulfide [(iPrO)₂P(O)CH₂SPh], which were prepared from diisopropyl α-hydroxymethylphosphonate [(iPrO)₂P(O)CH₂OH] by a reported procedure.⁹ Sulfones 5b-e were prepared from the corresponding chlorides (ZCH₂Cl) and sodium benzenesulfinate (PhSO₂Na) by a reported procedure.¹⁰

![Figure 1](attachment:Figure1.png)

It is known that when the substituents at the sulfine carbon are different, the sulfine exists as two geometrical isomers and the Diels-Alder reaction is stereospecific, as the geometry of the sulfine (Z/E) is retained in the cycloadduct (cis/trans). In our cases, Z/E (for the sulfine) and cis/trans (for the cycloadduct 7) indicate the relative position between the sulfonyl group and the oxygen of the thiocarbonyl S-oxide function (Scheme 3). Sulfones 5 reacted with thionyl chloride in the presence of a base (triethylamine or 2,6-lutidine) to generate the corresponding non-isolable sulfines, which reacted in situ with 2,3-dimethyl-1,3-butadiene or 1,3-butadiene to afford the expected cycloadducts 7.

The reaction between the sulfine prepared from phenylsulfonyl methylphosphonate 5a, SOCl₂ and triethylamine, and 2,3-dimethyl-1,3-butadiene was complete, leading to product 7a as a mixture of trans and cis isomers, in 75% yield (Table 1, entry 1). The ratio of the two isomers (major/minor) was 67/33, but the corresponding relative configuration was not assigned. Similarly, the reaction with 1,3-butadiene afforded cycloadduct 7a' with a ratio of isomers of 53/47 (Table 1, entry 2). In the case of phenylsulfonyl ethyl acetate 5b the base of choice was the 2,6-lutidine. Cycloaddition of sulfine 6b with 2,3-dimethyl-1,3-butadiene led to 7b as a mixture of two isomers in a 81/19 ratio and with 1,3-butadiene to cycloadduct 7b* in a 57/43 ratio (Table 1, entries 3 and 4). Crystallization of 7b* afforded a sample of pure minor isomer, from which a single crystal was isolated. The X-ray analysis showed a relative configuration in which the
phenylsulfonyl group is located cis to the sulfinyl oxygen atom (Figure 2). The results obtained with phenylsulfonylacetyl oxazolidinone 5c were similar to those obtained with 5a and 5b. Cycloadduct 7c resulting from 2,3-dimethyl-1,3-butadiene was obtained with a diastereomeric ratio of 87/13 and cycloadduct 7e' resulting from 1,3-butadiene with 67/33 dr (Table 1, entries 5 and 6). The assignment of the trans relative configuration for the major isomer of 7b' let suppose that the major isomer obtained in the other similar cases (7a, 7a', 7b, and 7c, 7c') also possesses the trans configuration. The differences observed in the cis/trans ratios of the cycloadducts resulting from the same sulfine (but different dienes) suggest sulfine isomerization, which could maybe occur under the reaction conditions via addition/elimination of a nucleophile (the tertiary amine used as the base or the Cl⁻ ion).

![Scheme 3](image)

**Table 1**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Sulfone</th>
<th>R</th>
<th>Base</th>
<th>Cycloadduct</th>
<th>dr a major/minor (%)</th>
<th>Isolated yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5a</td>
<td>Me</td>
<td>NEt₃</td>
<td>7a</td>
<td>67/33</td>
<td>75</td>
</tr>
<tr>
<td>2</td>
<td>5a</td>
<td>H</td>
<td>NEt₃</td>
<td>7a'</td>
<td>53/47</td>
<td>62</td>
</tr>
<tr>
<td>3</td>
<td>5b</td>
<td>Me</td>
<td>2,6-lutidine</td>
<td>7b</td>
<td>81/19</td>
<td>75</td>
</tr>
<tr>
<td>4</td>
<td>5b</td>
<td>H</td>
<td>2,6-lutidine</td>
<td>7b'</td>
<td>57/43 b</td>
<td>67</td>
</tr>
<tr>
<td>5</td>
<td>5c</td>
<td>Me</td>
<td>NEt₃</td>
<td>7c</td>
<td>87/13</td>
<td>78</td>
</tr>
<tr>
<td>6</td>
<td>5c</td>
<td>H</td>
<td>NEt₃</td>
<td>7c'</td>
<td>67/33</td>
<td>66</td>
</tr>
<tr>
<td>7</td>
<td>5d</td>
<td>Me</td>
<td>2,6-lutidine</td>
<td>7d</td>
<td>100/0 b</td>
<td>88</td>
</tr>
<tr>
<td>8</td>
<td>5e</td>
<td>Me</td>
<td>2,6-lutidine</td>
<td>7e</td>
<td>100/0</td>
<td>74</td>
</tr>
</tbody>
</table>

aDiastereomeric ratio determinated by ¹H NMR; trans and cis isomers were not assigned. bTrans relative configuration was assigned to the major isomer.
Then, we performed the reaction between the sulfine generated from methyl-2-pyridyl phenylsulfone 5d with the 2,3-dimethyl-1,3-butadiene. The expected cycloadduct 7d was obtained with a good isolated yield of 88% and as a single isomer (Table 1, entry 7). It was possible again to obtain a single crystal of this product and its analysis by X-ray diffraction showed a relative trans stereochemical arrangement between the phenylsulfonyl group and the sulfinyl oxygen atom (Figure 3). This supposes that the E sulfine\textsuperscript{11} was selectively formed \textit{in situ}. A similar result was obtained starting from the quinoline sulfone derivative 5e, which led to cycloadduct 7e in 74% yield and as a single isomer, having very probably also trans configuration (Table 1, entry 8).

![Figure 2. X-ray structure of the minor cis isomer of cycloadduct 7b.](image)

![Figure 3. X-ray structure of the single trans isomer of cycloadduct 7d.](image)

**Conclusions**

These results show that in the 5a-c sulfones series, when the sulfonyl group and the second substituent on the sulfine carbon have comparable electronwithdrawing effect, the sulfine is
formed as a mixture of \(Z\) and \(E\) isomers, leading respectively to the corresponding \(cis\) and \(trans\) isomers of the cycloadduct, with low to moderate selectivities (53/47 to 87/13 ratio). For sulfones \(5d\) and \(5e\), due to the much stronger electron-withdrawing effect of the sulfonyl group compared to pyridyl or quinolyl substituent, only one isomer of the cycloadduct was obtained. Crystals of cycloadducts \(7b'\) (carboxylsulfonylsulfine with butadiene) and \(7d\) (2-pyridyl sulfonylsulfine with 2,3-dimethylbutadiene) were isolated and analyzed by X-ray diffraction; the stereochemical arrangement was \(cis\) for the minor isomer of \(7b'\) and \(trans\) for the single isomer of \(7d\). Synthetic applications of the obtained cycloadducts are currently under examination in our laboratory.

**Experimental Section**

**General.** The solvents used in the reactions were purified using a PURESOLV™ apparatus developed by Innovative Technology Inc. Reactions were monitored by TLC using 0.25 mm thick Merck plates, silica gel 60 F254. Products were purified by flash column chromatography on silica gel Merck (40-63 \(\mu\)m, 60.08 g/mol). NMR spectra were recorded with a Bruker DRX 400 MHz or a Bruker DRX 500 MHz spectrometer in CDCl\(_3\). \(^{13}\)C and \(^{31}\)P NMR spectra were obtained with complete proton decoupling. The chemical shifts (\(\delta\)) are given in parts per millions (ppm) relative to tetramethylsilane (TMS) for \(^1\)H and \(^{13}\)C nuclei, and to H\(_2\)PO\(_4\) for \(^{31}\)P nucleus. Conventional abbreviations are used: \(s\) = singlet, \(d\) = doublet, \(t\) = triplet, \(q\) = quartet, \(qn\) = quintet, \(m\) = multiplet, \(br\) = broad. Coupling constants (\(J\)) are given in Hertz (Hz). Mass spectra were obtained on a GC/MS Saturn 2000 spectrometer. High-resolution mass spectra (HRMS) were performed on Q-TOF Micro Waters by electrospray ionisation (ESI). Infrared (IR) spectra were recorded with a Perkin Elmer 16 PC FT-IR spectrometer.

Sulfones \(5a\) (RN: 206256-73-7), \(^{12}\) \(5b\) (RN: 7605-30-3), \(^{5}\) \(5d\),\(^{10}\) and \(5e\) (RN: 65492-27-5)\(^{10}\) have been prepared as previously described in the literature.

**Synthesis of 3-(2-phenylsulfonylacetyl)oxazolidin-2-one (5c).** A mixture of 3-(2-chloroacetyl)oxazolidin-2-one (RN: 460313-68-2; 10 mmol), sodium benzenesulfinate (15 mmol), and catalytic amount of tetrapropylammonium bromide (2 mmol), in acetonitrile (20 mL), was refluxed for 12h. Then the solvent was removed under vacuum and the residue was dissolved in dichloromethane (20 mL), washed with brine (20 mL), dried (MgSO\(_4\)) and the solvent removed. The crude product was obtained in 56% as a white solid and was used without purification in the next step. \(^1\)H NMR (400.13 MHz, CDCl\(_3\) \(\delta\) 7.90 (d, \(J = 7.6\) Hz, 2H, H\(^ar\)), 7.62 (t, \(J = 6.0\) Hz, 1H, H\(^ap\)), 7.52 (m, 2H, H\(^ar\)), 4.87 (s, 2H, CH\(_2\)SO\(_2\)), 4.35 (t, \(J = 7.6\) Hz, 2H, CH\(_2\)O), 3.97 (t, \(J = 7.6\) Hz, 2H, CH\(_2\)N); \(^{13}\)C NMR (100.6 MHz, CDCl\(_3\) \(\delta\) 161.2 (C=O), 153.0 (NC=O), 139.3 (C\(^ar\)), 134.3 (C\(^ar\)), 129.3 (CH\(^ar\)), 128.5 (CH\(^ar\)), 62.2 (s, CH\(_2\)O), 59.5 (CH\(_2\)SO\(_2\)), 42.6 (CH\(_3\)N). HRMS Calcd for C\(_{11}\)H\(_{12}\)NO\(_5\)S [M+H] 270.0436. Found 270.0459. IR (neat): 2961,
1766, 1699, 1448, 1398, 1368, 1326, 1211, 1154, 1123, 1102, 1054, 1024, 998, 972, 759, 728, 687 cm⁻¹.

**General procedure for the thia-Diels-Alder reaction**

Under a nitrogen atmosphere a solution of sulfone 5 (1 mmol) and, as a base, 2,6-lutidine or triethylamine (2.1 mmol) in THF (5 mL), was added dropwise to a cooled (-78 °C) solution of thionyl chloride (88 µL, 1.2 mmol) and diene (2,3-dimethyl-1,3-butadiene or 1,3-butadiene, 5 to 10 mmol) in THF (10 mL). Once addition was complete, the temperature was allowed to rise slowly to room temperature and stirring was continued overnight. In the cases of substrates 5a-c, the crude reaction mixture was filtered, then the filtrate directly purified by chromatography on a silica gel column. In the cases of substrates 5d and 5e, the reaction mixture was poured into a saturated aqueous solution of NaHCO₃ (10 mL), the organic layer separated, the aqueous layer extracted again with CH₂Cl₂ (20 mL), and the combined organic layers were dried (MgSO₄) and filtered. Removal of the solvents in vacuum gave the cycloadduct 7, which was purified by column chromatography (silica gel, ethyl acetate/pentane).

2-Phenylsulfonyl-3,6-dihydro-4,5-dimethyl-1-oxo-2H-thiopyran-2-diisopropylphosphonate (7a).

Prepared by the general procedure from diisopropyl 2-phenylsulfonylmethylphosphonate 5a and 2,3-dimethyl-1,3-butadiene, using triethylamine as a base. Flash chromatography (pentane/EtOAc, 1:1) afforded 336 mg (75% yield) of a mixture of trans and cis isomers (major/minor ratio: 67/33), as a brown oil.

**Major diastereoisomer.** ³¹P NMR (162.0 MHz, CDCl₃) δ 9.5. ¹H NMR (400.13 MHz, CDCl₃) δ 8.13 (d, J = 8.4 Hz, 2H, H⁺α), 7.61 (t, J = 7.6 Hz, 1H, H⁺α), 7.51 (t, J = 8.4 Hz, 2H, H⁺β), 4.93-4.85 (m, 2H, 2xCH-O), 3.85 and 3.49 (AB system, J = 15.7 Hz, 2H, SCH₂), 2.98 and 2.71 (ABX system, J = 16.6 Hz, 21.9 Hz and 11.3 Hz, 2H, CH₂), 1.72 (s, 3H, CH₃), 1.38 (s, 3H, CH₃), 1.38-1.26 (m, 12H, 4xCH₃). ¹³C NMR (100.6 MHz, CDCl₃) δ 138.4 (C⁺α), 134.2 (CH⁺α), 131.3 (2xCH⁺α), 128.7 (Cq), 128.0 (2xCH⁺β), 124.7 (Cq), 82.4 (d, J = 132.4 Hz, Cq), 74.2-72.1 (m, 2xCH), 54.5 (CH₂), 30.6 (CH₂), 24.0-23.3 (m, 4xCH₃), 19.9 (CH₃), 19.5 (CH₃).

**Minor diastereoisomer.** ³¹P NMR (162.0 MHz, CDCl₃) δ 9.4. ¹H NMR (400.13 MHz, CDCl₃) δ 8.09 (d, J = 8.4 Hz, 2H, H⁺α), 7.68 (t, J = 7.6 Hz, 1H, H⁺α), 7.56 (t, J = 8.4 Hz, 2H, H⁺β), 4.89-4.81 (m, 2H, 2xCH-O), 4.04 and 3.49 (AB system, J = 14.0 Hz, 2H, SCH₂), 3.20 and 2.80 (AB system, J = 15.2 Hz, 2H, CH₂), 1.82 (s, 6H, 2xCH₃), 1.34-1.17 (m, 12H, 4xCH₃). ¹³C NMR (100.6 MHz, CDCl₃) δ 137.1 (C⁺α), 134.4 (CH⁺α), 131.6 (2xCH⁺α), 129.1 (Cq), 128.4 (2xCH⁺β), 120.3 (Cq), 86.5 (d, J = 135.2 Hz, Cq), 73.4-73.0 (m, 2xCH), 53.6 (CH₂), 33.6 (CH₂), 24.2-23.2 (m, 4xCH₃), 20.1 (CH₃), 19.7 (CH₃). MSMS: [M+H]: 449 (27), 407 (100), 365 (29), 307 (13), 267 (21), 183 (14), 141 (10).HRMS Calcd for C₁₉H₉₀O₈PS₂ [M+H] 449.1221. Found 449.1244. IR (neat): 2980, 1145, 1382, 1310, 1255, 1144, 1076, 981, 881, 811, 754, 680 cm⁻¹.

2-Phenylsulfonyl-3,6-dihydro-1-oxo-2H-thiopyran-2-diisopropylphosphonate (7a*).

Prepared by the general procedure from diisopropyl 2-phenylsulfonylmethylphosphonate 5a and 1,3-butadiene, using triethylamine as a base. Flash chromatography (pentane/EtOAc, 2:8)
afforded 260 mg (62% yield) of a mixture of *trans* and *cis* isomers (major/minor ratio: 53/47), as a brown oil.

**Major diastereoisomer.** \(^{31}\)P NMR (162.0 MHz, CDCl\(_3\)) \(\delta\) 8.7. \(^1\)H NMR (400.13 MHz, CDCl\(_3\)) \(\delta\) 8.05 (d, \(J = 7.3\) Hz, 2H, H\(^{ar}\)), 7.62 (t, \(J = 7.2\) Hz, 1H, H\(^{ar}\)), 7.50 (t, \(J = 8.4\) Hz, 2H, H\(^{ar}\)), 5.90-5.82 (m, 1H, CH), 5.70-5.62 (m, 1H, CH), 4.96-4.80 (m, 2H, 2xCH-O), 4.00 and 3.52 (ABX system, \(J = 17.2\) Hz and 4.9 Hz, 2H, SCH\(_2\)), 3.06-2.81 (m, 2H, CH\(_2\)), 1.39-1.18 (m, 12H, 4xCH\(_3\)). \(^{13}\)C NMR (100.6 MHz, CDCl\(_3\)) \(\delta\) 137.8 (C\(^{ar}\)), 134.4 (CH\(^{ar}\)), 131.6 (2xCH\(^{ar}\)), 128.3 (2xCH\(^{ar}\)), 127.3 (CH), 117.9 (CH), 84.7 (d, \(J = 133.2\) Hz, Cq), 74.0-73.7 (m, 2xCH), 50.0 (CH\(_2\)), 26.9 (CH\(_2\)), 24.4-23.7 (m, 4xCH\(_3\)).

**Minor diastereoisomer.** \(^{31}\)P NMR (162.0 MHz, CDCl\(_3\)) \(\delta\) 9.3. \(^1\)H NMR (400.13 MHz, CDCl\(_3\)) \(\delta\) 8.09 (d, \(J = 7.3\) Hz, 2H, 2Har), 7.68 (t, \(J = 7.4\) Hz, 1H, Har), 7.55 (t, \(J = 8.0\) Hz, 2H, Har), 5.94 (dt, \(J = 9.9\) Hz and 4.8 Hz, 1H, CH), 5.78 (dt, \(J = 10.2\) Hz and 5.2 Hz, 1H, CH), 4.96-4.82 (m, 2H, 2xCH-O), 4.05 and 3.81 (ABX system, \(J = 14.7\) Hz, 6.0 Hz and 5.0 Hz, 2H, SCH\(_2\)), 3.24 and 2.92 (ABX system, \(J = 13.0\) Hz, 5.4 Hz and 4.7 Hz, 2H, CH\(_2\)), 1.39-1.20 (m, 12H, 4xCH\(_3\)). \(^{13}\)C NMR (100.6 MHz, CDCl\(_3\)) \(\delta\) 137.8 (C\(^{ar}\)), 134.6 (CH\(^{ar}\)), 131.5 (2xCH\(^{ar}\)), 128.5 (2xCH\(^{ar}\)), 127.3 (CH), 119.9 (CH), 84.7 (d, \(J = 133.2\) Hz, Cq), 74.0-73.7 (m, 2xCH), 48.7 (CH\(_2\)), 26.9 (CH\(_2\)), 24.4-23.7 (m, 4xCH\(_3\)).

**2-Phenylsulfonyl-3,6-dihydro-4,5-dimethyl-1-oxo-2\(^{1}\)H-thiopyran-2-ethylcarboxylate (7b).** Prepared by the general procedure from ethyl 2-methylsulfonylacetate 5b and 2,3-dimethyl-1,3-butadiene, using 2,6-lutidine as a base. Flash chromatography (pentane/EtOAc, 1:1) afforded 267 mg (75% yield) of a mixture of *trans* and *cis* isomers (major/minor ratio: 81/19), as a brown oil. As this compound was already described, \(^5\) only some spectral and physical data of the major isomer are given here.

**Major diastereoisomer.** \(^1\)H NMR (400.13 MHz, CDCl\(_3\)) \(\delta\) 7.92 (d, \(J = 8.4\) Hz, 2H, H\(^{ar}\)), 7.69 (t, \(J = 8.4\) Hz, 1H, H\(^{ar}\)), 7.56 (t, \(J = 16.5\) Hz, 2H, SCH\(_2\)), 7.56 (t, \(J = 16.5\) Hz, 2H, SCH\(_2\)), 1.75 (s, 3H, CH\(_3\)), 1.72 (s, 3H, CH\(_3\)), 1.11 (t, \(J = 7.0\) Hz, 3H, CH\(_3\)). MSMS: [M+H] 357 (57), 215 (100), 197 (97), 169 (13), 165 (38). HRMS Calcd for C\(_{17}\)H\(_{26}\)O\(_5\)S\(_2\) [M+H] 357.0830. Found 357.0827. IR (neat): 2985, 1729, 1448, 1393, 1325, 1225, 1147, 1059, 1022, 912, 854, 800, 761, 687.

**2-Phenylsulfonyl-3,6-dihydro-1-oxo-2\(^{1}\)H-thiopyran-2-ethylcarboxylate (7b’).** Prepared by the general procedure from ethyl 2-methylsulfonylacetate 5b and 1,3-butadiene, using 2,6-lutidine as a base. Flash chromatography (pentane/EtOAc, 4:6) afforded 220 mg (67% yield) of a mixture of *trans* and *cis* isomers (major/minor ratio: 57/43), as a brown oil. The product (100 mg) was dissolved in a mixture of pentane/EtOAc 8:2 (1 mL) and by a long standing at the room temperature (about two weeks on the bench), crystals of minor 7b’ were separated from the solution which contained both isomers in the mixture.

**Major diastereoisomer.** Aspect: brown oil. \(^1\)H NMR (400.13 MHz, CDCl\(_3\)) \(\delta\) 7.92 (d, \(J = 8.4\) Hz, 2H, H\(^{ar}\)), 7.71 (t, \(J = 7.6\) Hz, 1H, H\(^{ar}\)), 7.61-7.26 (m, 2H, H\(^{ar}\)), 6.03-5.93 (m, 1H, CH), 5.77-5.65 (m, 1H, CH), 4.27-4.17 (m, 2H, OCH\(_2\)), 4.03-3.93 and 3.65-3.58 (m, 2H, SCH\(_2\)).
and 2.99-2.96 (m, 2H, CH₂), 1.11 (t, J = 7.2 Hz, 3H, CH₃). ¹³C NMR (100.6 MHz, CDCl₃) δ 163.8 (C=O), 136.8 (Cₐr), 135.2 (CHₐr), 130.1 (2xCHₐr), 129.1 (2xCHₐr), 125.3 (CH), 116.7 (CH), 85.5 (Cq), 63.7 (O-CH₂), 47.6 (CH₂), 24.5 (CH₂), 13.6 (CH₃).

**Minor diastereoisomer.** Aspect: brown crystals; mp 135-136 °C. ¹H NMR (400.13 MHz, CDCl₃) δ 8.00 (d, J = 8.4 Hz, 2H, Har), 7.74 (t, J = 7.4 Hz, 1H, Har), 7.61 (t, J = 8.2 Hz, 2H, Har), 6.02-5.98 (m, 1H, CH), 5.57-5.53 (m, 1H, CH), 4.26-4.20 (m, 2H, OCH₂), 3.35-3.32 (m, 2H, SCH₂), 3.01-2.97 (m, 2H, CH₂), 1.27 (t, J = 7.1 Hz, 3H, CH₃). ¹³C NMR (100.6 MHz, CDCl₃) δ 163.5 (C=O), 136.8 (Cₐr), 135.2 (CHₐr), 130.7 (2xCHₐr), 129.1 (2xCHₐr), 126.4 (CH), 115.1 (CH), 86.1 (Cq), 63.6 (O-CH₂), 47.4 (CH₂), 20.8 (CH₂), 13.7 (CH₃). MSMS: [M+Na] 351 (50), [M+H] 329 (100), 187 (41), 186 (55). HRMS Calcd for C₁₄H₁₇O₅S₂ [M+H] 329.0517. Found 329.0527. IR (neat): 2985, 1729, 1448, 1393, 1325, 1225, 1147, 1059, 1022, 912, 854, 800, 761, 716, 687.

Crystal data of minor 7b’. Bruker Kappa APEXII CCD diffractometer (Mo Kα λ=0.71073 Å; graphite monochromator; T=100(2)K). Formula C₁₄H₁₆O₅S₂, formula weight 328.39, crystal system monoclinic, space group P2₁, crystal dimensions 0.39 x 0.26 x 0.11 mm³, a=8.5112(2), b=7.5858(2), c=11.4014(2) Å, β=101.299(1)°, V=721.86(3) Å³, Z=2, ρcalcld=1.511 Mgm⁻³, μ=0.39 mm⁻¹, θmax=74.00°, 25175 measured reflections, 5279 independent reflections (Rint=0.025), R₁ [I>2σ(I)]=0.023, wR2 [I>2σ(I)]= 0.058, GO=1.04, 254 parameters, final difference map within 0.31 and -0.23 eÅ⁻³. The structure was solved using direct methods and refined by full-matrix least-squares analysis on F². Numerical absorption corrections were applied (G. M. Sheldrick SHELXTL, Bruker ACS Inc.: Madison, WI, 2008). CCDC 784819 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif. Selected bond lengths (Å) and angles (deg): S₁-O₁ 1.4954(8), S₁-C₁ 1.8625(8), S₂-O₄ 1.4390(9), S₂-O₅ 1.4396(8), S₂-C₁ 1.8508(9), C₄-C₃ 1.3307(15), S₁-C₁-S₂ 108.21(4), S₁-C₁-C₂ 109.41(7), C₄-C₃-C₅ 126.19(9), C₂-C₃-C₄ 125.20(9).

2-Phenylsulfonyl-3,6-dihydro-4,5-dimethyl-1-oxo-2H-thiopyran-2-(acetoxazolidin-2-one) (7c). Prepared by the general procedure from sulfone 5c and 2,3-dimethyl-1,3-butadiene, using triethylamine as a base. Flash chromatography (pentane/EtOAc, 1:1) afforded 309 mg (78% yield) of a mixture of trans and cis isomers (major/minor ratio: 87/13), as a brown oil.

**Major diastereoisomer.** Aspect: brown paste; Rf (cyclohexane/EtOAc: 1:1) = 0.15.

¹H NMR (500.13 MHz, CDCl₃) δ 7.88 (d, J = 7.4 Hz, 2H, Hₐr), 7.69 (t, J = 7.6 Hz, 1H, Hₐr), 7.56 (t, J = 8.2 Hz, 2H, Hₐr), 4.49 (t, J = 7.8 Hz, 2H, CH₂O), 4.19 (t, J = 7.8 Hz, 2H, CH₂N), 4.06 and 3.32 (AB system, J = 17.7 Hz, 2H, SCH₂), 3.17 and 2.85 (AB system, J = 18.3 Hz, 2H, CH₂), 1.67 (s, 3H, CH₃), 1.63 (s, 3H, CH₃). ¹³C NMR (100.6 MHz, CDCl₃) δ 163.8 (C=O), 151.7 (C=O), 138.0 (Cₐr), 134.5 (CHₐr), 131.9 (CHₐr), 130.0 (CHₐr), 128.6 (CHₐr), 124.8 (Cq), 118.6 (Cq), 89.6 (Cq), 62.7 (O-CH₂), 52.2 (CH₂), 45.0 (N-CH₂), 30.9 (CH₂), 19.5 (CH₃), 19.3 (CH₃).

**Minor diastereoisomer.** Aspect: brown oil; Rf (cyclohexane/EtOAc: 1:1) = 0.54.

¹H NMR (500.13 MHz, CDCl₃) δ 7.90 (d, J = 8.5 Hz, 2H, Hₐr), 7.68 (t, J = 7.5 Hz, 1H, Hₐr), 7.56 (t, J = 8.0 Hz, 2H, Hₐr), 4.62-4.35 (m, 2H, CH₂O), 4.43-4.24 (m, 2H, CH₂N), 3.12 and 2.82 (AB
system, $J = 14.2$ Hz, 2H, SCH$_2$), 3.09 and 2.45 (AB system, $J = 14.2$ Hz, 2H, CH$_2$), 1.76 (s, 3H, CH$_3$), 1.72 (s, 3H, CH$_3$). $^{13}$C NMR (100.6 MHz, CDCl$_3$) δ 164.6 (C=O), 152.4 (C=O), 135.5 (C$^\alpha$), 134.5 (CH$^\alpha$), 130.5 (CH$^{\beta}$), 129.5 (CH$^\alpha$), 128.8 (CH$^{\beta}$), 128.1 (Cq), 125.5 (Cq), 83.8 (Cq), 62.5 (O-CH$_2$), 45.6 (N-CH$_2$), 37.9 (CH$_2$), 32.7 (CH$_2$), 19.2 (CH$_3$), 18.4 (CH$_3$). HRMS Calcd for C$_{17}$H$_{20}$NO$_6$S$_2$ [M+H]$^+$ 398.0732. Found 398.0724. IR (neat): 2915, 1784, 1673, 1582, 1476, 1447, 1438, 1385, 1361, 1308, 1197, 1147, 1120, 1040, 998, 778, 753, 720, 688 cm$^{-1}$.

2-Phenylsulfonyl-3,6-dihydro-1-oxo-2H-thiopyran-2-(acetyloxazolidin-2-one) (7c'). Prepared by the general procedure from sulfone 5c and 1,3-butadiene, using triethylamine as a base. Flash chromatography (pentane/EtOAc, 2:8) afforded 243 mg (66% yield) of a mixture of trans and cis isomers (major/minor ratio: 67/33), as a brown oil.

**Major diastereoisomer.** Aspect: brown oil; Rf (cyclohexane/EtOAc: 2/8) = 0.72. $^1$H NMR (500.13 MHz, CDCl$_3$) δ 7.95 (d, $J = 8.3$ Hz, 2H, H$^{\alpha}$), 7.68 (t, $J = 7.5$ Hz, 1H, H$^{\beta}$), 7.56 (t, $J = 7.5$ Hz, 2H, H$^{\alpha}$), 6.10-5.95 (m, 1H, CH), 5.89-5.85 (m, 1H, CH), 4.56-4.36 (m, 2H, CH$_2$O), 4.42-4.27 (m, 2H, CH$_2$N), 4.20-4.03 and 3.27-3.13 (m, AB system, 2H, SCH$_2$), 3.27 and 2.71 (AB system, $J = 14.7$ Hz, 2H, CH$_2$). $^{13}$C NMR (100.6 MHz, CDCl$_3$) δ 165.0 (C=O), 152.2 (C=O), 136.1 (C$^\alpha$), 134.5 (CH$^\alpha$), 130.9 (2xCH$^{\beta}$), 128.4 (2xCH$^\alpha$), 126.3 (CH), 124.7 (CH), 80.4 (Cq), 62.6 (O-CH$_2$), 45.7 (N-CH$_2$), 30.1 (CH$_2$), 26.5 (CH$_2$). HRMS Calcd for C$_{15}$H$_{16}$NO$_6$S$_2$ [M+H]$^+$ 370.0419. Found 370.0424. IR (neat): 3063, 2981, 2924, 1778, 1682, 1583, 1476, 1447, 1385, 1362, 1308, 1217, 1191, 1079, 1038, 998, 982, 911, 754, 728, 717, 686 cm$^{-1}$.

Minor diastereoisomer. Aspect: brown oil; Rf (cyclohexane/EtOAc: 1/1) = 0.32. $^1$H NMR (500.13 MHz, CDCl$_3$) δ 8.10 (d, $J = 8.5$ Hz, 2H, H$^{\alpha}$), 7.68 (t, $J = 7.5$ Hz, 1H, H$^{\beta}$), 7.56 (t, $J = 8.0$ Hz, 2H, H$^{\alpha}$), 5.91-5.84 (m, 1H, CH), 5.64-5.59 (m, 1H, CH), 5.52-5.39 (m, 2H, CH$_2$O), 4.23-3.95 (m, 2H, CH$_2$N), 3.78 and 3.24 (ABX system, $J = 17.9$ Hz, 2.7 Hz and 2.0 Hz, 2H, CH$_2$). $^{13}$C NMR (100.6 MHz, CDCl$_3$) δ 164.6 (C=O), 151.3 (C=O), 135.0 (C$^\alpha$), 132.7 (CH$^{\beta}$), 131.9 (CH$^{\alpha}$), 128.9 (CH$^\alpha$), 128.4 (CH$^{\beta}$), 125.9 (CH), 119.1 (CH), 90.6 (Cq), 62.6 (O-CH$_2$), 59.0 (CH$_2$), 50.1 (CH$_2$). HRMS Calcd for C$_{15}$H$_{16}$NO$_6$S$_2$ [M+H]$^+$ 370.0419. Found 370.0424. IR (neat): 3063, 2981, 2924, 1778, 1682, 1583, 1476, 1447, 1385, 1362, 1308, 1217, 1142, 1079, 1038, 998, 982, 911, 754, 728, 717, 686 cm$^{-1}$.

2-Phenylsulfonyl-3,6-dihydro-4,5-dimethyl-1-oxo-2H-thiopyran-2-(2-pyridine) (7d). Prepared by the general procedure from 2-phenylsulfonylmethylpyridine 5d and 2,3-dimethyl-1,3-butadiene, using 2,6-lutidine as a base. Flash chromatography (pentane/EtOAc, 2:1 to 1:2) afforded 0.319 g (88% yield) of a white crystalline solid, mp 151 °C. The product (100 mg) was dissolved in a mixture of pentane/EtOAc 6:4 (1 mL) and by standing at the room temperature, on the bench, about three days, crystals of 7d were separated from the solution.

$^1$H NMR (400.13 MHz, CDCl$_3$) δ 8.42 (m, 1H), 7.93 (m, 1H), 7.51 (m, 4H), 7.31 (m, 2H), 7.19 (m, 2H), 3.50 (AB, $J = 16.2$ Hz, 2H, SCH$_2$), 2.97 & 2.82 (AB, $J = 17.3$ Hz, 2H, CH$_2$), 1.68 (s, 3H, CH$_3$), 1.49 (s, 3H, CH$_3$). $^{13}$C NMR (100.6 MHz, CDCl$_3$) δ 149.1, 148.6, 135.9, 134.3, 130.3, 128.6, 127.3, 126.8, 124.4, 117.3, 85.8, 53.1, 33.4, 19.6, 19.4. HRMS Calcd for C$_{18}$H$_{20}$NO$_6$S$_2$ (M+H) 362.0885. Found 362.0888. IR (neat) 1582, 1434, 1310, 1148, 1082, 1059, 877, 845, 797, 746, 715, 688 cm$^{-1}$.
Crystal data of (7d). Bruker Kappa APEXII CCD diffractometer (Mo Kα λ=0.71073 Å; graphite monochromator; T=291(2)K). Formula C_{15}H_{19}NO_{3}S_{2}, formula weight 361.46, crystal system orthorhombic, space group Pca₂₁, crystal dimensions 0.48 x 0.38 x 0.28 mm³, a=13.311(4), b=8.819(2), c=15.078(6) Å, α=β=γ=90.00°, V=1769.9(10) Å³, Z=4, ρ_{calc}=1.357 Mgm⁻³, μ=0.32 mm⁻¹, 2θ_{max}=63.26°, 47345 measured reflections, 5897 independent reflections (R_{int}= 0.024), R₁ [I>2σ(I)]=0.032, wR₂ [I>2σ(I)]= 0.090, GOF=1.03, 219 parameters, final difference map within 0.35 and -0.20 eÅ⁻³. The structure was solved using direct methods and refined by full-matrix least-squares analysis on F². Numerical absorption corrections were applied (G. M. Sheldrick SHELXTL, Bruker ACS Inc.: Madison, WI, 2008). CCDC 784818 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif. Selected bond lengths (Å) and angles (deg): S1-O2 1.4345(12), S1-O3 1.4418(13), S1-C1 1.8282(15), S2-O1 1.4841(16), S2-C1 1.8677(13), C3-C4 1.334(2), C2-C3-C4 124.30(14), C3-C4-C5 122.75(14), C8-C1-S2 115.68(9), C2-C1-S2 102.97(9), S1-C1-S2 103.45(6).

2-Phenylsulfonyl-3,6-dihydro-4,5-dimethyl-1-oxo-2H-thiopyran-2-(2-quinoline) (7e). Prepared by the general procedure from 2-phenylsulfonylmethylquinoline 5e and 2,3-dimethyl-1,3-butadiene, using 2,6-lutidine as a base. Flash chromatography (pentane/EtOAc, 2:1 to 1:2) afforded 0.305 g (74% yield) of a white powder, mp 181 °C. ¹H NMR (400.13 MHz, CDCl₃) δ 8.21 (d, J = 11.4 Hz, 1H), 7.88 (d, J = 17.5 Hz, 1H), 7.15-7.35 (m, 7H), 7.42 (m, 2H), 3.66 (AB, J = 17.4 Hz, 1H, CH₃), 3.27 & 3.09 (AB, J = 17.5 Hz, 2H, CH₂), 2.90 (AB, J = 17.4 Hz, 1H, CH₃), 1.60 (s, 3H, CH₃), 1.46 (s, 3H, CH₃); ¹³C NMR (100.6 MHz, CDCl₃) δ 152.3, 146.8, 136.8, 135.4, 134.3, 130.8, 130.0, 129.2, 128.4, 127.8, 127.6, 127.5, 124.9, 120.6, 116.5, 85.5, 51.9, 25.6, 20.8, 19.1. HRMS Calcd for C_{22}H_{22}NO_{3}S_{2} (M+H) 412.1041. Found 412.1022. IR (neat) 1501, 1310, 1146, 1082, 1060, 832, 803, 759, 691 cm⁻¹.

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