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

Hélène Dentel, Jean-François Lohier and Mihaela Gulea*

Laboratoire de Chimie Moléculaire et Thioorganique, UMR CNRS 6507, INC3M, FR 3038, ENSICAEN, Université de Caen Basse Normandie, 6, Bd. Maréchal Juin, 14050 Caen, France
E-mail: mihaela.gulea@ensicaen.fr

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

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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.

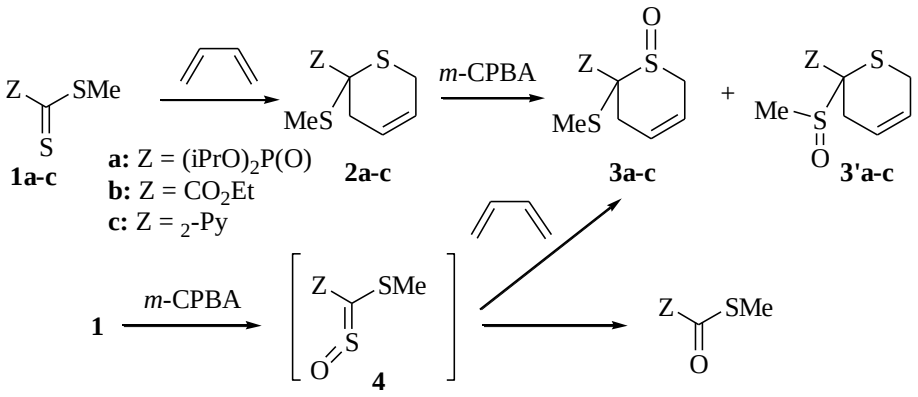
Keywords: *thia*-Diels-Alder reaction, sulfones, sulfines, thiopyran *S*-oxide

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

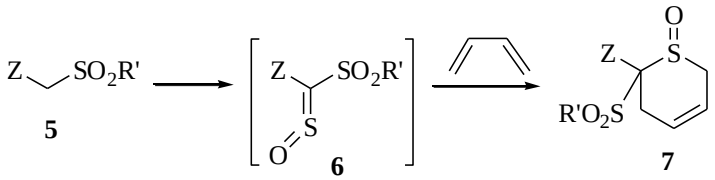
step, as they belong to the thiocarbonyl heterodienophile or to the diene, or they were introduced by subsequent reactions in particular on the cycloadduct double bond.

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.[1k, 3] 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**[3a] and **3b**,[4] 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 complexe mixture.[4] 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 **1** (Scheme 1).[5] 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].[6] 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 electronwithdrawing 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 ($SOCl_2$), in the presence of a base,[5, 7] then trapped *in situ* by a HDA reaction with a diene.[8]



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** (ZCH_2SO_2Ph) in which the substituent Z is a phosphonyl, carboxylate, carboxyoxazolidinone, 2-pyridyl, or a 2-quinolyl group (Figure 1). The corresponding dithioesters (ZCS_2Me) having the same Z substituents have already been used in our laboratory in HDA reaction.[1h-j, 4] Sulfonyl methylphosphonate **5a** was obtained by oxidation with *m*-CPBA of the corresponding sulfide [$(iPrO)_2P(O)CH_2SPh$], which were prepared from diisopropyl α-hydroxymethylphosphonate [$(iPrO)_2P(O)CH_2OH$] by a reported procedure.[9] Sulfones **5b-e** were prepared from the corresponding chlorides (ZCH_2Cl) and sodium benzenesulfinate ($PhSO_2Na$) by a reported procedure.[10]

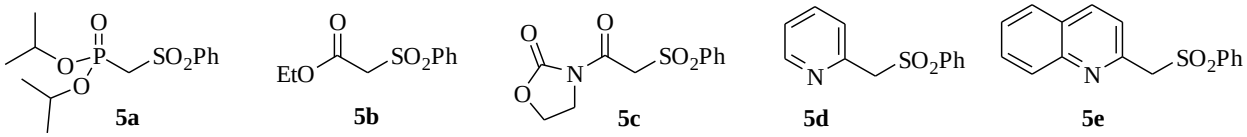
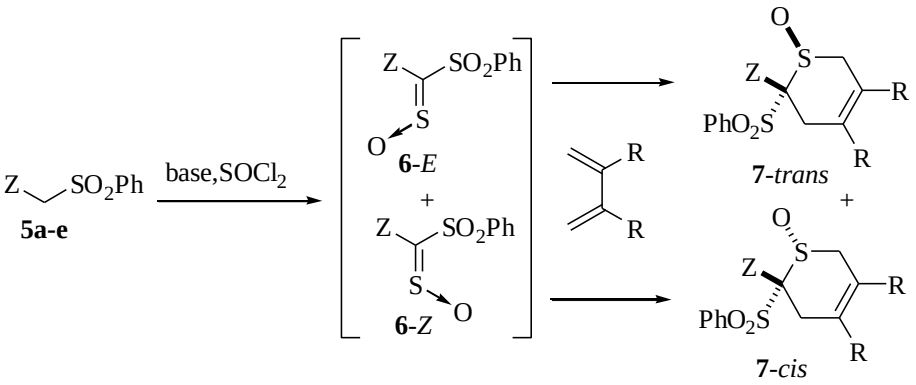


Figure 1

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**, $SOCl_2$ 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 **7c'** 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**,**a'**, **7b**, and **7c**,**c'**) 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

Table 1

Entry	Sulfone	R	Base	Cycloadduct	dr [a] major/minor (%)	Isolated yield (%)
1	**5a**	Me	NEt_3	**7a**	67/33	75
2	**5a**	H	NEt_3	**7a'**	53/47	62
3	**5b**	Me	2,6-lutidine	**7b**	81/19	75
4	**5b**	H	2,6-lutidine	**7b'**	57/43 [b]	67
5	**5c**	Me	NEt_3	**7c**	87/13	78
6	**5c**	H	NEt_3	**7c'**	67/33	66
7	**5d**	Me	2,6-lutidine	**7d**	100/0 [b]	88
8	**5e**	Me	2,6-lutidine	**7e**	100/0	74

[a]Diastereomeric ratio determinated by ^{1}H NMR; *trans* and *cis* isomers were not assigned. [b]*Trans* 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[11] was selectively formed *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).

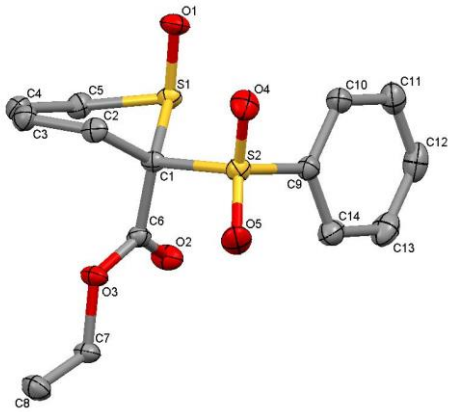


Figure 2. X-ray structure of the minor *cis* isomer of cycloadduct **7b'.**

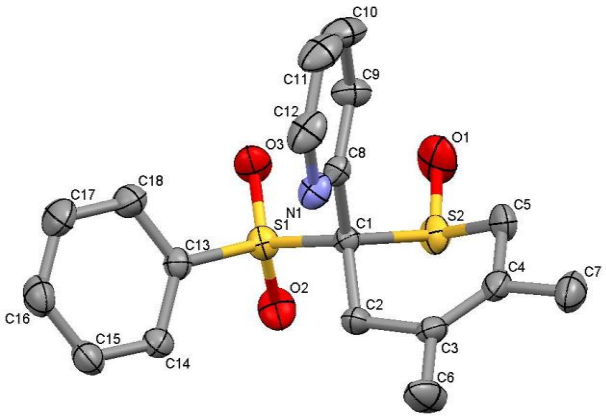


Figure 3. X-ray structure of the single *trans* isomer of cycloadduct **7d.**

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 electronwithdrawing 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 μm, 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 (δ) are given in parts per millions (ppm) relative to tetramethylsilane (TMS) for ^{1}H and ^{13}C nuclei, and to H_3PO_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, $CDCl_3$) δ 7.90 (d, *J* = 7.6 Hz, 2H, H^{ar}), 7.62 (t, *J* = 6.0 Hz, 1H, H^{ar}), 7.52 (m, 2H, H^{ar}), 4.87 (s, 2H, CH_2SO_2), 4.35 (t, *J* = 7.6 Hz, 2H, CH_2-O),

3.97 (t, *J* = 7.6 Hz, 2H, CH_2N); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 161.2 (C=O), 153.0 (NC=O), 139.3 (C^{ar}), 134.3 (CH^{ar}), 129.3 (CH^{ar}), 128.5 (CH^{ar}), 62.2 (s, CH_2O), 59.5 (CH_2SO_2), 42.6 (CH_2N). HRMS Calcd for $C_{11}H_{12}NO_5S$ [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 $NaHCO_3$ (10 mL), the organic layer separated, the aqueous layer extracted again with CH_2Cl_2 (20 mL), and the combined organic layers were dried ($MgSO_4$) 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-2*H*-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. ^{31}P NMR (162.0 MHz, $CDCl_3$) δ 9.5. ^1H NMR (400.13 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.4 Hz, 2H, H^{ar}), 7.61 (t, *J* = 7.6 Hz, 1H, H^{ar}), 7.51 (t, *J* = 8.4 Hz, 2H, H^{ar}), 4.93-4.85 (m, 2H, 2xCH-O), 3.85 and 3.49 (AB system, *J* = 15.7 Hz, 2H, SCH_2), 2.98 and 2.71 (ABX system, *J* = 16.6 Hz, 21.9 Hz and 11.3 Hz, 2H, CH_2), 1.72 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 1.38-1.26 (m, 12H, 4xCH_3). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 138.4 (C^{ar}), 134.2 (CH^{ar}), 131.3 (2xCH^{ar}), 128.7 (Cq), 128.0 (2xCH^{ar}), 124.7 (Cq), 82.4 (d, *J* = 132.4 Hz, Cq), 74.2-72.1 (m, 2xCH), 54.5 (CH_2), 30.6 (CH_2), 24.0-23.3 (m, 4xCH_3), 19.9 (CH_3), 19.5 (CH_3).

Minor diastereoisomer. ^{31}P NMR (162.0 MHz, $CDCl_3$) δ 9.4. ^1H NMR (400.13 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.4 Hz, 2H, H^{ar}), 7.68 (t, *J* = 7.6 Hz, 1H, H^{ar}), 7.56 (t, *J* = 8.4 Hz, 2H, H^{ar}), 4.89-4.81 (m, 2H, 2xCH-O), 4.04 and 3.49 (AB system, *J* = 14.0 Hz, 2H, SCH_2), 3.20 and 2.80 (AB system, *J* = 15.2 Hz, 2H, CH_2), 1.82 (s, 6H, 2xCH_3), 1.34-1.17 (m, 12H, 4xCH_3). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 137.1 (C^{ar}), 134.4 (CH^{ar}), 131.6 (2xCH^{ar}), 129.1 (Cq), 128.4 (2xCH^{ar}), 120.3 (Cq), 86.5 (d, *J* = 135.2 Hz, Cq), 73.4-73.0 (m, 2xCH), 53.6 (CH_2), 33.6 (CH_2), 24.2-23.2 (m, 4xCH_3), 20.1 (CH_3), 19.7 (CH_3). MSMS: [M+H]: 449 (27), 407 (100), 365 (29), 307 (13), 267 (21), 183 (14), 141 (10).HRMS Calcd for $C_{19}H_{30}O_6PS_2$ [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-2*H*-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, $CDCl_3$) δ 8.7. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 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, $CDCl_3$) δ 9.3. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 8.09 (d, *J* = 7.3 Hz, 2H, 2H^{ar}), 7.68 (t, *J* = 7.4 Hz, 1H, H^{ar}), 7.55 (t, *J* = 8.0 Hz, 2H, H^{ar}), 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, $CDCl_3$) δ 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). HRMS Calcd for $C_{17}H_{26}O_6PS_2$ [M+H] 421.0908. Found 421.0898. IR (neat): 2981, 1148, 1386, 1312, 1255, 1146, 1078, 981, 889, 813, 754, 686 cm^{-1}.

2-Phenylsulfonyl-3,6-dihydro-4,5-dimethyl-1-oxo-2*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, $CDCl_3$) δ 7.92 (d, *J* = 8.4 Hz, 2H, H^{ar}), 7.69 (t, *J* = 8.4 Hz, 1H, H^{ar}) 7.56 (t, *J* = 8.4 Hz, 2H, H^{ar}), 4.12-3.95 (m, 2H, O-CH_2), 3.76 and 3.52 (AB system, 2H, *J* = 16.5 Hz, 2H, SCH_2), 3.17 and 2.77 (AB system, *J* = 17.6 Hz, 2H, CH_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 $C_{16}H_{21}O_5S_2$ [M+H] 357.0830. Found 357.0827. IR (neat): 2985, 1729, 1448, 1393, 1325, 1225, 1147, 1059, 1022, 912, 854, 800, 761, 716, 687.

2-Phenylsulfonyl-3,6-dihydro-1-oxo-2*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, $CDCl_3$) δ 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), 3.21-3.12 and 2.99-2.96 (m, 2H, CH_2), 1.11 (t, *J* = 7.2 Hz, 3H, CH_3). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 163.8 (C=O), 136.8 (C^{ar}), 135.2 (CH^{ar}), 130.1 (2xCH^{ar}), 129.1 (2xCH^{ar}), 125.3 (CH), 116.7 (CH), 85.5 (Cq), 63.7 (O-CH_2), 47.6 (CH_2), 24.5 (CH_2), 13.6 (CH_3).

Minor diastereoisomer. Aspect: brown crystals; mp 135-136 °C. ^{1}H NMR (400.13 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.4 Hz, 2H, H^{ar}), 7.74 (t, *J* = 7.4 Hz, 1H, H^{ar}), 7.61 (t, *J* = 8.2 Hz, 2H, H^{ar}), 6,02-5.98 (m, 1H, CH), 5.57-5.53 (m, 1H, CH), 4.26-4.20 (m, 2H, OCH_2), 3.35-3.32 (m, 2H, SCH_2), 3.01-2.97 (m, 2H, CH_2), 1.27 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 163.5 (C=O), 136.8 (C^{ar}), 135.2 (CH^{ar}), 130.7 (2xCH^{ar}), 129.1 (2xCH^{ar}), 126.4 (CH), 115.1 (CH), 86.1 (Cq), 63.6 (O-CH_2), 47.4 (CH_2), 20.8 (CH_2), 13.7 (CH_3). MSMS: [M+Na] 351 (50), [M+H] 329 (100), 187 (41), 186 (55). HRMS Calcd for $C_{14}H_{17}O_5S_2$ [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 ($Mo_{K\alpha}$ λ=0.71073 Å; graphite monochromator; *T*=100(2)K). Formula $C_{14}H_{16}O_5S_2$, formula weight 328.39, crystal system monoclinic, space group $P2_1$, crystal dimensions 0.39 x 0.26 x 0.11 mm^3, *a*=8.5112(2), *b*=7.5858(2), *c*=11.4014(2) Å, β=101.299(1)°, *V*=721.86(3) $Å^3$, Z=2, ρ_{calcd}=1.511 Mgm^{-3}, μ□=0.39 mm^{-1}, $2\theta_{max}$=74.00°, 25175 measured reflections, 5279 independent reflections (R_{int}= 0.025), *R*1 [*I*>2σ(*I*)]=0.023, *wR*2 [*I*>2σ(*I*)]= 0.058, GOF=1.04, 254 parameters, final difference map within 0.31 and -0.23 e$Å^{-3}$. The structure was solved using direct methods and refined by full-matrix least-squares analysis on F^2. 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), C3-C4-C5 126.19(9), C2-C3-C4 125.20(9).

2-Phenylsulfonyl-3,6-dihydro-4,5-dimethyl-1-oxo-2*H*-thiopyran-2-(acetyloxazolidin-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.

^{1}H NMR (500.13 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.4 Hz, 2H, H^{ar}), 7.69 (t, *J* = 7.6 Hz, 1H, H^{ar}), 7.56 (t, *J* = 8.2 Hz, 2H, H^{ar}), 4.49 (t, *J* = 7.8 Hz, 2H, CH_2O), 4.19 (t, *J* = 7.8 Hz, 2H, CH_2N), 4.06 and 3.32 (AB system, *J* = 17.7 Hz, 2H, SCH_2), 3.17 and 2.85 (AB system, *J* = 18.3 Hz, 2H, CH_2), 1.67 (s, 3H, CH_3), 1.63 (s, 3H, CH_3). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 163.8 (C=O), 151.7 (C=O), 138.0 (C^{ar}), 134.5 (CH^{ar}), 131.9 (CH^{ar}), 130.0 (CH^{ar}), 128.6 (CH^{ar}), 124.8 (Cq), 118.6 (Cq), 89.6 (Cq), 62.7 (O-CH_2), 52.2 (CH_2), 45.0 (N-CH_2), 30.9 (CH_2), 19.5 (CH_3), 19.3 (CH_3).

Minor diastereoisomer. Aspect: brown oil; Rf (cyclohexane/EtOAc: 1/1) = 0.54.
^{1}H NMR (500.13 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.5 Hz, 2H, H^{ar}), 7.68 (t, *J* = 7.5 Hz, 1H, H^{ar}), 7.56 (t, *J* = 8.0 Hz, 2H, H^{ar}), 4.62-4.35 (m, 2H, CH_2O), 4.43-4.24 (m, 2H, CH_2N), 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^{ar}), 134.5 (CH^{ar}), 130.5 (CH^{ar}), 129.5 (CH^{ar}), 128.8 (CH^{ar}), 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 $C_{17}H_{20}NO_6S_2$ [M+H] 398.0732. Found 398.07245. 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-2*H*-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^{ar}), 7.68 (t, *J* = 7.5 Hz, 1H, H^{ar}), 7.56 (t, *J* = 7.5 Hz, 2H, H^{ar}), 6.10-5.95 (m, 1H, CH), 5.89-5.85 (m, 1H, CH), 4.56-4.36 (m, 2H, CH_2O), 4.42-4.27 (m, 2H, CH_2N), 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^{ar}), 134.5 (CH^{ar}), 130.9 (2xCH^{ar}), 128.4 (2xCH^{ar}), 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).

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^{ar}), 7.68 (t, *J* = 7.5 Hz, 1H, H^{ar}), 7.56 (t, *J* = 8.0 Hz, 2H, H^{ar}), 5.91-5.84 (m, 1H, CH), 5.64-5.59 (m, 1H, CH), 5.52-5.39 (m, 2H, CH_2O), 4.23-3.95 (m, 2H, CH_2N), 3.78 and 3.24 (ABX system, *J* = 17.9 Hz, 7.6 Hz and 2.5 Hz, 2H, SCH_2), 3.55 and 3.19 (ABX system, *J* = 18.4 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^{ar}), 132.7 (CH^{ar}), 131.9 (CH^{ar}), 130.9 (CH^{ar}), 128.8 (CH^{ar}), 128.4 (CH^{ar}), 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 $C_{15}H_{16}NO_6S_2$ [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-2*H*-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 $C_{18}H_{20}NO_3S_2$

(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 ($Mo_{K\alpha}$ λ=0.71073 Å; graphite monochromator; *T*=291(2)K). Formula $C_{18}H_{19}NO_3S_2$, formula weight 361.46, crystal system orthorhombic, space group $Pca2_1$, crystal dimensions 0.48 x 0.38 x 0.28 mm^3, *a*=13.311(4), *b*=8.819(2), *c*=15.078(6) Å, α=β=γ=90.00°, *V*=1769.9(10) $Å^3$, Z=4, ρ_{calcd}=1.357 Mgm^{-3}, μ□=0.32 mm^{-1}, $2\theta_{max}$=63.26°, 47345 measured reflections, 5897 independent reflections (R_{int}= 0.024), *R*1 [*I*>2σ(*I*)]=0.032, *wR*2 [*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 F^2. 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-2*H*-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. ^{1}H NMR (400.13 MHz, $CDCl_3$) 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, C<u>H</u>H), 3.27 & 3.09 (AB, *J* = 17.5 Hz, 2H, CH_2), 2.90 (AB, *J* = 17.4 Hz, 1H, CH<u>H</u>), 1.60 (s, 3H, CH_3), 1.46 (s, 3H, CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) 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 $C_{22}H_{22}NO_3S_2$ (M+H) 412.1041. Found 412.1022. IR (neat) 1501, 1310, 1146, 1082, 1060, 832, 803, 759, 691 cm^{-1}.

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