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[2+4] vs [4+2] Cycloaddition reactions of *o*-thioquinones with 1,3-dienes

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Abstract—Under kinetic control, the reaction of *o*-thioquinones with acyclic 1,3-dienes afforded, as main products, the spiro cycloadducts deriving from the participation of the thiones as dienophiles. Under thermodynamic control, or with cyclic dienes, the thioquinones behave as hetero dienes to give the benzoxathiin derivatives with complete regioselectivity.

1. Introduction

Mono-*ortho*-thioquinones, of general formula **1**, first reported by Chapman in 1971,[1] only rarely appeared in the literature[2–4] despite their promising structure, and did not find any practical application mainly due to the harsh reaction conditions required for their generation. The situation changed with we developed a simple methodology for the formation of **1** under very mild conditions by reacting the corresponding *ortho*-hydroxythiophthalimides **2** with bases. Compounds **2**, in turn, are the product of the *ortho* regiospecific S_EAr of phthalimidesulfenyl chloride **3** (PhthNSCl, Phth=Phthaloyl) with phenols[5–7] (Scheme 1). This chemistry allowed us to study in detail the reactivity of thioquinones **1** and to demonstrate their efficiency as electron-poor heterodienes towards a large number of electron rich-alkenes as dienophiles,[7] including glycals[8] and styrenes,[9] in inverse electron-demand Diels–Alder reactions leading to the formation of promising benzoxathiin cycloadducts (Scheme 1).

Actually, in order to verify the effective formation of a thioketone intermediate, our first effort was directed toward the trapping of species **1** as hetero dienophiles across the carbon–sulfur double bond. Indeed we reported[7] that thione **1a**, generated from the corresponding thiophthalimide and pyridine in $CHCl_3$ at 60°C, reacts with 2,3-dimethyl-1,3-butadiene (**4a**) to give the spiro derivative **5aa** isolated, after 240 h, in 46% yield (Fig. 1).

Recently Nair and co-workers published a series of papers describing the reaction of thiones **1**, prepared by a slight modification of our previously described methodology, (i.e. thiophthalimides **2**, pyridine, $CHCl_3$, sealed tube, 70°C), with acyclic[10] and cyclic[11–14] 1,3-dienes assessing the formation, as the only cycloaddition products, of the oxathiin derivatives **6**, obtained via the participation of the oxothione moiety as a heterodiene, without evidence of the corresponding spiro compounds **5** (Fig. 1).

Keeping in mind such results we decided to collect more insights on the reaction of *o*-thioquinones with 1,3-dienes. In this paper we report our findings.

2. Results and discussion

First of all we decided to unambiguously verify the formation of spiro **5aa** in the reaction of **1a** with **4a**. In the hope of carrying out the reaction under even milder reaction conditions and, at the same time, to speed up the process, we generated thione **1a** using Et_3N as base in $CHCl_3$ at rt, a procedure found effective for the formation of related *p*-thioquinones.[15] Under these conditions derivative **5aa** was isolated in 76% yield after 54 h at rt. The spiro structure of **5aa** was undoubtedly demonstrated by IR and NMR spectroscopy, which in particularly showed the presence of an α,β-unsaturated ketone (IR stretching band at 1658 cm^{-1}; ^{13}C NMR signal at 195.1 δ) indicating reaction of the carbon–sulfur double bond of **1a** as a dienophile. The next step was to verify the generality of this behaviour by reacting different *o*-thioquinones **1a–c** with acyclic and cyclic 1,3-dienes **4a–f** (Fig. 2).

All the reactions were carried out generating the thiones **1**

Keywords: cycloadditions; diene; dienophile; *ortho*-thioquinones; sulfur heterocycle.

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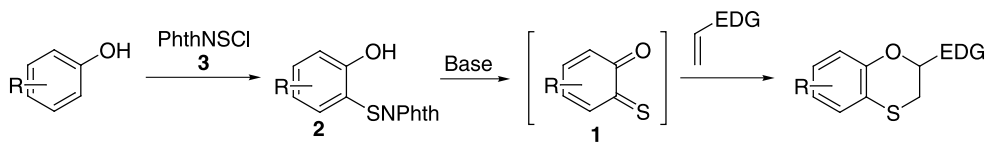


Scheme 1.

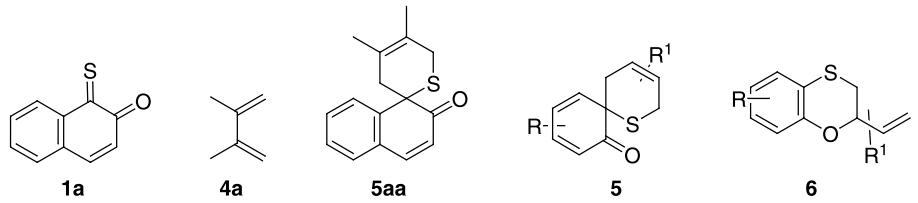


Figure 1. Spiro **5** and oxathiin **6** sulfur heterocycles deriving from the [2+4] or [4+2] cycloaddition of *o*-thioquinones with 1,3-dienes.

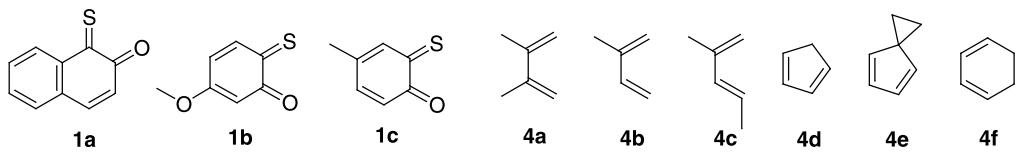


Figure 2. *o*-Thioquinones **1a–c** and 1,4-dienes **4a–f** used in this study.

from the corresponding thiophthalimides **2** (roughly 0.1 M in $CHCl_3$) with 1 equiv. of Et_3N at rt, in the presence of 2–3 equiv. of the dienes **4**. In any case the reactions were also carried out in a NMR tube in $CDCl_3$ and monitored until the disappearance of phthalimides **2** either by ^1H NMR or TLC. Evaporation of the solvent and column chromatography on silica gel (see Section 4) allowed isolation of the cycloadducts.

In Table 1 are collected the result obtained using acylic dienes **4a–c** as trapping reagent. The reaction of *o*-thioquinones **1a–c** with simple acyclic dienes **4a** and **4b** indeed gave formation of the corresponding spiro cycloadducts **5**. The structure of the thione plays a role in the [2+4] vs [4+2] reaction pathway. In fact, while spiro compounds **5aa** and **5ba** were obtained as single products and easily isolated form the crude reaction mixtures, thione **1c** reacted with **4a** to give, after 168 h at rt, a 2:1 mixture of spiro derivative **5ca** and oxathiin **6ca**, respectively. Monitoring the reaction by ^1H NMR we observed the initial formation of **5ca** while trace amounts of **6ca** were detectable only after 26 h at rt. Moreover, keeping the reaction mixture at rt after the complete disappearance of **2c** (168 h), we monitored a decrease of the **5ac/6ac** ratio.

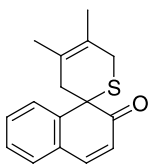
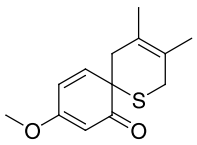
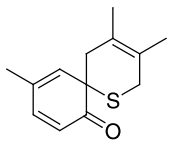
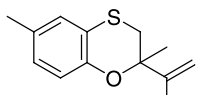
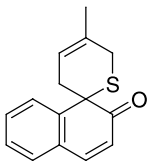
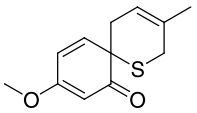
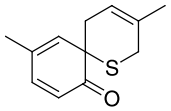
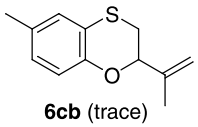
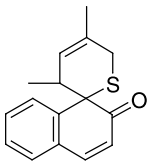
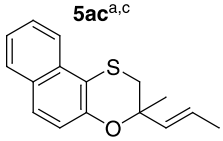
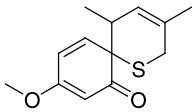
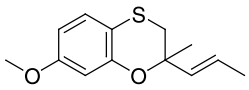
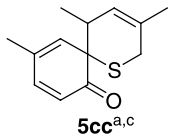
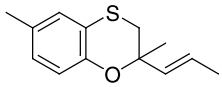
The formation of **5ca** was demonstrated by spectroscopy on the crude which showed the presence of a ketonic carbon by IR (1670 cm^{-1}) and ^{13}C NMR (195.8 δ), but all attempts to isolate this spiro derivative were unsuccessful, while **6ca** was obtained, after column chromatography, in 26% yield.

A reasonable explanation is that in this case both [2+4] and [4+2] cycloadditions, as well as a retro Diels–Alder process from **5ca**, were operative at 23°C, and hence only **6ca** was stable under these conditions. Thus the structure of the thiones plays a role in the rates of such direct and retro Diels–Alder processes even as a function of the substituents on the phenyl ring of mono-benzo-*o*-thioquinones and not only, as expected,[16] moving from benzo- to naphthothiones. As a matter of fact, spiro compound **5ba** was stable for weeks at rt, but when heated at 60°C in $CDCl_3$ we monitored by ^1H NMR its complete disappearance after 70 h and the formation of very small amounts of oxathiin **6ba** clearly via a retro Diels–Alder/[4+2] sequence. On the other hand, compound **5aa** was stable at 60°C for more than 240 h and actually it was firstly prepared under similar conditions using pyridine as base.[7]

Similarly using isoprene **4b** as trapping reagent for thiones **1**, we observed the formation of the spiro derivatives **5ba** and **5bb** as the only cycloaddition products, while in the crude reaction mixture of **1c** with **4b** it was possible to verify the presence, together with compound **5cb**, of trace amounts of oxathiin **6cb**. In any case however the spiro derivatives **5** were isolated, as a mixture of regioisomers,[15] by flash chromatography, even though the low yield obtained for **5cb** can be again due to a slow retro Diels–Alder process operative from this spiro compound.

When 1,3-dimethyl butadiene **4c** was reacted with thiones **1a–c** we observed, immediately after the mixing of the reagents, the presence of complex mixtures of [2+4] and [4+2] cycloadducts. Also in this case, spiro derivatives **5** represented the main cycloaddition products but we were able to isolate only the oxathiin derivatives **6**. Thus the balance between dienic or dienophile behaviour seems very sensitive to steric hindrance on the 1,3-diene, since substitution at one of the dienic termini in **4c** appears sufficient to slow down the [2+4] reaction leading to derivatives **5** and/or to accelerate the corresponding retro Diels–Alder process. The sensitivity of such reactions to steric hindrance is further demonstrated by the participation

Table 1. Cycloadducts **5** and **6** obtained in the reaction of thiones **1a–c** with acyclic dienes **4a–c**

	1a	**1b**	**1c**
4a	 **5aa** (54h, 76%)	 **5ba** (117h, 54%)	 **5ca**[a]  **6ca** (168h, 26%)[b]
4b	 **5ba** (49h, 95%)[c]	 **5bb** (72h, 65%)[c]	 **5cb** (72h, 36%)[c]  **6cb** (trace)
4c	 **5ac**[a,c]  **6ac** (70h, 36%)[d]	 **5bc**[a,c]  **6bc** (70h, 17%)[e]	 **5cc**[a,c]  **6cc** (70h, 30%)[e]

[a] Not isolated.
[b] **5ca/6ca**=2/1 after 168 h.
[c] Mixture of regioisomers.
[d] **5ac/6ac**=1/1.
[e] Ratio spiro derivatives **5**/oxathiins **6** rougly 2/1.

of 2-methyl-1,3-pentadiene (**4c**) as dienophile exclusively with the 1,2-double bond as also reported by Nair.[10]

Thus, at least for the combination of thiones **1a–c** and dienes **4a–c**, the spiro derivatives **5** seem to represent the kinetically favoured products which however in some case undergo a retro Diels–Alder process that prevents their isolation. As already published,[10] with these substrates the formation of the thermodynamically stable oxathiin cycloadducts **6** occurs as the only detectable event working at higher temperature.

The reaction of **1a–c** with cyclopentadienes **4d**,**e** gave the corresponding oxathiins **6** as the only reaction products isolated in very good yields. Probably in this case the remarkable steric hindrance of the transition state leading to the spiro cycloadduct transforms the behaviour of *o*-thioquinones as dienes in the kinetic and

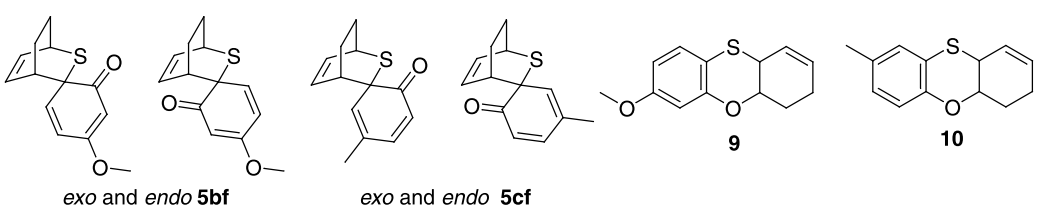
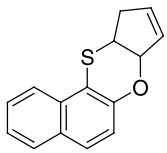
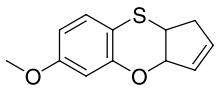
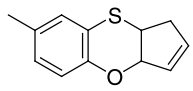
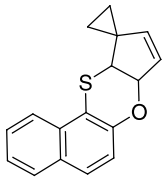
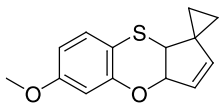
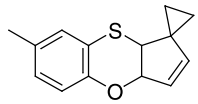
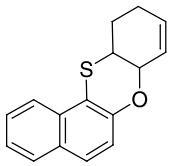
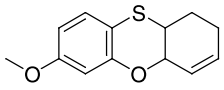
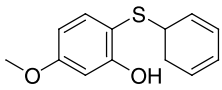
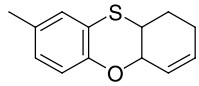
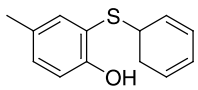


Figure 3. Possible cycloadducts from the reaction of **1b**,**c** with **4f** ruled out for compounds **7** and **8**.

Table 2. Cycloadducts **6** obtained in the reaction of thiones **1a–c** with cyclic dienes **4d–f**

	1a	**1b**	**1c**
4d	 **6ad** (46h, 87%)	 **6bd** (25h, 93%)	 **6cd** (114h, 92%)
4e	 **6ae** (94h, 84%)	 **6be** (70h, 58%)	 **6ce** (24h, 74%)
4f	 **6af** (116h, 70%)	 **6bf** (144h, 73%)[a,b]  **7**	 **6cf** (138h, 85%)[a,c]  **8**

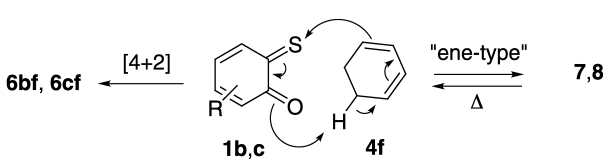
[a]Overall yield.
[b]**6bf/7**=3/1.
[c]**6cf/8**=2/1.

thermodynamic favoured process under any reaction conditions (Table 2).

Reacting cyclohexadiene **4f** with thiones **1a–c**, we observed the formation of derivative **6af** as the only product, while oxathiins **6bf** and **6cf** where isolated together derivatives **7** and **8**, respectively (3:1 and 2:1 mixtures; see Section 4).

Spectroscopic data of these by-products allowed us to rule out the possibility that spiro derivatives **5bf** and **5cf** (*exo* or *endo*) as well as oxathiins **9** and **10** were formed in these reactions (Fig. 3), and suggested for **7** and **8** the structures reported in Table 2 deriving from a thiophilic 'ene-type' reaction of thiones **1b**,**c** with **4f** leading to the formation of a cyclic 1,3-diene bearing a phenolic group (Scheme 2).

Derivatives similar to **7** and **8** with a free phenolic hydroxyl group were also isolated by Nair[10,12] who included in fact an 'ene-type' reaction as one of the possible explanations for their formation together with some thermal rearrangements from the oxathiin or spiro cycloadducts.[10] Since we isolated **7** and **8** reacting **1b**,**c** with **4f** at rt, the possibility of a thermal rearrangement can be reasonably ruled out in favour of an 'ene-type' reaction.[17]



Scheme 2.

Interestingly in a previous mentioned paper[12] the reaction of *o*-thioquinone **1c** with cyclohexadiene (**4f**) afforded only the oxathiin **6cf** while derivative **8** was not reported. This can be explained considering the possibility of a 'retro-ene' process operative at 70°C leading to the exclusive formation of the thermodynamic [4+2] cycloadduct **6cf** (Scheme 2).

In all the reactions, oxathiin heterocycles **6** were obtained as single regioisomers, in particular those with the oxygen of the oxothione linked to the allylic carbon of the oxathiin ring, perfect agreement with the previous reported papers regarding the inverse electron demand Diels–Alder reactions of *o*-thioquinones, and with the orbital coefficients of the reacting species.

The reaction of thiones **1** with 1,3-dienes represents one of the peculiar examples where both partners can behave as diene and as dienophile.[18] Molecular mechanics *ab initio* calculations[21] clearly showed that the energetically favoured interaction is in any case between the HOMO of the 1,3-diene and LUMO of the thione. However the symmetry of such orbitals allows the formation of spiro derivatives **5** as well as oxathiin cycloadducts **6**, thus a fine tuning of the structure of the reagents and the reaction conditions chosen make the difference in these reactions driving the interaction between *o*-thioquinones

and 1,3-dienes to the formation of the [2+4] dihydrothiopyran spiro and/or the [4+2] benzoxathiin cycloadducts.

3. Conclusion

The generation under very mild reaction conditions of *o*-thioquinones allowed us to demonstrate that, under kinetic control, they behave as hetero dienophiles in the presence of acyclic 1,3-dienes to give, mainly or exclusively, the spiro dihydrothiopyran cycloadducts. The oxathiin cycloadducts are obtained under thermodynamic control with acyclic dienes or in any case with cyclic dienes. Further applications of the chemistry of *o*-thioquinone are currently under investigation in these laboratories.

4. Experimental

4.1. General

^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 300 and 75 MHz, respectively, using residual $CHCl_3$ at δ_H 7.26 and the central line of $CDCl_3$ at δ_D 77.0 as reference. FTIR spectra were recorded on a Perkin–Elmer 1600. Melting points are uncorrected. $CHCl_3$ and Et_3N were dried using standard procedures. Phthalimidesulfenyl chloride[22] **3**, and *N*-thiophthalimides **2a–c**[7] were prepared as published elsewhere.

Data for derivative **2c** are as follows.

4.1.1. 2-(2-Hydroxy-5 methyl-phenylsulfanyl)-isoindole-1,3-dione 2c. White solid from column flash chromatography with CH_2Cl_2 as eluent. Mp 185–186°C, 81% yield.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.25 (s, 3H); 6.92 (d, 1H, J=8.4 Hz); 7.18 (d, 1H, J=8.4, 2.1 Hz); 7.65 (d, 1H, J=2.1 Hz); 7.51–7.92 (m, 4H); 8.16 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.1 (q, 1C); 116.7 (d, 1C); 117.8 (s, 1C); 124.2 (d, 2C); 130.0 (s, 2C); 131.9 (s, 1C); 134.8 (d, 2C); 135.6 (d, 1C); 138.2 (d, 1C); 156.7 (s, 1C); 168.5 (s, 2C). IR (nujol) 3403, 1778, 1735, 1707, 1487, 1283 cm^{-1}. Anal. calcd for $C_{15}H_{11}NO_3S$: C, 63.14; H, 3.89; N, 4.91. Found: C, 63.39; H, 3.91; N, 4.84.

4.2. Cycloaddition reactions: general procedure

To a solution of thiophthalimides **2** in dry $CHCl_3$ (roughly 0.1 M) diene **4** (2–3 equiv.) and freshly distilled Et_3N (1 equiv.) were added in sequence and the reactions monitored, either by ^{1}H NMR or TLC, until the disappearance of phthalimides **2**. Evaporation of the solvent and flash chromatography on silica gel allowed the isolation of the cycloadducts as reported in Tables 1 and 2. Spectroscopic data are as follows.

4.2.1. 3,4-Dimethyl-1-thia-spiro[5.5]undeca-3,8-dien-[9,10]benzo-7-one 5aa. Yellow oil from flash chromatography with CH_2Cl_2 as eluent, 76% yield.[7]

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.81 (s, 3H); 1.84 (s, 3H); 2.63–2.83 (m, 3H); 3.16–3.23 (m, 1H); 6.20 (d, 1H, J=9.6 Hz); 7.30–7.33 (m, 3H); 7.36–7.43 (m, 1H); 7.56 (d, 1H, J=7.8 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.7 (q, 1C); 20.3 (q, 1C); 30.5 (t, 1C); 36.6 (t, 1C); 51.3 (s, 1C); 122.9 (d, 1C); 124.4 (d, 1C); 127.1 (d, 1C); 127.7 (s, 1C); 127.9 (d, 1C); 129.4, 129.8, 129.9 (2s, 1d, 3C); 141.8 (s, 1C); 142.5 (d, 1C); 195.1 (s, 1C). IR (neat) 3063, 2989, 2912, 2887, 1658, 1595, 1565, 1445 cm^{-1}. Anal. calcd for $C_{16}H_{16}OS$: C, 74.96; H, 6.29. Found: C, 74.78; H, 6.50.

4.2.2. 9-Methoxy-3,4-dimethyl-1-thia-spiro[5.5]undeca-3,8,10-trien-7-one 5ba. Yellow oil from flash chromatography with CH_2Cl_2 as eluent, 54% yield.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.71 (bs, 3H); 1.79 (bs, 3H); 2.05 (bd, 1H, J=17.1 Hz); 2.78 (bd, 1H, J=17.1 Hz); 3.19 (bs, 2H); 3.76 (s, 3H); 5.49 (d, 1H, J=2.1 Hz); 6.07 (dd, 1H, J=9.9, 2.1 Hz); 6.45 (d, 1H, J=9.9 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.3 (q, 1C); 20.4 (q, 1C); 29.6 (t, 1C); 37.9 (t, 1C); 49.0 (s, 1C); 55.8 (q, 1C); 99.3 (d, 1C); 119.8 (d, 1C); 122.7 (s, 1C); 125.5 (s, 1C); 143.0 (d, 1C); 169.8 (s, 1C); 197.2 (s, 1C). IR (neat) 2979, 2913, 2877, 1771, 1733, 1650, 1573, 1445 cm^{-1}. Anal. calcd for $C_{13}H_{16}O_2S$: C, 66.07; H, 6.82. Found: C, 66.00; H, 6.61.

4.2.3. 3-Isopropenyl-3,6-dimethyl-2,3-dihydro-benzo[1,4]oxathiine 6ca. Yellow oil from flash chromatography with petroleum ether/EtOAc 15:1 as eluent, 26% yield.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.53 (s, 3H); 1.84 (s, 3H); 2.21 (s, 3H); 2.95 (d, A part of an AB system, 1H, J=13.2 Hz); 3.02 (d, B part of an AB system, 1H, J=13.2 Hz);4.91–4.92 (m, 1H); 5.01–5.02 (m, 1H); 6.75–6.85 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 18.2 (q, 1C); 20.4 (q, 1C); 26.1 (q, 1C); 32.7 (t, 1C); 77.2 (s, 1C); 112.6 (d, 1C); 116.3 (s, 1C); 118.5 (d, 1C); 126.7 (t, 1C); 127.3 (d, 1C); 130.1 (s, 1C); 145.7 (s, 1C); 148.3 (s, 1C). IR (neat) 3010, 2977, 2923, 1646, 1486, 1268, 1233 cm^{-1}. Anal. calcd for $C_{13}H_{16}OS$: C, 70.87; H, 7.32. Found: C, 71.01; H, 7.45.

4.2.4. 3- and 4-Methyl-1-thia-spiro[5.5]undeca-3,8-dien-[9,10]benzo-7-one 5ab. Glassy yellow solid (2:1 mixture of regioisomers) after flash chromatography with petroleum ether/EtOAc 4:1 as eluent, 95% yield.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.84 (s, 3H); 2.68–2.78 (m, 2H); 2.88–2.99 (m, 1H); 3.15–3.22 (m, 1H); 5.76–5.78 (m, 1H); 6.21 (d, 1H, J=9.9 Hz); 7.29–7.45 (m, 4H); 7.57 (t, 1H, J=7.3 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.3 (q, 1C) 24.8 (q, 1C); 25.6 (t, 1C); 28.9 (t, 1C); 30.8 (t, 1C); 34.4 (t, 1C); 49.4 (s, 1C); 50.8 (s, 1C); 117.0 (1C); 122.1 (1C); 124.3 (1C); 127.6 (2C); 128.0 (3C); 129.8 (2C); 130.0 (4C); 130.1 (1C); 135.3 (1C); 141.1 (1C); 141.2 (1C); 142.4 (2C); 194.7 (2C). IR (neat) 3046, 2968, 2927, 2882, 1657, 1620, 1564, 1445 cm^{-1}. Anal. calcd for $C_{15}H_{14}OS$: C, 74.34; H, 5.82. Found: C, 74.26; H, 5.69.

4.2.5. 9-Methoxy-3(and 4)-methyl-1-thia-spiro[5.5]undeca-3,8,10-trien-7-one 5bb. The reaction carried out following the general procedure allowed the isolation, by flash chromatography on silica gel (petroleum ether/EtOAc 5:1), of a 3:1 mixture of oxathiin **6bf** and derivative **7** as a

pale yellow oil (65% overall). By further flash chromatography with petroleum ether/EtOAc 10:1 as eluent it was isolated a mixture enriched in major regioisomer (major R/minor r=5:1) which allowed the attribution of the spectroscopic data of both regioisomers. Signals unlabelled with R or r state coincident proton or carbon resonances.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.75 (bs, 3H, r); 1.81 (bs, 3H, R); 1.99 (bd, 1H, J=17.1 Hz, r); 2.12–2.20 (m, 1H, R); 2.68–2.86 (m, 2H); 3.16 (bs, 2H, R); 3.28 (bs, 2H, r); 3.76 (s, 3H, R); 3.77 (s, 3H, r); 5.48–5.50 (m, 2H); 5.59 (bs, 1H, R); 5.71 (bs, 1H, r); 6.07–6.12 (m, 2H); 6.43–6.49 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.2 (q, 1C, R); 24.6 (q, 1C, r); 27.9 (t, 2C); 32.0 (t, 2C); 47.1 (s, 2C); 55.8 (q, 2C); 99.4 (d, 2C); 120.3 (d, 2C); 120.4 (s, 2C); 129.7 (d, 2C); 142.6 (d, 2C); 169.7 (s, 2C); 196.8 (s, 1C, r); 197.0 (s, 1C, R). IR (neat) 3045, 2970, 2920, 1650, 1620, 1564 cm^{-1}. Anal. calcd for $C_{12}H_{14}O_2S$: C, 64.83; H, 6.35. Found: C, 64.72; H, 6.47.

4.2.6. 4 and 3,10-Dimethyl-1-thia-spiro[5.5]undeca-3,8,10-trien-7-one 5cb. The reaction carried out following the general procedure allowed the isolation, by flash chromatography on silica gel (petroleum ether/EtOAc 10:1), of a 3:1 mixture regioisomers as a pale yellow oil (36% overall). The following data refer to such mixture where the major R or minor r regioisomer are indicated when clearly differentiated.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.80 (s, 3H, r); 1.95 (s, 3H, R); 2.10–3.18 (3m, 8H); 5.60 (bs, 1H, R); 5.68 (bs, 1H, r); 5.97 (bs, 2H); 6.06 (d, 2H, J=9.9 Hz); 6.73 (dd, 1H J=2.1, 9.9 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.0 (q, 1C); 24.3 (q, 1C); 27.2 (t, 1C); 32.0 (t, 1C); 48.3 (s, 1C); 120.7 (d, 1C); 125.5 (d, 1 C); 129.5 (s, 1 C); 130.7 (s, 1 C); 136.1 (d, 1C); 142.6 (d, 1C); 196.2 (s, 1C). IR (neat) 3040, 2985, 2920, 1657, 1620, 1564 cm^{-1}. Anal. calcd for $C_{12}H_{14}OS$: C, 69.86; H, 6.84. Found: C, 69.69; H, 6.75.

4.2.7. 3-Methyl-3-propenyl-2,3-dihydro-naphtho[2,1-*b*][1,4]oxathiine 6ac. Glassy solid after flash chromatography with CH_2Cl_2 as eluent, 36% yield.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.56 (s, 3H); 1.70 (d, 3H, J=1.2, 6.0 Hz); 2.99 (bs, 2H); 5.63–5.82 (m, 2H); 7.08 (d, 1H, J=9.0 Hz); 7.36 (t, 1H, J=7.5 Hz); 7.46–7.54 (m, 2H); 7.74 (d, 1H, J=7.8 Hz); 7.89 (d, 1H, J=7.8 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 17.8 (q, 1C); 26.3 (q, 1C); 34.2 (t, 1C); 73.4 (s, 1C); 109.5 (s, 1C); 120.4 (d, 1C); 122.4 (d, 1C); 123.8 (d, 1C); 125.7 (d, 1C); 125.8 (d, 1C); 126.1 (d, 1C); 128.2 (d, 1C); 129.0 (s, 1C); 131.1 (s, 1C); 133.2 (s, 1C); 148.2 (s, 1C). Anal. calcd for $C_{16}H_{16}OS$: C, 74.96; H, 6.29. Found: C, 74.81; H, 6.34.

4.2.8. 7-Methoxy-2-methyl-2-propenyl-2,3-dihydro-benzo[1,4]oxathiine 6bc. Yellow oil from flash chromatography with petroleum ether/EtOAc 10:1 as eluent, 17% yield.

^{1}H NMR ($CDCl_3$, 300 MHz) 1.50 (s, 3H); 1.70 (d, 3H, J=6.1 Hz); 2.85 (s, 2H); 3.74 (s, 3H); 5.58–5.82 (m, 2H); 6.46–6.49 (m, 2H); 6.93 (d, 1H, J=9.3 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 17.8 (q, 1C); 26.2 (q, 1C); 34.6 (t, 1C); 55.3 (q, 1C); 74.0 (s, 1C); 103.9 (d, 1C); 107.3 (s, 1C); 108.4 (d, 1C); 125.8 (d, 1C); 127.7 (d, 1C); 133.3 (d, 1C); 151.4 (s, 1C); 158.1 (s, 1C). IR (neat) 2928, 1606, 1488 cm^{-1}. Anal. calcd for $C_{13}H_{16}O_2S$: C, 66.07; H, 6.82. Found: C, 65.98; H, 6.74.

4.2.9. 2,6-Dimethyl-2-propenyl-2,3-dihydro-benzo[1,4]oxathiine 6cc.[10] Colourless oil from flash chromatography with petroleum ether/EtOAc 10:1 as eluent, 30% yield.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.49 (s, 3H); 1.70 (d, 3H, J=5.7 Hz); 2.23 (s, 3H); 2.87 (bs, 2H); 5.57–5.81 (m, 2H); 6.74–6.86 (m, 3H). Anal. calcd for $C_{13}H_{16}OS$: C, 70.87; H, 7.32. Found: C, 70.68; H, 7.26.

4.2.10. 10,10a-Dihydro-7aH-7-oxa-11-thia-cyclopenta[b]phenanthrene 6ad. White solid from column flash chromatography with petroleum ether/EtOAc 10:1 as eluent. Mp 66–68°C, 87% yield.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.50–2.59 (m, 1H); 2.87 (dd, 1H, J=18.0, 8.1 Hz); 4.02 (m, 1H); 5.31 (d, 1H, J=6.9 Hz); 5.98–6.05 (m, 2H); 7.22 (d, 1H, J=8.7 Hz); 7.43 (t, 1H, J=7.8 Hz); 7.55 (t, 1H, J=7.8 Hz); 7.65 (d, 1H, J=8.7 Hz); 7.81 (d, 1H, J=8.1 Hz); 8.15 (d, 1H, J=8.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 41 (t, 1C); 42.5 (d, 1C); 86.5 (d, 1C); 118.0 (s, 1C); 120.4 (d, 1C); 123.1 (d, 1C); 124.4 (d, 1C); 126.2 (d, 1C); 126.6 (d, 1C); 128.3 (d, 1C); 129.7 (d, 1C); 130.1 (s, 1C); 132.2 (s, 1C); 136.4 (d, 1C); 152.7 (s, 1C). Anal. calcd for $C_{15}H_{12}OS$: C, 74.97; H, 5.03. Found: C, 74.73; H, 5.18.

4.2.11. 6-Methoxy-3a,9a-dihydro-1H-4-oxa-9-thia-cyclopenta[*b*]naphthalene 6bd. Viscous colourless oil from column chromatography with petroleum ether/EtOAc 10:1 as eluent, 93% yield.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.43–2.51 (m, 1H); 2.52–2.86 (m, 1H); 3.76 (s, 3H); 3.89–3.85 (m, 1H); 5.22–5.26 (m, 1H); 5.85–5.89 (m, 1H); 6.00–6.04 (m, 1H); 6.54–6.58 (m, 2H); 7.11–7.15 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 40.8 (t, 1C); 42.5 (d, 1C); 55.3 (q, 1C); 86.9 (d, 1C); 105.8 (d, 1C); 109.1 (d, 1C); 114.8 (s, 1C); 129.3 (d, 1C); 129.3 (d, 1C); 136.3 (d, 1C); 156.0 (s, 1C); 159.3 (s, 1C). IR 3061, 2936, 2834, 1597, 1478, 1155 cm^{-1}. Anal. calcd for $C_{12}H_{12}O_2S$: C, 65.43; H, 5.49. Found: C, 65.61; H, 5.32.

4.2.12. 7-Methyl-3a,9a-dihydro-1H-4-oxa-9-thia-cyclopenta[*b*]naphthalene 6cd. Viscous pale yellow oil from column chromatography with petroleum ether/EtOAc 15:1 as eluent, 92% yield.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.26 (s, 3H); 2.47–2.54 (m, 1H); 2.78–2.87 (m, 1H); 3.87–3.94 (m, 1H); 5.13–5.15 (m, 1H); 5.89–5.92 (m, 1H); 6.03–6.07 (m, 1H); 6.84 (d, 1H, J=8.1 Hz); 6.89–6.92 (m, 1H) 7.05 (bs, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.7 (q, 1C); 41.0 (t, 1C); 42.5 (d, 1C); 86.2 (d, 1C); 119.3 (d, 1C); 123.7 (s, 1C); 127.7 (d, 1C); 129.1 (d, 1C); 129.6 (d, 1C); 132.4 (s, 1C); 136.5 (d, 1C); 152.5 (s, 1C). IR (neat) 3060, 2919, 2849, 1483, 1225 cm^{-1}. Anal. calcd for $C_{15}H_{12}OS$: C, 70.55; H, 5.92. Found: C, 70.39; H, 5.74.

4.2.13. Oxathiin 6ae. White solid from column flash

chromatography with petroleum ether/EtOAc 20:1 as eluent. Mp 110–111°C, 84% yield.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.53–0.57 (m, 1H); 0.78–0.83 (m, 1H); 0.90–1.09 (m, 2H); 3.96 (d, 1H, J=7.5 Hz); 5.54 (d, 1H, J=6.0 Hz); 5.66 (dd, 1H, J=7.5, 2.1 Hz); 5.92 (dd, 1H, J=6.0, 2.1 Hz); 7. 18 (d, 1H, J=8.7 Hz); 7.40 (t, 1H, J=7.5 Hz); 7.52 (t, 1H, J=7.5 Hz); 7.63 (d, 1H, J=8.7 Hz); 7.79 (d, 1H, J=8.1 Hz); 8.13 (d, 1H, J=8.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 11.9 (t, 1C); 12.8 (t, 1C); 32.6 (s, 1C); 50.0 (d, 1C); 87.5 (d, 1C); 117.4 (s, 1C); 120.5 (d, 1C); 123.0 (d, 1C); 124.2 (d, 1C); 126.3 (d, 1C); 126.8 (d, 1C); 127.3 (d, 1C); 128.3 (d, 1C); 130.2 (s, 1C); 132.5 (s, 1C); 143.0 (d, 1C); 153.4 (s, 1C). Anal. calcd for $C_{17}H_{14}OS$: C, 76.66; H, 5.30. Found: C, 76.81; H, 5.41.

4.2.14. Oxathiin 6be. White solid from column flash chromatography with petroleum ether/EtOAc 50:1 as eluent. Mp 67–69°C, 58% yield.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.61–0.68 (m, 1H); 0.75–0.88 (m, 2H); 0.94–1.00 (m, 1H); 3.75 (s, 3H); 3.78 (d, 1H, J=7.6 Hz); 5.51 (dd, 1H, J=6.0, 0.8 Hz); 5.58 (dd, 1H, J=7.6, 2.1 Hz); 5.80 (dd, 1H, J=6.0, 2.1 Hz); 6.52–6.57 (m, 2H); 7.10 (dd, 1H, J=8.1, 0.6 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 12.3 (t, 1C); 13.3 (t, 1C); 32.5 (s, 1C); 49.9 (d, 1C); 55.3 (q, 1C); 87.9 (d, 1C); 105.8 (d, 1C); 109.1 (d, 1C); 114.6 (s, 1C); 126.8 (d, 1C); 129.7 (d, 1C); 143.1 (d, 1C); 156.3 (s, 1C); 159.4 (s, 1C). IR (neat) 2923, 2852, 1599, 1463 cm^{-1}. Anal. calcd for $C_{14}H_{14}O_2S$: C, 68.26; H, 5.73. Found: C, 68.43; H, 5.92.

4.2.15. Oxathiin 6ce. White solid from column flash chromatography with petroleum ether/EtOAc 20:1 as eluent. Mp 81–83°C, 74% yield.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.64–0.70 (m, 1H); 0.71–0.89 (m, 2H); 0.98–1.05 (m, 1H); 2.26 (s, 3H); 3.79 (d, 1H, J=7.5 Hz); 5.50 (dd, 1H, J=7.5, 2.1 Hz); 5.54 (dd, 1H, J=6.0, 0.6 Hz); 5.81 (dd, 1H, J=6.0, 2.1 Hz); 6.84 (d, 1H, J=8.1 Hz); 6.91 (dd, 1H, J=8.1, 1.2 Hz); 7.04 (d, 1H, J=2.1, Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 12.1 (t, 1C); 13.1 (t, 1C); 20.7 (t, 1C); 32.8 (s, 1C); 49.8 (d, 1C); 87.2 (d, 1C); 119.3 (d, 1C); 123.3 (s, 1C); 127.1 (d, 1C); 127.9 (d, 1C); 129.5 (d, 1C); 132.3 (s, 1C); 143.0 (d, 1C); 152.8 (s, 1C). IR (neat) 2923, 1609, 1482, 1223 cm^{-1}. Anal. calcd for $C_{14}H_{14}OS$: C, 73.01; H, 6.13. Found: C, 73.17; H, 6.22.

4.2.16. 7a,10,11,11a-Tetrahydro-7-oxa-12-thia-benzo[*a*]antracene 6af. White solid from column flash chromatography with petroleum ether/EtOAc 100:1 as eluent. Mp 95–97°C, 70% yield.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.2.00–2.44 (m, 4H); 3.50–3.56 (m, 1H); 4.59–4.61 (m, 1H); 5.99–6.10 (m, 2H); 7.10 (d, 1H, J=8.7 Hz); 7.35–7.41 (m, 1H); 7.47–7.53 (m, 1H); 7.74–7.77 (m, 1H); 7.88–7.91 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.7 (t, 1C); 26.3 (t, 1C); 37.6 (d, 1C); 69.1 (d, 1C); 111.0 (s, 1C); 119.8 (d, 1C); 122.4 (d, 1C); 124.1 (d, 1C); 125.2 (d, 1C); 125.6 (d, 1C); 126.1 (d, 1C); 128.3 (d, 1C); 129.6 (s, 1C); 130.7 (s, 1C); 133.0 (d, 1C); 148.3 (s, 1C). IR (neat) 3039, 1614, 1594, 1563, 1229 cm^{-1}. Anal. calcd for $C_{16}H_{14}OS$: C, 75.55; H, 5.55. Found: C, 75.71; H, 5.38.

4.3. Reaction of thione 1b with cyclohexadiene 4f. The reaction carried out following the general procedure allowed the isolation, by flash chromatography on silica gel (petroleum ether/EtOAc 30:1), of a 3:1 mixture of oxathiin **6bf** and derivative **7** as a pale yellow oil (73% overall). The following data refer to the individual signals deduced from the spectra of the mixture.

4.3.1. 7-Methoxy-1,2,4a,10a-tetrahydro-phenoxathiine 6bf. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.92–2.35 (m, 4H); 3.33–3.39 (m, 1H); 3.74 (s, 3H); 4.47–4.49 (m, 1H); 5.92–5.98 (m, 1H); 6.01–6.07 (m, 1H); 6.48–6.52 (m, 2H); 6.92–6.96 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 25.6 (t, 1C); 26.2 (t, 1C); 37.8 (d, 1C); 37.8 (d, 1C); 55.3 (q, 1C); 69.6 (d, 1C); 103.8 (d, 1C); 108.7 (s, 1C); 109.1 (d, 1C); 125.3 (d, 1C); 126.9 (d, 1C); 132.9 (d, 1C); 151.7 (s, 1C); 157.6 (s, 1C).

4.3.2. 2-(Cyclohexa-2,4-dienylsulfanyl)-5-methoxy-phenol 7. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.36–2.54 (m, 2H); 3.64–3.70 (m, 1H); 3.78 (s, 3H); 5.77–5.86 (m, 2H); 6.01–6.10 (m, 2H);6.45 (dd, 1H, J=2.7, 8.4 Hz); 6.54 (d, 1H, J=2.7 Hz); 7.34 (d, 1H, J=8.4 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 28.2 (t, 1C); 44.1 (d, 1C); 55.3 (q, 1C); 99.6 (d, 1C); 107.4 (d, 1C); 108.0 (s, 1C); 123.9 (d, 1C); 124.5 (d, 1C); 125.0 (d, 1C); 126.6 (d, 1C); 137.5 (d, 1C); 159.1 (s, 1C); 162.4 (s, 1C). IR (neat) on the mixture 3403, 3032, 1604, 1573, 1487, 1161 cm^1. Analysis on the mixture: calcd for $C_{13}H_{14}O_2S$: C, 66.64; H, 6.02. Found: C, 66.64; H, 5.93.

4.4. Reaction of thione 1c with cyclohexadiene 4f. The reaction carried out following the general procedure allowed the isolation, by flash chromatography on silica gel (petroleum ether/EtOAc 40:1), of a 2:1 mixture of oxathiin **6cf** and derivative **8** as a pale yellow oil (85% overall). The following data refer to the individual signals deduced from the spectra of the mixture.

4.4.1. 8-Methyl-1,2,4a,10a-tetrahydro-phenoxathiine 6cf.[12] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.93–2.37 (m, 3H); 2.23 (s, 3H); 3.36–3.42 (m, 1H); 4.41–4.43 (m, 1H); 5.91–5.97 (m, 1H); 6.01–6.06 (m, 1H); 6.77 (bs, 2H); 6.87 (bs, 1H).

4.4.2. 2-(Cyclohexa-2,4-dienylsulfanyl)-4-methyl-phenol 8. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.27 (s, 3H); 2.39–2.57 (m, 2H); 3.73–3.79 (m, 1H); 5.80–5.90 (m, 2H); 6.04–6.13 (m, 2H); 6.89 (d, 1H, J=8.7 Hz); 7.08 (dd, 1H, J=2.1, 8.7 Hz); 7.27 (d, 1H, J=2.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 20.3 (q, 1C); 28.3 (t, 1C); 44.2 (d, 1C); 114.3 (d, 1C); 116.6 (s, 1C); 124.0 (d, 1C); 124.7 (d, 1C); 125.1 (d, 1C); 126.7 (d, 1C); 129.8 (s, 1C); 132.1 (d, 1C); 136.8 (d, 1C); 155.8 (s, 1C). IR (neat) on the mixture 3396, 3032, 2925, 1650, 1611, 1560, 1486 cm^{-1}. Analysis on the mixture: calcd for $C_{13}H_{14}OS$: C, 71.52; H, 6.46. Found: C, 71.74; H, 6.57.

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