Notes

Phthalimidesulfenyl Chloride.[1] 11. Generation, General Reactivity, and Synthetic Applications of *o*-Thioquinones[†]

G. Capozzi,* C. Falciani, S. Menichetti,* and C. Nativi

*Centro C.N.R. "Chimica dei Composti Eterociclici",
Dipartimento di Chimica Organica,
Universita' di Firenze, Via G. Capponi 9,
I-50121, Firenze, Italy*

Introduction

Hetero Diels–Alder reactions represent one of the main topics of contemporary organic chemistry.[2] Among the diverse heterodienes, *o*-quinones[3] and *o*-quinomethides[4] have been found several applications which have also been used for the construction of biologically active compounds. Less attention has been devoted to the corresponding sulfur-substituted species[5] despite the interest in the building of thio-substituted rings fused to aromatic systems.

We have recently reported a new method to prepare α,α′-dioxothiones, a new class of electron poor heterodienes, on the basis of the reactivity of phthalimidesulfenyl chloride.[6,7] In preliminary reports[8–10] we have shown that following a similar approach, it is possible to obtain *o*-thioquinones, a hitherto unknown class of electron poor dienes, which are possible intermediates for the synthesis of various benzo-condensed thio-substituted heterocycles and which has been used for stereoselective preparation of *O*-aryl-2-deoxy glycosides.[9] In this paper we report our studies on the generation and trapping of *o*-thioquinones, *o*-thionaphthoquinones, and *o*-thiophenanthroquinones,

Scheme 1
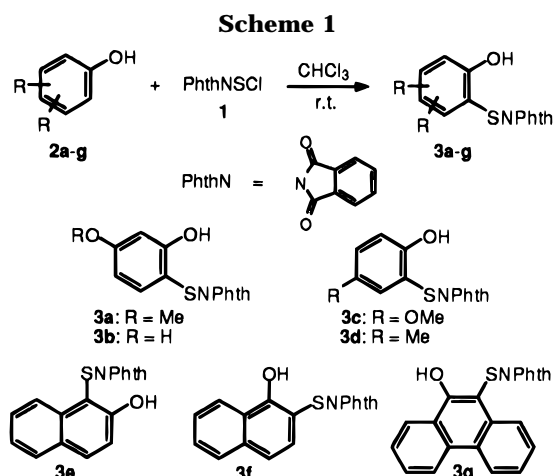
as well as a selected synthetic application toward a new synthesis of isovanillin sweeteners.

Results and Discussion

The reaction of phthalimidesulfenyl chloride **1** with activated hydroxyl arenes **2a–g** in chloroform at room temperature forms the key intermediates for the generation of *o*-thioquinones (Scheme 1). *o*-Hydroxythiophthalimides **3a–g** are generally obtained in good yields, with complete regioselectivity and without polysubstitution byproducts even when using an excess of **1** with highly activated phenols.[1] Derivatives **3a–g** are solids which can be purified by flash chromatography and/or recrystallization and stored at room temperature for prolonged times without decomposition.

The reaction of phthalimides **3a–g** with 2 equiv of pyridine and 2 equiv of ethyl vinyl ether **4** in chloroform at 60 °C gave 1,4-benzooxathiin cycloadducts **5a–g** (Scheme 2). A reasonable mechanism involves pyridine deprotonation of the hydroxyl group to give phenates **6a–g** which undergo phthalimide anion elimination with the formation of *o*-thioquinones **7a–g**. These reactive electron poor dienes are then trapped[11] by the electron rich alkene **4** to give **5** via an inverse electron demand Diels–Alder reaction (Scheme 2).

In all the examples reported in Scheme 2 we observed the formation of a single regioisomeric 1,4-benzooxathiin where the oxygen of the *o*-thioquinone is linked to the hetero-substituted carbon of vinyl ether **4**. Quantum mechanic calculations[12] carried out on *o*-thioquinone **7e** and ethyl vinyl ether **4** indicated that HOMO–LUMO orbital energies are in agreement with an inverse electron demand Diels–Alder reaction. Moreover the orbital coefficients show that the favorite interaction involves the oxygen of **7e** and the hetero-substituted carbon of **4**. The reaction of *o*-thioquinones with enol ethers can be carried out also using cyclic systems like 2,3-dihydrofuran, 5,6-dihydro-2*H*-pyran, and 6-ethoxy-5,6-dihydro-2*H*-pyran which react with derivatives **3e–g**, in the previous reported conditions, to give cycloadducts **8–12**.

^{1}H NMR coupling constants of benzooxathiins **8–11** indicate a *cis* fusion of the two heterocyclic rings with the oxygen and the sulfur of the oxathiin in pseudoaxial and pseudoequatorial positions, respectively.

[†] Dedicated to Prof. Richard W. Franck on the occasion of his 60th birthday.

(1) For part 10 of this series see: Capozzi, G.; Falciani, C.; Menichetti, S.; Nativi, C. *Gazz. Chim. Ital.* **1996**, *126*, 227.

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(6) Capozzi, G.; Franck, R. W.; Mattioli, M.; Menichetti, S.; Nativi, C.; Valle, G. *J. Org. Chem.* **1995**, *60*, 6416.
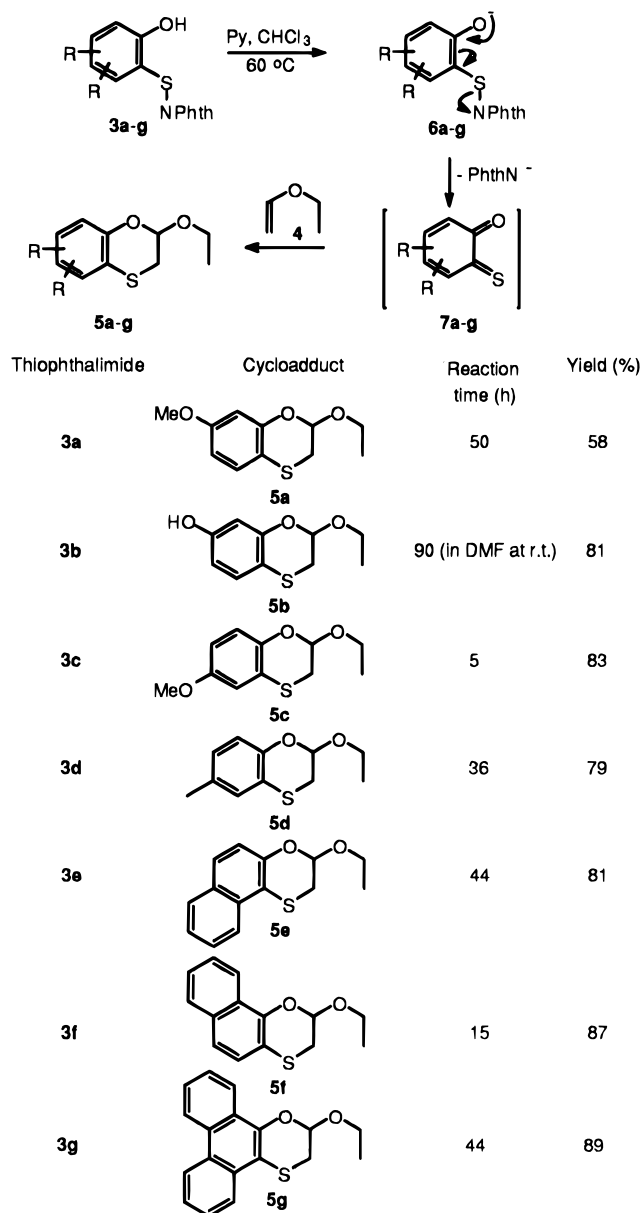
(7) Capozzi, G.; Dios, A.; Franck, R. W.; Geer, A.; Marzabaldi, C.; Menichetti, S.; Nativi, C.; Tamarez, M. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 777.

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Scheme 2

Thiophthalimide	Cycloadduct	Reaction time (h)	Yield (%)
3a	5a	50	58
3b	5b	90 (in DMF at r.t.)	81
3c	5c	5	83
3d	5d	36	79
3e	5e	44	81
3f	5f	15	87
3g	5g	44	89

Derivative **12** was isolated as a 80/20 mixture of diastereoisomers. Also in this case, the analysis of the ¹H NMR chemical shifts and coupling constants support the same structure of the oxathiin ring for both isomers, and show that the ethoxy group in the major isomer lies in a pseudoequatorial position.
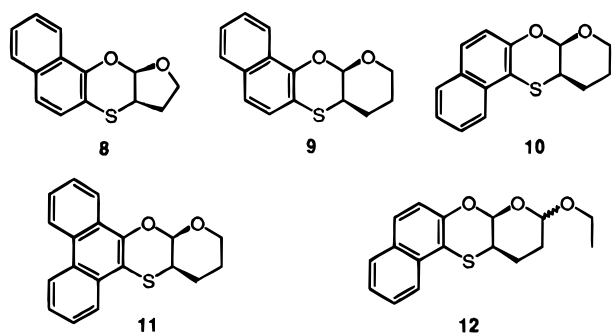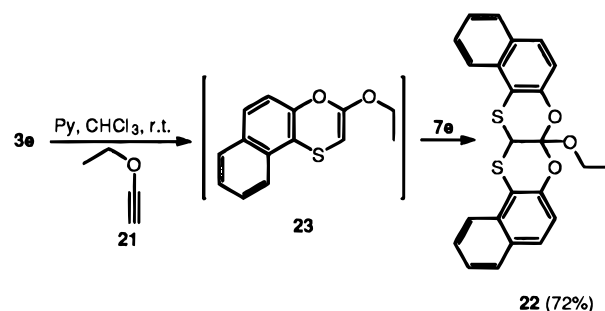

We showed that it was possible to use electron rich alkenes other than vinyl ethers in this Diels–Alder reaction by using *o*-thioquinone **7e** as a model substrate.

Table 1. Reaction of *o*-Thioquinone 7e with Dienophiles 13–16

| Entry	Dienophile	Product (react. time, Isolated yield)
1	13	17 (108 h, 89%)
2	14	18 (22 h, 71%)
3	15	19 (22 h, 70%)
4	16	20 (28 h, 62%)

Scheme 3

Indeed **7e** reacts with silyl enol ether **13**, phenyl vinyl sulfide (**14**), vinylpyrrolidone (**15**), and *p*-methoxystyrene (**16**) to give the expected cycloadducts **17–20** as single regioisomers (Table 1).

The versatility of *o*-thioquinones as efficient electron poor dienes has been verified in the reaction of **7e** with ethoxyethyne **21** giving bis-adduct **22** which was isolated in 72% yield after 10 h at room temperature (see Experimental Section). As in the case of α,α′-dioxothiones,[6] this result can easily be explained, assuming the reaction of **7e** with **21** gives monoadduct **23** and is followed by a second, faster, cycloadditon of **7e** with the intermediate **23** giving the final product (Scheme 3).

In a preliminary communication[7] we have shown that the carbon–sulfur double bond of *o*-thioquinones can also behave as a dienophile. In fact, generating **7e** in the

(11) Attempts to detect the transient *o*-thioquinines by ¹H NMR, in the absence of trapping agents, were unsuccessful as well as the possibility to trap the thioquinones as a metal legands.

(12) Ab initio calculations were obtained minimizing using a 3-21G* basis set with a geometric optimization implemented via a Spartan program running on an IBM-RISC 6000 workstation. Calculated energies (eV): **7e** HOMO −8.977; LUMO −0.261. **4**:[6] HOMO, −9.088; LUMO, 5.578.

Scheme 4
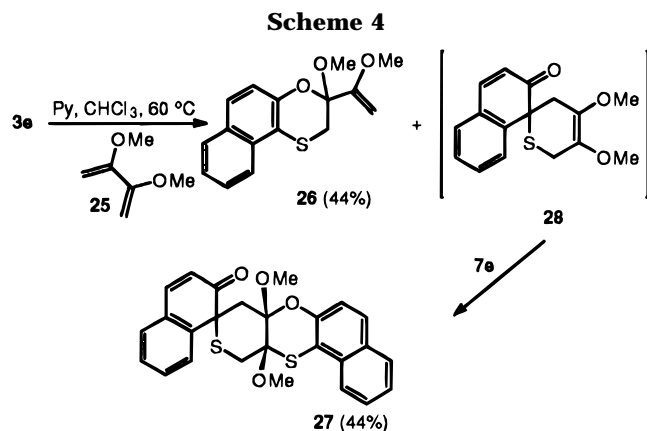
presence of 2,3-dimethyl-1,3-butadiene leads to a very slow cycloaddition reaction to give the spiro derivative **24**, isolated in 46% yield after 10 days at 60 °C.
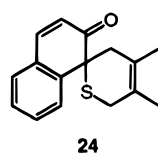

Two conclusions can be drawn from this result. First of all, *o*-thioquinones seem to be the real intermediates formed by basic treatment of sulfenamides **3**, since only the presence of a carbon−sulfur double bond can rationalize the formation of **24**. Secondly, the very low cycloaddition rate observed indicates that the carbon−sulfur double bond in *o*-thioquinone **7e** is a low-efficiency dienophile.

We verify this hypothesis by reacting **7e** with 2,3-dimethoxy-1,3-butadiene (**25**) which, in principle, can act both as an electron rich diene or as a dienophile. Under the usual reaction conditions equimolar amounts of **3e** and **25** gave oxathiin **26** and bis-adduct **27**[13] in 2:1 ratio and an 88% overall yield (Scheme 4). Compound **26** derives from the reaction of **7e** with one of the activated double bonds of **25**. The formation of **27** can be explained, assuming the reaction of the dienophilic thiocarbonyl residue of **7e** with the diene **25** to gives the spiro derivative **28**, which in turn is a very reactive dienophile for further reaction with 1 equiv of *o*-thioquinone.

In a similar experiment α,α′-dioxothiones gave, as the sole isolated product, the compound deriving from the reaction of the thione acting as dienophile.[6] This result indicates that, in contrast with the aliphatic species, for *o*-thioquinones the reactivity as dienes is higher than the reactivity as dienophiles. The reconstruction of the aromaticity in the final cycloadduct could play a role in this behavior.

The sweetening activity of a number of isovanillin-containing heterocyclic systems has been reported.[14] The structure of these compounds is strictly related to that of derivative **20** (see Table 1).

In this light we prepared a number of 5-aryl-1,4-benzooxathiins using *o*-thioquinones **7c** or **7e** as dienes and β-*trans*-methyl-4-methoxystyrene (anethole), β-*trans*-methyl-4-hydroxy-3-methoxystyrene (*trans*-isoeugenole), or 4-methoxy-3-hydroxystyrene (**29**) as electron-rich dienophiles. Cycloadducts **30**−**32** were obtained in good yield with control of the regiochemistry and with retention of the alkene geometry.
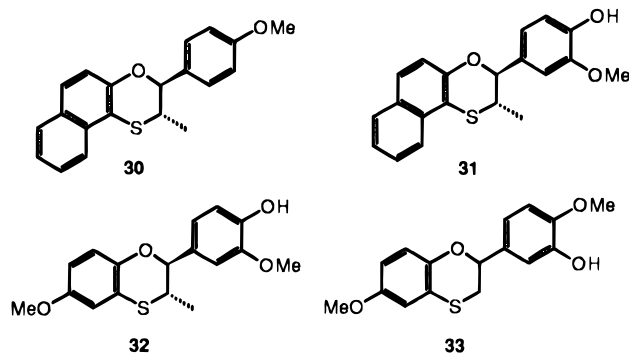
The versatility of this new approach to potentially sweet compounds has been verified in the total synthesis of isovanillin-containing derivative **34** which has been reported to be 500 times as sweet as sucrose.[14] As described in Scheme 5, the synthesis was carried out starting from *p*-hydroquinone. Thus, monoprotection of one of the hydroxyl groups of hydroquinone with *tert*-butyldimethylsilyl chloride, followed by the regiospecific sulfenylation with **1**, affords the thiophthalimide **35** which, under the standard conditions, generates the corresponding *o*-thioquinone **36**. Cycloaddition of **36** to the styrene **29** affords the silyl-derivative **37** which can be desilylated with cesium fluoride in methanol to give the expected non-glycoside sweetener **34** (Scheme 5).

Conclusion

In conclusion, we have shown that *o*-hydroxythiophthalimides, simply obtained from hydroxyl arenes and phthalimidesulfenyl chloride, are the precursors of *o*-thioquionones, which represent an interesting class of electron poor dienes. These reactive intermediates can be trapped by a number of different electron-rich alkenes and alkynes with complete regiochemical control to give 1,4-benzooxathiin systems.

Using activated styrenes as dienophiles, the cycloaddition of *o*-thioquinones affords derivatives with potential biological activity in a single step. Following this approach, the total synthesis of a non-glycoside sweetener was achieved in four steps starting from hydroquinone.

Further aspects of the reactivity of *o*-thioquinones, as well as the 1,4-benzooxathiins, are under investigation in this laboratory.

Experimental Section

^{1}H and ^{13}C NMR spectra were recorded (when not specified) in CDCl$_3$ at 200 and 50 MHz, respectively, using the residual CHCl$_3$ peak at 7.26 ppm for ^{1}H and the central peak of CDCl$_3$ at 77 ppm for ^{13}C as reference lines. Mass spectra and GC-MS analyses were obtained using a gas chromatograph, equipped with an OV101 30 m capillary column, interfaced to a mass spectrometer. Melting points are uncorrected. CHCl$_3$ and CH$_2$Cl$_2$ were dried following standard procedures. All commercial reagents were used without further purification as obtained from freshly opened containers. Monoprotection of

(13) In the crude reaction mixture, bis-adduct **27** was actually present as a 95:5 mixture of regioisomers. The structure reported for the major isomer, isolated by flash chromatography, was tentatively assigned in analogy with the parallel result obtained in the case of α,α′-dioxothiones.[6]

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Scheme 5
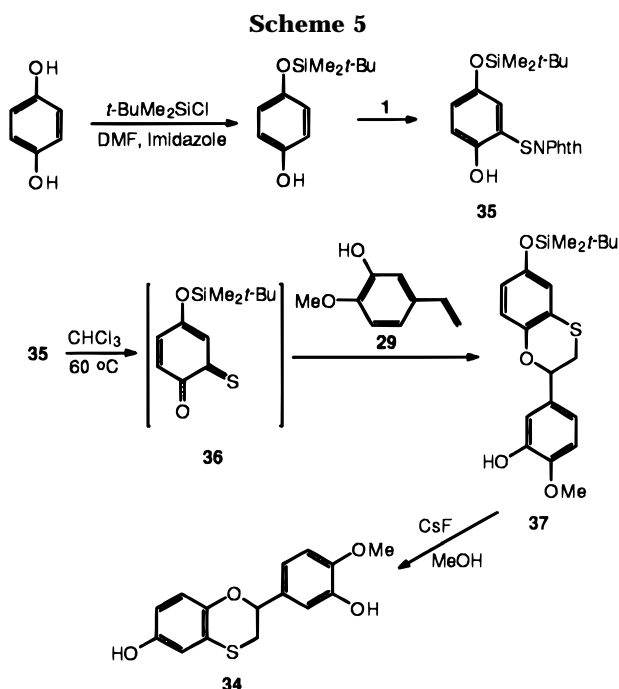
hydroquinone was done following standard procedures.[15] Phthalimidesulfenyl chloride (**1**),[16] thiophthalimides **3a**–**g**,[1] and cyclodducts **5c**–**e,g**, **10**, and **11**[10] were prepared as reported elsewhere. Thiophthalimide **35** and cyclodducts **5a,b,f**, **8**, **12**, **17**–**20**, **24**, **26**, **27**, **30**–**33**, and **37** have been similarly prepared; physical and spectroscopic data are as follows.

N-[[(2-Hydroxy-5-[(*tert*-butyldimethylsilyl)oxy]phenyl]-thio]phthalimide (35): 60% yield; white solid; mp 154–156 °C; ¹H NMR δ 0.17 (s, 6H), 0.94 (s, 9H), 6.88–6.89 (m, 2 H), 7.33 (bs, 1H), 7.76–7.91 (m, 4H), 7.94 (s, 1H). Anal. Calcd for $C_{20}H_{23}NO_4SSi$: C, 59.82; H, 5.77; N, 3.49. Found: C, 59.50; H, 5.81; N, 3.50.

2-Ethoxy-2,3-dihydro-7-methoxy-1,4-benzoxathiin (5a): 58% yield; glassy solid; ¹H NMR δ 1.25 (X₃ part of an ABX₃ system, $J_{AX} = J_{BX} = 7.1$ Hz, 3H), 3.04 (AB part of an ABX system, $J_{AB} = 13.0$ Hz, 2H), 3.65–4.15 (m, 5H), 5.37 (X part of an ABX system, $J = 4.8, 2.2$ Hz, 1H), 6.44–6.55 (m, 2H), 6.95 (d, $J = 8.4$ Hz, 1H); ¹³C NMR δ 15.1 (q), 29.2 (t), 55.4, 64.4 (q), 95.0 (d), 101.7 (s), 104.2, 108.8, 127.7 (d), 150.53, 158.3 (s); MS *m/z* (rel int) 226 (M⁺•, 81), 197 (11), 181 (21), 165 (100). Anal. Calcd for $C_{11}H_{14}O_3S$: C, 58.39; H, 6.24. Found: C, 58.17; H, 6.37.

2-Ethoxy-2,3-dihydro-1,4-benzoxathiin-7-ol (5b): 81% yield; glassy solid; ¹H NMR δ 1.24 (X₃ part of an ABX₃ system, $J_{AX} = J_{BX} = 7.0$ Hz, 3H), 3.03 (AB part of an ABX system, $J_{AB} = 13.0$ Hz, 2H), 3.65–4.04 (m, 2H), 5.63 (s, 1H), 5.36 (X part of an ABX system, $J = 4.6, 2.2$ Hz, 1H), 6.40–6.50 (m, 2H), 6.89 (d, $J = 9.2$ Hz, 1H); ¹³C NMR δ 15.0 (q), 29.1, 64.4 (t), 94.8, 105.8 (d), 108.5 (s), 109.7, 127.9 (d), 150.4, 154.1 (s); MS *m/z* (rel int) 212 (M⁺•, 100), 183 (13), 167 (14). Anal. Calcd for $C_{10}H_{12}O_3S$: C, 56.58; H, 5.70. Found: C, 56.27; H, 5.67.

6-Ethoxy-6,7-dihydro-5-oxa-8-thiaphenanthrene (5f): 87% yield; glassy solid; ¹H NMR δ 1.26 (X₃ part of an ABX₃ system, $J_{AX} = J_{BX} = 7.1$ Hz, 3H), 3.20 (AB part of an ABX system, $J_{AB} = 12.8$ Hz, 2H), 3.75–4.11 (AB part of an ABX₃, $J_{AB} = 16.8$ Hz, 2H), 5.59 (X part of an ABX system, $J = 4.6, 2.2$ Hz, 1H), 7.12 (d, $J = 8.8$ Hz, 1H), 7.30–7.55 (m, 3H), 7.37–7.73 (m, 3H), 8.01–8.19 (m, 1H); ¹³C NMR δ 15.1 (q), 29.3, 64.54 (t), 94.6 (d), 111.7 (s), 120.3, 121.1, 125.1, 125.3, 125.9 (d), 126.1 (s), 127.7 (d), 132.3, 143.8 (s); MS *m/z* (rel int) 246 (M⁺•, 100), 217 (4), 201 (7), 144 (15). Anal. Calcd for $C_{14}H_{14}O_2S$: C, 68.26; H, 5.73. Found: C, 68.49; H, 6.08.

Tetrahydrofurano[6a,7a-*b*]-5-oxa-8-thiaphenanthrene (6aα,7aα) (8): 73% yield; white solid; mp 90–93 °C; ¹H NMR δ

1.94–2.14 (m, 1H), 2.18–2.32 (m, 1H), 3.69–3.80 (m, 1H), 3.93–4.05 (m, 1H), 4.12–4.22 (m, 1H), 5.81 (d, $J = 4.4$ Hz, 1H), 7.22 (d, $J = 9.0$ Hz, 1H), 7.40–7.54 (m, 3H), 7.70–7.80 (m, 1H), 8.21–8.27 (m, 1H); ¹³C NMR δ 30.8 (t), 41.7 (d), 68.4 (t), 101.3 (d), 112.6 (s), 120.9, 122.0, 125.3, 125.8, 126.2, 127.5 (d), 126.3, 132.7, 148.8 (s); MS *m/z* (rel int) 244 (M⁺•, 100), 211 (64), 183 (55), 146 (95). Anal. Calcd for $C_{14}H_{12}O_2S$: C, 68.84; H, 4.96. Found: C, 68.90; H, 5.07.

5a,5,6,6,7,7a-Hexahydro-7,9-dioxa-10-thiabenz[*a*]anthracene (5aα,7aα) (9):[17] 81% yield; pale yellow solid; mp 96–99 °C; ¹H NMR δ 1.77–2.04 (m, 4H), 3.27–3.34 (m, 1H), 3.78–3.86 (m, 1H), 4.08–4.24 (m, 1H), 5.77 (d, $J = 2.6$ Hz, 1H), 7.12 (d, $J = 8.8$ Hz, 1H), 7.36–7.54 (m, 3H), 7.69–7.79 (m, 1H), 8.20–8.29 (m, 1H). Anal. Calcd for $C_{15}H_{14}O_2S$: C, 69.75; H, 5.47. Found: C, 69.68; H, 5.20.

6-Ethoxy-5a,5,6,6,7,7a-hexahydro-5,9-dioxa-10-thiabenz-[*a*]anthracene (5aα,7aα) (12).[17] Analysis of the crude reaction mixture showed the presence of two isomers in a 80/20 ratio isolated in 90% overall yield. Pure samples of both compounds were obtained by further flash chromatography (petroleum ether:ethyl acetate = 5:1). Major isomer: oil; ¹H NMR δ 1.29 (X₃ part of an ABX₃ system, $J_{AX} = J_{BX} = 7.0$ Hz, 3H), 1.68–1.80 (m, 2H), 1.95–2.35 (m, 2H), 3.48–3.56 (m, 1H), 3.56–3.70 (m, 1H), 3.94–4.09 (m, 1H), 5.13 (dd, $J = 2.8, 6.4$ Hz, 1H), 5.78 (d, $J = 2.2$ Hz, 1H), 7.12 (d, $J = 8.8$ Hz, 1H), 7.38–7.57 (m, 3H), 7.28–7.89 (m, 2H); ¹³C NMR δ 15.2 (q), 24.1, 28.2 (t), 35.9 (d), 64.1 (t), 92.1 (d), 97.6 (d), 109.0 (s), 119.3, 122.6, 124.3, 126.0, 126.4, 128.3 (d), 129.6, 130.9, 147.0 (s); MS *m/z* (rel int) 302 (M⁺•, 100), 256 (15). Anal. Calcd for $C_{17}H_{18}O_3S$: C, 67.52; H, 6.00. Found: C, 67.24; H, 6.34.

Minor isomer: yellowish oil; ¹H NMR δ 1.29 (X₃ part of an ABX₃ system, $J_{AX} = J_{BX} = 7.0$ Hz, 3H), 1.68–1.80 (m, 2H), 1.95–2.35 (m, 2H), 3.40–3.52 (m, 1H), 3.50–3.64 (m, 1H), 3.94–4.08 (m, 1H), 4.87 (bt, $J = 4.0$ Hz, 1H), 5.65 (d, $J = 2.2$ Hz, 1H), 7.07 (d, $J = 8.8$ Hz, 1H), 7.34–7.58 (m, 3H), 7.73–7.82 (m, 2H).

(5a)-[(Trimethylsilyl)oxy]-5a,5,6,7,8,8a-hexahydro-5-oxa-10-thiabenz[*a*]anthracene (17): 89% yield; white solid; mp 88 °C; ¹H NMR δ 0.03 (s, 9H), 1.28–1.80 (m, 5H), 1.82–1.97 (m, 2H), 2.30–2.44 (m, 1H), 3.06 (dd, $J = 4.0, 10.0$ Hz, 1H), 7.02 (d, $J = 8.0$ Hz, 1H), 7.32–7.53 (m, 3H), 7.73–7.80 (m, 1H), 7.91–7.98 (m, 1H); ¹³C NMR δ 1.5 (q), 23.4 (t), 25.3, 31.7 (t), 39.9 (d), 44.6 (t), 95.2 (s), 109.9 (s), 119.8, 122.8, 123.9, 125.3, 126.0, 128.6 (d), 129.42, 131.2, 146.2 (s); MS *m/z* (rel int) 344 (M⁺•, 77), 271 (1), 73 (100). Anal. Calcd for $C_{19}H_{24}O_2SSi$: C, 66.24; H, 7.02. Found: C, 66.10; H, 6.90.

7-(Phenylthio)-6,7-dihydro-5-thia-8-oxaphenanthrene (18): 70% yield; yellow oil; ¹H NMR δ 3.50 (AB part of an ABX system, $J_{AB} = 12.8$ Hz, 2H), 5.95 (X part of an ABX system, $J = 3.0, 4.6$ Hz, 1H), 7.10 (d, $J = 8.0$ Hz, 1H), 7.31–7.65 (m, 8H), 7.73–7.98 (m, 2H); ¹³C NMR δ 30.1 (t), 81.6 (d), 110.7 (s), 120.1, 122.5, 124.4, 126.2, 126.4, 127.9, 128.3, 129.0 (d), 129.64, 131.0, 132.6, 133.2, 146.8 (s); MS *m/z* (rel int) 310 (M⁺•, 50), 201 (69), 135 (100). Anal. Calcd for $C_{18}H_{14}OS_2$: C, 69.65; H, 4.55. Found: C, 69.58; H, 4.71.

7-(2'-Oxo-2',3',4',5'-tetrahydropyrrolidino)-6,7-dihydro-5-thia-8-oxaphenanthrene (19): 70% yield; white solid; mp 168–170 °C; IR 1692 cm⁻¹; ¹H NMR δ 2.00–2.20 (m, 2H), 2.46–2.54 (m, 2H), 3.07 (A part of an ABX system, $J_{AB} = 12.8$ Hz, 1H), 3.31 (B part of an ABX $J_{AB} = 12.8$ Hz, 1H), 3.41–3.58 (m, 1H), 3.60–3.72 (m, 1H), 6.21 (X part of an ABX system, $J = 2.2, 8.8$ Hz, 1H), 7.03 (d, $J = 8.0$ Hz, 1H), 7.34–7.56 (m, 3H), 7.72–7.88 (m, 2H); ¹³C NMR δ 18.1, 29.6, 31.2, 42.5 (t), 77.3 (d), 109.7 (s), 119.4, 122.7, 124.3, 126.4, 126.5, 128.2 (d), 129.3, 130.9, 149.4, 175.4 (s); MS *m/z* (rel int) 285 (M⁺•, 31), 200 (75), 110 (100). Anal. Calcd for $C_{16}H_{15}NO_2S$: C, 67.34; H, 5.30, N, 4.91. Found: C, 67.42; H, 5.54, N, 4.74.

7-(4'-Methoxyphenyl)-6,7-dihydro-5-thia-8-oxaphenanthrene (20): 62% yield; white solid; mp 100 °C; ¹H NMR δ 3.30 (AB part of an ABX system, $J_{AB} = 13.2$ Hz, 2H), 3.85 (s, 3H), 5.25 (X part of an ABX system, $J = 8.8, 2.6$ Hz, 1H), 6.94–7.01 (m, 2H), 7.14 (d, $J = 8.8$ Hz, 1H), 7.36–7.57 (m, 5H), 7.76–7.94 (m, 2H); ¹³C NMR δ 31.3 (t), 55.3 (q), 76.2 (d), 110.2 (s), 114.1, 120.0, 122.6, 124.1, 125.7, 126.3 (d), 127.3 (d, 2C), 128.9, 131.1, 132.4, 150.1, 159.7 (s); MS *m/z* (rel int) 308 (M⁺•, 63), 149 (100). Anal. Calcd for $C_{19}H_{16}O_2S$: C, 74.00; H, 5.23. Found: C, 73.61; H, 5.48.

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Bis-Adduct (22). Due to the high volatility of ethoxyethyne **21**, the reaction was carried out at room temperature adding 4 mol equiv of the acetylene in small aliquots during 10 h. The usual workup and column chromatography gave **22**, 72% yield as n yellow oil; ¹H NMR δ 1.23 (t, *J* = 7.0 Hz, 3H), 4.17 (q, *J* = 7.0, Hz, 2H), 5.00 (s, 1H), 7.13 (d, *J* = 8.8 Hz, 2H), 7.37−7.83 (m, 10 H); MS *m/z* (rel int) 418 (M⁺•, 9); 244 (100). Anal. Calcd for C₂₄H₁₈O₃S₂: C, 68.88; H, 4.33. Found: C, 68.67; H, 4.58.

Spiro derivative 24: 46% yield; glassy solid; ¹H NMR δ 1.78−1.88 (m, 6H), 2.58−2.88 (m, 3H), 3.20 (A part of an AB system, *J* = 16.8 Hz, 1H), 6.21 (d, *J* = 9.8 Hz, 1H), 7.24−7.60 (m, 5H); ¹³C NMR δ 19.7, 20.3 (q), 30.5, 36.6 (t), 51.3 (s), 122.9, 124.4, 127.1 (d), 127.7 (s), 127.9 (d), 129.4, 129.8, 129.9 (2s + 1d), 141.8 (s) 142.5 (d), 195.1 (s); MS *m/z* (rel int) 256 (M⁺•, 14), 254 (100), 209 (17). Anal. Calcd for C₁₆H₁₆OS: C, 74.96; H, 6.29. Found: C, 75.12; H, 6.19.

7-(1′-Methoxyethynyl)-7-methoxy-5-thia-8-oxa-7,8-dihydrophenanthrene (26): 44% yield; white solid; mp 95−97 °C; ¹H NMR δ 3.28 (AB system, *J*ₐᵦ = 13.2 Hz, 2H), 3.34 (s, 3H), 3.70 (s, 3H), 4.42 (d, *J* = 2.5 Hz, 1H), 4.79 (d, *J* = 2.5 Hz, 1H), 7.16 (d, *J* = 8.8 Hz, 1H), 7.26−7.51 (m, 2H), 7.58 (d, *J* = 8.8 Hz, 1H), 7.77 (dd, *J* = 8.6, 1.4 Hz, 1H), 7.94 (dd, *J* = 8.6, 0.6 Hz, 1H); ¹³C NMR δ 31.7 (t), 50.8, 55.5 (q), 85.7 (t), 95.0, 111.6 (s), 119.7, 122.8, 124.3, 125.9, 126.3, 128.1 (d), 129.4, 130.9, 146.7, 157.9 (s); MS *m/z* (rel int) 288 (M⁺•, 10); 256 (25); 43 (100). Anal. Calcd for C₁₆H₁₆O₃S: C, 66.64; H, 5.59. Found: C, 66.72; H, 5.77.

Bis-adduct (27): 44% yield; yellow solid; mp 179−182 °C; ₁H NMR δ 2.94 (AB system, *J*ₐᵦ = 14.0 Hz, 2H), 3.28 (A part of an AY system, *J*ₐY = 13.9 Hz, 1H), 3.38 (s, 3H), 3.53 (s, 3H), 4.16 (Y part of an AY system, *J*ₐM = 13.9 Hz, 1H), 6.28 (d, *J* = 10.0 Hz, 1H), 6.99 (d, *J* = 9.2 Hz, 1H), 7.21−7.58 (m, 8H), 7.65−8.01 (m, 2H); ¹³C NMR δ 33.7, 47.9 (t), 50.89, 52.1 (q), 59.6, 86.9, 99.3, 109.3, 112.8 (s), 119.4 (d), 124.1 (s), 124.7 (d), 125.2 (s), 126.9, 127.1, 128.0, 128.6, 128.8, 129.8, 134.8 (d), 130.1, 131.8, 133.1 (s), 142.4 (d), 148.1 (s), 200.4 (s); MS *m/z* (rel int) 461 ((M − 1)⁺•, 1), 288 (22), 256 (100). Anal. Calcd for C₂₆H₂₂O₄S₂: C, 67.52; H, 4.80. Found: C, 67.07; H, 4.99.

3-Hydroxy-4-methoxystyrene (29). To a solution of 1.08 g (2.6 mmol) of instant ylide in 50 mL of dry THF kept at −78 °C was added 3-hydroxy-4-methoxybenzaldehyde (isovanillin) 200 mg (1.3 mmol) in THF (2 mL) dropwise. The reaction mixture was allowed to reach room temperature and stirred 10 h. The crude mixture was then diluted with petroleum ether and washed with saturated NH₄Cl (20 mL) and with water (2 × 20 mL). Flash chromatography (petroleum ether/ethyl acetate 3:1) afforded 66 mg (87% yield) of **29** which was used without further purification: ¹H NMR δ 3.89 (s, 3H), 5.15 (dd, *J* = 11.0, 1.0 Hz, 1H), 5.61 (dd, *J* = 17.6, 1.0 Hz, 1H), 5.78 (s, 1H, OH), 6.63 (dd, *J* = 17.6, 11.0 Hz, 1H), 6.78−7.08 (m, 3H).

(*E*)-6-Methyl-7-(4′-methoxyphenyl)-6,7-dihydro-5-thia-8-oxaphenanthrene (30): 74% yield; white solid; mp 123−125 °C; ¹H NMR δ 1.22 (d, X₃ part of an AMX₃ system, *J* = 7.0 Hz, 3H), 3.54 (dq, M part of an AMX₃ system, *J* = 7.0, 8.4 Hz, 1H), 3.86 (s, 3H), 4.83 (d, A part of an AMX₃ system, *J* = 8.4 Hz, 1H), 6.93−7.03 (m, 2H), 7.13 (d, *J* = 8.8 Hz, 1H), 7.31−7.56 (m, 5H) 7.77−7.82 (m, 1H), 7.89−7.93 (m, 1H); ¹³C NMR δ 18.2 (q), 38.4 (d), 55.8 (q), 83.1 (d), 112.3 (s), 114.6, 120.2, 123.1, 124.6, 126.0, 126.8, 128.8, 129.0, 129.2 (d, 11C), 131.3, 131.4, 150.5, 160.4 (s); MS *m/z* (rel int) 322 (M⁺•, 1), 147 (100). Anal. Calcd for C₂₀H₁₈O₂S: C, 74.50; H, 5.63. Found: C, 74.30; H, 5.68.

(*E*)-6-Methyl-7-(3′-hydroxy-4′-methoxyphenyl)-6,7-dihydro-5-thia-8-oxaphenanthrene (31): 69% yield; white solid; mp 130−133 °C; ¹H NMR δ 1.22 (d, X₃ part of an AMX₃ system, *J* = 8.0 Hz, 3H), 3.53 (dq, M part of an AMX₃ system, *J* = 6.0, 8.0 Hz, 1H), 3.93 (s, 3H), 4 .78 (d, A part of an AMX₃ system, *J* = 8.0 Hz, 1H), 5.77 (bs, 1H, OH), 6.89−7.02 (m, 3H), 7.14 (d, *J* = 10.0 Hz, 1H), 7.39−7.57 (m, 3H), 7.77−7.95 (m, 2H); ¹³C NMR δ 18.2 (q), 38.4 (d), 56.5 (q), 83.45 (d), 109.7 (d), 112.4 (s), 114.9, 120.2, 121.3, 123.1, 124.6, 126.0, 126.8, 128.8 (d), 129.9, 131.0, 131.3, 146.6, 147.5, 150.5 (s); MS *m/z* (rel int) 338 (M⁺•, 54), 164 (100). Anal. Calcd for C₂₀H₁₈O₃S: C, 70.98; H, 5.36. Found: C, 71.21; H, 5.29.

(*E*)-2-(3-Methoxy-4-hydroxyphenyl)-3-methyl-2,3-dihydro-6-methoxy-1,4-benzoxathiin (32): 85% yield; pale yellow solid; mp 148−150 °C; ¹H NMR δ 1.06 (d, X₃ part of an AMX₃ system, *J* = 6.6 Hz, 3H), 3.47 (dq, M part of an AMX₃ system, *J* = 6.6, 8.8 Hz, 1H), 3.76 (s, 3H), 3.92 (s, 3H), 4.57 (d, A part of an AMX₃ system, *J* = 8.8 Hz, 1H), 5.69 (s, 1H, OH), 6.58−6.63 (m, 2H), 6.80−6.93 (m, 4H); ¹³C NMR δ 17.5 (q), 38.5 (d), 55.7, 55.9 (q), 82.9, 109.0, 110.4, 111.8, 114.3, 119.0 (d), 119.8 (s), 120.7 (d), 130.5, 145.9, 146.5, 146.8, 154.1 (s); MS *m/z* (rel int) 318 (M⁺•, 33), 181 (20), 164 (100). Anal. Calcd for C₁₇H₁₈O₄S: C, 64.13; H, 5.70. Found: C, 64.02; H, 5.77.

2-(3-Hydroxy-4-methoxyphenyl)-2,3-dihydro-6-methoxy-1,4-benzoxathiin (33): 51% yield; oil; ¹H NMR δ 3.14 (AB part of an ABX system, *J*ₐᵦ = 13.0 Hz, 2H), 3.75 (s, 3H), 3.91 (s, 3H), 5.02 (X part of an ABX system, *J* = 1.8, 9.5 Hz, 1H), 5.67 (s, 1H, -OH), 6.56−6.89 (m, 6H); ¹³C NMR δ 31.8 (t), 55.7, 56.0 (q), 76.1, 110.6 (d), 111.3 (s), 112.1, 112.4 (d), 117.7 (s), 117.8, 119.3, 133.6 (d), 145.8, 146.5, 146.6, 154.0 (s); MS *m/z* (rel int) 304 (M⁺•, 36), 150 (100). Anal. Calcd for C₁₆H₁₆O₄S: C, 63.14; H, 5.30. Found: C, 63.13; H, 5.52.

2-(3-Hydroxy-4-methoxyphenyl)-2,3-dihydro-6-[(*tert*-butyldimethylsilyl)oxy]-1,4-benzoxathiin (37): 47% yield; oil; ¹H NMR δ 0.17 (s, 6H), 0.97 (s, 9H), 3.01 (A part of an ABX system, *J*ₐᵦ = 12.9 Hz, 1H), 3.25 (B part of an ABX system, *J*ₐᵦ = 12.9 Hz, 1H), 3.91 (s, 3H), 5.01 (X part of an ABX system, *J* = 9.8, 2.0 Hz, 1H), 6.20 (s, 1H, OH), 6.46−6.99 (m, 6H). Anal. Calcd for C₂₁H₂₈O₄SSi: C, 62.34; H, 6.98. Found: C, 62.23; H, 6.72.

2-(3-Hydroxy-4-methoxyphenyl)-2,3-dihydro-1,4-benzoxathiin-6-ol (34). A solution of **37** (32 mg, 0.08 mmol) and cesium fluoride (16 mg, 0.12 mmol) in 2 mL of methanol was maintained under stirring at room temperature for 3 h. The mixture was then diluted with diethyl ether (30 mL), washed twice with saturated NH₄Cl, and dried over anhydrous Na₂SO₄. Flash chromatography (petroleum ether:ethyl acetate = 3:1) afforded 12 mg (52% yield) of **34** which was identified by comparison with literature data:[14] ¹H NMR δ 2.98−3.31 (AB part of an ABX system, *J*ₐᵦ = 13.2 Hz, 2 H), 3.91 (s, 3 H), 4.51 (bs, 1H, OH), 5.01 (X part of an ABX system, *J* = 9.4, 2 Hz, 1 H), 5.66 (bs, 1H, OH), 6.47−6.98 (m, 6 H).