Synthesis of *p*-phenylthio- *peri*-hydroxy polyaromatic compounds by strong-base-induced [4+2] cycloaddition of 4-(phenylthio)homophthalic anhydrides with phenylsulfinyl-dienophiles

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Dedicated to Professor Keiichiro Fukumoto on the occasion of his 70th birthday

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Abstract

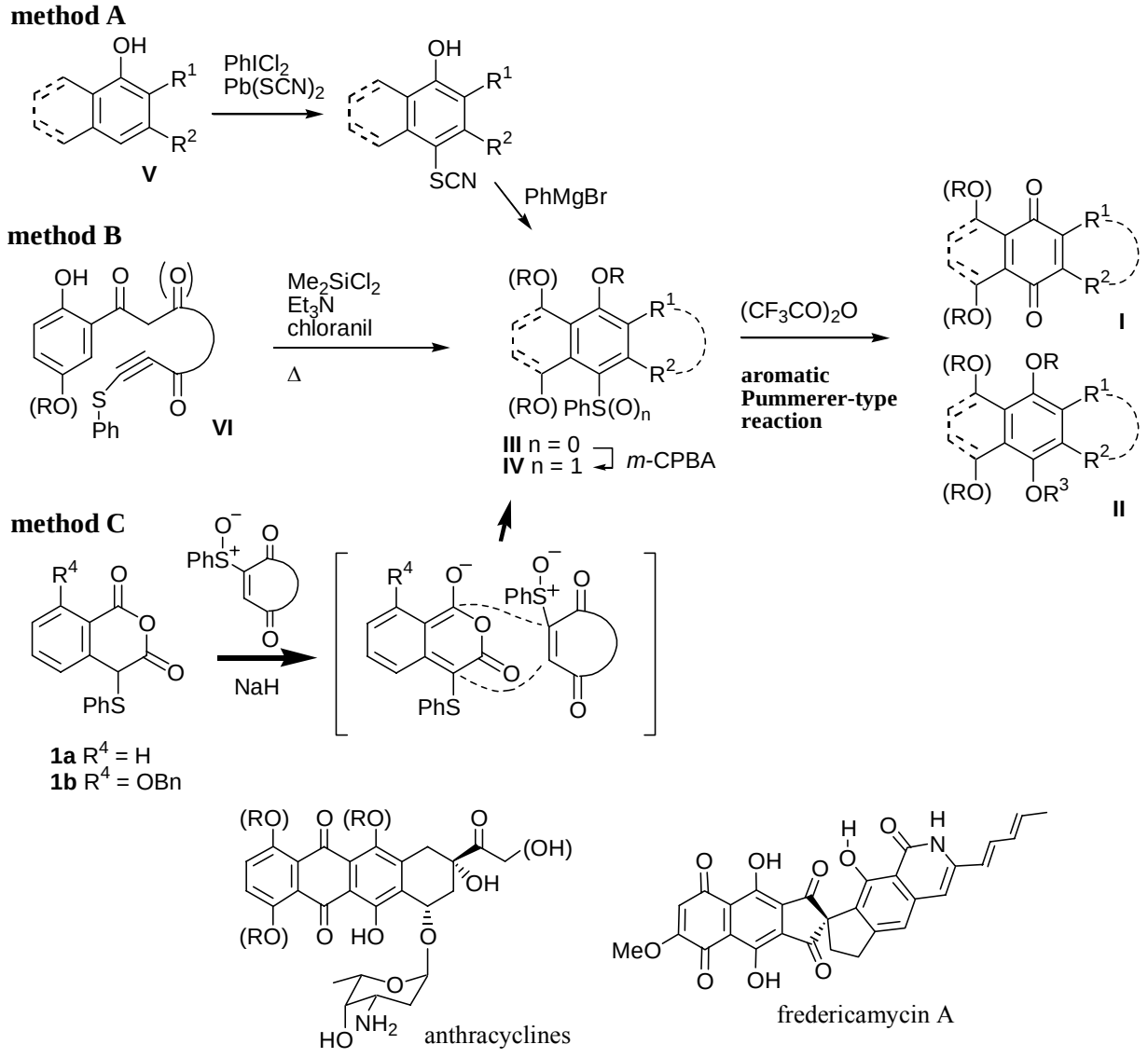
A direct and regioselective synthesis of *p*-phenylthio-substituted *peri*-hydroxy polyaromatic compounds (**9**–**12**) was developed via the strong-base-induced [4+2] cycloaddition of the 4-(phenylthio)homophthalic anhydrides (**1a**–**d**) to the phenylsulfinyl-substituted dienophiles (**5**–**8**). The sulfinyl group in **5**–**8** is the key to producing the desired reaction under mild conditions (at –20 °C to room temperature) in good yields. A reaction mechanism explaining the remarkable effect of the sulfinyl group is discussed.

Keywords: *peri*-Hydroxy polyaromatic compounds, strong-base-induced [4+2] cycloaddition, homophthalic anhydride, sulfinyl-substituted dienophile

Introduction

General and efficient syntheses of *peri*-hydroxy polyaromatic *p*-quinones (**I**) and their dihydroquinone derivatives (**II**) are important in recent synthetic organic- and medicinal chemistry because these compounds are key components of many biologically important natural products such as anthracyclines[1] and fredericamycin A.[2] For the synthesis of these quinone compounds, the transformation of phenols into *p*-benzoquinones or *p*-dihydrobenzoquinone derivatives has been one of the most important steps.[3] Recently, we reported a new method for the synthesis of **I** and **II** from *p*-(phenylthio)phenols (**III**) *via* the aromatic Pummerer-type reaction of the derived sulfoxides (**IV**).[4] The synthesis of **III** has been achieved by two methods; *viz*, the *p*-specific thiocyanation of phenols (**V**) using the combination of $PhICl_2$ and $Pb(SCN)_2$

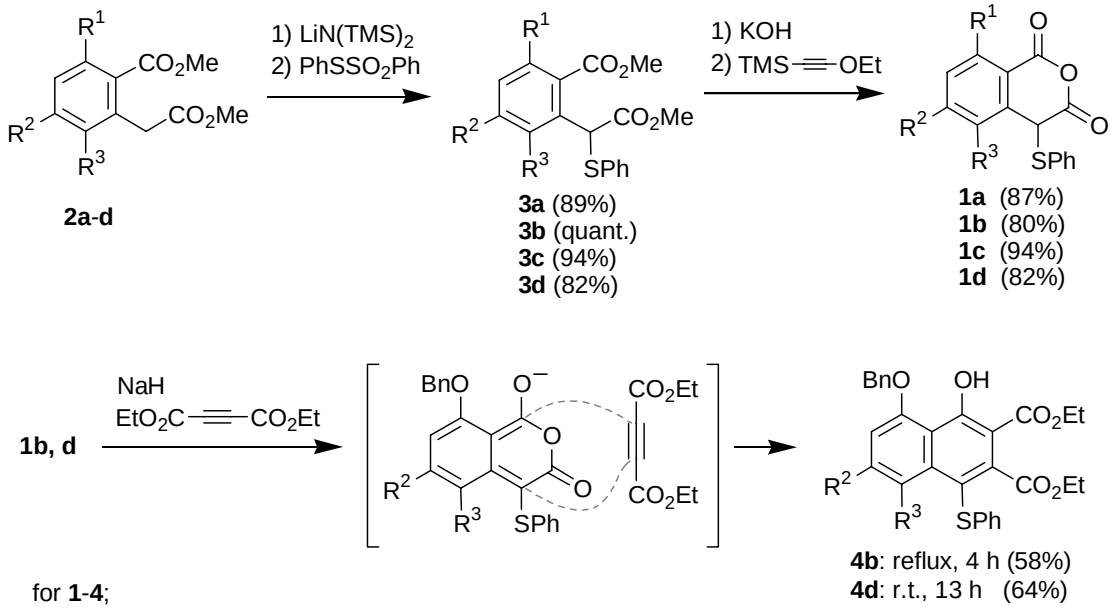
followed by reaction with PhMgBr (method A)[4d,5] and the oxidative intramolecular [4+2] cycloaddition of *o*-[(ω-phenylthio-ethynyl)acyl]-phenols (**VI**) (method B).[6] Recently, we briefly reported a third method, based on the strong-base-induced [4+2] cycloaddition of 4-(phenylthio)-homophthalic anhydrides (**1a**,**b**) to sulfinyl-substituted dienophiles, in which we found that the sulfinyl groups were essential for producing the desired reaction under mild conditions in good yields (method C) (Scheme 1).[7] We now give a full account of our studies on method C, with additional examples using the new homophthalic anhydrides (**1c** and **1d**). A reaction mechanism to explain the remarkable effect of the sulfinyl group is also discussed.



Scheme 1

Results and Discussion

The starting 4-(phenylthio)homophthalic anhydrides (**1a**–**d**) were readily prepared from the corresponding homophthalic acid dimethyl esters (**2a**–**d**), in good overall yields. That is, the reaction of **2** with lithium bis-(trimethylsilyl)amide followed by treatment with $PhSSO_2Ph$ afforded the phenylthio-substituted diesters (**3**). Alkaline hydrolysis of **3** and dehydration of the resultant dicarboxylic acids with trimethylsilyl(ethoxy)acetylene[8] afforded **1**. As in our previous study using the related homophthalic anhydrides,[9] the cycloaddition of **1b**, **d** with acetylenedicarboxylic acid diethyl ester took place in the presence of NaH to give directly the *p*-phenylthio-substituted adducts (**4b** and **4d**) in 58% and 64% yields, respectively (Scheme 2).



Scheme 2

In order to establish the regioselective synthesis of the *p*-phenylthio-substituted *peri*-hydroxy polyaromatic compounds, we examined the strong-base-induced [4+2] cycloaddition of **1a** with naphthoquinones (**5a**–**d**) bearing various types of activating groups (**X**). The reactions of **1a** with the known halogen-substituted naphthoquinones (**5a,b**)[1e,f,10] took a long time to produce the tetracyclic product (**9a**), in 65–67 yields (Table 1, runs 1 and 2). The similar reaction with the phenylthio derivative (**5c**)[11] did not proceed at all, even in refluxing THF (run 3). On the other hand, the reaction with the phenylsulfinyl derivative (**5d**)[12] was very fast at room temperature, to give **9a** in 72% yield (run 4).

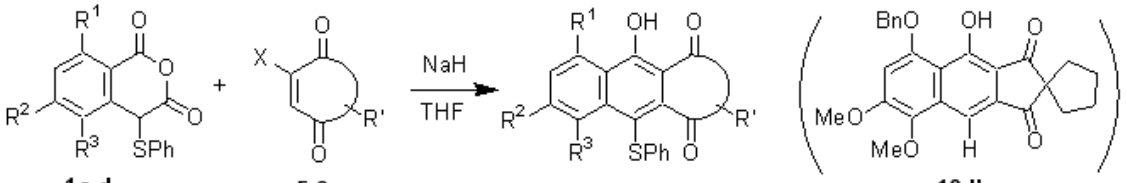
In a like manner, the reactions of a highly-oxygen-substituted homophthalic anhydride (**1d**) and the spiro-dienophiles (**6a**–**e**) were investigated. The reaction of **1d** with the bromide (**6a**) required refluxing in THF to give a mixture of the desired product **10d** and the product lacking the phenylthio group, (**10d'**), in low yield (run 5). Similar low reactivity and/or the formation of **10d'** were also observed in the reactions with the arylthio- (**6b**, **c**) and the phenylsulfonyl-derivative (**6e**) (runs 6, 7 and 9). In contrast, the reaction with the sulfinyl derivative (**6d**) was again very fast at room temperature, to afford **10d** (77% yield) without forming **10d'** (run 8). Thus, the sulfinyl group was unique, because other electron-withdrawing substituents, viz., the p-nitrophenylthio- (**6c**), and the phenylsulfonyl- (**6e**) groups, were not efficient.

The NaH-induced [4+2] cycloaddition reaction of **1** was found to be generally applicable for a range of sulfinyl-substituted dienophiles (**5d**, **6d**, **7**, and **8**) as summarized in Table 1. All the reactions were completed at or below room temperature and gave the expected adducts (**9**–**12**) in 66–82% yields. The reactions with a set of two regioisomers (**5d** and **7**) afforded the corresponding products (**9** and **11**) as a single product, and thus, the regiochemistry of each reaction was proved to be controlled exclusively by the position of the sulfinyl group. Some results of the reactions with the corresponding bromo-substituted dienophiles are also given in brackets (runs 10, 14, 17, and 21) to emphasize the general superiority of the phenylsulfinyl group over the halogen substituents.

In order to obtain some insights into the reactivity of dienophiles, the frontier molecular orbital (FMO) energy levels of **5**–**8** and some related compounds were calculated using the PM3 Hamiltonian in the Spartan (ver. 3.1.2) program (Table 2). The results show that the LUMO levels of the sulfinyl-substituted dienophiles (**5d**, **6d**, **7**, and **8**) are similar to, or lower than, those of the halogen derivatives (**5a**, **5b**, **6a**, etc.) but higher than that of the sulfonyl derivative (**6e**). Therefore, the LUMO levels are not the only factor that causes the remarkable effect of the sulfinyl group in our case.

The following reaction mechanism seems plausible. First, the δ-oxy-quinodimethanes **A**, generated by the treatment with NaH, would produce the oxyanion-assisted Diels–Alder type cycloaddition[9,13] to dienophiles to provide the adduct **B** in which the X and H groups are situated syn- to each other. In the case of the sulfinyl-substituted dienophiles [X = S(O)Ph], the easy syn-elimination of PhSOH followed by the oxyanion-assisted retro-Diels–Alder reaction[14] of the resultant **C** would give the cycloadducts (**9**–**12**) with CO_2 release[15] (Scheme 3). These irreversible reactions from **B** to the final products could proceed at or below room temperature, as reported in the literature.[12,14] Thereby, the fast and exclusive formation of **10d** from **6d** was attained.[16] On the other hand,, the reactions of the halogen- and sulfonyl-substituted dienophiles must have suffered a slow elimination of the X and H groups in **B**, which not only retarded the overall reaction but also brought about the side reaction leading to **10d'**. This explanation may be consistent with the fact that the reaction of **1d** with diethyl acetylenedicarboxylate gave exclusively **4d**, in which the intermediate (**C'**) was formed directly from **A**.

Table 1. Reaction of 4-(phenylthio)homophthalic anhydrides **(1a-d)** with dienophiles **(5-8)**[a]



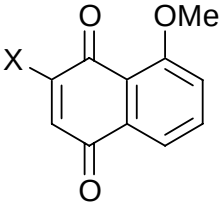
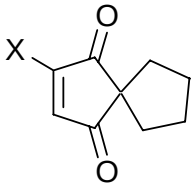
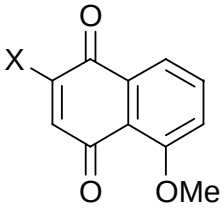
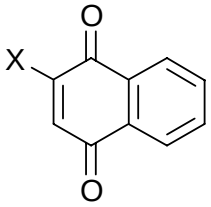
1a-d **5-8** **9-12** **10d'**

for **1**, **9-12**; **a** $R^1 = R^2 = R^3 = H$; **b** $R^1 = OBn$, $R^2 = R^3 = H$;
c $R^1 = OBn$, $R^2 = H$, $R^3 = OMe$; **d** $R^1 = OBn$, $R^2 = R^3 = OMe$

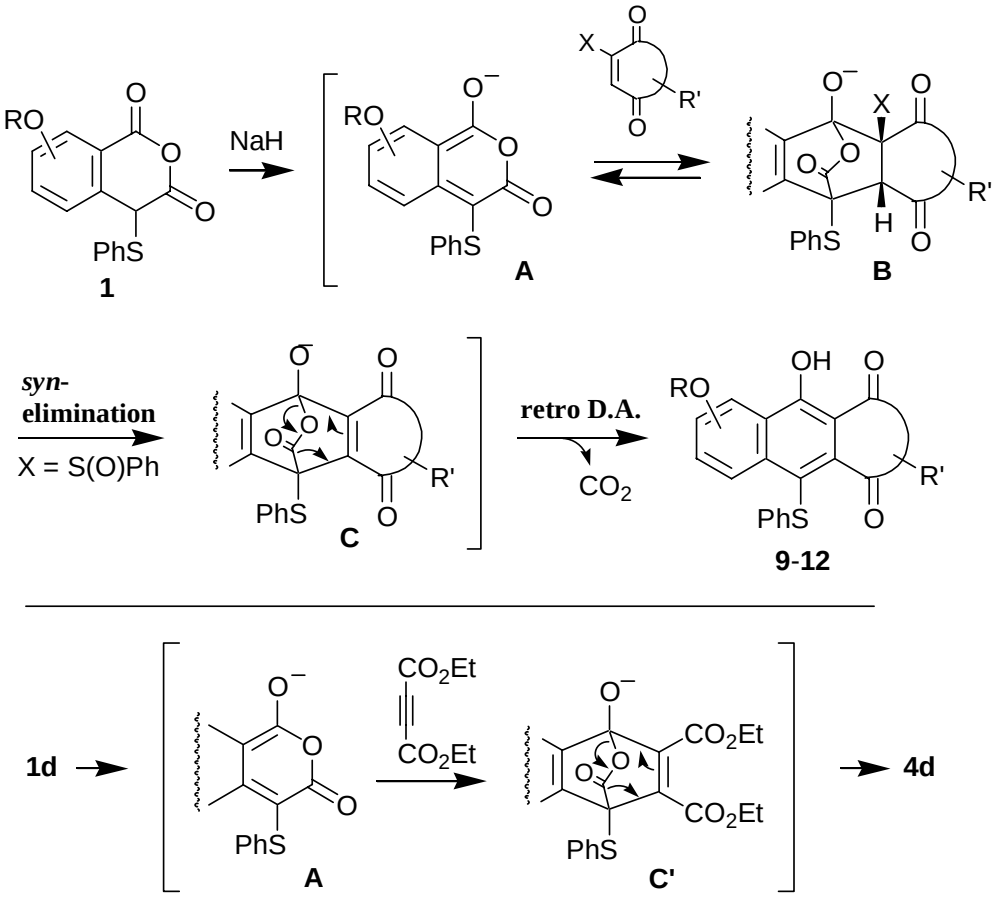
run	1	dienophile	reaction conditions	product	yield (%)[b]
1	**1a**	**5a** X = Cl	r.t., 4 d		**9a** 65
2	//	**5b** Br	r.t., 42 h		// 67
3	//	**5c** SPh	reflux, 15 h		// No Rxn.
4	//	**5d** S(O)Ph	r.t., 1 h		// 72
5	**1d**	**6a** X = Br	reflux, 12 h		**10d** 15 **10d'** 4
6	//	**6b** SPh	reflux, 12 h		// 0 // 19
7	//	**6c** S-C_6H_4-*p*-NO_2	r.t., 2 h		// 0 // 51
8	//	**6d** S(O)Ph	r.t., 2 h		// 77 // 0
9	//	**6e** SO_2Ph	r.t., 2 h		// 64 // 22
10	**1b**	**5d**	r.t., 1 h		**9b** 73 [r.t., 7 d, 48%][c]
11	**1c**		r.t., 15 h		**9c** 75
12	**1d**		r.t., 12 h		**9d** 78
13	**1a**	**6d**	r.t., 1 h		**10a** 76
14	**1b**		r.t., 0.5 h		**10b** 82 [r.t., 3 d, 32%][c]
15	**1c**		r.t., 2 h		**10c** 71
16	**1a**	**7**	r.t., 0.5 h		**11a** 73
17	**1b**		r.t., 1 h		**11b** 67 [r.t., 3 d, 52%][c]
18	**1c**		r.t., 5 h		**11c** 70
19	**1d**		r.t., 1 h		**11d** 72
20	**1a**	**8**	–20 to 0 °C, 1.5 h		**12a** 70
21	**1b**		–20 to 0 °C, 2 h		**12b** 66 [r.t., 7 d, 48%][c]
22	**1c**		–20 to 0 °C, 1.5 h		**12c** 68
23	**1d**		–20 to 0 °C, 3 h		**12d** 70

[a] The molar ratio of the reagents is generally as follows: **1** (1.3 equiv), and **5-8** (1.0 equiv).
[b] Isolated yield of the product based on **5-8**. [c] The reaction conditions and the yield of the product of the similar reaction with the corresponding bromo-subtituted dienophile are given in the bracket.

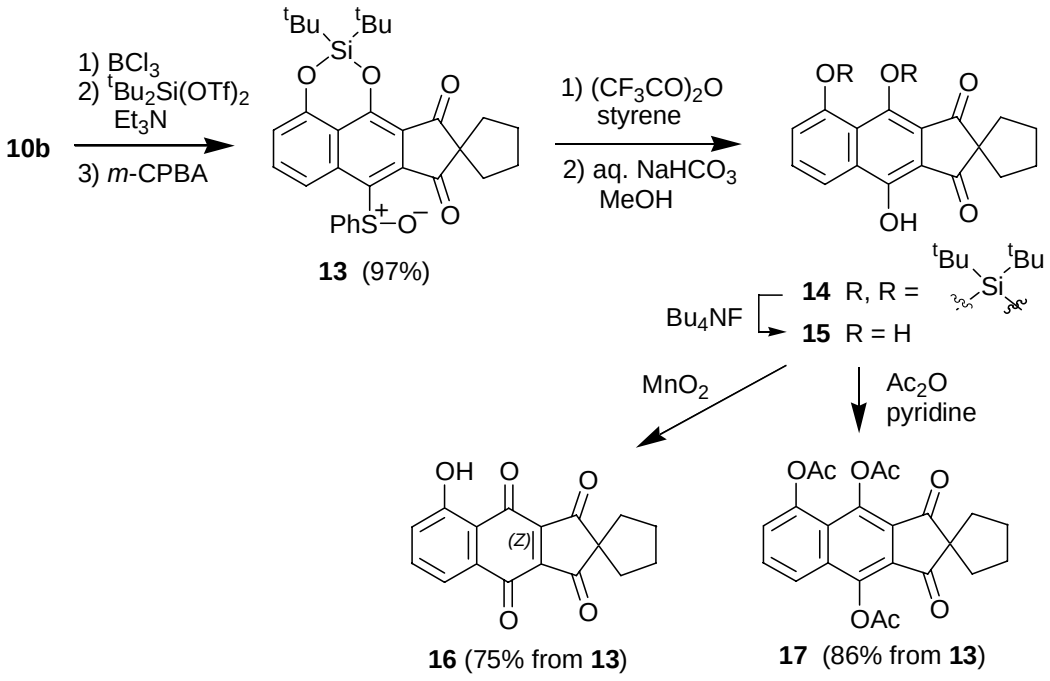
Table 2. HOMO and LUMO level values of **5**–**8** and some related compounds using the PM3 calculation

dienophile			HOMO/eV	LUMO/eV
		X = H	–9.982	–1.285
	5a	X = Cl	–9.664	–1.349
	b	X = Br	–9.639	–1.583
	c	X = SPh	–9.048	–1.250
	d	X = S(O)Ph	–9.358	–1.480
		X = H	–10.598	–0.991
		X = Cl	–10.163	–1.184
	6a	X = Br	–10.740	–1.222
	b	X = SPh	–9.143	–1.092
	d	X = S(O)Ph	–9.510	–1.400
	e	X = SO_2Ph	–10.307	–1.566
		X = Br	–9.693	–1.372
	7	X = S(O)Ph	–9.375	–1.473
		X = H	–10.249	–1.311
		X = Br	–10.352	–1.461
	8	X = S(O)Ph	–9.485	–1.764

We have applied this anionic cycloaddition to the synthesis of the ABCD-ring analog of fredericamycin A.[2] The tetracyclic compound (**10b**), obtained in 82% yield from **1b** and **6d** (Table 1, run 14), was subjected successively to debenzylation by BCl_3, protection of the diol by silylene formation, and the oxidation of the phenylthio group to give **13** in 97% overall yield. The aromatic Pummerer-type reaction[4c] of **13** followed by sequential deprotection using aqueous $NaHCO_3$ and Bu_4NF provided the ABCD-ring analog, **15**. Since **15** was susceptible to autoxidation during chromatography, to give a mixture of **15** and the *p*-quinone **16**, the product was isolated as either **16** or **17** (Scheme 4).


RO
NaH
PhS
1
A
X
R'
B
syn-
elimination
X = S(O)Ph
C
retro D.A.
CO2
OH
9-12
1d
CO2Et
4d
C'

Scheme 3


10b
1) BCl3
2) tBu2Si(OTf)2
Et3N
3) m-CPBA
13 (97%)
1) (CF3CO)2O
styrene
2) aq. NaHCO3
MeOH
14 R, R =
Bu4NF
15 R = H
MnO2
Ac2O
pyridine
16 (75% from 13)
17 (86% from 13)

Scheme 4

Conclusions

We have succeeded in producing the efficient and versatile synthesis of *p*-phenylthio-substituted *peri*-hydroxy polyaromatic compounds, whose structure is expected to be capable of various modifications. In this cycloaddition, use of the sulfinyl-substituted dienophile is crucial, and this method offers very mild reaction conditions and the direct formation of the desired compounds in good yields.

Experimental Section

General Procedures. All melting points are uncorrected. The ^{1}H NMR spectra were measured using 200–500 MHz spectrometers with $SiMe_4$ as internal standard. Infrared (IR) absorption spectra were recorded in CH_2Cl_2 solutions or by diffuse reflectance measurement of the samples dispersed in KBr powder. Column chromatographic purification was performed on silica gel BW-300 (200–400 mesh, Fuji Silysia Chemical Co., Ltd., Japan). RT denotes room temperature.

Methyl 6-benzyloxy-2-(methoxycarbonylmethyl)benzoate (2b). was prepared similar to the reported preparation method of substituted homophthalates.[2c] Under an argon atmosphere, *n*-BuLi (1.6 M in hexane, 33 mL, 56 mmol) was added to a solution of diisopropylamine (2.6 mL, 19 mmol) in anhydrous THF (40 mL) at -78 °C. The reaction mixture was stirred for 30 min at -78 °C, and a solution of dimethyl malonate (4.3 mL, 37 mmol) in anhydrous THF (30 mL) was added. After 1 h, a solution of 3-benzyloxy-1-bromobenzene (4.9 g, 8.6 mmol) in anhydrous THF (30 mL) was added at -78 °C. The reaction mixture was stirred for 30 min at -78 °C, quenched with saturated aqueous NH_4Cl and extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (hexane–EtOAc, 10:1 $\rightarrow$ 3:1) to give **2b** (2.2 g, 38%) as a yellow solid, mp 66–67 °C: IR (KBr) cm^{-1}: 1736, 1586. ^{1}H NMR ($CDCl_3$) δ 3.69 (5H, s), 3.89 (3H, s), 5.12 (2H, s), 6.92 (2H, d, *J* = 8.0 Hz), 7.27–7.42 (6H, m). Anal. Calcd for $C_{18}H_{18}O_5$: C, 68.78; H, 5.77. Found: C, 68.97; H, 5.78.

Methyl 6-benzyloxy-3-methoxy-2-(methoxycarbonylmethyl)benzoate (2c). As in the preparation of **2b**, methyl 3,6-dimethoxy-2-(methoxycarbonylmethyl)benzoate (2.3 g, 37%) was obtained, but using 2,2,6,6-tetramethylpiperidine (5.4 mL, 32 mmol) as base (instead of diisopropylamine), *n*-BuLi (1.6 *M* in hexane, 44 mL, 69 mmol), dimethyl malonate (5.3 mL, 46 mmol) and 1-bromo-2,5-dimethoxybenzene (5.0 g, 23 mmol). An orange oil: IR (KBr) cm^{-1}:

1740, 1736, 1599. ^{1}H NMR ($CDCl_3$) δ 3.65 (2H, s), 3.67 (3H, s), 3.79 (6H, s), 3.88 (3H, s), 6.83 (1H, d, *J* = 9.0 Hz), 6.89 (1H, d, *J* = 9.0 Hz). Anal. Calcd for $C_{13}H_{16}O_6$: C, 58.20; H, 6.01. Found: C, 57.95; H, 5.97%. Under a nitrogen atmosphere, BCl_3 (1.0 *M* in CH_2Cl_2, 9.8 mL, 9.8 mmol) was added to a solution of the methyl 3,6-dimethoxy-2-(methoxycarbonyl-methyl)benzoate (2.2 g, 8.2 mmol) in anhydrous CH_2Cl_2 (80 mL) at 0 °C. The reaction mixture was stirred at RT for 10 min, quenched with ice-water and extracted with CH_2Cl_2. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (hexane–Et_2O, 2:1) to give methyl 6-hydroxy-3-methoxy-2-(methoxycarbonylmethyl)benzoate (1.9 g, 89%) as a yellow solid, mp 78–79 °C (Et_2O). IR (KBr) cm^{-1}: 1740, 1673, 1607. ^{1}H NMR ($CDCl_3$) δ: 3.69 (3H, s), 3.79 (3H, s), 3.90 (3H, s), 4.04 (2H, s), 6.95 (1H, d, *J* = 9.0 Hz), 7.13 (1H, d, *J* = 9.0 Hz), 10.56 (1H, s). Anal. Calcd for $C_{12}H_{14}O_6$: C, 56.69; H, 5.55. Found: C, 56.66; H, 5.50%. Under a nitrogen atmosphere, K_2CO_3 (2.1 g, 15 mmol) and benzyl bromide (0.86 mL, 7.2 mmol) were added to a solution of methyl 6-hydroxy-3-methoxy-2-(methoxycarbonylmethyl)benzoate (1.8 g, 6.9 mmol) in anhydrous DMF (25 mL) at 0 °C. The reaction mixture was stirred at RT overnight, quenched with water and extracted with Et_2O. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was recrystallized from hexane–Et_2O to give **2c** (2.0 g, 83%) as a colorless solid, mp 96–97 °C. IR (KBr) cm^{-1}: 1732, 1599. ^{1}H NMR ($CDCl_3$) δ: 3.67 (2H, s), 3.68 (3H, s), 3.77 (3H, s), 3.87 (3H, s), 5.05 (2H, s), 6.83–6.91 (2H, m), 7.28–7.39 (5H, m). Anal. Calcd for $C_{19}H_{20}O_6$: C, 66.27; H, 5.85. Found: C, 66.29; H, 5.79%.

Methyl 6-benzyloxy-3,4-dimethoxy-2-(methoxycarbonylmethyl)benzoate (2d). As in the preparation of **2c**, the reaction of methyl 3,4,6-trimethoxy-2-(methoxycarbonylmethyl)benzoate[2c] (1.7 g, 5.7 mmol) with BCl_3 (1.0 *M* in CH_2Cl_2, 6.5 mL, 6.5 mmol) gave methyl 6-hydroxy-3,4-dimethoxy-2-(methoxycarbonylmethyl)benzoate (1.6 g, 96%), a colorless solid, mp 77–78 °C (hexane–Et_2O). IR (KBr) cm^{-1}: 1740, 1661, 1609, 1586. ^{1}H NMR ($CDCl_3$) δ: 3.70 (3H, s), 3.73 (3H, s), 3.86 (3H, s), 3.89 (3H, s), 4.04 (2H, s), 6.48 (1H, s), 11.49 (1H, s). Anal. Calcd for $C_{13}H_{16}O_7$: C, 54.93; H, 5.67. Found: C, 54.90; H, 5.59%. As in the preparation of **2c**, **2d** (1.8 g, 96%) was obtained from methyl 6-hydroxy-3,4-dimethoxy-2-(methoxycarbonylmethyl)benzoate (1.4 g, 5.1 mmol), K_2CO_3 (1.7 g, 12 mmol) and benzyl bromide (0.65 mL, 5.5 mmol). A yellow solid, mp 78–79 °C (hexane–Et_2O). IR (KBr) cm^{-1}: 1736, 1600. ^{1}H NMR ($CDCl_3$) δ: 3.69 (3H, s), 3.76 (3H, s), 3.77 (2H, s), 3.83 (6H, s). 5.09 (2H, s), 6.50 (1H, s), 7.30 (1H, t, *J* = 7.5 Hz), 7.35–7.42 (4H, m). Anal. Calcd for $C_{20}H_{22}O_7$: C, 64.16; H, 5.92. Found: C, 64.14; H, 5.88%.

Typical procedure for preparation of 3. Methyl 2-[methoxycarbonyl(phenylthio)methyl]benzoate (3a)

Under a nitrogen atmosphere, $LiN(TMS)_2$ (1.0 *M* in THF, 8.0 mL, 8.0 mmol) was added to a solution of **2a** (1.4 g, 6.6 mmol) in anhydrous THF (20 mL) at -78 °C. The reaction mixture was stirred at -78 °C for 1 h, and a solution of $PhSSO_2Ph$ (1.7 g, 7.0 mmol) in anhydrous THF

(12 mL) was added. The reaction mixture was stirred at -78 °C for 30 min, quenched with saturated aqueous NH_4Cl and extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (hexane–benzene, 2:1) to give **3a** (1.9 g, 89%) as a yellow oil : IR (KBr) cm^{-1}: 1740, 1719, 1599, 1578. ^1H NMR ($CDCl_3$) δ: 3.69 (3H, s), 3.85 (3H, s), 6.15 (1H, s), 7.22–7.26 (3H, m), 7.33 (1H, dd, *J* = 7.5, 1.5 Hz), 7.37–7.41 (2H, m), 7.49 (1H, dt, *J* = 7.5, 1.5 Hz), 7.68 (1H, dd, *J* = 7.5, 1.5 Hz), 7.91 (1H, dd, *J* = 7.5, 1.5 Hz). Anal. Calcd for $C_{17}H_{16}O_4S$: C, 64.54; H, 5.10; S, 10.13. Found: C, 64.62; H, 5.16; S, 10.00%.

Methyl 6-benzyloxy-2-[methoxycarbonyl(phenylthio)methyl]benzoate (3b). Compound **2b** (1.1 g, 3.4 mmol) was converted into **3b** (1.4 g, quant.). A yellow oil. IR (KBr) cm-1: 1730, 1584. ^1H NMR ($CDCl_3$) δ: 3.61 (3H, s), 3.77 (3H, s), 5.04 (3H, s), 6.83–6.86 (1H, m), 7.18–7.36 (12H, m). Anal. Calcd for $C_{24}H_{22}O_5S$: C, 68.23; H, 5.25; S, 7.59. Found: C, 68.27; H, 5.27. S, 7.60%.

Methyl 6-benzyloxy-3-methoxy-2-[methoxycarbonyl(phenylthio)methyl]benzoate (3c). Compound **2c** (2.0 g, 5.7 mmol) was converted into **3c** (2.4 g, 94%). A colorless solid, mp 91–92 °C (hexane–Et_2O). IR (KBr) cm^{-1}: 1736, 1732, 1595. ^1H NMR ($CDCl_3$) δ 3.69 (3H, s), 3.71 (3H, s), 3.72 (3H, s), 5.04 (2H, s), 5.25 (1H, s), 6.81 (1H, d, *J* = 9.0 Hz), 6.86 (1H, d, *J* = 9.0 Hz), 7.21–7.46 (10H, m). Anal. Calcd for $C_{25}H_{24}O_6S$: C, 66.36; H, 5.35; S, 7.08. Found: C, 66.20; H, 5.31; S, 6.87.

Methyl 6-benzyloxy-3,4-dimethoxy-2-[methoxycarbonyl(phenylthio)methyl]benzoate (3d). Compound **2d** (2.5 g, 6.8 mmol) was converted into **3d** (2.7 g, 82%). A colorless solid, mp 124–125 °C (hexane–Et_2O). IR (KBr) cm-1: 1736, 1595. ^1H NMR ($CDCl_3$) δ 3.63 (3H, s), 3.73 (3H, s), 3.74 (3H, s), 3.80 (3H, s), 5.08 (2H, s), 5.48 (1H, s), 6.48 (1H, s), 7.20–7.46 (10H, m). Anal. Calcd for $C_{26}H_{26}O_7S$: C, 64.72; H, 5.43; S, 6.64. Found: C, 64.64; H, 5.45; S, 6.58%.

Typical procedure for preparation of 1 from 3. 4-(phenylthio)homophthalic anhydride (1a)

A mixture of **3a** (1.4 g, 4.4 mmol) and KOH (4.9 g, 88 mmol) in EtOH (25 mL) and water (5 mL) was heated at reflux for 1 h and concentrated *in vacuo* to one-fifth of the original volume. The residual aqueous layer was washed with CH_2Cl_2. To the aqueous layer was added CH_2Cl_2, and the mixture cooled to 0 °C and acidified with 10% HCl to pH 2–3 with vigorous stirring. The organic layer was separated, and the aqueous layer extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residual solid was washed with EtOAc to give 2-[carboxy(phenylthio)methyl]benzoic acid (1.3 g, quant.) as a colorless solid, mp 138–140 °C: IR (KBr) cm^{-1}: 3400–2600, 1714, 1599, 1576. ^1H NMR ($CDCl_3$) δ 5.87 (1H, s), 7.21–7.26 (3H, m), 7.36–7.44 (3H, m), 7.56 (1H, td, *J* = 7.5, 1.5 Hz), 7.71 (1H, d, *J* = 7.0 Hz), 8.09 (1H, dd, *J* = 8.0, 1.5 Hz), 9.58 (2H, br. s). High resolution FAB-MS Calcd for $C_{15}H_{13}O_4S$ (M^++H): 289.0535. Found 289.0555. Similarly to the reported method,[8] a mixture of 2-[carboxy(phenylthio)methyl]benzoic acid (0.43 g, 1.5 mmol) and trimethylsilyl(ethoxy)-

acetylene (0.35 mL, 2.4 mmol) in anhydrous CH_2Cl_2 (10 mL) was stirred at RT for 2.5 h. The reaction mixture was concentrated *in vacuo,* and the residual solid was washed with hexane–benzene and dried *in vacuo* to give **1a** (0.35 g, 87%) as a colorless solid, mp 144–145 °C (hexane–benzene). IR (CH_2Cl_2) cm^{-1}: 1798, 1757, 1603. ^1H NMR ($CDCl_3$) δ: 4.99 (1H, s), 7.20–7.43 (5H, m), 7.49 (1H, td, *J* = 8.0, 1.0 Hz), 7.59 (1H, dd, *J* = 8.0, 1.0 Hz), 7.76 (1H, td, *J* = 8.0, 1.0 Hz), 7.95 (1H, dd, *J* = 8.0, 1.0 Hz). Anal. Calcd for $C_{15}H_{10}O_3S$: C, 66.65; H, 3.73; S, 11.86. Found: C, 66.30; H, 3.89; S, 11.72%.

8-Benzyloxy-4-(phenylthio)homophthalic anhydride (1b). Compound **3b** (1.4 g, 3.4 mmol) was converted into 6-benzyloxy-2-[carboxy(phenylthio)methyl]benzoic acid (1.2 g, 90%); δ0, 7.5 Hz), 7.37 (1H, t, *J* = 7.5 Hz), 7.42 (2H, dd, *J* = 8.0, 7.5 Hz), 7.48 (1H, t, *J* = 8.0 Hz), 7.56 (2H, d, *J* = 7.5 Hz), 8.07 (1H, d, *J* = 8.0 Hz), 12.70 (1H, s). High resolution MS, calcd for $C_{29}H_{26}O_6S$: 502.1450. Found 502.1451.

8-Benzyloxy-2,3-bis-(ethoxycarbonyl)-1-hydroxy-5,6-dimethoxy-4-(phenylthio)naphthalene (4d). As in the preparation of **4b**, **1d** (36 mg, 0.082 mmol) and diethyl acetylenedicarboxylate (0.040 mL, 0.25 mmol) were converted into **4d** (29 mg, 64%). A yellow oil. IR (KBr) cm^{-1}: 1779, 1744, 1653, 1595, 1570. ^1H NMR ($CDCl_3$) δ: 0.97 (3H, t, *J* = 7.0 Hz), 1.35 (3H, t, *J* = 7.0 Hz), 2.52 (1H, br s), 3.85 (3H, s), 3.88 (3H, s), 3.95–4.03 (2H, m), 4.27–4.34 (2H, m), 5.15 (2H, s), 6.50 (1H, s), 7.19–7.23 (5H, m), 7.31–7.34 (1H, m), 7.37–7.40 (3H, m), 7.44 (2H, d, *J* = 7.5 Hz). High resolution MS Calcd for $C_{31}H_{30}O_8S$: 562.1161. Found 562.1673.

The known compounds (**5a**,[17] **5b**,[18] **5c**,[11c] **8**[12c,19]) were prepared according to the literature, and new compounds were prepared as follows.

8-Methoxy-2-phenylsulfinyl-1,4-naphthaquinone (5d). A solution of *m*-CPBA (80% purity, 36 mg, 0.17 mmol) in CH_2Cl_2 (5 mL) was gradually added to an ice-cooled solution of **5c** (50 mg, 0.17 mmol) in CH_2Cl_2 (10 mL). The reaction mixture was stirred for 4 h, quenched with saturated aqueous $Na_2S_2O_3$ and extracted with CH_2Cl_2. The organic layer was washed with saturated aqueous $NaHCO_3$, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (CH_2Cl_2–MeOH, 50:1) to give **5d** (53 mg, quant.) as an orange solid, mp 212–214 °C. IR (KBr) cm^{-1}: 1667, 1586. ^1H NMR ($CDCl_3$) δ 3.97 (3H, s), 7.29 (1H, d, *J* = 8.0 Hz), 7.46–7.48 (3H, m), 7.58 (1H, s), 7.68–7.75 (2H, m), 7.86–7.88 (2H, m). High resolution MS Calcd for $C_{17}H_{12}O_4S$: 312.0456. Found: 312.0492.

2-Bromo-spiro-[4,4]-non-2-ene-1,4-dione (6a). Under a nitrogen atmosphere, a solution of phenyltrimethylammonium tribromide (1.4 g, 3.8 mmol) in THF (20 mL) was slowly added to a solution of spiro-[4,4]-nonane-1,4-dione[20] (0.50 g, 3.3 mmol) in THF (20 mL) at RT. The mixture was stirred for 3 h, quenched with saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (hexane:EtOAc, 10:1) to give **6a** (0.22 g, 29%) as a yellow solid, mp 74–75 °C (hexane–Et_2O). IR (KBr) cm^{-1}: 1754, 1705, 1561. ^1H NMR ($CDCl_3$) δ 1.89 (8H, br. s), 7.45 (1H, s). High resolution MS Calcd for $C_9H_9O_2Br$: 227.9785. Found 227.9811.

2-(Phenylthio)-spiro-[4,4]-on-2-ene-1,4-dione (6b). Under a nitrogen atmosphere, a solution of PhSCl (ca. 4.9 mmol), prepared *in situ* from PhSSPh (0.54 g, 2.5 mmol) and SO_2Cl_2 (0.20 mL, 2.5 mmol), in CH_3CN (7 mL) was added to a solution of spiro-[4,4]-nonane-1,4-dione (0.30 g, 2.0 mmol) in CH_3CN (8 mL) at 0 °C. The reaction mixture was stirred at RT for 1 day and concentrated *in vacuo*. The residue was purified by column chromatography (hexane–EtOAc, 8:1) to give **6b** (0.42 g, 82%) as a yellow solid, mp 103–104 °C (hexane–Et_2O). IR (KBr) cm^{-1}: 1742, 1694, 1541. ^1H NMR ($CDCl_3$) δ 1.87 (8H, s), 6.27 (1H, s), 7.46–7.57 (5H, m). Anal. Calcd for $C_{15}H_{14}O_2S$: C, 69.74; H, 5.46; S, 12.41. Found: C, 69.71; H, 5.54; S, 12.39.

2-(4-Nitrophenylthio)-spiro-[4,4]-non-2-ene-1,4-dione (6c). Under a nitrogen atmosphere, Et_3N (0.050 mL, 0.36 mmol) and 4-nitrothiophenol (55 mg, 0.35 mmol) were added to a solution of **6a** (41 mg, 0.18 mmol) in THF (3 mL) at 0 °C. The mixture was stirred at RT for 3 h, quenched with water and extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (hexane–EtOAc, 3:1) to give **6c** (46 mg, 86%), a yellow solid, mp 130–132 °C. IR (KBr) cm^{-1}: 1741, 1698, 1541, 1522. ^1H NMR ($CDCl_3$) δ1.89 (8H, s), 6.39 (1H, s), 7.76 (2H, d, *J* = 8.5 Hz), 8.34 (2H, d, *J* = 8.5 Hz). High resolution MS Calcd for $C_{15}H_{13}NO_4S$: 303.0565. Found 303.0563.

2-(Phenylsulfinyl)-spiro-[4,4]-non-2-ene-1,4-dione (6d). As in the preparation of **5d**, **6b** (0.28 g, 1.1 mmol) was converted into **6d** (0.29 g, 99%), a yellow solid, mp 102–103 °C (hexane–Et_2O). IR (KBr) cm^{-1}: 1748, 1707. ^1H NMR ($CDCl_3$) δ 1.46–1.57 (2H, m), 1.65–1.93 (6H, m), 7.51–7.57 (3H, m), 7.64 (1H, s), 7.76–7.83 (2H, m). Anal. Calcd for $C_{15}H_{14}O_3S$: C, 65.67; H, 5.14; S, 11.69. Found: C, 65.58; H, 5.20; S, 11.55.

2-(Phenylsulfonyl)-spiro-[4,4]-non-2-ene-1,4-dione (6e). To a solution of **6b** (49 mg, 0.19 mmol) in CH_2Cl_2 (2 mL) was added dimethyldioxirane[21] (*ca*. 0.06 *M* in acetone, 7.3 mL, *ca*. 0.45 mmol) at RT. The reaction mixture was stirred for 2 h and concentrated *in vacuo*. The residue was recrystallized from hexane–Et_2O to give **6e** (45 mg, 82%) as a yellow solid, mp 148–150 °C (hexane–Et_2O). IR (KBr) cm^{-1}: 1755, 1713. ^1H NMR ($CDCl_3$) δ1.79–1.83 (8H, m), 7.62 (2H, t, *J* = 8.0 Hz), 7.63 (1H, s), 7.74 (1H, t, *J* = 8.0 Hz), 8.11 (2H, d, *J* = 8.0 Hz). High resolution MS Calcd for $C_{15}H_{14}O_4S$: 290.0613. Found 290.0613.

5-Methoxy-2-phenylsulfinyl-1,4-naphthaquinone (7). As in the preparation of **5d**, 5-methoxy-2-phenylthio-1,4-naphthoquinone[11c] (160 mg, 0.54 mmol) was converted into **7** (143 mg, 85 %). An orange solid, mp 215–217 °C. IR (KBr) cm^{-1}: 1667, 1584. ^1H NMR ($CDCl_3$) δ: 4.00 (3H, s), 7.30–7.35 (1H, m), 7.46–7.52 (4H, m), 7.62–7.72 (2H, m), 7.83–7.87 (2H, m). Anal. Calcd for $C_{17}H_{12}O_4S$: C, 65.37; H, 3.87; S, 10.26. Found: C, 65.19; H, 3.94; S, 10.25%.

Typical procedure for [4+2]-cycloaddition of 1 with the sulfinyl-substituted dienophiles. 5-Benzyloxy-4-hydroxy-9-phenylthio-2,2-tetramethylenebenz-[*f*]-indane-1,3-dione (10b) (Table 1, run 14)

Under a nitrogen atmosphere, a solution of **1b** (94 mg, 0.25 mmol) in anhydrous THF (4 mL) was added to a suspension of sodium hydride (60% in mineral oil, 11 mg, 0.27 mmol) in THF (4 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 1.5 h, and a solution of **6d** (53 mg, 0.19 mmol) in anhydrous THF (8 mL) was added. The mixture was stirred at RT for 30 min, then quenched with saturated aqueous NH_4Cl and extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (hexane–EtOAc) to give **10b** (76 mg, 82%), a yellow solid, mp 164–165 °C (CH_2Cl_2–Et_2O). IR (KBr) cm^{-1}: 1734, 1705, 1671, 1607, 1580. ^1H NMR ($CDCl_3$) δ 1.91–2.00 (8H, m), 5.33 (2H, s), 7.04–7.08 (3H, m), 7.13–7.16 (3H, m), 7.39–7.46 (3H, m), 7.55 (2H, d, *J* = 7.5 Hz), 7.62 (1H, t, *J* = 8.5 Hz), 8.49 (1H, d, *J* = 8.5 Hz), 11.26 (1H, s). Anal. Calcd for $C_{30}H_{24}O_4S$: C, 74.98; H, 5.03; S, 6.67. Found: C, 74.63; H, 5.08; S, 6.59.

11-Hydroxy-1-methoxy-6-(phenylthio)naphthacene-5,12-dione (9a) (run 4). 1a (29 mg, 0.11 mmol) and **5d** (26 mg, 0.083 mmol) were converted into **9a** (25 mg, 72%), an orange solid, mp 257–259 °C (EtOAc). IR (KBr) cm^{-1}: 1673, 1622, 1568, 1547. ^1H NMR ($CDCl_3$) δ: 4.09 (3H, s), 7.01–7.05 (3H, m), 7.10–7.13 (2H, dd, *J* = 8.0, 7.5 Hz), 7.32 (1H, d, *J* = 7.5 Hz), 7.59–7.63 (2H, m), 7.72 (1H, dd, *J* = 8.5, 8.0 Hz), 7.88 (1H, d, *J* = 8.0 Hz), 8.58–8.60 (2H, m), 15.47 (1H, s). Anal. Calcd for $C_{25}H_{16}O_4S$: C, 72.80; H, 3.91; S, 7.77. Found: C, 72.73; H, 4.03; S, 7.89.

5-Benzyloxy-4-hydroxy-7,8-dimethoxy-9-phenylthio-2,2-tetramethylenebenz-[*f*]-indane-1,3-dione (10d) (run 8). 1d (62 mg, 0.14 mmol) and **6d** (33 mg, 0.12 mmol) were converted to **10d** (50 mg, 77%), a brown solid, mp 186–187 °C (EtOAc). IR (KBr) cm^{-1}: 1726, 1700, 1663, 1595. ^1H NMR ($CDCl_3$) δ 1.52–1.94 (8H, m), 3.94 (3H, s), 3.98 (3H, s), 5.33 (2H, s), 6.90 (1H, s), 7.11–7.16 (4H, m), 7.40–7.48 (4H, m), 7.58 (2H, dd, *J* = 7.5, 1.5 Hz), 11.15 (1H, s). High resolution MS Calcd for $C_{32}H_{28}O_6S$: 540.1606. Found 540.1633.

10-Benzyloxy-11-hydroxy-1-methoxy-6-(phenylthio)naphthacene-5,12-dione (9b) (run 10). 1b (37 mg, 0.099 mmol) and **5d** (24 mg, 0.076 mmol) were converted into **9b** (29 mg, 73%), a purple solid, mp 256–257 °C (EtOAc). IR (KBr) cm^{-1}: 1663, 1614, 1586, 1572. ^1H NMR ($CDCl_3$) δ: 4.08 (3H, s), 5.30 (2H, s), 7.00–7.14 (6H, m), 7.31 (1H, d, *J* = 8.0 Hz), 7.35 (1H, d, *J* = 7.5 Hz), 7.42 (2H, t, *J* = 7.5 Hz), 7.50 (1H, t, *J* = 8.0 Hz), 7.66 (2H, d, *J* = 7.5 Hz), 7.71 (1H, d, *J* = 8.0 Hz), 7.84 (1H, d, *J* = 7.5 Hz), 8.29 (1H, d, *J* = 8.0 Hz), 16.48 (1H, s). Anal. Calcd for $C_{32}H_{22}O_5S$: C, 74.12; H, 4.28; S, 6.18. Found: C, 73.76; H, 4.41; S, 6.47.

10-Benzyloxy-11-hydroxy-1,7-dimethoxy-6-(phenylthio)naphthacene-5,12-dione (9c) (run 11). 1c (47 mg, 0.12 mmol) and **5d** (28 mg, 0.090 mmol) were converted into **9c** (37 mg, 75%), a purple solid, mp 220–221 °C (EtOAc). IR (KBr) cm^{-1}: 1615, 1584, 1541. ^1H NMR ($CDCl_3$) δ 3.67 (3H, s), 4.07 (3H, s), 5.22 (2H, s), 6.82 (1H, d, *J* = 9.0 Hz), 6.93–7.05 (7H, m), 7.26 (1H, d, *J* = 8.0 Hz), 7.31–7.45 (3H, m), 7.59–7.66 (2H, m), 7.75 (1H, d, *J* = 6.5 Hz), 16.59 (1H, s). High resolution MS Calcd for $C_{33}H_{24}O_6S$: 548.1293. Found 548.1293.

10-Benzyloxy-11-hydroxy-1,7,8-trimethoxy-6-(phenylthio)naphthacene-5,12-dione (9d) (run 12). 1d (19 mg, 0.044 mmol) and **5d** (11 mg, 0.037 mmol) were converted into **9d** (16 mg, 78%). A

purple solid, mp 218–219 °C (EtOAc). IR (KBr) cm^{-1}: 1617, 1586. ^1H NMR ($CDCl_3$) δ 3.82 (3H, s), 3.84 (3H, s), 4.06 (3H, s), 5.28 (2H, s), 6.79 (1H, s), 6.94 (1H, dd, *J* = 7.5, 6.5 Hz), 7.02 (2H, dd, *J* = 8.0, 7.5 Hz), 7.07 (2H, d, *J* = 7.5 Hz), 7.24 (1H, d, *J* = 8.0 Hz), 7.35 (1H, t, *J* = 7.5 Hz), 7.43 (2H, t, *J* = 7.5 Hz), 7.58 (1H, dd, *J* = 7.5, 8.0 Hz), 7.63–7.64 (3H, m), 16.85 (1H, s). High resolution MS Calcd for $C_{34}H_{26}O_7S$: 578.1399. Found 578.1418.

4-Hydroxy-9-phenylthio-2,2-tetramethylenebenz-[*f*]-indane-1,3-dione (10a) (run 13). 1a (37 mg, 0.14 mmol) and **6d** (29 mg, 0.11 mmol) were converted into **10a** (30 mg, 76%), a yellow solid, mp 172–173 °C. IR (KBr) cm^{-1}: 1736, 1678, 1617, 1595, 1582. ^1H NMR ($CDCl_3$) δ 1.96–2.05 (8H, m), 7.05–7.18 (5H, m), 7.71 (1H, dd, *J* = 7.5, 2.0 Hz), 7.77 (1H, dd, *J* = 7.5, 2.0 Hz), 8.51 (1H, d, *J* = 9.0 Hz), 8.79 (1H, d, *J* = 9.0 Hz), 10.46 (1H, br. s). Anal. Calcd for $C_{23}H_{18}O_3S$: C, 73.78; H, 4.84; S, 8.56. Found: C, 73.62; H, 4.93; S, 8.57.

5-Benzyloxy-4-hydroxy-8-methoxy-9-phenylthio-2,2-tetramethylenebenz-[*f*]-indane-1,3-dione (10c) (run 15). 1c (65 mg, 0.16 mmol) and **6d** (34 mg, 0.12 mmol) were converted into **10c** (45 mg, 71%), a yellow solid, mp 163–164 °C (EtOAc). IR (KBr) cm^{-1}: 1728, 1703, 1673, 1605. ^1H NMR ($CDCl_3$) δ 1.61–1.91 (8H, m), 3.91 (3H, s), 5.28 (2H, s), 7.01 (1H, d, *J* = 8.0 Hz), 7.03–7.14 (6H, m), 7.39–7.46 (3H, m), 7.53 (2H, d, *J* = 7.5 Hz), 11.14 (1H, s). Anal. Calcd for $C_{31}H_{26}O_5S$: C, 72.92; H, 5.13; S, 6.28. Found: C, 73.05; H, 5.19; S, 6.23%.

6-Hydroxy-1-methoxy-11-(phenylthio)naphthacene-5,12-dione (11a) (run 16). 1a (15 mg, 0.056 mmol) and **7** (14 mg, 0.043 mmol) were converted into **11a** (13 mg, 73%), an orange solid, mp 235–236 °C (EtOAc). IR (KBr) cm^{-1}: 1676, 1673, 1665, 1619, 1582. ^1H NMR ($CDCl_3$) δ 4.00 (3H, s), 7.02–7.12 (5H, m), 7.32 (1H, d, *J* = 8.0 Hz), 7.58–7.60 (2H, m), 7.70 (1H, dd, *J* = 8.0, 7.5 Hz), 7.97 (1H, d, *J* = 7.5 Hz), 8.51–8.55 (2H, m), 14.97 (1H, s). Anal. Calcd for $C_{25}H_{16}O_4S$: C, 72.80; H, 3.91; S, 7.77. Found: C, 72.71; H, 4.03; S, 7.69.

7-Benzyloxy-6-hydroxy-1-methoxy-11-(phenylthio)naphthacene-5,12-dione (11b) (run 17). 1b (35 mg, 0.088 mmol) and **7** (22 mg, 0.071 mmol) were converted into **11b** (25 mg, 67%), an orange solid, mp 217–218 °C (EtOAc). IR (KBr) cm^{-1}: 1674, 1622, 1617, 1601, 1576. ^1H NMR ($CDCl_3$) δ 3.99 (3H, s), 5.31 (2H, s), 7.01–7.10 (5H, m), 7.27–7.51 (6H, m), 7.62–7.72 (3H, m), 7.98 (1H, d, *J* = 6.5 Hz), 8.23 (1H, d, *J* = 8.5 Hz), 16.05 (1H, s). Anal. Calcd for $C_{32}H_{22}O_5S$: C, 74.12; H, 4.28; S, 6.18. Found: C, 74.04; H, 4.39; S, 6.07%.

7-Benzyloxy-6-hydroxy-1,10-dimethoxy-11-(phenylthio)naphthacene-5,12-dione (11c) (run 18). 1c (35 mg, 0.087 mmol) and **7** (23 mg, 0.072 mmol) were converted into **11c** (28 mg, 70%), a purple solid, mp 224–225 °C (EtOAc). IR (KBr) cm^{-1}: 1646, 1619, 1584, 1547. ^1H NMR ($CDCl_3$) δ 3.64 (3H, s), 3.92 (3H, s), 5.24 (2H, s), 6.82 (1H, d, *J* = 8.5 Hz), 6.94–7.01 (6H, m), 7.22 (1H, d, *J* = 9.0 Hz), 7.34–7.45 (3H, m), 7.59–7.67 (3H, m), 7.95 (1H, d, *J* = 8.5 Hz), 16.09 (1H, s). Anal. Calcd for $C_{33}H_{24}O_6S$: C, 72.25; H, 4.41; S, 5.84. Found: C, 72.04; H, 4.53; S, 5.74.

7-Benzyloxy-6-hydroxy-1,9,10-trimethoxy-11-(phenylthio)naphthacene-5,12-dione (11d) (run 19). 1d (10 mg, 0.024 mmol) and **7** (5.7 mg, 0.018 mmol) were converted into **11d** (7.6 mg, 72%), purple solid, mp 239–240 °C (EtOAc). IR (KBr) cm^{-1}: 1667, 1615, 1574. ^1H NMR

($CDCl_3$) δ: 3.79 (3H, s), 3.82 (3H, s), 3.90 (3H, s), 5.30 (2H, s), 6.75 (1H, s), 6.95 (1H, t, *J* = 7.5 Hz), 7.00 (2H, t, *J* = 7.5 Hz), 7.06 (2H, d, *J* = 7.5 Hz), 7.19 (1H, d, *J* = 8.0 Hz), 7.36 (1H, t, *J* = 7.5 Hz), 7.44 (2H, dd, *J* = 8.0, 7.5 Hz), 7.61–7.65 (3H, m), 7.93 (1H, d, *J* = 8.0 Hz), 16.43 (1H, s). High resolution MS Calcd for $C_{34}H_{26}O_7S$: 578.1399. Found 578.1407.

6-Hydroxy-11-(phenylthio)naphthacene-5,12-dione (12a) (run 20). 1a (30 mg, 0.11 mmol) and **8** (24 mg, 0.086 mmol) were converted into **12a** (23 mg, 70%), an orange solid, mp 217–218 °C. IR (KBr) cm^{-1}: 1659, 1622, 1592, 1576, 1549. ^1H NMR ($CDCl_3$) δ 7.03–7.15 (5H, m), 7.61–7.64 (2H, m), 7.77–7.81 (2H, m), 8.25–8.28 (1H, m), 8.33–8.37 (1H, m), 8.56–8.64 (2H, m), 15.37 (1H, s). Anal. Calcd for $C_{24}H_{14}O_3S$: C, 75.38; H, 3.69; S, 8.38. Found: C, 75.09; H, 3.87; S, 8.42.

7-Benzyloxy-6-hydroxy-11-(phenylthio)naphthacene-5,12-dione (12b) (run 21). 1b (44 mg, 0.11 mmol) and **8** (25 mg, 0.090 mmol) were converted into **12b** (29 mg, 66%), an orange solid, mp 222–223 °C (EtOAc). IR (KBr) cm^{-1}: 1669, 1619, 1593, 1578. ^1H NMR ($CDCl_3$) δ 5.30 (2H, s), 7.00–7.14 (6H, m), 7.32–7.52 (4H, m), 7.63 (2H, d, *J* = 7.5 Hz), 7.72–7.75 (2H, m), 8.21–8.37 (3H, m), 16.45 (1H, s). Anal. Calcd for $C_{31}H_{20}O_4S$: C, 76.21; H, 4.13; S, 6.56. Found: C, 76.14; H, 4.21; S, 6.45.

7-Benzyloxy-6-hydroxy-10-methoxy-11-(phenylthio)naphthacene-5,12-dione (12c) (run 22). 1c (41 mg, 0.10 mmol) and **8** (22 mg, 0.077 mmol) were converted into **12c** (27 mg, 68%), a purple solid, mp 194–195 °C (EtOAc). IR (KBr) cm^{-1}: 1642, 1619, 1590, 1541. ^1H NMR ($CDCl_3$) δ 3.66 (3H, s), 5.26 (2H, s), 6.81 (1H, d, *J* = 9.0 Hz), 6.96–7.05 (5H, m), 7.35–7.50 (4H, m), 7.62 (2H, d, *J* = 7.5 Hz), 7.72–7.75 (2H, m), 8.16–8.20 (1H, m), 8.32–8.36 (1H, m), 16.50 (1H, s). Anal. Calcd for $C_{32}H_{22}O_5S$: C, 74.12; H, 4.28; S, 6.18. Found: C, 74.02; H, 4.44; S, 6.01.

7-Benzyloxy-6-hydroxy-9,10-dimethoxy-11-(phenylthio)naphthacene-5,12-dione (12d) (run 23). 1d (44 mg, 0.10 mmol) and **8** (22 mg, 0.078 mmol) were converted into **12d** (30 mg, 70%), a purple solid, mp 184–185 °C (EtOAc). IR (KBr) cm^{-1}: 1665, 1615, 1589. ^1H NMR ($CDCl_3$) δ 3.81 (3H, s), 3.82 (3H, s), 5.30 (2H, s), 6.77 (1H, s), 6.94–7.09 (5H, m), 7.36–7.47 (4H, m) 7.61–7.73 (3H, m), 8.08 (1H, d, *J* = 7.5 Hz), 8.30 (1H, d, *J* = 7.5 Hz), 16.82 (1H, s). High resolution MS Calcd for $C_{33}H_{24}O_6S$: 548.1293. Found 548.1267.

4,5-(Di-*tert*-butylsilylenedioxy)-9-phenylsulfinyl-2,2-tetramethylenebenz-[*f*]-indane-1,3-dione (13). Under a nitrogen atmosphere, a solution of BCl_3 (1.0 *M* in CH_2Cl_2, 0.10 mL, 0.10 mmol) was added to a solution of **10b** (47 mg, 0.098 mmol) in anhydrous CH_2Cl_2 (2 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min and then at RT for another 30 min, quenched with ice–water and extracted twice with CH_2Cl_2. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. Benzene (5 mL) was added to the residue, and then evaporated *in vacuo* to give 4,5-dihydroxy-9-phenylthio-2,2-tetramethylenebenz-[*f*]-indane-1,3-dione. This was dissolved in anhydrous DMF (2 mL), and Et_3N (0.055 mL, 0.40 mmol) and $(t\text{-}Bu)_2Si(OTf)_2$ (0.072 mL, 0.20 mmol) were added at 0 °C. The reaction mixture

was stirred at RT overnight, quenched with ice–water and extracted twice with Et_2O. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (hexane–EtOAc, 6:1) to give 4,5-(di-*tert*-butylsilylenedioxy)-9-phenylthio-2,2-tetramethylenebenz-[*f*]-indane-1,3-dione. This product was dissolved in anhydrous CH_2Cl_2 (1.5 mL), cooled to -60 °C, and *m*-CPBA (80% purity, 21 mg, 0.098 mmol) was added, the reaction mixture stirred at -30 °C for 1 h and then at 0 °C for 1 h. The mixture was worked up as in the preparation of **5d**, and the product purified by column chromatography (hexane–CH_2Cl_2, 1:1 → CH_2Cl_2→ CH_2Cl_2–MeOH, 20:1) to give **13** (52 mg, 97 % from **10b**) as a yellow gum, IR (KBr) cm-1 1736, 1709, 1578. ^{1}H NMR ($CDCl_3$) δ 1.13 (9H, s), 1.15 (9H, s), 1.92–2.13 (8H, m), 7.07 (1H, d, *J* = 8.0 Hz), 7.37–7.78 (6H, m), 8.69 (1H, d, *J* = 9.0 Hz). High resolution MS Calcd for $C_{31}H_{34}O_5SSi$: 546.1893. Found 546.1890.

5-Hydroxy-2,2-tetramethylenebenz-[*f*]-indane-1,3,4,9-tetra-one (16). Under a nitrogen atmosphere, trifluoroacetic anhydride (0.031 mL, 0.22 mmol) was added to an ice-cooled solution of **13** (12 mg, 0.022 mmol) and styrene (6.7 μl, 0.071 mmol) in anhydrous CH_3CN (1 mL), and the mixture stirred at 0 °C for 3 h. Ethyl acetate (5 mL) was added, and the whole mixture concentrated *in vacuo*. The residue was dissolved in MeOH (1 mL), and saturated aqueous $NaHCO_3$ (2 drops) was added. The reaction mixture was stirred at RT for 1 h, then EtOAc (5 mL) added, and saturated aq. NH_4Cl (2 drops). After stirring for 5 min, the mixture was dried over Na_2SO_4 and concentrated *in vacuo* to give crude **14**. This product was dissolved in THF (0.5 mL) and water (0.1 mL), and Bu_4NF (1.0 *M* in THF, 0.010 mL, 0.010 mmol) was added at 0 °C. The mixture was stirred at 0 °C for 2 h, quenched with saturated aq. NH_4Cl and extracted with CH_2Cl_2 three times. The combined organic layer was dried over Na_2SO_4 and concentrated *in vacuo* to give crude **15**. Purification by column chromatography (CH_2Cl_2–MeOH, 100:1) gave a mixture of **15** and **16**, which was dissolved in CH_2Cl_2 (1 mL), and MnO_2 (95 mg) added. The reaction mixture was stirred overnight, filtered through a Celite pad, concentrated *in vacuo*, and the residue purified by column chromatography (hexane–EtOAc, 5:1) to give **16** (4.8 mg, 75% from **13**) as a red–purple solid, mp >300 °C (EtOAc–hexane). IR (KBr) cm^{-1}: 1719, 1634, 1603, 1449. ^{1}H NMR ($CDCl_3$) δ 1.96–1.99 (8H, m), 7.41 (1H, d, *J* = 7.5 Hz), 7.69–7.79 (2H, m), 11.91 (1H, s). High resolution MS Calcd for $C_{17}H_{12}O_5$: 296.0685. Found 296.0674.

4,5,9-Triacetoxy-2,2-tetramethylenebenz-[*f*]-indane-1,3-dione (17). As in the preparation of **16**, **13** (15 mg, 0.027 mmol) was converted into **15**. The crude product was immediately dissolved in pyridine (1.0 mL, 13 mmol), and acetic anhydride (0.40 mL, 4.0 mmol) was added. The reaction mixture was then stirred overnight under nitrogen, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane–EtOAc, 2:1) to give **17** (9.8 mg, 86% from **13**) as a pale yellow solid, mp 245–247 °C (hexane–EtOAc). IR (KBr) cm^{-1}: 1775, 1736, 1711. ^{1}H NMR ($CDCl_3$) δ: 1.94–1.98 (8H, m), 2.45 (3H, s), 2.55 (3H, s), 2.58 (3H, s), 7.39 (1H, d, *J* = 7.5 Hz), 7.73 (1H, dd, *J* = 7.5, 8.0 Hz), 8.16 (1H, d, *J* = 8.0 Hz). High resolution MS Calcd for $C_{23}H_{20}O_8Si$: 424.1158. Found 424.1163.

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