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Utilization of Sulfide, Sulfoxide, and Sulfone Groups as Regiochemical Control Elements in the Diels-Alder Reaction of Naphthoquinones

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The Diels-Alder reactions of 2-phenylthio-, 2-phenylsulfinyl-, and 2-phenylsulfonyl-1,4-naphthoquinones, which were unsymmetrically substituted by methoxyl group on the benzenoid ring, with some vinylketene acetals were studied. The regioselectivity of the reactions was cleanly controlled by each of these sulfur substituents. In addition, the reactivity of the naphthoquinones were greatly enhanced by introduction of the sulfone or sulfoxide group. As a result of this study, several anthraquinones including natural products, such as pachybasin and phomarin 6-methyl ether, and 11-deoxyanthracyclinones were efficiently synthesized.

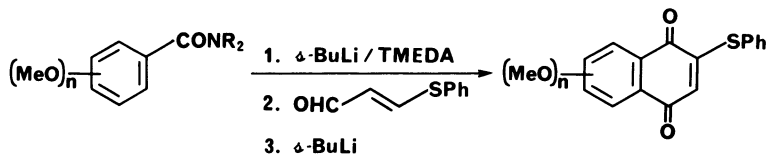
The Diels-Alder reaction of naphthoquinone derivatives with a variety of polarized dienes has been regarded as one of the most efficient methods for the synthesis of highly substituted anthraquinones[1] and tetracyclic anthracyclinone systems.[2] The regioselectivity of this reaction has been proved to be controlled by several factors in the naphthoquinone moiety, such as intramolecular hydrogen bonding between peri hydroxyl group and quinone carbonyl,[3] resonance effect of oxygen functionalities on the benzenoid ring,[3,4] and inductive effect of halo substituents (Cl, Br) on the quinonoid ring.[1,2] Of these, the directing priority of the halo substituents seems to be the highest and consequently they have been employed most widely as regiochemical control elements of the reactions. However, it is sometimes difficult[5] to synthesize pure halonaphthoquinones regiospecifically in a few steps, except by the Diels-Alder approaches developed independently by Brassard[1c,f] and Cameron[1b,g,h]. Therefore, it is desirable to devise new directing groups which may be readily and regiospecifically introduced into the quinonoid ring.

Recently, we have developed[6] a regiospecific one-pot synthesis of 2-phenylthionaphthoquinones from substituted tertiary benzamides using directed lithiation strategy (Scheme 1). We expected that the phenylthio group in these quinones could excert a powerful regiochemical controlling effect for the Diels-Alder reaction by its conversion into the corresponding electron-withdrawing sulfoxide or sulfone groups. Boeckman et al.[3,7] were the first to examine the Diels-Alder reaction of this type of quinone, namely, tolylsulfinyljuglones, with isoprene or the diene derived from 7,7-dimethoxybicyclo-[4.2.0]oct-1(6)-en-2-one, and observed modest regioselectivities. In addition, Kraus and Woo[8] reported recently on a similar reaction using several different types of dienes but did not pursue regiochemical studies. In this paper, we describe the regioselective Diels-Alder reaction of naphthoquinone sulfoxides **2a—c**, sulfones **3a—c**, and sulfides **1a—c** with the vinylketene acetals **5**, **6**, **26**, and isoprene (**33**).

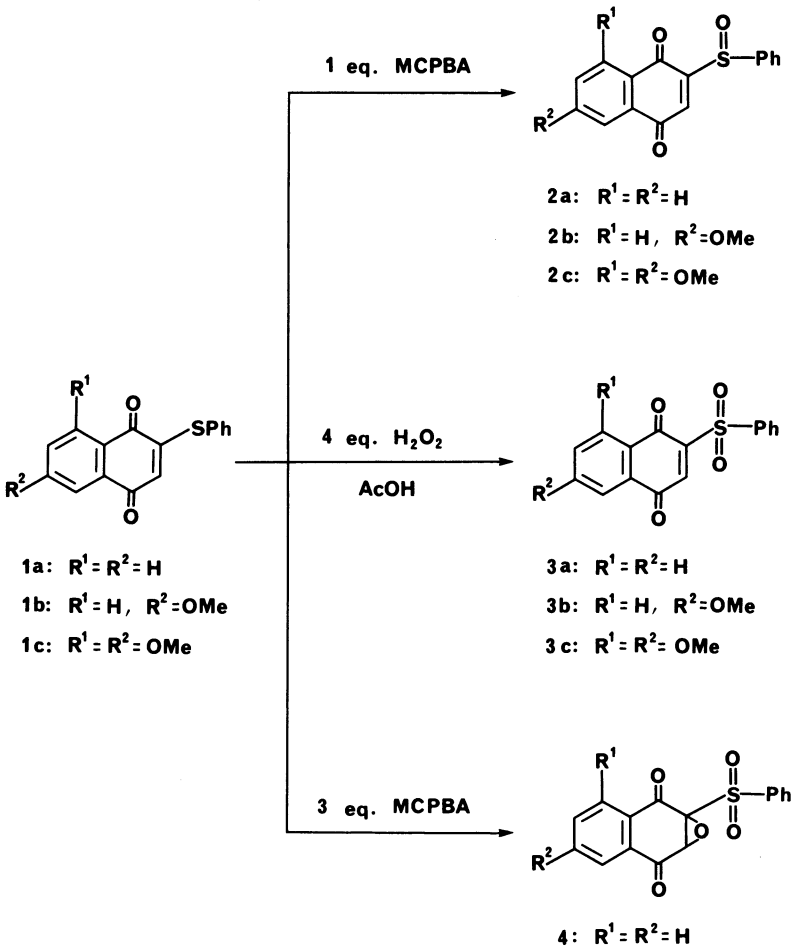
Results and Discussion

The sulfoxides **2a—c** were easily prepared in good yields from the corresponding sulfides **1a—c** by treatment with 1 equivalent of *m*-chloroperbenzoic acid (MCPBA)[3] in chloroform at 0 °C. However, the corresponding sulfone could not be obtained by MCPBA oxidation. Thus, TLC indicated that treatment of **1a** with 2 equivalents of MCPBA did not produce the sulfone **3a**, but a mixture of **1a**, **2a**, **4**, and another unidentified product. The epoxy sulfone **4** was obtained in good yield by treatment of **3a** with 3 equivalents of MCPBA. On the other hand, oxidation of **1a** with 4 equivalents of hydrogen peroxide[9] in refluxing acetic acid for 15 minutes gave the desired sulfone **3a** in 84% yield. In a similar manner, **3b** was obtained in 83% yield from **1b**. Oxidation of **1c** under similar conditions gave tarry material. However, at a lower temperature (80 °C), the sulfone **3c** was obtained in 66% yield.

We examined initially the Diels-Alder reaction of the quinones **2a**, **3a**, and **1a**, unsubstituted on the benzenoid ring, with mixed vinylketene acetal **5**[1d] readily prepared from methyl 3-methyl-2-butenoate. The sulfoxide **2a** was treated with 2 equivalents of **5** in



Scheme 1.



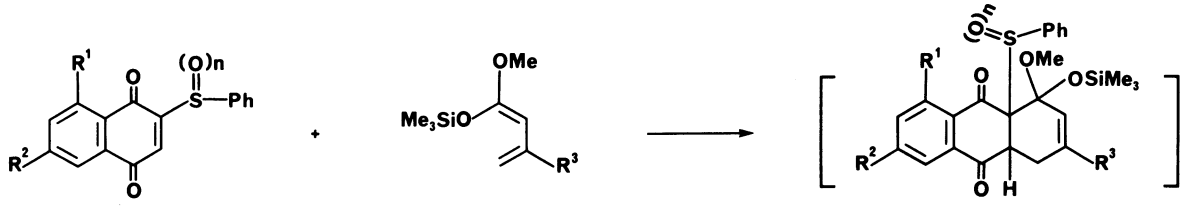
Scheme 2.

toluene at 0 °C. After 1 hour, TLC indicated the disappearance of starting quinone **2a**. However, the yellow color of the quinone did not disappear during this period which may indicate that the elimination of benzenesulfenic acid from the Diels–Alder adduct **7** (n=1, R^1=R^2=H, R^3=Me) is spontaneous under these conditions to regenerate the quinonoid structure. After evaporation of toluene, the residual oil was treated with aqueous methanolic HCl to effect aromatization to give 1-hydroxy-3-methylnaphthoquinone (pachybasin) (**8**) and its *O*-methyl derivative **9** in low yields and poor selectivity (**8**: 28%; **9**: 14%). On the other hand, the base-catalyzed aromatization using triethylamine which was employed at first by Rapoport[2g] in their aklavinone synthesis provided **8** almost exclusively although the yield again was low (Table 1: Entry 1). We used this mild and highly selective aromatization method as a standard procedure for other cases described below. The Diels–Alder reaction of the sulfone **3a** with **5** is very rapid. When **5** was added to a toluene solution of **3a** at 0 °C, the yellow color of **3a** disappeared almost instantaneously and TLC indicated the absence of starting quinone **3a**. On treatment with triethylamine, smooth elimination of benzenesulfinic acid and methanol from the adduct **7** (n=2, R^1=R^2=H, R^3=Me) took place and **8** was obtained in 86% yield accompanying with a trace amount of **9** (Entry 2). The sulfide **1a** is much less reactive toward **5** compared with **2a** and **3a**. It took 12 hours to complete the Diels–Alder reaction in refluxing benzene and additional 2 days for the triethylamine-catalyzed aromatization. In this reaction, the selectivity of **8** to **9** is somewhat low, but the total yield of the quinonoid products is excellent (Entry 3).

Next, we examined the Diels–Alder reaction of 6-methoxynaphthoquinones **2b**, **3b**, and **1b** with vinylketene acetal **5** to see the regiochemical controlling effect of the sulfoxide, sulfone, and sulfide groups (Entries 4—6). In every case, the reaction proceeded regiospecifically to give 1-hydroxy-6-methoxy-3-methylanthraquinone (phomarin 6-methyl ether) (**10**) as a major product in addition to a minor amount of its *O*-methyl derivative **11**.

In order to confirm the regiospecificity of these reactions, we have synthesized the regioisomer of **10**, 1-hydroxy-7-methoxy-3-methylanthraquinone (**24**), using the directed lithiation strategy developed by

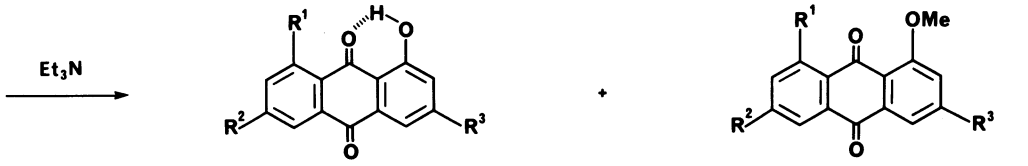
Table 1. Diels-Alder Reaction of Sulfur-Substituted Naphthoquinones with Vinylketene Acetals



1a-c: n=0
2a-c: n=1
3a-c: n=2

5: R^3 = Me
6: R^3 = OMe

7



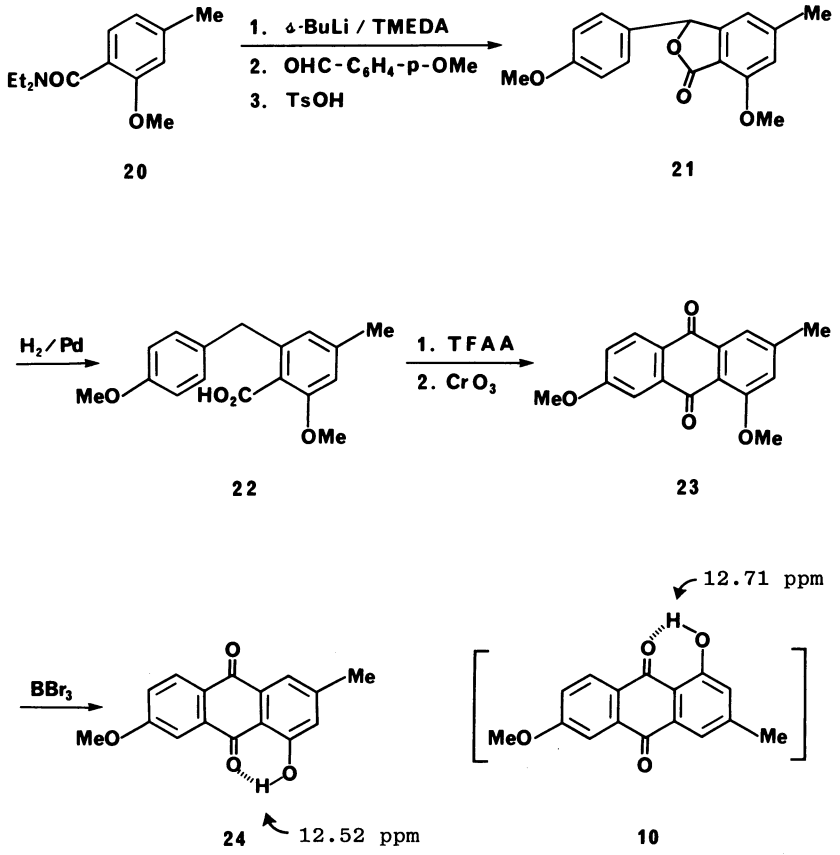
8: R^1 = R^2 = H, R^3 = Me
10: R^1 = H, R^2 = OMe, R^3 = Me
12: R^1 = R^2 = OMe, R^3 = Me
14: R^1 = R^2 = H, R^3 = OMe
16: R^1 = H, R^2 = R^3 = OMe
18: R^1 = R^2 = R^3 = OMe

9: R^1 = R^2 = H, R^3 = Me
11: R^1 = H, R^2 = OMe, R^3 = Me
13: R^1 = R^2 = OMe, R^3 = Me
15: R^1 = R^2 = H, R^3 = OMe
17: R^1 = H, R^2 = R^3 = OMe
19: R^1 = R^2 = R^3 = OMe

Entry	Naphthoquinone	Vinylketene acetal	Solvent[a]	Condition[b]		Anthraquinone(yield/%)[c]	
				Diels-Alder	Aromatization		
1	**2a**	**5**	T	A (1 h)	A (4 h)	**8**(41)	**9**(<1)
2	**3a**	**5**	T	A (1 h)	A (4 h)	**8**(86)	**9**(<1)
3	**1a**	**5**	B	D (12 h)	D (48 h)	**8**(81)	**9** (11)
4	**2b**	**5**	T	A (1 h)	A (4 h)	**10**(43)	**11**(<1)
5	**3b**	**5**	T	A (1 h)	A (4 h)	**10**(84)	**11** (1)
6	**1b**	**5**	B	D (30 h)	D (24 h)	**10**(81)	**11** (9)
7	**2c**	**5**	T	C (5 h)	B (18 h)	**12**(42)	**13** (5)
8	**3c**	**5**	T	C (1 h)	B (18 h)	**12**(81)	**13** (8)
9	**1c**	**5**	B	D (68 h)	D (24 h)	**12**(50)	**13** (11)
10	**2a**	**6**	T	A (0.5 h)	A (6 h)	**14**(73)	**15**(<1)
11	**3a**	**6**	T	A (0.5 h)	A (6 h)	**14**(66)	**15**(<1)
12	**1a**	**6**	B	C (120 h)	D (40 h)	**14**(77)	**15** (1)
13	**2b**	**6**	T	A (1 h)	A (3 h)	**16**(81)	**17** (6)
14	**2c**	**6**	T	C (1 h)	B (18 h)	**18**(65)	**19** (19)

a) T: Toluene; B: benzene. b) A: 0 °C; B: 0°C→room temperature; C: room temperature; D: reflux. c) Isolated yield after chromatography.

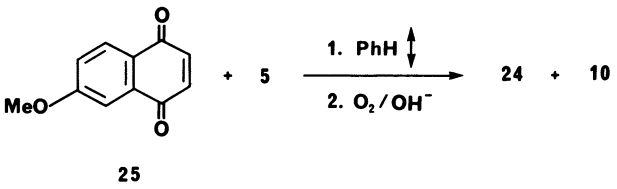
Snieckus[10] (Scheme 3). Thus *N,N*-diethyl-2-methoxy-4-methylbenzamide (**20**) was sequentially ortho-lithiated (*s*-BuLi-TMEDA-ether/−78 °C) and treated with *p*-anisaldehyde. The crude condensation product was treated with *p*-toluenesulfonic acid in refluxing benzene to give the phthalide **21** in 45% yield. Compound **21** was hydrogenated over palladium on charcoal to give the benzylbenzoic acid **22**. Without purification, crude **22** was treated with trifluoroacetic anhydride (TFAA) in dichloromethane followed by chromium trioxide to give the anthraquinone **23** in 29% overall yield from **21**. Selective demethylation of **23** with boron tribromide afforded the desired isomer **24** in 86% yield. The most characteristic difference between **10** and **24** was observed in their ^{1}H NMR spectra. Thus, the



Scheme 3.

absorptions of the strongly hydrogen-bonded peri hydroxyl protons for these compounds appeared at considerably different chemical shifts (**10**: δ 12.71, **24**: δ 12.52). This is apparently due to the difference of the resonance effect[2b,g] of the methoxyl group in the hydrogen-bonded quinone carbonyl in each isomer. This result suggests that the regioselectivity of the Diels–Alder reaction of mixed vinylketene acetals of type **5** with methoxy-substituted naphthoquinones could be generally established by ^{1}H NMR spectroscopy.

Next, we carried out the Diels–Alder reaction of 6-methoxy-1,4-naphthoquinone (**25**) with **5** to confirm the necessity of the sulfur substituents for the regiospecific Diels–Alder reactions (Scheme 4). When **25** was treated with **5** in refluxing benzene for 20 hours, and the crude Diels–Alder adduct was oxygenated under alkaline conditions, a 3.1 : 1 mixture of **24** and **10** was obtained in 78% yield. The ratio of **24** to **10** was determined by integration of the hydroxyl proton NMR absorptions of each isomer in the mixture. This result could be rationalized[4,23] as follows. The electron-donating effect of the methoxyl group at the 6 position weakens the electron-withdrawing effect of the C-1 carbonyl compared with C-4 which causes the electron-rich center of **5** to react preferentially at the C-2 position of the quinone **25** to give the anthraquinone **24** as a major product after



Scheme 4.

oxidative and hydrolytic work-up. This experiment revealed that the sulfur substituents on the quinonoid ring of **2b**, **3b**, and **1b** can overcome the electronic effect of 6-methoxyl group, and are essential for the regiospecific Diels–Alder reactions.

It is of interest to determine the effect of an additional methoxyl group in 5,7-dimethoxynaphthoquinone derivatives **2c**, **3c**, and **1c** on the regioselectivity of the Diels–Alder reaction. In these compounds, the electron-releasing effect of two methoxyl groups at 5 and 7 positions should result in considerable increase of electron density of the quinonoid ring and decrease of the electron-withdrawing effect of C-4 carbonyl rather than C-1. These effects should reduce both reactivity and regioselectivity of these compounds compared with monomethoxylated quinones described above.

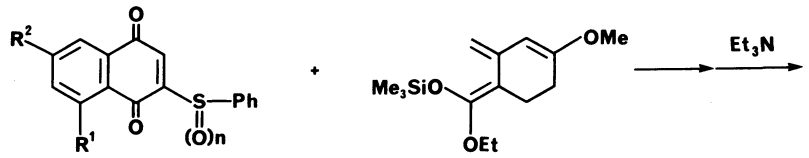
The sulfoxide **2c** was actually much less reactive

toward **5** compared with unsubstituted sulfoxide **2a** or mono-methoxylated compound **2b**. However, the Diels–Alder reaction was completed within 5 hours at room temperature and, after triethylamine-catalyzed aromatization, 1-hydroxy-6,8-dimethoxy-3-methylanthraquinone (emodin 6,8-dimethyl ether) (**12**) and its *O*-methyl derivative **13** were obtained in 42% and 5% yields, respectively (Table 1: Entry 7). The regioselectivity of this reaction was proved by careful examination of the hydroxyl proton region of ^{1}H NMR spectrum of the crude product, which showed only a sharp singlet at δ 13.09 which was identical with a reported value[1e] for emodin 6,8-dimethyl ether. In addition, structure of **13** was identified by direct spectroscopic and TLC comparisons with an authentic sample.[11] The sulfone **3c** was more reactive than the sulfoxide **2c**, and the Diels–Alder reaction with **5** was completed within 1 hour at room temperature. After triethylamine-catalyzed aromatization, **12** was obtained in good yield (81%) in addition to a small amount of **13** (8%) (Entry 8). The sulfide **1c** was much less reactive toward **5**. It took 68 hours in refluxing benzene to complete the reaction. However, the reaction was again regiospecific, and emodin derivatives were obtained in modest yields after triethylamine-catalyzed aromatization (Entry 9). Therefore, it was revealed from these experiments that the directing and activating effects of the sulfur substituents attached directly on the quinonoid ring were quite strong to outweigh the electronic effect of two methoxyl groups on the benzenoid ring. It appears that the effects of the sulfur substituents are stronger than those of the halo substituents since Brassard has reported[1d] that 3-chloro-5,7-dimethoxynaphthoquinone was almost unreactive toward the vinylketene acetals of type **5**.

The vinylketene acetal **6**[1d] was also allowed to react with some sulfur-substituted naphthoquinones, and the expected anthraquinone products were obtained regiospecifically in good yields (Table 1: Entries 10—14).

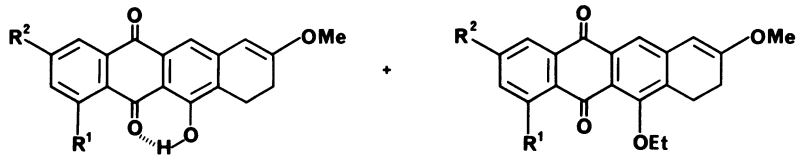
The synthesis of anthracyclinone aglycone is of current interest due to the potent antitumor activity of anthracycline antibiotics.[12] Based on the studies described above, some 11-deoxyanthracyclinones were easily synthesized regiospecifically by cycloaddition of

Table 2. Synthesis of 11-Deoxyanthracyclinones



2a-c: n=1
3a-c: n=2

26



27: $R^1 = R^2 = H$
29: $R^1 = H$, $R^2 = OMe$
31: $R^1 = R^2 = OMe$

28: $R^1 = R^2 = H$
30: $R^1 = H$, $R^2 = OMe$
32: $R^1 = R^2 = OMe$

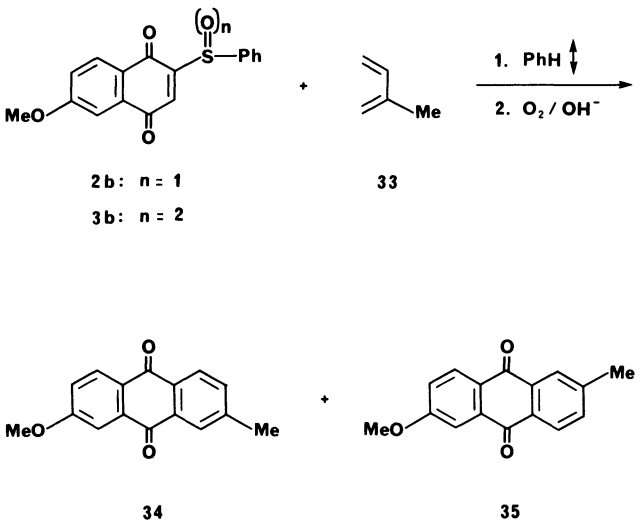
Entry	Naphthoquinone	Condition[a]	Anthracyclinone (yield/%)[b]	
1	**2a**	A	**27** (56)	**28** (34)
2	**3a**	A	**27** (57)	**28** (4)
3	**2b**	A	**29** (44)	**30** (47)
4	**3b**	A	**29** (69)	**30** (10)
5	**2c**	B	**31** (27)	**32** (32)
6	**3c**	B	**31** (37)	**32** (3)

a) A: Diels-Alder(0 °C, 1 h), aromatization(0 °C→room temperature, 18 h); B: Diels-Alder(room temperature, 1 h), aromatization(0 °C→room temperature, 18 h). All reactions were carried out in toluene. b) Isolated yield after chromatography.

Gesson's vinylketene acetal **26**,[2d] prepared in two steps from commercially available Hageman's ester, with the naphthoquinone sulfoxides **2a—c** and sulfones **3a—c**. The results are summarized in Table 2. In general, the sulfoxides reacted with **26** in good yields to give, after triethylamine-catalyzed aromatization, mixtures of 5-hydroxyanthracyclinones and their *O*-ethyl derivatives. However, the selectivity of the former compounds to the latter was very poor (Entries 1,3,5). On the other hand, the total yields of anthracyclinone products from the sulfones were somewhat lower, but the hydroxy compounds were obtained in good selectivity (Entries 2,4,6).

Finally, the regiochemical outcome of the Diels–Alder reactions of the sulfoxide **2b** and the sulfone **3b** with isoprene (**33**) was briefly examined (Scheme 5). Although the sulfoxide **2b** reacted smoothly with **33** in refluxing benzene, the reaction was not regiospecific and, after oxidation, a mixture of the anthraquinone products **34** and **35** was obtained in the ratio of 7:3, as determined by gas chromatography using nematic liquid crystals[4,13] as stationary phase. From the sulfone **3b**, a mixture of **34** and **35** was obtained in a somewhat improved ratio (8:2). It therefore appears that both sulfoxide and sulfone groups are insufficiently strong directing group for the regiospecific Diels–Alder reaction with relatively unpolarized diene **33**. Therefore, use of the polarized dienes such as vinylketene acetals is essential[14] for the regiospecific Diels–Alder reaction of the sulfur-substituted naphthoquinones.

In conclusion, we have shown that the sulfone, sulfoxide and sulfide groups, especially the former two, offer effective regiochemical control and activating elements in the Diels–Alder reaction of naphthoquinones. Since the regiospecific synthesis of 2-phenylthionaphthoquinones has been established,[6] the sulfur-directed Diels–Alder reaction described herein provides easy access to a wide range of highly substituted anthraquinones and anthracyclinones under mild conditions.



Scheme 5.

Experimental

General. All melting points are uncorrected. Mass spectra (MS) were determined on JEOL JMS-DX303 spectrometer. IR spectra were obtained in Nujol mulls with JASCO A-100 spectrometer. UV spectra were recorded in 95% ethanol on Hitachi 323 spectrometer. High field ^{1}H NMR spectra (400 MHz) were obtained with JEOL JNM-GX400 spectrometer using $CDCl_3$ as a solvent and TMS as an internal standard. Routine ^{1}H NMR spectra (60 MHz) were recorded on Hitachi R-600 machine. Elemental analyses were performed at microanalytical laboratory in Nagasaki University. Gas chromatography was performed on a Shimadzu GC-8A apparatus using flame ionization detector. Thin-layer chromatography was performed on Merck 0.2 mm precoated aluminum sheets of silica gel 60 F_{254} (Art 5554). For column chromatography, Merck silica gel 60 (230—400 mesh) (Art 9385) was employed.

2-Phenylsulfinyl-1,4-naphthoquinone (2a): Under ice-cooling, 2.16 g (10 mmol) of 80% MCPBA was added portionwise to a solution of 2.66 g (10 mmol) of **1a** in 150 ml of chloroform, and stirred for 4 h. The chloroform solution was washed with sodium hydrogencarbonate solution, dried over sodium sulfate, and evaporated. The residue was recrystallized from dichloromethane–hexane to give 2.64 g (94%) of **2a** as orange needles. An analytical sample was purified by recrystallization from methanol; mp 158.5—160 °C. IR: 1655, 1580, 1055, and 1050 cm^{-1}. ^{1}H NMR (400 MHz) δ=7.49 (m, 3H, H-3′, H-4′, H-5′), 7.65 (s, 1H, H-3), 7.76 (m, 2H, H-6, H-7), 7.85 (m, 2H, H-2′, H-6′), 8.00 (near d, 1H, H-5 or H-8, J=ca. 8 Hz), and 8.10 (near d, 1H, H-8 or H-5, J=ca. 8 Hz). Found: C, 68.10; H, 3.48; S, 11.50%. Calcd for $C_{16}H_{10}O_3S$: C, 68.07; H, 3.57; S, 11.36%.

6-Methoxy-2-phenylsulfinyl-1,4-naphthoquinone (2b): This compound was obtained from **1b** in a similar manner as described above in 89% yield; yellow needles from methanol; mp 181—181.5 °C. IR: 1670, 1650, 1585, and 1045 cm^{-1}. ^{1}H NMR (400 MHz) δ=3.94 (s, 3H, OMe), 7.18 (dd, 1H, H-7, J=8.8 and 2.6 Hz), 7.49 (m, 3H, H-3′, H-4′, H-5′), 7.52 (d, 1H, H-5, J=2.9 Hz), 7.60 (s, 1H, H-3), 7.85 (m, 2H, H-2′, H-6′), and 7.94 (d, 1H, H-8, J=8.8 Hz). Found: C, 65.23; H, 3.78; S, 10.31%. Calcd for $C_{17}H_{12}O_4S$: C, 65.37; H, 3.87; S, 10.27%.

5,7-Dimethoxy-3-phenylsulfinyl-1,4-naphthoquinone (2c): This compound was prepared from **1c** in a similar manner as described for **2a** in 98% yield; yellow needles from dichloromethane–methanol; mp 231.5—233.5 °C (decomp). IR: 1650, 1635, 1595, and 1045 cm^{-1}. ^{1}H NMR (400 MHz) δ=3.93 (s, 3H, OMe), 3.94 (s, 3H, OMe), 6.69 (d, 1H, H-6, J=2.2 Hz), 7.25 (d, 1H, H-8, J=2.2 Hz), 7.46 (m, 3H, H-3′, H-4′, H-5′), 7.53 (s, 1H, H-3), and 7.87 (m, 2H, H-2′, H-6′). Found: C, 63.29; H, 4.03; S. 9.37%. Calcd for $C_{18}H_{14}O_5S$: C, 63.15; H, 4.12; S, 9.37%.

2-Phenylsulfonyl-1,4-naphthoquinone (3a): To a hot solution of 1133 mg (4.25 mmol) of **1a** in 100 ml of acetic acid was added 2.0 ml (17.6 mmol) of 30% hydrogen peroxide solution, and the mixture was refluxed for 15 min. The solution was concentrated under reduced pressure to several

ml to precipitate yellow fine crystals, which were collected by filtration and washed with methanol giving 1061 mg (84%) of practically pure sulfone **3a**. Recrystallization from methanol afforded yellow fine plates; mp 190—191.5 °C (lit,[15] mp 192 °C). IR: 1665, 1585, 1330, and 1165 cm^{-1}. ^1H NMR (400 MHz) δ=7.59 (near t, 2H, H-3′, H-5′, J=ca. 7.5 Hz), 7.68 (near t, 1H, H-4′, J=ca. 7.5 Hz), 7.78 (m, 2H, H-6, H-7), 7.85 (s, 1H, H-3), 8.03 (m, 1H, H-5 or H-8), 8.08 (m, 1H, H-8 or H-5), and 8.15 (d, 2H, H-2′, H-6, J=7.7 Hz). Found: C, 64.20; H, 3.33; S, 10.86%. Calcd for $C_{16}H_{10}O_4S$: C, 64.42; H, 3.38; S, 10.75%.

6-Methoxy-2-phenylsulfonyl-1,4-naphthoquinone (3b): This compound was obtained from **1b** in a similar manner as described for **3a**; Yellow needles from methanol, mp 201—203 °C (decomp). IR: 1670, 1660, 1595, 1340, and 1155 cm^{-1}. ^1H NMR (400 MHz) δ=3.95 (s, 3H, OMe), 7.22 (dd, 1H, H-7, J=8.8 and 2.6 Hz), 7.48 (d, 1H, H-5, J=2.6 Hz), 7.59 (near t, 2H, H-3′, H-5′, J=ca. 7.5 Hz), 7.68 (near t, 1H, H-4′, J=ca. 7.5 Hz), 7.80 (s, 1H, H-3), 7.97 (d, 1H, H-8, J=8.8 Hz), and 8.15 (d, 2H, H-2′, J=7.7 Hz). Found: C, 62.20; H, 3.68; S, 9.82%. Calcd for $C_{17}H_{12}O_5S$: C, 62.19; H, 3.68; S, 9.77%.

5,7-Dimethoxy-3-phenylsulfonyl-1,4-naphthoquinone (3c): To a warm solution of 326 mg (1.00 mmol) of **3a** in 30 ml of acetic acid was added 0.45 ml (4.0 mmol) of 30% hydrogen peroxide solution. The mixture was kept at 80 °C for 4 h, and evaporated to dryness. The residue was recrystallized from dichloromethane-ethanol giving 235 mg (66%) of orange needles of **3c**. Mp 230—234.5 °C (decomp) was measured in a sealed capillary. IR: 1690, 1660, 1595, 1550, 1340, 1325, and 1160 cm^{-1}. ^1H NMR (400 MHz) δ=3.92 (s, 3H, OMe), 3.95 (s, 3H, OMe), 6.73 (d, 1H, H-6, J=2.2 Hz), 7.20 (d, 1H, H-8, J=2.2 Hz), 7.56 (near t, 2H, H-3′, H-5′, J=ca. 7.5 Hz), 7.64 (near t, 1H, H-4′, J=ca. 7.5 Hz), 7.76 (s, 1H, H-2), and 8.15 (d, 2H, H-2′, H-6′, J=7.7 Hz). Found: C, 60.17; H, 3.78; S, 9.16%. Calcd for $C_{18}H_{14}O_6S$: C, 60.33; H, 3.94; S, 8.95%.

2,3-Epoxy-2-phenylsulfonyl-1,4-naphthoquinone (4): Under ice-cooling, 4.50 g (21 mmol) of 80% MCPBA was added all at once to a stirred solution of 1.85 g (7.0 mmol) of **1a** in 170 ml of chloroform. The mixture was stirred for 2 h at 0 °C and left overnight at room temperature. An additional 0.20 g (0.9 mmol) of 80% MCPBA was added, and the mixture was stirred for further 8 h. The chloroform solution was washed with sodium hydrogencarbonate solution, dried over sodium sulfate and evaporated. The residual oil was crystallized by trituration with ether and the crystals were collected by filtration to give 2.01 g (92%) of **4**. Recrystallization from dichloromethane-ether (charcoal) afforded colorless prisms, mp 151.5—153.5 °C. MS m/z=314 (M^+). IR: 1695, 1585, 1575, 1345, 1335, 1165, and 1145 cm^{-1}. ^1H NMR (400 MHz) δ=4.80 (s, 1H, H-3), 7.64 (near t, 2H, H-3′, H-5′, J=ca. 7.5 Hz), 7.75 (near t, 1H, H-4′, J=ca. 7.5 Hz), 7.78 (m, 2H, H-6, H-7), 7.94 (dd, 1H, H-5 or H-8, J=7.0 and 1.8 Hz), 8.02 (dd, 1H, H-8 or H-5, J=7.5 and 1.5 Hz), and 8.19 (d, 2H, H-2′, H-6′, J=7.3 Hz). Found: C, 61.38; H, 3.07; S, 10.33%. Calcd for $C_{16}H_{10}O_5S$: C, 61.14; H, 3.21; S, 10.20%.

Diels-Alder Reaction of the Naphthoquinones 1a—c, 2a—c, and 3a—c with the Vinylketene Acetals 5, 6, and 26; General Procedure: Under nitrogen atmosphere, 2.0 mmol of the vinylketene acetal was added to a solution or suspension of 1.0 mmol of the naphthoquinone in 50 ml of dry toluene or benzene. After completion of the Diels-Alder reaction, 1.0 ml of triethylamine was added and the aromatization reaction was conducted. The reaction conditions for both the Diels-Alder and aromatization reactions were shown in Table 1 or 2 for each cases. When the Diels-Alder reaction was slow (Table 1: Entries 6,9,12), small portions of additional vinylketene acetal were added until the starting quinone had disappeared (TLC analysis) (Entry 6: 2 equiv of the vinylketene acetal for the quinone; Entry 9: 25 equiv; Entry 12: 3 equiv). When the reaction was completed, the reaction mixture was evaporated to dryness under reduced pressure. The residue was washed with methanol and filtered giving the quinonoid products, which were chromatographed on silica gel using dichloromethane or a mixture of dichloromethane and acetone (20:1) as eluents. From the first yellow band, the hydroxy quinone was obtained, and its *O*-alkylated derivative was obtained from the next yellow band. The yield of each compound is shown in Table 1 or 2. The following quinones were obtained in this manner.

1-Hydroxy-3-methylanthraquinone (Pachybasin) (8): Yellow needles from ethanol; mp 176.5—177.5 °C (lit,[16,17] mp 176—177 °C; lit,[1j] mp 179—180 °C). IR: 1670, 1635, 1585, and 1570 cm^{-1}. ^1H NMR (400 MHz) δ=2.47 (s, 3H, Me), 7.11 (s, 1H, H-2), 7.64 (s, 1H, H-4), 7.80 (m, 2H, H-6, H-7), 8.29 (m, 2H, H-5, H-8), and 12.57 (s, 1H, OH). Found: C, 75.70; H, 4.16%. Calcd for $C_{15}H_{10}O_3$: C, 75.62; H, 4.23%.

1-Methoxy-3-methylanthraquinone (9): Yellow needles from methanol; mp 190—191 °C (lit,[16] mp 187—188 °C; lit,[17] mp 185—187 °C. IR: 1670, 1655, 1595, and 1590 cm^{-1}. ^1H NMR (400 MHz) δ=2.50 (s, 3H, Me), 4.04 (s, 3H, OMe), 7.14 (s, 1H, H-2), 7.7—7.8 (m, 2H, H-6, H-7), 7.77 (s, 1H, H-4), 8.21 (dd, 1H, H-8 or H-5, J=7.6 and 1.4 Hz), and 8.27 (dd, 1H, H-5 or H-8, J=7.5 and 1.4 Hz). Found: C, 76.04; H, 4.67%. Calcd for $C_{16}H_{12}O_3$: C, 76.18; H, 4.79%.

1-Hydroxy-6-methoxy-3-methylanthraquinone (Phomarin 6-Methyl Ether) (10): Yellow needles from ethanol; mp 188.5—189 °C (lit,[1f] mp 187.0—187.5 °C; lit,[18] mp 193 °C). R_f (TLC-benzene)=0.41. IR: 1670, 1630, and 1590 cm^{-1}. UV: 267.5 (log ε 4.61), 292sh (4.25), and 411 nm (3.93). ^1H NMR (400 MHz) δ=2.46 (s, 3H, Me), 3.99 (s, 3H, OMe), 7.10 (s, 1H, H-2), 7.26 (dd, 1H, H-7, J=8.4 and 2.8 Hz), 7.63 (s, 1H, H-4), 7.71 (d, 1H, H-5, J=2.8 Hz), 8.24 (d, 1H, H-8, J=8.8 Hz), and 12.71 (s, 1H, OH). Found: C, 71.85; H, 4.39%. Calcd for $C_{16}H_{12}O_4$: C, 71.64; H, 4.51%.

1,6-Dimethoxy-3-methylanthraquinone (11): Yellow needles from methanol; mp 189.5—190 °C. IR: 1665, 1650, 1600, 1575, and 1560 cm^{-1}. ^1H NMR (400 MHz) δ=2.50 (s, 3H, Me), 3.96 (s, 3H, OMe), 4.03 (s, 3H, OMe), 7.13 (s, 1H, H-2), 7.25 (dd, 1H, J=8.4 and 2.6 Hz), 7.63 (d, 1H, H-5, J=2.6 Hz), 7.76 (s, 1H, H-4), and 8.21 (d, 1H, H-8, J=8.4 Hz). Found: C, 72.36; H, 5.04%. Calcd for $C_{17}H_{14}O_4$: C, 72.33; H, 5.00%.

1-Hydroxy-6,8-dimethoxy-3-methylanthraquinone (Emodin 6,8-Dimethyl Ether) (12): Orange needles from ethanol; mp 211.5—213 °C (lit,[19] mp 211.0 °C; lit,[1e] mp 204—205 °C). IR: 1665, 1625, 1590, and 1550 cm^{-1}. ^1H NMR (400 MHz) δ=2.43 (s, 3H, Me), 3.99 (s, 3H, OMe), 4.02 (s, 3H, OMe), 6.78 (d, 1H, H-7, J=2.3 Hz), 7.07 (s, 1H, H-2), 7.45 (d, 1H, H-5, J=2.8 Hz), 7.56 (s, 1H, H-4), and 13.09 (s, 1H, OH). Found: C, 68.55; H, 4.64%. Calcd for $C_{17}H_{14}O_5$: C, 68.45; H, 4.73%.

1,3,8-Trimethoxy-6-methylanthraquinone (13): Hygroscopic yellow needles from methanol; mp 228.5—229.5 °C (lit,[20] mp 227—228 °C; lit,[11] mp 229 °C). IR: 1650, 1600,

and 1555 cm^{-1}. ^{1}H NMR (400 MHz) δ=2.47 (s, 3H, Me), 3.95 (s, 3H, OMe), 3.96 (s, 3H, OMe), 3.99 (s, 3H, OMe), 6.77 (d, 1H, H-2, J=2.6 Hz), 7.10 (s, 1H, H-7), 7.32 (d, 1H, H-4, J=2.6 Hz), and 7.64 (s, 1H, H-5). This compound was shown to be identical with an authentic sample[11] by spectroscopic and TLC comparisons.

1-Hydroxy-3-methoxyanthraquinone (Xanthopurprine 3-Methyl Ether) (14): Yellow needles from ethanol; mp 195—196.5 °C (lit,[21] mp 193—194 °C; lit,[1d] mp 193.5—194.5 °C). IR: 1675, 1630, 1590, and 1565 cm^{-1}. ^{1}H NMR (400 MHz) δ=3.93 (s, 3H, OMe), 6.68 (d, 1H, H-2, J=2.3 Hz), 7.34 (d, 1H, H-4, J=2.3 Hz), 7.77 (m, 2H, H-6, H-7), 8.26 (m, 2H, H-5, H-8), and 12.86 (s, 1H, OH). Found: C, 70.75; H, 3.85%. Calcd for $C_{15}H_{10}O_4$: C, 70.86; H, 3.96%.

1,3-Dimethoxyanthraquinone (15): Yellow needles from methanol; mp 163.5—164 °C (lit,[22] mp 163 °C; lit,[21] mp 154—155 °C). IR: 1665, 1655, 1590, 1580, and 1555 cm^{-1}. ^{1}H NMR (400 MHz) δ=3.99 (s, 3H, OMe), 4.02 (s, 3H, OMe), 6.79 (d, 1H, H-2, J=2.3 Hz), 7.46 (d, 1H, H-4, J=2.3 Hz), 7.71 (dt, 1H, H-6 or H-7, J=7.8 and 1.4 Hz), 7.77 (dt, 1H, H-7 or H-6, J=7.3 and 1.4 Hz), 8.21 (dd, 1H, H-8 or H-5, J=7.8 and 0.9 Hz), and 8.27 (dd, 1H, H-5 or H-8, J=7.8 and 0.9 Hz). Found: C, 71.50; H, 4.52%. Calcd for $C_{16}H_{12}O_4$: C, 71.64; H, 4.51%.

1-Hydroxy-3,6-dimethoxyanthraquinone (16): Orange needles from ethanol; mp 220—221 °C. IR: 1675, 1620, and 1585 cm^{-1}. ^{1}H NMR (400 MHz) δ=3.94 (s, 3H, OMe), 3.98 (s, 3H, OMe), 6.71 (d, 1H, H-2, J=2.3 Hz), 7.27 (dd, 1H, H-7, J=8.8 and 2.8 Hz), 7.36 (d, 1H, H-4, J=2.8 Hz), 7.70 (d, 1H, H-5, J=2.3 Hz), 8.23 (d, 1H, H-8, J=8.8 Hz), and 13.01 (s, 1H, OH). Found: C, 67.63; H, 4.21%. Calcd for $C_{16}H_{12}O_5$: C, 67.60; H, 4.25%.

1,3,6-Trimethoxyanthraquinone (17): Yellow microcrystals from ethanol; mp 242—243 °C (lit,[23] mp 240—241.5 °C). IR: 1655, 1645, 1595, 1575, and 1560 cm^{-1}. ^{1}H NMR (400 MHz) δ=3.96 (s, 3H, OMe), 3.98 (s, 3H, OMe), 4.01 (s, 3H, OMe), 6.79 (d, 1H, H-2, J=2.6 Hz), 7.25 (dd, 1H, H-7, J=8.8 and 2.6 Hz), 7.45 (d, 1H, H-4, J=2.6 Hz), 7.63 (d, 1H, H-5, J=2.6 Hz), and 8.22 (d, 1H, H-8, J=8.8 Hz). Found: C, 68.54; H, 4.70%. Calcd for $C_{17}H_{14}O_5$: C, 68.45; H, 4.73%.

1-Hydroxy-3,6,8-trimethoxyanthraquinone (18): Orange microcrystals from chloroform–ethanol; mp 257—258 °C. IR: 1620, 1590, and 1550 cm^{-1}. ^{1}H NMR (400 MHz) δ=3.92 (s, 3H, OMe), 3.99 (s, 3H, OMe), 4.03 (s, 3H, OMe), 6.71 (d, 1H, H-2, J=2.3 Hz), 6.80 (d, 1H, H-7, J=2.3 Hz), 7.30 (d, 1H, H-4, J=2.8 Hz), 7.47 (d, 1H, H-5, J=2.3 Hz), and 13.40 (s, 1H, OH). Found: C, 65.12; H, 4.44%. Calcd for $C_{17}H_{14}O_6$: C, 64.97; H, 4.49%.

1,3,6,8-Tetramethoxyanthraquinone (19): Hygroscopic yellow microcrystals from ethanol, mp 222—223 °C (lit,[22] mp 220—221 °C, lit,[24] mp 224—225 °C). IR: 1655, 1600, and 1560 cm^{-1}. ^{1}H NMR (400 MHz) δ=3.96 (s, 6H, OMe), 3.99 (s, 6H, OMe), 6.76 (d, 2H, H-2, H-7, J=2.6 Hz), and 7.31 (d, 2H, H-4, H-5, J=2.6 Hz). An analytical sample was obtained by sublimation at 150—180 °C/0.15 mmHg (1 mmHg=133.322 Pa). Found: C, 65.66; H, 4.88%. Calcd for $C_{18}H_{16}O_6$: C, 65.85; H, 4.91%.

6-Hydroxy-9-methoxy-7,8-dihydro-5,12-naphthacenedione (27): Orange needles from dichloromethane; mp 243—244 °C. MS m/z=306 (M$^+$). IR: 1665, 1615, 1590, 1570, and 1550 cm^{-1}. ^{1}H NMR (400 MHz) δ=2.49 (near t, 2H, H-8, J=ca. 8.5 Hz), 3.03 (near t, 2H, H-7, J=ca. 8.5 Hz), 3.78 (s, 3H, OMe), 5.65 (s, 1H, H-10), 7.45 (s, 1H, H-11), 7.77 (m, 2H, H-2, H-3), 8.27 (m, H-1, H-4), and 12.99 (s, 1H, OH). Found: C, 74.42; H, 4.52%. Calcd for $C_{19}H_{14}O_4$: C, 74.45; H, 4.60%.

6-Ethoxy-9-methoxy-7,8-dihydro-5,12-naphthacenedione (28): Yellow needles from dichloromethane–hexane, mp 203.5—204.5 °C. MS m/z=334 (M$^+$). IR: 1670, 1630, 1575, and 1540 cm^{-1}. ^{1}H NMR (400 MHz) δ=1.53 (t, 3H, CH_3 of OEt, J=7.0 Hz), 2.46 (near t, 2H, H-8, J=ca. 8 Hz), 3.08 (near t, 2H, H-7, J=ca. 8 Hz), 3.78 (s, 3H, OMe), 4.03 (q, 2H, CH_2 of OEt, J=7.0 Hz), 5.71 (s, 1H, H-10), 7.72 (s, 1H, H-11), 7.7—7.8 (m, 2H, H-2, H-3), 8.21 (dd, 1H, H-4 or H-1, J=7.3 and 1.5 Hz), and 8.26 (dd, 1H, H-1 or H-4, J=7.7 and 1.5 Hz). Found: C, 75.37; H, 5.42%. Calcd for $C_{21}H_{18}O_4$: C, 75.43; H, 5.43%.

6-Hydroxy-2,9-dimethoxy-7,8-dihydro-5,12-naphthacenedione (29): Orange needles from dichloromethane–hexane; mp 232—233 °C. MS m/z=336 (M$^+$). IR: 1670, 1630, 1615, 1595, 1560, and 1550 cm^{-1}. ^{1}H NMR (400 MHz) δ=2.49 (near t, 2H, H-8, J=ca. 8.5 Hz), 3.02 (near t, 2H, H-7, J=ca. 8.5 Hz), 3.78 (s, 3H, OMe), 3.98 (s, 3H, OMe), 5.64 (s, 1H, H-10), 7.23 (dd, 1H, H-3, J=8.8 and 2.9 Hz), 7.43 (s, 1H, H-11), 7.68 (d, 1H, H-1, J=2.9 Hz), 8.21 (d, 1H, H-4, J=8.8 Hz), and 13.10 (s, 1H, OH). Found: C, 71.36; H, 4.75%. Calcd for $C_{20}H_{16}O_5$: C, 71.42; H, 4,79%.

6-Ethoxy-2,9-dimethoxy-7,8-dihydro-5,12-naphthacenedione (30): Yellow needles from dichloromethane–ether–hexane; mp 224—225 °C. MS m/z=364 (M$^+$). IR: 1670, 1630, 1600, 1570, and 1540 cm^{-1}. ^{1}H NMR (400 MHz) δ=1.52 (t, 3H, CH_3 of OEt, J=7.0 Hz), 2.45 (near t, 2H, H-8, J=ca. 8 Hz), 3.07 (near t, 2H, H-7, J=ca. 8 Hz), 3.77 (s, 3H, OMe), 3.96 (s, 3H, OMe), 4.02 (q, 2H, CH_2 of OEt, J=7.0 Hz), 5.69 (s, 1H, H-10), 7.23 (dd, 1H, H-3, J=8.8 and 2.6 Hz), 7.63 (d, 1H, H-1, J=2.6 Hz), 7.69 (s, 1H, H-11), and 8.20 (d, 1H, H-4, J=8.8 Hz). Found: C, 72.61; H, 5.50%. Calcd for $C_{22}H_{20}O_5$: C, 72.51; H, 5.53%.

6-Hydroxy-2,4,9-trimethoxy-7,8-dihydro-5,12-naphthacenedione (31): Orange needles from dichloromethane–ether–hexane; mp 257—259 °C (decomp). MS m/z=366 (M$^+$). IR: 1670, 1630, 1615, 1595, and 1550 cm^{-1}. ^{1}H NMR (400 MHz) δ=2.47 (near t, 2H, H-8, J=ca. 8.5 Hz), 3.02 (near t, 2H, H-7, J=ca. 8.5 Hz), 3.77 (s, 3H, OMe), 3.98 (s, 3H, OMe), 4.03 (s, 3H, OMe), 5.62 (s, 1H, H-10), 6.78 (d, 1H, H-3, J=2.3 Hz), 7.39 (s, 1H, H-11), 7.46 (d, 1H, H-1, J=2.3 Hz), and 13.48 (s, 1H, OH). Found: C, 68.57; H, 4.92%. Calcd for $C_{21}H_{18}O_6$: C, 68.85; H, 4.95%.

6-Ethoxy-2,4,9-trimethoxy-7,8-dihydro-5,12-naphthacenedione (32): Yellow needles from dichloromethane–ether; mp 207.5—209.5 °C. MS m/z=394 (M$^+$). IR: 1665, 1635, 1595, 1580, and 1565 cm^{-1}. ^{1}H NMR (400 MHz) δ=1.50 (t, 3H, CH_3 of OEt, J=7.0 Hz), 2.43 (near t, 2H, H-8, J=ca. 8 Hz), 3.06 (near t, 2H, H-7, J=ca. 8 Hz), 3.76 (s, 3H, OMe), 3.95 (s, 3H, OMe), 3.97 (s, 3H, OMe), 4.07 (q, 2H, CH_2 of OEt, J=7.0 Hz), 5.67 (s, 1H, H-10), 6.76 (d, 1H, H-3, J=2.2 Hz), 7.34 (d, 1H, H-1, J=2.6 Hz), and 7.60 (s, 1H, H-11). Found: C, 69.89; H, 5.64%. Calcd for $C_{23}H_{22}O_6$: C, 70.04; H, 5.62%.

***N,N*-Diethyl-2-methoxy-4-methylbenzamide (20):** This amide was prepared under standard conditions[10] from the corresponding acid via the acid chloride and purified by Kugelrohr distillation, bp 130 °C/0.1 mmHg. Colorless solid, mp 60—62 °C. IR: 1610, 1575, and 1510 cm^{-1}. ^{1}H NMR (400 MHz) δ=1.02 (near t, 3H, CH_3 of NEt_2, J=ca. 7 Hz), 1.23 (near t, 3H, CH_3 of NEt_2, J=ca. 7 Hz), 2.35 (s, 3H,

Me), 3.15 (q, 2H, CH_2 of NEt_2, J=ca. 7 Hz), 3.56 (br s, 2H, CH_2 of NEt_2), 3.79 (s, 3H, OMe), 6.71 (s, 1H, H-3), 6.77 (d, 1H, H-5, J=7.3 Hz), and 7.06 (d, 1H, H-6, J=7.7 Hz). Found: C, 70.66; H, 8.69; N, 6.15%. Calcd for $C_{13}H_{19}NO_2$: C, 70.56; H, 8.65; N, 6.33%.

7-Methoxy-3-(4-methoxyphenyl)-5-methyl-1(3*H*)-isobenzofuranone (21): A solution of 13.8 ml (16.5 mmol) of *s*-BuLi (1.20 M in cyclohexane (1 M=1 mol dm^{-3})) was slowly injected into a stirred solution of 3320 mg (15 mmol) of **20** and 2.5 ml of TMEDA in 250 ml of anhydrous ether at −78 °C under nitrogen atmosphere. After stirring for 1 h, a solution of 2246 mg (16.5 mmol) of *p*-anisaldehyde in ether was injected. After 1 h, Dry Ice-acetone bath was removed and the solution was stirred overnight. The reaction mixture was quenched by saturated ammonium chloride solution, washed successively with water and brine solution, dried over sodium sulfate and evaporated to give an oily residue. A solution of this material and 1 g of *p*-toluenesulfonic acid in 200 ml of benzene was refluxed for 6 h. The reaction mixture was washed twice with sodium hydrogencarbonate solution, dried over sodium sulfate and evaporated. The residual oil was dissolved in ether and the mixture was left overnight. The precipitate was collected by filtration giving 1167 mg of **21**. An additional 765 mg of **21** was obtained from the mother liquor after silica-gel chromatography using dichloromethane as eluent. The total yield was 1932 mg (45%). An analytical sample was obtained by recrystallization from dichloromethane-ether-hexane to give colorless needles; mp 118—118.5 °C. IR: 1750 and 1605 cm^{-1}. ^1H NMR (400 MHz) δ=2.40 (s, 3H, Me), 3.80 (s, 3H, OMe), 4.00 (s, 3H, OMe), 6.21 (s, 1H, H-3), 6.62 (s, 1H, H-6), 6.73 (s, 1H, H-4), 6.89 (d, 2H, H-3′, H-5′, J=8.4 Hz), and 7.18 (d, H-2′, H-6′, J=8.8 Hz). Found: C, 72.10; H, 5.55%. Calcd for $C_{17}H_{16}O_4$: C, 71.82; H, 5.67%.

1,7-Dimethoxy-3-methylanthraquinone (23): A mixture of 1008 mg (3.55 mmol) of **21** and 370 mg of 5% palladium on charcoal in 100 ml of glacial acetic acid was stirred at 80 °C overnight under an atmosphere of hydrogen. The catalyst was removed by filtration, and the filtrate was evaporated under reduced pressure giving an oily residue. In order to remove acetic acid contaminant, toluene was added and the whole was evaporated. The residual crude acid **22** was dissolved in 150 ml of dry dichloromethane, and 3 ml of trifluoroacetic anhydride was added at 0 °C. The mixture was stirred at room temperature for 5 h and evaporated. Methanol was added to the residue and the whole was evaporated. The residue was dissolved in dichloromethane and the solution was washed with sodium hydrogencarbonate solution, dried over sodium sulfate and evaporated to give a dark oil. A mixture of this oil, 0.4 g of chromium trioxide and a few drops of water in 90 ml of acetic acid was stirred at room temperature for 3.5 h. The mixture was evaporated to dryness, and the residue was dissolved in dichloromethane. The solution was washed with sodium hydrogencarbonate solution, filtered through celite, dried over sodium sulfate and evaporated. The residue was chromatographed over silica gel using a mixture of dichloromethane and ether (20:1) giving 294 mg (29%) of **23**. An analytical sample was obtained by recrystallization from methanol to give yellow needles; mp 181—182 °C (lit,[25] mp 183—184 °C). IR: 1665, 1650, 1595, and 1555 cm^{-1}. ^1H NMR δ=2.50 (s, 3H, Me), 3.97 (s, 3H, OMe), 4.04 (s, 3H, OMe), 7.11 (s, 1H, H-2), 7.20 (dd, 1H, H-6, J=8.8 and 2.6 Hz), 7.70 (d, 1H, H-8, J=2.6 Hz), 7.77 (s, 1H, H-4), and 8.17 (d, 1H, H-5, J=8.8 Hz). Found: C, 72.61; 4.85%. Calcd for $C_{17}H_{14}O_4$: C, 72.33; H, 5.00%.

1-Hydroxy-7-methoxy-3-methylanthraquinone (24): A solution of 85 mg (0.34 mmol) of boron tribromide in 5 ml of dichloromethane was added to a stirred solution of 80 mg (0.28 mmol) of **23** in 40 ml of dry dichloromethane at −78 °C. After 1 h, Dry Ice-acetone bath was removed and the mixture was stirred for 1.5 h. The mixture was washed with 5% sodium carbonate solution, dried over sodium sulfate and evaporated. The residue was purified by silica-gel chromatography using benzene as eluent giving 65 mg (86%) of **24**. An analytical sample was obtained by recrystallization from ethanol to give yellow needles; mp 191—192 °C and 201—201.5 °C (double melting point) (lit,[25] mp 198—199 °C). R_f (TLC-benzene)=0.37. IR: 1670, 1630, 1590, and 1565 cm^{-1}. UV: 272.5 (log ε 4.59), 295 (4.29), and 390 nm (3.90). ^1H NMR (400 MHz) δ=2.46 (s, 3H, Me), 3.99 (s, 3H, OMe), 7.08 (s, 1H, H-2), 7.26 (dd, 1H, H-6, J=8.7 and 2.8 Hz), 7.64 (s, 1H, H-4), 7.72 (d, 1H, H-8, J=2.8 Hz), 8.23 (d, 1H, H-5, J=8.7 Hz), and 12.52 (s, 1H, OH). Found: C, 71.41: H, 4.37%. Calcd for $C_{16}H_{12}O_4$: C, 71.64; H, 4.51%.

Diels-Alder Reaction of 6-Methoxynaphthoquinone (25) and the Vinylketene Acetal 5: A solution of 188 mg (1.0 mmol) of **25**[4,26] and 373 mg (2.0 mmol) of **5** in 50 ml of benzene was refluxed for 20 h, and evaporated to dryness. The residual oil was dissolved in a mixture of 10 ml each of THF and ethanol, 10 ml of 5% aqueous sodium hydroxide was added, and oxygen was bubbled through the resulting solution for 3 h. The mixture was acidified with hydrochloric acid and diluted with water. The yellow precipitate was collected by filtration and washed with water. Chromatography of the precipitate over silica gel using dichloromethane as eluent afforded 210 mg (78%) of a 3.1:1 mixture of the hydroxy quinones **24** and **10**, and 39 mg (14%) of a mixture of the methoxy quinones **23** and **11**. The ratio of **24** to **10** was determined by integration of the absorptions of the hydroxyl proton of each isomer by 400 MHz NMR. The ratio of **23** to **11** could not be estimated correctly by 400 MHz NMR because of the similarity of the spectra of the two isomers. However, it was apparent that **23** was a major product (**23**/**11**>5) from the comparison of the spectrum (aromatic region) of the mixture with those of authentic samples. Attempts to separate the mixture of **23** and **11** by GC or analytical HPLC were not successful.

Diels-Alder Reaction of 2b or 3b with Isoprene (33): A mixture of 156 mg (0.5 mmol) of **2b** and 1.0 ml (10 mmol) of isoprene in 20 ml of benzene was refluxed for 4 h, and evaporated to dryness. The residue was dissolved in a mixture of 5 ml each of THF and ethanol, and 5 ml of 5% aqueous sodium hydroxide was added. Oxygen was bubbled through this solution for 2 h. The mixture was diluted with water, and the precipitate was collected by filtration giving 77 mg (61%) of slightly colored fine needles of a 7:3 mixture of 2-methoxy-7-methylanthraquinone (**34**) and 2-methoxy-6-methylanthraquinone (**35**). The ratio was estimated by gas chromatography (2.5% BBBT/2 m×2.6 mm I.D./230 °C). Spectral data of the mixture were as follows. MS m/z=252 (M^+). ^1H NMR (400 MHz) δ=2.53 (s, Me of **34** and **35**), 3.99 (s, OMe of **34** and **35**), 7.25 (partially overlapped dd, H-3 of **34** and **35**), 7.56 (d, H-7 of **35**, J=8.1 Hz), 7.58 (d, H-6 of **34**, J=8.1 Hz), 7.72 (d, H-1 of **34** and **35**, J=2.6 Hz), 8.08 (s, H-8 of **34** and H-5 of **35**), 8.18 (d, H-8 of **35**, J=8.1 Hz), 8.19 (d,

H-5 of **34**, J=7.7 Hz), and 8.24 (d, H-4 of **34** and **35**, J=8.8 Hz). These values of the chemical shifts and coupling constants are almost identical with the reported values[4] for **34** and **35**. In a similar manner **2b** was treated with isoprene giving a 8:2 mixture of **34** and **35** in 84% combined yield.

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