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Polycyclic Hydroxyquinones. Part 29.[1] Regioselective Reactions of 5-Sulphur-substituted furan-2(5*H*)-one Anions with Naphthoquinone Monoketals. Application to the Synthesis of Anthracyclinone Precursors

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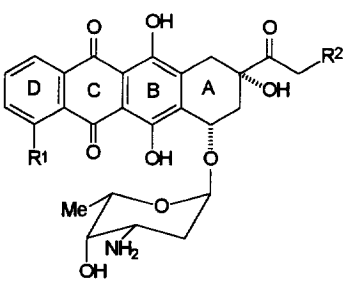
Abstract: The anions of furanones **7-10**, reacted with naphthoquinone monoketals **11-15** to afford exclusively the C-5 substituted Michael adducts in good yield. The annelation reactions of the anions generated from furanones **30** and **33** with naphthoquinone monoketals **11** and **12** lead to 2-sulphur-substituted 1,4-anthraquinones **32, 35** and **36**. Diels-Alder reaction of the 1,4-anthraquinones **41** and **42** with (*E*)-1,3-bis[(trimethylsilyl)oxy]buta-1,3-diene (**37**) affords ABCD tetracyclic systems related to those existing in anthracyclinones.

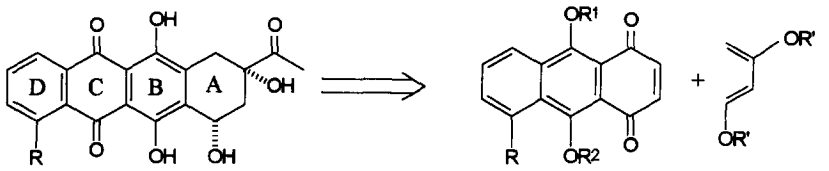
INTRODUCTION

The clinical importance of anthracycline antitumor antibiotics such as daunomycin (**1**) and adriamycin (**2**) in the treatment of a variety of human cancers has stimulated intense activity in the development of total synthesis of these antineoplastic agents.[2] However, these compounds display various side effects, the most serious being a cumulative dose-dependent cardiotoxicity, so that considerable efforts have been devoted to develop new structurally modified anthracyclines with an improved antineoplastic activity and a low cardiotoxicity. It is also well known that the synthetic 4-demethoxy derivatives of daunomycin and adriamycin (**3, 4**) are less toxic than the parent compounds while retaining the antitumor efficacy.[3]



1: R^1=OMe , R^2=H
2: R^1=OMe , R^2=OH
3: R^1=H , R^2= H
4: R^1=H , R^2=OH

In retrosynthetic analyses, numerous disconnections to the corresponding aglycones, the anthracyclinones, have been proposed. One of the most simple strategies is based on the formation of the A-ring by a Diels-Alder reaction with an appropriately substituted 1,4-anthraquinone as a BCD-ring synthon.

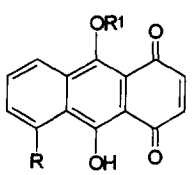


R=OMe
R=H

Some years ago,[4] as part of our studies on the synthesis of anthracyclinones, we have shown the utility of the Diels-Alder reaction with 1,4-anthraquinones in the synthesis of the tetracyclic systems. Recently[1,5] we have reported the first total synthesis of 5-iminodaunomycinone and its 4-demethoxy derivative. In our strategy, the key step is a regiocontrolled Diels-Alder reaction of an appropriately 1,3-disubstituted buta-1,3-diene with fixed derivatives of the 1,4-anthraquinonoid tautomer of 1,4-dihydroxy-9,10-anthraquinone imines, as suitable BCD-ring synthons.

It was therefore of interest to study the synthesis of partially blocked 1,4-anthraquinones as **5**, in which the presence of a sole strong hydrogen bond suggests a high regioselectivity in Diels-Alder reaction with polarized dienes.

Alternatively, we could use derivatives of type **6** as BCD synthons. We expected that the introduction of a halogen or a sulphur bearing group at 2-position, could be used to control the regiochemistry of the cycloaddition in accord with previous results reported for 1,4-naphthoquinones.[6,7]



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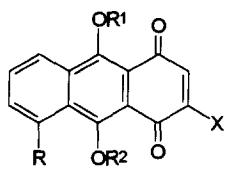

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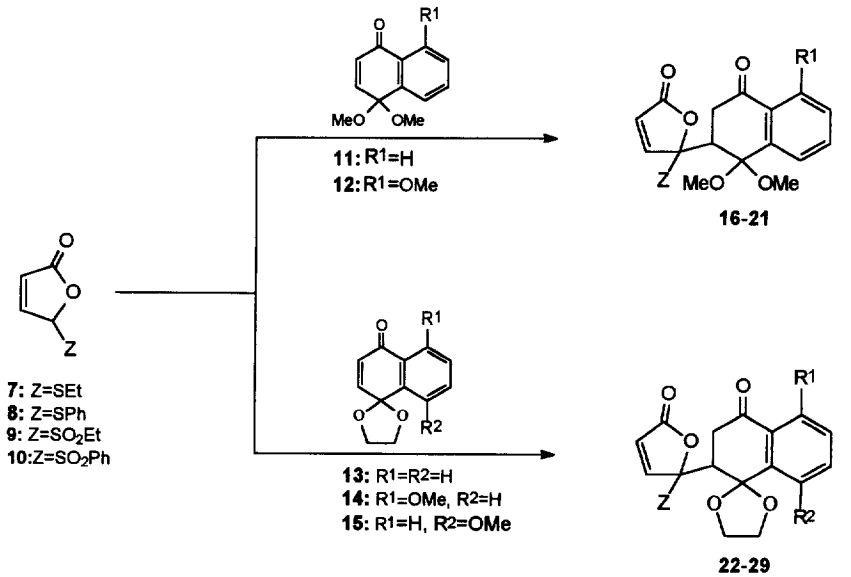
On the other hand, Michael addition followed by base-induced cyclization constitutes a versatile method for the construction of carbocyclic rings. This methodology has been employed for the preparation of 9,10-anthraquinones,[8] from sulphonylphthalides and benzoquinone monoketals. However, this route, has not been previously used for the preparation of 1,4-anthraquinones. In previous studies,[9] it has been shown that 5-

ethylthio- and 5-fluoroalkylfuran-2(5*H*)-ones were readily deprotonated to the corresponding anions, which reacts with Michael acceptors such as methyl acrylate or cyclohexenone in regiospecific manner. These results prompted us to investigate the annelation reactions of this type of furanone anions with quinone monoketals. It is interesting to note that in order to achieve direct routes to 1,4-anthraquinones of type **5**, it is necessary to have an adequate leaving group such as thioether or sulphone, at the 5-position of the furanone.

In the present paper, we study the behaviour of the anions generated from furan-2(5*H*)-ones substituted at the 5-position by sulphur bearing groups such as SEt, SPh, SO_2Et and SO_2Ph, toward several naphthoquinone monoketals. We have developed[10] and now report herein in full detail a novel route to differently substituted 1,4-anthraquinones, by annelation reactions of anions of 4-halo-5-sulphur-furan-2(5*H*)-ones with naphthoquinone monoketals, their Diels-Alder reactions with an appropriate 1,3-disubstituted buta-1,3-diene and also investigations about the subsequent conversion of cycloadducts into compounds related to anthracyclinones.

RESULTS AND DISCUSSION

We initially explored the reactions between anions generated from 5-ethylthio and 5-phenylthio-furan-2(5*H*)-ones (**7**,[11] **8**[12]) and the corresponding sulphones **9**[13] and **10**[12] with naphthoquinone monoketals[14] of type **11-12** and **13-15** (Scheme 1).



Scheme 1

The anions were generated with lithium diisopropylamide (LDA) at -78°C in tetrahydrofuran and the reaction was effected under conditions indicated in table 1. The reaction occurs regiospecifically at the 5 position of the furanone, in accord with our previous results with different types of Michael acceptors,[9a,15,16] to afford the corresponding adducts in good to excellent yield.

Table 1. Reactions of anions generated from furanones **7-10** with naphthoquinone monoketals **11-15**

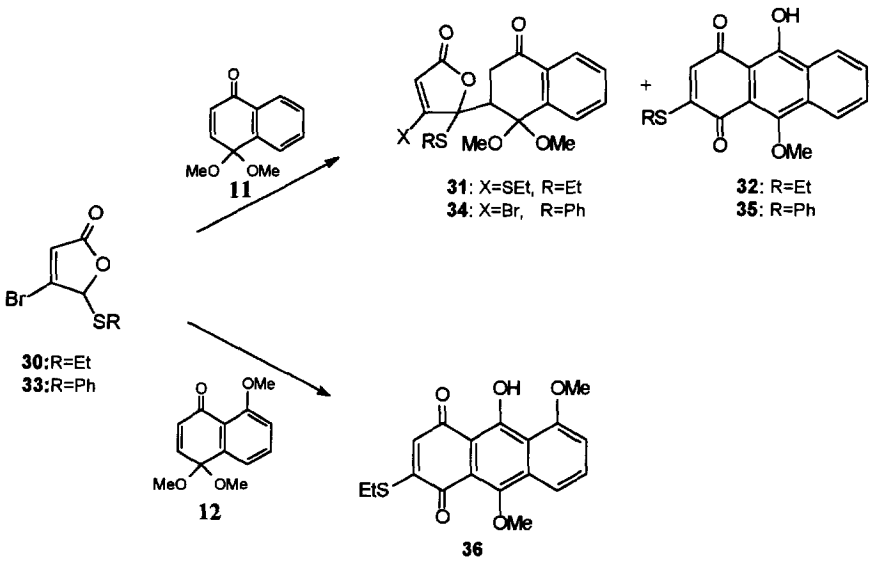
Furanone	Monoketal	Temp (°C)	Time (h)	Adduct	Yield (%)
7	**11**	-78	8	**16**	78
8	**11**	-22	60	**17a,b**	72
8	**12**	-7	32	**18a,b**	70
9	**11**	-22	27	**19**	79
10	**11**	25	48	**20**	68
10	**12**	-7	120	**21**	68
7	**13**	-78	1	**22**	90
8	**13**	-78	0.25	**23**	95
8	**14**	-78	7	**24**	90
8	**15**	-25	18	**25**	80
9	**13**	-22	7	**26**	90
10	**13**	25	24	**27**	83
10	**14**	-7	96	**28**	85
10	**15**	-7	96	**29**	70

The reaction proceeds in all cases without subsequent ring closure to the anthraquinones. The addition of methyl monoketals **11** and **12** takes place at slower rate than those of ethylene glycol monoketals **13-15**. The sulphones **9** and **10** react slower than those of the corresponding thioethers **7** and **8**. The reaction between furanone **8** and monoketals **11** and **12** afforded mixtures of diastereoisomeric Michael adducts. The ratio of diastereoisomers **17a,b** (40:60) and **18a,b** (66:44), has been determined by integration of the H-3 proton signal in ^{1}H-NMR spectra.

The structures of Michael adducts **16-29** were confirmed by their elemental analyses and spectral data. Thus, their ^{1}H-NMR spectra show the typical singlets of the two OMe (at δ ca. 2.70 and 3.90 ppm) or a

multiplet for the OCH_2-CH_2O group (δ ca. 4.00 ppm). Moreover, in furanones **16-29** lacked resonances corresponding to the H-5 acetal type protons, but contained signals assignable to the H-3 and H-4 olefinic protons. On the other hand, the ^{13}C-NMR spectra of **16-29**, show a quaternary carbon at δ 94.4-102.6 ppm. attributable to the C-5. Also the presence of two signals at δ ca. 170 and 190 ppm assignable to lactonic and ketonic group respectively, confirms the structure of adducts.

We then investigated the annelation reaction with the 4-bromo-5-ethylthiofuran-2(5*H*)-one (**30**) [13] and 4-bromo-5-phenylthiofuran-2(5*H*)-one (**33**) [17], in which the presence of a halogen atom in the 4-position of furanone could favour the formation of the anthraquinone.



Scheme 2

The reaction of the anion generated from furanone **30** with monoketal **11** after 7 days, at -7°C, afforded as main product the 1,4-anthraquinone **32** and a 45:55 mixture of diastereomeric Michael adducts **31a,b**. Similarly, the anion of furanone **33** reacted with monoketal **11** to afford, after 13 days, the 1,4-anthraquinone **35** and a 60:40 mixture of diastereoisomeric Michael adducts **34a,b** (Scheme 2, Table 2). However, the annelation reaction between the anion generated from furanone **30** with monoketal **12** lead exclusively to the 1,4-anthraquinone **36** in 40% yield. It is noteworthy, that the substitution of the bromine atom by the ethylthio group in adduct **31** and quinones **32** and **36,** takes place simultaneously to the annelation reaction, but only was observed substitution of the halogen by the phenylthio group in the quinone **35**.

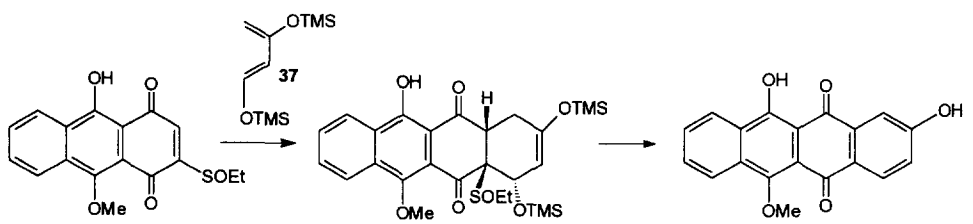
Table 2. Reactions of anions generated from furanones **30, 33** with naphthoquinone monoketals **11** and **12**

Furanone	Monoketal	Temperature (°C)	Time (days)	Anthraquinone Yield (%)	Michael Adduct Yield (%)
30	**11**	-7	7	**32** (45)	**31** (12)
30	**12**	-7	7	**36** (40)	---
33	**11**	-5	13	**35** (49)	**34** (10)

The formation of the anthraquinones was evidenced by their elemental analyses and spectral data. Thus, their ^{1}H-NMR spectra indicated the presence of a strongly chelated OH group (sharp singlet at δ ca. 15 ppm) and show the H-3 protons at δ 6.1-6.7 ppm, in accord with the chemical shift values expected for quinonoid protons. Moreover, the ^{13}C-NMR spectra show two signals at δ ca.186 and 180 ppm attributable to the quinonoid carbonyl groups.

Our first attempts of Diels-Alder reaction of the 1,4-anthraquinones **32** and **35** with an appropriate 1,3-disubstituted diene such as (*E*)-1,3-bis[(trimethylsilyl)oxy]buta-1,3-diene (**37**), in benzene under reflux, over a period of 15 days, failed to give the expected adducts.

In view of the above results, we explored further the Diels-Alder reaction with the 1,4-anthraquinone **38**, in which the presence of the ethylsulphinyl group should increase the dienophilic reactivity of the double bond. The sulphoxide **38** was prepared by oxidation of the thioether **32** with an equimolecular amount of *m*-chloroperbenzoic acid at 5°C in dichloromethane. The reaction of anthraquinone **38** with diene **37** in benzene at 3°C after 5h afforded adduct **39**, as main product (Scheme 3). This adduct was identified by ^{1}H-NMR in the crude reaction mixture as a single regioisomer, but all attempts to isolate them were unsuccessful, affording fully aromatized naphthacenedione **40**, in agreement with literature precedent.[18]



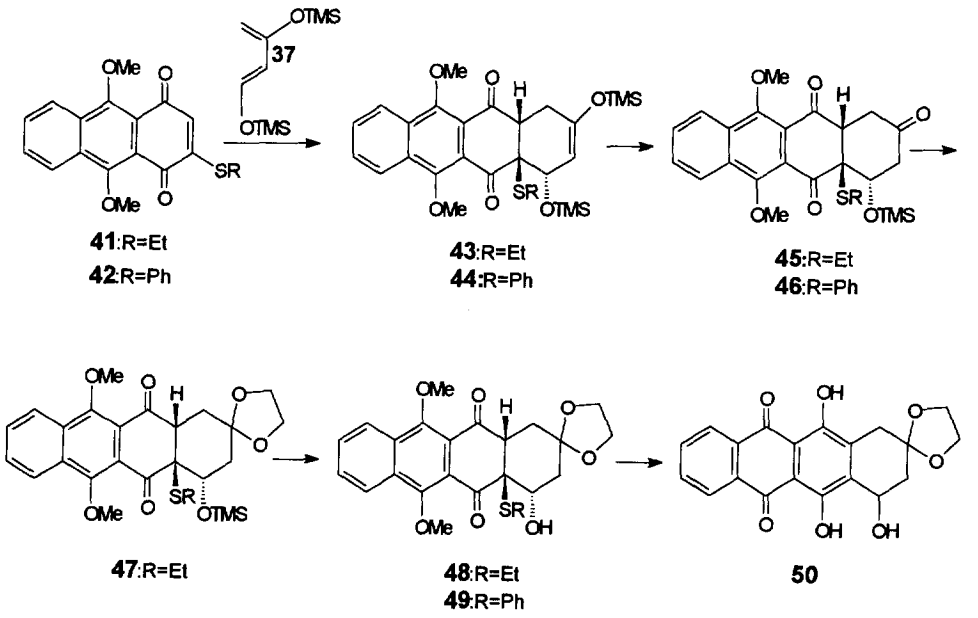
38 **39** **40**

Scheme 3

Since attempted cycloadditions to hydroxy-1,4-anthraquinones of type **5** were unsuccessful, we turned our attention to the Diels-Alder reaction with dienophiles of type **6**.

The Diels-Alder reaction of the anthraquinones **41** and **42**, prepared by methylation of 1,4-anthraquinones **32** and **35** with methyl iodide, in the presence of silver oxide, were carried out with an excess of the diene **37** in benzene affording regio- and stereospecifically a single adduct in excellent yields. Adducts **43** and **44** could not be isolated in pure state because of hydrolysis of the OTMS group in 9-position. The high-field ^{1}H-NMR spectra of the crude reaction mixtures obtained from 1,4-anthraquinones **41** and **42** and the diene **37** indicated the formation, in each case, of a single regioisomer, adduct **43** and **44** respectively.

The structures of the tetracyclic compounds **39**, **43** and **44** were confirmed on the basis of their ^{1}H-NMR spectra, in which the presence of only two sharp singlets (δ -0.24, -0.17, -0.22 and 0.29, 0.32, 0.19 ppm), attributable to the OTMS groups at the 7- and 9- position, respectively, indicates the absence of regioisomers. The regiochemistry was conclusively established taking into consideration that the methine proton on the carbon bearing the OTMS (C-7) appears as a doublet (δ 5.60, 5.67 and 4.55 ppm), coupled with the olefinic proton (δ 5.5, 5.5 and 4.98 ppm).



Scheme 4

These results suggest that the regiochemical course of the cycloaddition is controlled by the sulphenyl or sulphinyl group.

Because adducts **43** and **44** could not be isolated, their crude reaction mixtures were subjected to a mild selective hydrolysis with 3N hydrochloric acid in tetrahydrofuran at 0°C for 5 min to give excellent yields of tetracyclic ketones **45** and **46** by selective hydrolysis of the silyl enol ether.

The C-9 carbonyl group was appropriately protected as ethylene dioxyderivative, prior to the oxidative demethylation step, in order to avoid the aromatization of the A-ring. Reaction of ketone **45** with ethylene glycol in presence of *p*-toluenesulphonic acid (benzene, 80°C, 12 h) afforded dioxolane **47** in 97% yield. The trimethylsilyl group of ketal **47** was then removed using tartaric acid in tetrahydrofuran at room temperature to give **48** in 95% yield. Under similar conditions the ketone **46** underwent acetalization and simultaneous removal of TMS group to give dioxolane **49** in 63% yield.

Oxidative demethylation of **48** and **49** with silver(II) oxide and nitric acid, following a method previously reported by us[19] afforded quinone **50** in 80% yield. It is to note the elimination of RSH under the conditions employed for the oxidative demethylation. The physical and spectral data of the tetracyclic compound **50** were identical with those previously described.[20]

In summary, we have develop a novel procedure for the synthesis of 1,4-anthraquinones, starting from 4-bromo-5-ethylthio- or 5-phenylthio-2(5*H*)-furanones with dimethyl naphthoquinone monoketals. The synthetic methodology described herein, that uses the anthraquinones **41** and **42** as suitable BCD ring synthon, may also be relevant for the construction of novel unnatural anthracyclinones.

EXPERIMENTAL

Melting points were determined with a Kofler hot-stage apparatus and are uncorrected. Microanalyses were performed with a Heraeus analyzer model CHN-O-rapid. IR spectra were recorded on a Perkin-Elmer model 681 grating spectrophotometer as nujol mulls, ν values in cm^{-1}. ^{1}H-NMR spectra were determined with either a Varian Gemini 200, a Bruker AM-200 or a Varian XL-300 spectrometer, in $CDCl_3$ solution, unless otherwise stated. ^{13}C-NMR were determined with either a Varian XL-300 or a Bruker AM-200 in $CDCl_3$ solution, unless otherwise stated. Chemical shifts were reported in ppm (δ) downfield from Me_4Si. Mass spectra were determined on a VG-12-250 spectrometer. Silica gel Merck 60 (70- 230 mesh) and DC-alufolien $60F_{254}$ were used for column chromatography and analytical tlc, respectively.

Furanones **7**,[11] **8**,[12] **9**,[13] **10**,[12] **30**,[13] **33**[17] and monoketals[14] were prepared according to the methods previously reported by us.

Generation of furanone anions and reaction with naphthoquinone monoketals. General procedure.

A solution of lithium diisopropylamide was prepared by addition at -78°C, under argon, of a solution of *n*-butyllithium in *n*-hexane (1.15 mmol) to a solution of diisopropylamine (1.15 mmol) in dry tetrahydrofuran (4 ml). A solution of furanone (1.0 mmol) in dry tetrahydrofuran (3 ml) was added and the mixture was stirred for 15 min at -78°C. A solution of the naphthoquinone monoketal (1.0 mmol) in tetrahydrofuran was then added, and the reaction mixture was kept under the conditions indicated in each case (Table 1). The solution was poured into saturated aqueous ammonium chloride and extracted with ethyl acetate. The combined extracts were dried ($MgSO_4$) filtered and concentrated under reduced pressure. The crude products were purified by column chromatography on silica gel or crystallization.

5-Ethylthio-5-(1',1'-dimethoxy-4'-oxo-1',2',3',4'-tetrahydronaphth-2'-yl)furan-2(5*H*)-one (16)

Purified by column chromatography (petroleum ether-ethyl acetate, 5:1). (78%). M.p. 140-143°C (from cyclohexane). Anal. Calcd. for $C_{18}H_{20}O_5S$: C, 62.05; H, 5.78; S, 9.20. Found: C, 62.27; H, 6.00; S, 9.04. IR: 1780, 1680, 1600, 1250, 1060. ^{1}H-NMR: 8.00-7.97 (m, 1H, H-5'), 7.51-7.45 (m, 3H, H-6', H-7', H-8'), 7.28 (d, 1H, $J_{3,4}$=5.5 Hz, H-4), 5.59 (d, 1H, H-3), 3.44 (s, 3H, OCH_3), 3.36-3.16 (m, 2H, H-3'), 2.99 (m, 1H, H-2'), 2.79 (s, 3H, OCH_3), 2.13 (q, 2H, J=7.5 Hz, SCH_2), 1.12 (t, 3H, CH_3). ^{13}C-NMR: 195.4, 175.0, 157.0, 136.9, 133.2, 132.1, 129.5, 127.1, 126.1, 116.8, 103.0, 94.4, 48.9, 48.1, 46.6, 38.1, 21.8, 13.9. MS (*m/z*): 348 (M^+, 0.2), 287, 255, 163 (100).

5-Phenylthio-5-(1',1'-dimethoxy-4'-oxo-1',2',3',4'-tetrahydronaphth-2'-yl)furan-2(5*H*)-one (17a,b)

Purified by column chromatography (petroleum ether-ethyl acetate, 6:1). (72%), (ratio **17a**:**17b** 2:3). Anal. Calcd. for $C_{22}H_{20}O_5S$: C, 66.65; H, 5.08; S, 8.09. Found: C, 66.60; H, 4.79; S, 7.85. IR(KBr): 1780, 1695, 1600, 1290, 1250, 1080, 1070. ^{1}H-NMR **17a**: 8.03-7.98 (m, 1H, H-5'), 7.70-7.22 (m, 8H, 5H arom., H-6', H-7', H-8'), 6.65 (d, 1H, $J_{3,4}$=5.5 Hz, H-4), 5.28 (d, 1H, H-3), 3.58-2.90 (m, 3H, H-2', H-3'), 3.38 (s, 3H, OCH_3), 2.82 (s, 3H, OCH_3). ^{1}H-NMR **17b**: 7.89 (m, 1H, H-5'), 7.43-7.14 (m, 8H, 5H arom., H-6', H-7', H-8'), 7.14 (d, 1H, $J_{3,4}$=5.5 Hz, H-4), 5.04 (d, 1H, H-3), 3.39-3.18 (m, 3H, H-2', H-3'), 3.39 (s, 3H, OCH_3), 2.73 (s, 3H, OCH_3). ^{13}C-NMR **17a**: 195.5, 170.1, 154.3, 139.9, 137.7, 133.3, 132.2, 130.2, 129.5, 128.9, 127.2, 127.0, 126.7, 119.1, 98.1, 97.2, 49.2, 48.6, 46.2, 38.4. MS (*m/z*): 287 (M^+-SPh, 91), 255, 218, 163 (100), 113, 109, 77.

5-Phenylthio-5-(1',1',5'-trimethoxy-4'-oxo-1',2',3',4'-tetrahydronaphth-2'-yl)furan-2(5*H*)-one (18a,b)

Purified by column chromatography (petroleum ether-ethyl acetate, 3:1). (70%), (ratio **18a**:**18b** 2:1). IR (neat): 1780, 1690, 1595, 1270, 1230, 1060. ^{1}H-NMR: 7.47-7.21 (m, 6H, 5H arom., H-7', **18a**, **18b**), 7.14 (d, 0.66H, $J_{3,4}$=5.5 Hz, H-4, **18a**), 7.04-6.95 (m, 2H, H-6', H-8', **18a**, **18b**), 6.75 (d, 0.34H, $J_{3,4}$=5.6 Hz, H-4, **18b**), 5.31 (d,

0.34H, H-3, **18b**), 5.16 (d, 0.66H, H-3, **18a**), 3.93 (s, 1.02H, OCH_3, **18b**), 3.90 (s, 1.98H, OCH_3, **18a**), 3.44 (s, 1.98H, OCH_3, **18a**), 3.35 (s, 1.02H, OCH_3, **18b**), 3.39-3.14 (m, 3H, H-2', 2H-3', **18a**, **18b**), 2.80 (s, 1.98H, OCH_3, **18a**), 2.78 (s, 1.02H, OCH_3, **18b**). ^{13}C-NMR: 194.1, 171.0, 169.0, 158.3, 156.0, 139.2, 137.8, 132.6, 130.2, 129.0, 126.6, 122.2, 117.8, 117.0, 113.5, 97.9, 95.2, 60.0, 56.2, 48.8, 48.1, 43.9, 38.7. MS (*m/z*): 317 (M^+-SPh, 52), 287, 193 (100), 163, 113, 77.

5-Ethylsulfonyl-5-(1',1'-dimethoxy-4'-oxo-1',2',3',4'-tetrahydronaphth-2'-yl)furan-2(5*H*)-one (19)

Purified by column chromatography (*n*-hexane-ethyl acetate, 3:1). (79%). M.p. 151-153°C (from cyclohexane). IR: 1800, 1685, 1600, 1320, 1160, 1130, 1050. ^{1}H-NMR: 7.95 (dd, 1H, $J_{5',6'}$=6.4 Hz, $J_{5',7'}$=2.4 Hz, H-5'), 7.66 (d, 1H, $J_{3,4}$=5.7 Hz, H-4), 7.55-7.43 (m, 3H, H-6', H-7', H-8'), 5.78 (d, 1H, H-3), 3.99 (m, 1H, H-2'), 3.56 (s, 3H, OCH_3), 3.33-3.13 (m, 2H, H-3'), 3.00-2.68 (m, 2H, SCH_2), 2.85 (s, 3H, OCH_3), 1.35 (t, 3H, J=7.5 Hz, CH_3). ^{13}C-NMR: 194.8, 167.8, 153.7, 136.7, 132.4, 132.1, 129.7, 127.1, 126.7, 121.4, 100.8, 97.7, 49.0, 47.9, 40.8, 40.6, 37.9, 5.4. MS (*m/z*): 287 (M^+-SO_2Et, 45), 255, 163 (100), 113, 77.

5-Phenylsulfonyl-5-(1',1'-dimethoxy-4'-oxo-1',2',3',4'-tetrahydronaphth-2'-yl)furan-2(5*H*)-one (20)

Purified by column chromatography (*n*-hexane-ethyl acetate, 4:1). (68%). M.p. 170-172°C (from ethanol). Anal. Calcd. for $C_{22}H_{20}O_7S$: C, 61.67; H, 4.70; S, 7.48. Found: C, 61.57; H, 4.75; S, 7.47. IR: 1805, 1695, 1600, 1595, 1325, 1160, 1075, 1040. ^{1}H-NMR: 7.91-7.39 (m, 9H, 5H arom., H-5', H-6', H-7', H-8'), 7.56 (d, 1H, $J_{3,4}$=5.8 Hz, H-4), 5.40 (d, 1H, H-3), 4.08 (m, 1H, H-2'), 3.62 (s, 3H, OCH_3), 3.20 (dd, 1H, J_{gem}=18.9 Hz, $J_{2',3'}$=5.8 Hz, H-3'), 3.06 (dd, 1H, $J_{2',3'}$=2.0 Hz, H'-3'), 2.83 (s, 3H, OCH_3). ^{13}C-NMR: 194.9, 167.5, 152.3, 136.8, 135.3, 132.5, 132.0, 131.5, 130.9, 129.7, 129.0, 127.1, 126.5, 122.2, 100.9, 98.0, 49.1, 48.1, 40.9, 37.7. MS (*m/z*): 287 (M^+-SO_2Ph, 1), 250, 218 (100), 141, 109, 77.

5-Phenylsulfonyl-5-(1',1',5'-trimethoxy-4'-oxo-1',2',3',4'-tetrahydronaphth-2'-yl)furan-2(5*H*)-one (21)

Purified by column chromatography (petroleum ether-ethyl acetate, 2:1). (68%). M.p. 157-158°C. IR: 1810, 1680, 1595, 1330, 1160, 1060. ^{1}H-NMR: 7.81-7.70 (m, 2H, arom.), 7.68-7.65 (m, 1H, arom.), 7.54-7.49 (m, 2H, arom.), 7.51 (d, 1H, $J_{3,4}$=5.7 Hz, H-4), 7.31 (t, 1H, J=7.7 Hz, J=8.4 Hz, H-7'), 7.03 (dd, 1H, J=0.9 Hz, J=7.7 Hz, H-6' or H-8'), 6.93 (d, 1H, J=8.4 Hz, H-8' or H-6'), 5.5 (d, 1H, H-3), 3.98 (dd, 1H, H-2'), 3.85 (s, 3H, OCH_3), 3.60 (s, 3H, OCH_3), 2.97 (dd, 1H, J_{gem}=19.0 Hz, $J_{2',3'}$=6.6 Hz, H-3'), 2.85 (dd, 1H, $J_{2',3'}$=1.5 Hz, H'-3'), 2.84 (s, 3H, OCH_3). ^{13}C-NMR: 194.0, 167.7, 158.5, 151.6, 138.7, 135.2, 132.3, 131.8, 130.8, 129.0, 122.6, 122.0, 118.5, 113.7, 100.9, 98.0, 56.3, 49.0, 48.0, 39.2, 38.1. MS (*m/z*): 458 (M^+, 1), 317, 285, 193 (100), 113, 77.

5-Ethylthio-5-(1',1'-ethylendioxy-4'-oxo-1',2',3',4'-tetrahydronaphth-2'-yl)furan-2(5*H*)-one (22)

Purified by column chromatography (petroleum ether-ethyl acetate, 5:2). (90%). M.p. 163-166°C (from cyclohexane). IR: 1780, 1760, 1690, 1600, 1290, 1250, 1070. ^{1}H-NMR: 8.01 (dd, 1H, $J_{5',6'}$=7.6 Hz, $J_{5',7'}$=1.5 Hz, H-5'), 7.55-7.43 (m, 2H, H-6', H-7'), 7.48 (d, 1H, $J_{3,4}$=5.5 Hz, H-4), 7.34 (dd, 1H, $J_{7',8'}$=7.9 Hz, $J_{6',8'}$=1.6 Hz, H-8'), 5.77 (d, 1H, H-3), 4.15-3.98 (m, 4H, OCH_2), 3.40 (dd, 1H, J_{gem}=18.3 Hz, $J_{2',3'}$=8.1 Hz, H-3'), 3.32 (dd, 1H, $J_{2',3'}$=5.7 Hz, H'-3'), 2.96 (m, 1H, H-2'), 2.20 (q, 2H, J=7.5 Hz, SCH_2), 1.15 (t, 3H, CH_3). ^{13}C-NMR: 194.8, 170.1, 157.7, 140.1, 133.2, 132.6, 129.6, 127.0, 124.0, 116.0, 106.3, 94.6, 65.6, 64.5, 50.2, 39.4, 21.9, 14.0. MS (*m/z*): 346 (M^+, 0.3), 285 (100), 202, 148.

5-Phenylthio-5-(1',1'-ethylendioxy-4'-oxo-1',2',3',4'-tetrahydronaphth-2'-yl)furan-2(5*H*)-one (23)

(95%). M.p. 190-193°C (from cyclohexane). Anal. Calcd. for $C_{22}H_{18}O_5S$: C, 66.99; H, 4.60; S, 8.13. Found: C, 67.08; H, 4.79; S, 8.30. IR: 1775, 1690, 1605, 1295, 1250, 1075. ^{1}H-NMR: 8.04-8.01 (m, 1H, H-5'), 7.55-7.23 (m, 8H, 5H arom., H-6', H-7', H-8'), 7.39 (d, 1H, $J_{3,4}$=5.4 Hz, H-4), 5.32 (d, 1H, H-3), 4.20-3.99 (m, 4H, OCH_2), 3.53 (dd, 1H, J_{gem}=18.3 Hz, $J_{2',3'}$=6.0 Hz, H-3'), 3.42 (dd, $J_{2',3'}$=5.6 Hz, H'-3'), 3.13 (m, 1H, H-2'). ^{13}C-NMR: 194.5, 169.5, 157.0, 140.3, 137.9, 133.2, 132.6, 130.2, 129.5, 128.8, 128.0, 127.0, 124.0, 116.1 106.4, 95.5, 65.5, 64.5, 49.6, 38.4. MS (*m/z*): 394 (M^+, 1), 285 (100), 148, 109.

5-Phenylthio-5-(1',1'-ethylendioxy-5'-methoxy-4'-oxo-1',2',3',4'-tetrahydronaphth-2'-yl)furan-2(5*H*)-one (24)

(90%). M.p. 188°C (from cyclohexane). Anal. Calcd. for $C_{23}H_{20}O_6S$: C, 65.09; H, 4.75; S, 7.52. Found: C, 65.35; H, 5.00; S, 7.38. IR: 1770, 1680, 1590, 1270, 1235, 1050. ^{1}H-NMR: 7.41 (dt, 1H, $J_{6',7'}$=$J_{7',8'}$=7.6 Hz, H-7'), 7.37 (d, 1H, $J_{3,4}$=5.5 Hz, H-4), 7.37-7.23 (m, 5H, arom.), 6.99 (dd, 1H, J=7.6 Hz, J=1.0 Hz, H-6' or H-8'), 6.93 (dd, 1H, J=7.6 Hz, J=1.0 Hz, H-8' or H-6'), 5.35 (d, 1H, H-3), 4.10-3.94 (m, 4H, OCH_2), 3.91 (s, 3H, OCH_3), 3.41 (dd, 1H, J_{gem}=18.5 Hz, $J_{2',3'}$=6.0 Hz, H-3'), 3.28 (dd, 1H, $J_{2',3'}$=6.6 Hz, H'-3'), 3.07 (t, 1H, H-2'). ^{13}C-NMR: 194.6, 171.4, 160.4, 157.8, 139.1, 135.1, 134.8, 131.3, 129.9, 127.4, 125.1, 117.3, 116.7, 114.4, 107.5, 96.6, 66.4, 65.7, 57.2, 49.2, 40.1. MS (*m/z*): 424 (M^+, 1), 315 (100), 285, 218, 149, 109, 83.

5-Phenylthio-5-(1',1'-ethylendioxy-8'-methoxy-4'-oxo-1',2',3',4'-tetrahydronaphth-2'-yl)furan-2(5*H*)-one (25)

Purified by column chromatography (petroleum ether-ethyl acetate, 3:1). (80%). M.p. 169-170°C (from cyclohexane) Anal. Calcd. for $C_{23}H_{20}O_6S$: C, 65.08; H, 4.75; S, 7.55. Found: C, 65.25; H, 4.36; S, 7.21. IR: 1780, 1685, 1600, 1280, 1160. ^{1}H-NMR: 7.59 (dd, 1H, $J_{5',6'}$=7.7 Hz, $J_{5',7'}$=1.2 Hz, H-5'); 7.36 (d, 1H, $J_{3,4}$=5.5 Hz, H-4), 7.34-7.16 (m, 6H, 5H arom., H-6'), 7.04 (dd, 1H, $J_{7',6'}$=8,3 Hz, H-7'), 5.22 (d, 1H, H-3), 4.15-4.06 (m,

3H, OCH_2), 3.92-3.90 (m, 1H, OCH_2), 3.76 (s, 3H, OCH_3), 3.39 (dd, 1H, J_{gem}=17.6 Hz, $J_{2',3'}$=5.6 Hz, H-3'), 3.29 (dd, 1H, $J_{2',3'}$=5.3 Hz, H'-3'), 2.99 (t, 1H, H-2'). ^{13}C-NMR: 194.8, 169.7, 157.3, 156.7, 138.0, 134.7, 130.3, 130.1, 128.7, 127.8, 126.8, 119.4, 117.9, 115.8, 107.1, 95.7, 66.3, 65.5, 56.6, 51.4, 38.4. MS (*m/z*): 315 (M^+-SPh, 100), 178, 109.

5-Ethylsulfonyl-5-(1',1'-ethylendioxy-4'-oxo-1',2',3',4'-tetrahydronaphth-2'-yl)furan-2(5*H*)-one (26)

Purified by column chromatography (*n*-hexane-ethyl acetate, 2:1). (90%). IR (neat): 1800, 1690, 1605, 1315, 1150, 1070. ^{1}H-NMR: 7.99 (dd, 1H, $J_{5',6'}$=7.5 Hz, $J_{5',7'}$=1.5 Hz, H-5'), 7.87 (d, 1H, $J_{3,4}$=5.7 Hz, H-4), 7.68-7.44 (m, 2H, H-6', H-7'), 7.38 (dd, 1H, $J_{8',7'}$=7.3 Hz, $J_{8',6'}$=1.7 Hz, H-8'), 5.86 (d, 1H, H-3), 4.32-4.27 (m, 2H, OCH_2), 4.14-3.98 (m, 2H, OCH_2), 3.68 (m, 1H, H-2'), 3.45 (dd, 1H, J_{gem}=18.4 Hz, $J_{2',3'}$=3.1 Hz, H-3'), 3.41 (dd, 1H, $J_{2',3'}$=5.6 Hz, H'-3'), 3.00-2.70 (m, 2H, SCH_2), 1.35 (t, 3H, J=7.5 Hz, CH_3). ^{13}C-NMR: 194.0, 168.2, 154.0, 138.9, 133.3, 132.4, 129.9, 127.0, 124.3, 121.0, 105.6, 101.1, 66.4, 64.4, 44.0, 41.3, 38.2, 5.4. MS (*m/z*): 286 (M^++1-SO_2Et, 20), 285 (M^+-SO_2Et, 100), 203, 148.

5-Phenylsulfonyl-5-(1',1'-ethylendioxy-4'-oxo-1',2',3',4'-tetrahydronaphth-2'-yl)furan-2(5*H*)-one (27)

Purified by column chromatography (petroleum ether-ethyl acetate, 2:1). (83%). M.p. 188-189°C. Anal. Calcd. for $C_{22}H_{18}O_7S$: C, 61.96; H, 4.25; S, 7.52. Found: C, 62.00; H, 4.16; S, 7.45. IR: 1810, 1695, 1600, 1325, 1160, 1070. ^{1}H-NMR: 7.87 (dd, 1H, $J_{5',6'}$=7.2 Hz, $J_{5',7'}$=1.9 Hz, H-5'), 7.72 (d, 1H, $J_{3,4}$=5.7 Hz, H-4), 7.73-7.70 (m, 2H, arom.), 7.60-7.56 (m, 1H, H-6' or H-7'), 7.45-7.26 (m, 5H, 3H arom., H-8', H-7' or H-6'), 5.39 (d, 1H, H-3), 4.27-4.22 (m, 2H, OCH_2), 4.07-3.90 (m, 2H, OCH_2), 3.73 (t, 1H, $J_{2',3}$=4.4 Hz, H-2'), 3.28 (d, 2H, H-3'). ^{13}C-NMR: 195.1, 168.8, 154.4, 139.8, 136.3, 134.2, 133.6, 132.6, 132.0, 131.0, 130.0, 128.1, 125.2, 122.7, 107.1, 102.1, 67.5, 65.5, 45.1, 39.1. MS (*m/z*): 285 (M^+-SO_2Ph, 100), 148, 77.

5-Phenylsulfonyl-5-(1',1'-ethylendioxy-5'-methoxy-4'-oxo-1',2',3',4'-tetrahydronaphth-2'-yl)furan-2(5*H*)-one (28)

Purified by column chromatography (petroleum ether-ethyl acetate, 1:1). (85%). M.p. 216-218°C. IR: 1790, 1780, 1685, 1595, 1330, 1160, 1055. ^{1}H-NMR: 7.80-7.64 (m, 3H, arom.), 7.74 (d, 1H, $J_{3,4}$=5.7 Hz, H-4), 7.52-7.47 (m, 2H, arom), 7.36 (dd, 1H, J=7.7 Hz, J=8.6 Hz, H-7'), 6.96 (dd, 1H, J=1.0 Hz, H-6' or H-8'), 6.90 (dd, 1H, H-8' or H-6'), 5.54 (d, 1H, H-3), 4.26-3.92 (m, 4H, OCH_2), 3.86 (s, 3H, OCH_3), 3.69 (t, 1H, $J_{2',3'}$=4.9 Hz, H-2'), 3.20 (d, 2H, H-3'). ^{13}C-NMR: 193.4, 168.4, 159.5, 152.8, 141.3, 135.6, 133.9, 132.2, 131.2, 129.4, 122.3, 116.0, 114.2, 106.2, 101.5, 66.7, 64.8, 56.8, 43.1, 38.8. MS (*m/z*): 456 (M^+, 0.5), 315 (100).

5-Phenylsulfonyl-5-(1',1'-ethylendioxy-8'-methoxy-4'-oxo-1',2',3',4'-tetrahydronaphth-2'-yl)furan-2(5*H*)-one (29)

Purified by column chromatography (petroleum ether-ethyl acetate, 5:1). (70%). IR: 1805, 1705, 1595, 1585, 1330, 1290, 1155. ^{1}H-NMR: 7.87 (d, 1H, $J_{3,4}$=5.7 Hz, H-4), 7.82-7.03 (m, 8H, 5H arom., H-5', H-6', H-7'), 5.47 (d, 1H, H-3), 4.33-4.29 (m, 2H, OCH_2), 4.16-4.11 (m, 2H, OCH_2), 3.84 (s, 3H, OCH_3), 3.69 (dd, 1H, J=3.1 Hz, J=3.3 Hz, H-2'), 3.30 (dd, 1H, J_{gem}=18.0 Hz, H-3'), 3.22 (dd, 1H, H-3'). ^{13}C-NMR: 184.1, 169.2, 157.9, 144.6, 132.5, 130.4, 129.0, 128.8, 127.9, 127.6, 127.1, 126.8, 119.0, 116.8, 104.5, 100.8, 66.7, 56.3, 29.7. MS *(m/z)*: 316 (M^++1-SO_2Ph, 27), 315 (M^+-SO_2Ph, 100), 178, 77.

Generations of 4-halofuranone anions and reaction with monoketals 11 and 12.

Reaction of furanone 30 with monoketal 11

Following the general procedure, the reaction mixture was kept under the conditions indicated in table 2. The crude reaction mixture was chromatographied (dichloromethane-ethyl acetate, 2:1) to afford **2-ethylthio-10-hydroxy-9-methoxy-1,4-anthraquinone (32)** (143 mg, 45%). M.p. 209-210°C. (from benzene-*n*-hexane). Anal. Calcd. for $C_{17}H_{14}O_4S$: C, 64.97; H, 4.46; S, 10.20. Found: C, 64.91; H, 4.51; S, 9.98. IR: 1655, 1610, 1590, 1560, 1255, 1095. ^{1}H-NMR: 14.85 (s, 1H, OH), 8.50-8.48 (m, 1H, H-8), 8.35-8.31 (m, 1H, H-5), 7.78-7.73 (m, 2H, H-7, H-6), 6.63 (s, 1H, H-3), 4.03 (s, 3H, OCH_3), 2.87 (q, 2H, J=7.5 Hz, SCH_2), 1.45 (t, 3H, CH_3). ^{13}C-NMR: 185.6, 179.7, 160.2, 158.7, 154.4, 132.8, 131.2, 130.0, 129.6, 126.5, 125.1, 124.9, 116.3, 107.4, 62.4, 24.9, 12.4. MS (*m/z*): 315 (M^++1, 12), 314 (M^+, 67), 299 (100), 281, 265, and **4,5-di(ethyilthio)-5-(1',1'-dimethoxy-4'-oxo-1',2',3',4'-tetrahydronaphth-2'-yl)furan-2(5*H*)-one (31a,b)** (50 mg, 12%), (ratio **31a**:**31b**, 56:44). Anal. Calcd. for $C_{20}H_{24}O_5S_2$: C, 58.82; H, 5.89; S, 15.68. Found: C, 59.20; H, 6.10; S, 15.89. IR: 1765, 1670 , 1600, 1245, 1220, 1080, 1050. ^{1}H-NMR: 8.01 (m, 0.44H, $J_{5',6}$=7.3 Hz, $J_{5',7}$=1.8 Hz, H-5' **31b**), 7.94 (dd, 0.56H, $J_{5',6}$=7.5 Hz, $J_{5',7}$=1.6 Hz, H-5' **31a**), 7.76 (dd, 0.56H, $J_{8',7}$=7.7 Hz, $J_{8',6}$=1.4 Hz, H-8' **31a**), 7.59-7.44 (m, 2.44H, H-6', H-7', **31a,b**, H-8', **31b**), 5.54 (s, 0.56H, H-3, **31a**), 5.52 (s, 0.44H, H-3, **31b**), 3.51 (s, 1.68H, OCH_3, **31a**), 3.45-3.15 (m, 2H, H-3', **31a,b**), 3.38 (s, 1.32H, OCH_3, **31b**), 2.79-2.67 (m, 1H, H-2', **31a,b**), 2.76 (s, 1.68H, OCH_3, **31a**), 2.75 (s, 1.32H, OCH_3, **31b**), 2.95, 2.65, 2.47, 2.44 (q, 2H, SCH_2, **31a,b**), 2.29-2.07 (m, 2H, SCH_2, **31a,b**), 1.47, 1.26, 1.13, 1.06 (t, 6H, J=7.5 Hz, CH_3, **31a,b**). ^{13}C-NMR: 195.3, 194.9, 173.3, 171.6, 167.9, 167.3, 138.8, 138.5, 133.2, 133.1, 132.2, 132.1, 128.8, 126.7, 126.4, 125.6, 111.4, 110.2, 98.6, 98.5, 96.5, 50.5, 49.3, 48.9, 48.7, 46.3, 45.5, 39.0, 37.1, 27.4, 27.2, 22.1, 21.7, 12.8, 12.6. MS (*m/z*): 347 (M^+-SEt, 18), 315, 203, 173, 163 (100).

Reaction of furanone 30 with monoketal 12

Following the general procedure, the reaction mixture was kept under the conditions indicated in table 2. The crude product was crystallized from benzene-*n*-hexane.

2-Ethylthio-10-hydroxy-5,9-dimethoxy-1,4-anthraquinone (36)

M.P. 206-208°C . IR: 1655, 1610, 1580, 1555, 1260, 1060. ^{1}H-NMR: 16.04 (s, 1H, OH), 7.94 (d, 1H, $J_{6,7}$=8.3 Hz, H-6), 7.68 (t, 1H, $J_{6,7}$=$J_{7,8}$=8.1 Hz, H-7), 7.14 (d, 1H, H-8), 6.62 (s, 1H, H-3), 4.06 (s, 3H, OCH_3), 3.98 (s, 3H, OCH_3), 2.86 (q, 2H, J=7.4 Hz, SCH_2), 1.44 (t, 3H, CH_3). ^{13}C-NMR: 185.0, 179.7, 163.6, 160.3, 157.6, 153.8, 135.6, 134.8, 132.2, 126.9, 117.5, 116.5, 111.4, 107.2, 62.2, 56.5, 24.8, 12.5. MS (*m/z*): 344 (M^+, 100), 329, 315, 283.

Reaction of furanone 33 with monoketal 11

Following the general procedure, from furanone **33** (405 mg, 1.5 mmol) and monoketal **11** (204 mg, 1 mmol), the reaction mixture was kept under the conditions indicated in table 2. The crude reaction mixture was chromatographied (petroleum ether-ethyl acetate, 7:1) to afford **2-phenylthio-10-hydroxy-9-methoxy-1,4-anthraquinone (35)** (177 mg, 49%). M.p. 165-168°C. (from benzene-*n*-hexane). Anal. Calcd. for $C_{21}H_{14}O_4S$: C, 69.61; H, 3.87; S, 8.84. Found: C, 69.38; H, 3.86; S, 8.60. IR: 1650, 1610, 1560, 1500, 1250. ^{1}H-NMR: 14.77 (s, 1H, OH), 8.49-8.45 (m, 1H, H-8), 8.44-8.31 (m, 1H, H-5), 7.78-7.71 (m, 2H, H-7, H-6), 7.57-7.48 (m. 5H, arom.), 6.13 (s, 1H, H-3), 4.05 (s, 3H, OCH_3). ^{13}C-NMR: 186.0, 179.7, 160.5, 160.3, 154.6, 135.8, 132.8, 131.3, 130.5, 130.4, 130.2, 129.7, 126.0, 127.9, 125.2, 125.0, 116.3, 107.6, 62.5. MS (*m/z*): 363 (M^++1, 0.8) (M^+, 3), 347, 253, 157, 109, 77 (100) and **4-bromo-5-(phenylthio)-5-(1',1'-dimethoxy-4'-oxo-1',2',3',4'-tetrahydronaphth-2'-yl)furan-2(5*H*)-one (34a,b)** (37 mg, 10%), (ratio **34a:34b**, 60:40). Anal. Calcd. for $C_{22}H_{19}O_5$ BrS: C, 55.61; H, 3.98; S, 6.52; Br, 16.81. Found: C, 55.54; H, 4.03; S, 6.74; Br, 16.40. IR: 1770, 1690, 1600. ^{1}H-NMR: 8.03-7.97 (m, 1H, H-5'), 7.80-7.75 (m, 0.6H, H-8', **34a**), 7.65-7.16 (m, 7.4H, H-6', H-7', 5H, arom., **34a,b**, 0.4H, H-8', **34b**), 5.71 (s, 0.6H, H-3, **34a**), 5.53 (s, 0.4H, H-3, **34b**), 3.57 (dd, 0.6H, $J_{2',3'}$=6.5 Hz, $J_{2',3'}$=2.8 Hz, H-2', **34a**), 3.61-3.36 (m, 1.2H, H.2', H-3', **34b**), 3.53 (s, 1.8H, OCH_3, **34a**), 3.39 (s, 1.2H, OCH_3, **34b**), 3.23 (dd, 0.6H, J_{gem}=18.6 Hz, $J_{2',3'}$=6.5 Hz, H-3', **34a**), 2.86 (s, 1.8H, OCH_3, **34a**), 2.78 (s, 1.2H, OCH_3, **34b**), 2.62 (d, 0.6H, H'-3', **34a**). ^{13}C-NMR: 195.2, 194.7, 167.1, 166.2, 151.6, 150.7, 138.4, 137.1, 137.0, 133.3, 133.0, 132.7, 130.6, 130.4, 129.3, 128.9, 127.5, 127.2, 127.1, 127.0, 126.9, 126.7, 125.9, 125.6, 123.5, 121.9, 99.7, 99.3, 98.9, 98.8, 51.0, 50.0, 49.4, 49.0, 44.4, 43.6, 38.8, 37.4. MS (*m/z*): 367, 365 (M^+-SPh, 29), 335, 333, 271, 269, 193, 191, 163 (100), 109, 77.

Attempted reaction of the anthraquinones 32 and 35 with (E)-1,3-bis [(trimethylsilyl)oxy]buta-1,3-diene (37)

A solution of (*E*)-1,3-[bis(trimethylsilyl)oxy]buta-1,3-diene (**37**) (1.3 ml) and the anthraquinone **32** or **35** (1.0 mmol) was heated in benzene (10 ml) under reflux in argon atmosphere for 12 or 5 days respectively. The solvent was removed, and the residue was stimated by ^{1}H-NMR to be recovered anthraquinone **32** or **35**.

2-Ethylsulphinyl-10-hydroxy-9-methoxy-1,4-anthraquinone (38)

To an ice-salt cooled (-5°C) solution of anthraquinone **32** (102 mg, 0.32 mmol) in dichloromethane (10 ml), was added drop-wise with stirring *m*-chloroperbenzoic acid (66 mg, 0.32 mmol) in dichloromethane (10 ml). The reaction mixture was kept at -5°C for 1 h, diluted with dichloromethane (10 ml), washed with 10% $NaHCO_3$ solution and then with water. After drying ($MgSO_4$), the solvent was removed at room temperature under reduced pressure, and the crude product crystallized from benzene- *n*-hexane to yield 106 mg (99%). M.p. 158-161°C. IR (KBr): 1645, 1630, 1595, 1435, 1255, 1060. ^{1}H-NMR: 14.81 (s, 1H, OH), 8.57-8.54 (m, 1H, H-8), 8.37-8.34 (m, 1H, H-5), 7.86-7.78 (m, 2H, H-6, H-7), 7.53 (s, 1H, H-3), 4.04 (s, 3H, OCH_3), 3.32 (q, 1H, J=7.4 Hz, SCH_2), 3.08 (q, 1H, J= 7.4 Hz, SCH_2), 1.35 (t, 3H, CH_3).

12a-Ethylsulphinyl-6-hydroxy-11-methoxy-1,3-bis[(trimethylsilyl)oxy]-1,4,4a,12a-tethrahydronaphthacene-5,12-dione (39)

A solution of (*E*)-1,3-bis[(trimethylsilyl)oxy]buta-1,3-diene **37** (0.3 ml, 0.56 mmol) and the anthraquinone **38** (33 mg, 0.1 mmol) in benzene (10 ml), was keep at 3°C under argon for 5 h. The solvent was removed, and the residue was show to be the adduct **39** by ^{1}H-NMR: 14.60 (s, 1H, OH), 8.45-8.42 (m, 1H, H-7), 8.32-8.28 (m, 1H, H-10), 7.74-7.63 (m, 2H, H-8, H-9), 5.67 (m, 1H, H-1), 5.50 (d, 1H, J=4.7 Hz, H-2), 3.99 (s, 3H, OCH_3), 3.76 (m, 1H, H-4a), 3.43-2.62 (m, 4H, H-4, SCH_2), 1.28 (t, 3H, J=7.4 Hz, CH_3), 0.29 (s, 9H, $OSiMe_3$), -0.24 (s, 9H, $OSiMe_3$).

2,11-Dihydroxy-6-methoxynaphthacene-5,12-dione (40).

M.p. 288-291°C. IR: 3260, 1655, 1590, 1580, 1435, 1270. ^{1}H-NMR: 15.2 (s, 1H, OH), 10.06 (br s, 1H, OH), 8.27-8.22 (m, 2H, H-7, H-10), 8.01 (d, 1H, $J_{3,4}$=8.6, H-4), 7.75-7.70 (m, 2H, H-8, H-9), 7.32 (d, 1H, $J_{1,3}$=2.5 Hz, H-1), 7.09 (dd, 1H, H-3), 3.89 (s, 3H, OCH_3). ^{13}C-NMR: 187.6, 178.0, 162.6, 160.1, 151.9, 135.0, 133.2, 132.0, 129.9, 127.9, 127.5, 126.1, 125.0, 124.6, 124.4, 122.4, 111.1, 62.0.

2-Ethylthio-9,10-dimethoxy-1,4-anthraquinone (41)

To a solution of **32** (157 mg, 0.5 mmol) in chloroform (4 ml) were added silver(I) oxide (150 mg) and methyl iodide (7 ml). The reaction mixture was stirred at 30-40ºC for 48 h. The crude product was filtered and the solvent was removed. The solid residue was purified by crystallization from benzene-*n*-hexane to give 160 mg (98%). M.p. 312-314ºC. Anal. Calcd. for $C_{18}H_{16}O_4S$: C, 65.85; H, 4.91; S, 9.76. Found: C, 65.60; H, 5.10; S, 9.51. IR: 1660, 1645, 1610, 1590, 1455, 1405, 1240, 1090. ^{1}H-NMR: 8.40-8.36 (m, 2H, H-5, H-8), 7.76-7.73 (m, 2H, H-6, H-7), 6.59 (s, 1H, H-3), 4.07 (s, 3H, OCH_3), 4.06 (s, 3H, OCH_3), 2.86 (q, 2H, J=7.5 Hz, SCH_2), 1.44 (t, 3H, CH_3). ^{13}C-NMR: 181.2, 180.8, 156.4, 155.6, 155.5, 133.2, 132.3, 130.3, 130.0, 129.1, 125.0, 124.8, 119.0, 63.1, 62.9, 24.6, 12.6. MS (*m/z*): 328 (M^+, 100), 313, 299, 297, 295, 269, 266.

2-Phenylthio-9,10-dimethoxy-1,4-anthraquinone (42)

To a solution of **35** (192 mg, 0.53 mmol) in chloroform (15 ml) were added silver(I) oxide (370 mg) and methyl iodide (15 ml). The reaction mixture was stirred at 30-40ºC for 48 hr. The crude product was filtered and the solvent was removed. The solid residue was purified by crystallization from benzene-*n*-hexane to give 198 mg (99%). M.p 206-208ºC. Anal. Calcd. for $C_{22}H_{16}O_4S$: C, 70.19; H, 4.28; S, 8.51. Found: C, 70.02; H, 4.52; S, 8.25. IR: 1660, 1640, 1610, 1590, 1400, 1350. ^{1}H-NMR: 8.41-8.34 (m, 2H, H-5, H-8), 7.77-7.72 (m, 2H, H-6, H-7), 7.59-7.47 (m, 5H, arom.), 6.10 (s, 1H, H-3), 4.10 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3). ^{13}C-NMR: 181.7, 181.5, 157.7, 156.9, 155.9, 136.4, 133.6, 132.8, 130.8, 130.7, 130.6, 130.5, 129.7, 128.4, 125.5, 125.3, 119.5, 119.3, 63.7, 63.4. MS (*m/z*): 378 (M^++2, 31), 377 (M^++1, 65), 376 (M^+, 100), 348, 330, 163, 109, 77.

12a-Ethylthio-6,11-dimethoxy-1,3-bis[(trimethylsilyl)oxy]-1,4,4a,12a-tetrahydronaphthacene-5,12-dione (43)

A solution of (*E*)-1,3-bis[(trimethylsilyl)oxy]buta-1,3-diene **37** (1.3 ml) and the anthraquinone **41** (157.0 mg, 0.5 mmol) in benzene (10 ml) was refluxed under argon for 12 days. The solvent was removed to afford 242 mg (86%). ^{1}H-NMR: 8.42-8.32 (m, 2H, H-7, H-10), 7.78-7.70 (m, 2H, H-8, H-9), 4.98 (d, 1H, $J_{1,2}$=5.9 Hz, H-2), 4.62 (d, 1H, H-1), 4.14 (s, 3H, OMe), 4.12 (s, 3H, OMe), 3.31 (d, 1H, $J_{4a,4}$=6.9 Hz, H-4a), 3.11 (d, 1H, J_{gem}=17.7 Hz, H-4), 2.79 (q, 2H, J=7.6 Hz, SCH_2), 2.38 (dd, 1H, H'-4), 1.24 (t, 3H, CH_3), 0.32 (s, 9H, $OSiMe_3$ in C-3), -0.17 (s, 9H, $OSiMe_3$ in C-1). MS (*m/z*): 486 (M^+-$SiMe_3$, 32), 426, 390, 355, 336, 309 (100), 269.

12a-Phenylthio-6,11-dimethoxy-1,3-bis[(trimethylsily)oxy]-1,4,4a,12a-tetrahydronaphthacene-5,12-dione (44)

A solution of (*E*)-1,3-bis[(trimethylsilyl)oxy]buta-1,3-diene **37** (1.3 ml) and the anthraquinone **42** (198 mg, 0.53 mmol) in benzene (5ml) was refluxed under argon for 4 days. The solvent was removed, to afford 260 mg (81%). ^{1}H-NMR: 8.34-8.23 (m, 2H, H-7, H-10), 7.66-7.63 (m, 2H, H-8, H-9), 7.57-7.55 (m, 2H, arom.), 7.19-7.17 (m, 3H, arom.), 4.98 (d, 1H, $J_{1,2}$=5.8 Hz, H-2), 4.55 (d, 1H, H-1), 4.04 (s, 3H, OMe), 4.03 (s, 3H, OMe), 3.17 (d, 1H, $J_{4a,4}$=6.5 Hz, H-4a), 3.06 (d, 1H, J_{gem}=17.7 Hz, H-4), 2.47 (dd, 1H, H′-4), 0.19 (s, 9H, $OSiMe_3$ in C-3), -0.22 (s, 9H, $OSiMe_3$ in C-1). ^{13}C-NMR: 194.9, 192.2, 154.7, 153.5, 150.4, 135.9, 132.1, 131.6, 130.5, 129.4, 129.0, 128.8, 128.7, 124.6, 124.2, 124.1, 123.1, 103.1, 72.0, 64.1, 63.7, 63.3, 48.3, 26.0, 0.4, -0.3. MS (*m/z*): 533 (M^+- $SiMe_3$, 1), 496, 448, 309, 215, 109, 73 (100).

12a-Ethylthio-6,11-dimethoxy-1-[(trimethylsily)loxy]-1,2,3,4,4a,12a-hexahydronaphthacene-3,5,12-trione (45)

A solution of adduct **43** (28 mg, 0.05 mmol) in tetrahydrofuran (20 ml) and 2 drop of 3 N HCl was kept at 0 °C under argon for 5 min. The mixture was poured into water and was extracted with dichloromethane. The organic layer was successively washed with water, NaCl solution, water and dried ($MgSO_4$). The solvent was removed, and the residue was recrystallized from diethyl ether/*n*-hexane to give 24 mg (98%). IR (KBr): 2955, 2925, 2855, 1720, 1680, 1620, 1350, 1260, 1255, 1060, 845. ^{1}H-NMR: 8.42-8.31 (m, 2H, H-7, H-10), 7.75-7.71 (m, 2H, H-8, H-9), 4.88 (t, 1H, $J_{1,2}$=3.1 Hz, H-1), 4.35 (s, 3H, OCH_3), 4.29 (s, 3H, OCH_3), 3.38-3.29 (m, 2H, H-4a, H-4), 3.10 (dd, 1H, J_{gem}=15.0 Hz, H-2), 3.03-2.87 (m, 2H, SCH_2), 2.79-2.72 (m, 1H, H′-4), 2.51-2.44 (m, 1H, H′-2), 1.28 (t, 3H, J=7.5 Hz, CH_3), -0.12 (s, 9H, $OSiMe_3$). MS (*m/z*): 487 (M^++1, 13), 486 (M^+, 41), 426, 390, 355, 336, 334, 329, 309 (100), 305, 269.

12a-Phenylthio-6,11-dimethoxy-1-[(trimethylsily)loxy]-1,2,3,4,4a,12a-hexahydronaphthacene-3,5,12-trione (46)

A solution of adduct **44** (260 mg, 0.42 mmol) in tetrahydrofuran (7 ml) and 1 ml of 3N HCl was kept at 0 °C under argon for 5 min. The mixture was poured into water and was extracted with dichloromethane. The organic layer was successively washed with water, NaCl solution, and water and dried ($MgSO_4$). The solvent was removed, and the residue was crystallized from diethyl ether/*n*-hexane to give 220 mg (96%). M.p. 72-74°. Anal. Calcd. for $C_{29}H_{30}O_6SSi$: C, 65.15; H, 5.66; S, 5.99. Found: C, 65.07; H, 5.83; S, 5.69. IR: 2960, 2940, 2860, 1720, 1690, 1610, 1350, 1060, 845. ^{1}H-NMR: 8.27-8.15 (m, 2H, H-7, H-10), 7.64-7.57 (m, 2H, H-8, H-9), 7.49-7.36 (m, 2H, arom.), 7.19-7.11 (m, 3H, arom.), 4.69 (t, 1H, $J_{1,2}$=2.9 Hz, H-1), 4.05 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 3.20 (dt, 1H, H-4a), 3.15 (m, 1H, $J_{4,4a}$= 1.9 Hz, H′-4), 3.02 (dd, 1H, J_{gem}=15.7 Hz, $J_{2,1}$=3.0 Hz, H-2), 2.74 (dd, 1H, $J_{4,4a}$=6.6 Hz, H′-4), 2.39 (dt, 1H, $J_{2,4}$= 2.4 Hz, H-2); -0.19 (s, 9H, $OSiMe_3$). ^{13}C-NMR: 205.7, 194.8, 191.5, 154.5, 150.8, 136.0, 132.5, 131.8, 129.9, 129.7, 129.3, 129.0,

124.7, 124.4, 123.6, 123.3, 76.4, 64.6, 63.8, 63.2, 50.9, 45.6, 35.9, -0.5. MS (*m/z*): 535 (M^+ +1, 25), 534 (M^+, 51), 446, 425 , 335 (100), 309, 109.

12a-Ethylthio-3,3-ethylenedioxy-6,11-dimethoxy-1-[(trimethylsilyl)oxy]-1,2,3,4,4a,12a-hexahydronaphthacene-5,12-dione (47)

A stirred mixture of ketone **45** (25 mg, 0.05 mmol), ethylene glycol (2 ml) and *p*-toluenesulphonic acid (2 mg) in tetrahydrofuran (12 ml) was heated at 80°C for 12 h. The reaction mixture was poured into water and extracted with dichloromethane. The organic layer was washed with water and dried ($MgSO_4$). The solvent was removed and the residue was tritured with diethyl ether-ligtht petroleum to give 26 mg (97 %) . ^{1}H-NMR: 8.41-8.36 (m, 2H, H-7, H-10), 7.79-7.75 (m, 2H, H-8, H-9), 4.25-4.22 (m, 1H, H-1), 4.07 (s, 3H, OCH_3), 4.04 (s, 3H, OCH_3), 4.03-3.95 (m, 4H, OCH_2), 3.17 (q, 1H, SCH_2), 3.09 (dd, 1H, $J_{4,4a}$=13.3 Hz, $J_{4,4a}$=4.1 Hz, H-4a), 2.58 (q, 1H, SCH_2), 2.28-2.16 (m, 2H, H-2), 2.02-1.96 (m, 1H, H-4), 1.80 (t, 1H, J_{gem}=$J_{4,4a}$=13.4 Hz, H'-4), 1.10 (t, 3H, J=7.5 Hz, CH_3), 0.07 (s, 9H, $SiMe_3$). MS (*m/z*): 531 (M^+, 3), 467, 451, 435, 405 (100), 329.

12a-Ethylthio-3,3-ethylenedioxy-1-hydroxy-6,11-dimethoxy-1,2,3,4,4a,12a-hexahydronaphthacene-5,12-dione (48)

A solution of **47** (23 mg, 0.05 mmol) in tetrahydrofuran (6 ml) was stirred with a saturated aqueus solution of tartaric acid for 15 min. The organic layer was separated, washed with sodium chloride solution and dried. The solvent was removed to give 19 mg (97%) of **48**. ^{1}H-NMR: 8.45-8.32 (m, 2H, H-7, H-10), 7.81-7.68 (m, 2H, H-8, H-9), 4.25 (m, 1H, H-1), 4.12 (m, 1H, OH), 4.08 (s, 3H, OCH_3), 4.05 (s, 3H, OCH_3), 4.02-3.88 (m, 4H, OCH_2), 3.18 (q, 1H, SCH_2), 3.07 (dd, 1H, $J_{4,4a}$=12.7 Hz, $J_{4,4a}$=4.3 Hz, H-4a), 2.56 (q, 1H, SCH_2), 2.40-2.20 (m, 2H, H-2), 2.20-2.02 (m, 1H, H-4), 1.9 (t, 1H, J_{gem}=$J_{4,4a}$=12.7 Hz, H'-4), 1.17 (t, 1H, J=7.5 Hz, CH_3). MS (*m/z*): 396 (M^+-HSEt, 28), 378 (100), 350, 349, 295, 291, 267.

12a-Phenylthio-3,3-ethylenedioxy-1-hydroxy-6,11-dimethoxy-1,2,3,4,4a,12a-hexahydronaphthacene-5,12- dione (49)

A solution of ketone **46** (160 mg, 0.28 mmol), ethylene glycol (2 ml) and *p*-toluenesulphonic acid (10 mg) in tetrahydrofuran (12 ml) was heated at 80°C for 12 h. The reaction mixture was poured into water and extracted with dichlomethane. The organic layer was washed with water and dried ($MgSO_4$). The solvent was removed and the residue was tritured with diethyl ether-ligtht petroleum to give 102 mg (63 %) of **49**. M.p. 185-187°C (from methanol). Anal. Calcd. for $C_{28}H_{26}O_7S$: C, 66.39; H, 5.17; S, 6.33. Found: C, 66.56: H, 5.31; S, 6.12. IR: 3500, 1690, 1600. ^{1}H-NMR: 8.43-8.32 (m, 2H, H-7, H-10), 7.81-7.70 (m, 2H, H-8, H-9), 7.57-7.47 (m, 2H, arom.), 7.40-7.20 (m, 3H, arom.), 4.20 (d, 1H, $J_{1,OH}$=11.3 Hz, OH), 4.07 (s, 3H, OCH_3),

3.91-3.88 (m, 4H, OCH_2), 3.85 (s, 3H, OCH_3), 3.83-3.70 (m, 1H, H-1), 3.11 (dd, 1H, $J_{4a,4}$= 4.4 Hz, $J_{4a,4}$= 13.4 Hz, H-4a), 2.22-2.18 (m, 2H, H-2), 2.01-1.92 (m, 1H, H-4), 1.77 (t, 1H, $J_{4,4}=J_{4,4a}$=13.4 Hz, H'-4). ^{13}C-NMR: 195.2, 193.5, 156.3, 155.1, 137.9, 133.3, 132.6, 130.2, 130.0, 129.9, 128.9, 128.0, 124.9, 124.7, 120.4, 119.4, 107.1, 72.9, 64.6, 64.5, 63.3, 63.1, 62.7, 53.2, 41.9, 37.1. MS (*m/z*): 508 (M^++2, 12), 507 (M^++1, 33), 506 (M^+, 100), 491, 447, 392, 378, 295, 115, 110, 109.

3,3-Ethylenedioxy-1,5,12-trihydroxy-1,2,3,4-tetrahydronaphthacene-6,11-dione (50)

a) A mixture of **48** (23 mg, 0.05 mmol), 30 mg of silver(II) oxide and 5 ml of dioxane was stirred for 5 min., 6N HNO_3 (0.1 ml) was added and stirred at room temperature for another 5 min. Then 15 ml of chloroform and 5 ml of water were added and the organic layer was washed with water and dried ($MgSO_4$). The solvent was removed to give 15.6 mg (85%). M.p. 217°C (M.p. lit 228°C).[20] The spectral data were identical with those reported in the literature.[20] ^{1}H-NMR: 13.72 (s, 1H, OH), 13.36 (s, 1H, OH), 8.37-8.31 (m, 2H, H-7, H-10), 7.84-7.80 (m, 2H, H-8, H-9), 5.33 (dt, 1H, $J_{1,OH}$=7.9 Hz, $J_{1,2}$=5.0 Hz, H-1), 4.12-4.03 (m, 4H, OCH_2), 3.98 (d, 1H, $J_{1,OH}$= 7.9 Hz, OH), 3.20 (d, 1H, J_{gem}=18.5 Hz, H-4), 2.92 (d, 1H, H'-4), 2.26 (d, 2H, H-2). MS (*m/z*): 368 (M^+, 22), 350 , 306, 282, 278, 254 (100), 239, 165, 87.

b) Reaction of compound **49** following the above procedure afforded **50** in 78% yield.

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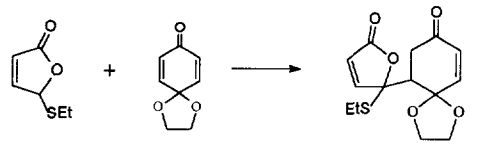

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