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GENERAL SYNTHESIS OF CHIRAL 2-P-TOLYLSULFINYLQUINONES.

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Abstract: Optically pure (S)-p-tolylsulfinyl substituted quinones were synthesized by deketalization of the corresponding quinone bisketals obtained by Andersen's type synthesis starting from 2-bromo-1,4-dimethoxy aromatic derivatives, followed by anodic oxidation of the resulting sulfoxide.

Quinones have been extensively used in synthesis of natural products[1]. In some cases, the high reactivity of the quinone moiety makes it necessary the use of protected derivatives such as quinone ketals and monoketals, which have been increasingly used in synthesis in the past ten years.[2] As an example, the regiospecific synthesis of daunomicynone from a functionalized lithiated quinone bisketal should be mentioned.[3] The most useful reactions of quinone monoketals are 1,2-[2,4] and 1,4-additions,[2,5] Diels-Alder[6] and acid catalyzed[7] cycloadditions. Quinone imine ketals can also be prepared starting from quinone monoketals.[8]

Despite of the ready availability of these derivatives, the only report on simple chiral protected quinones concerns (S)-2-p-tolylsulfinylquinone dimethyl bisketal (1)[9] which, upon acidic treatment, afforded (S)-2-p-tolylsulfinyl-p-benzoquinone (2). The presence of the chiral sulfinyl group in the quinone framework allowed for the diastereofacial selectivity to be controlled in Diels-Alder reaction of 2 with cyclopentadiene. Besides, the sulfinyl group makes this system a synthetic equivalent of the unknown triple bonded quinone *via* elimination of the sulfoxide in the resulting adduct, as was already shown in several racemic 2-sulfinylnaphthoquinones.[10]

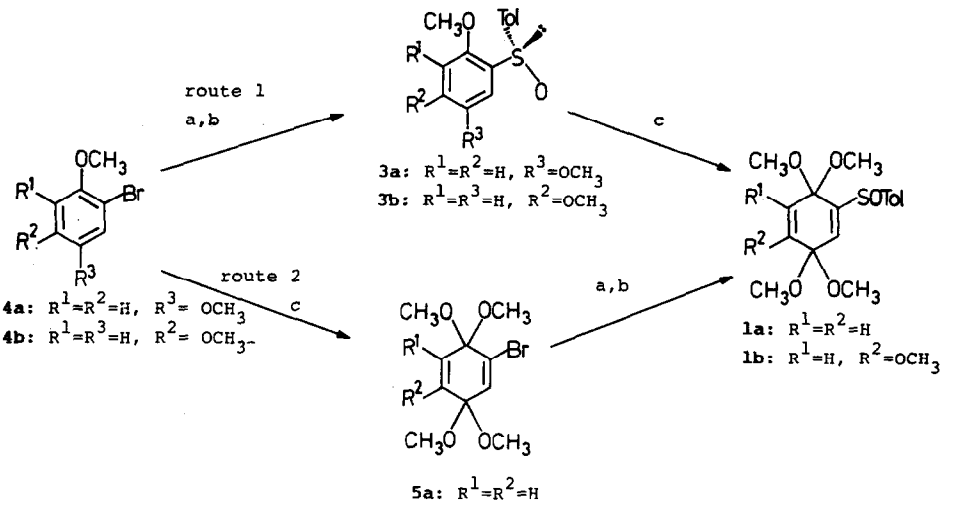
We hereby report a general synthesis of chiral 2-p-tolylsulfinylquinones based on the well known anodic oxidation of 1,4-dialkoxyaromatic derivatives to give the quinone bisketals.[11] This method is extended, in the case of p-benzoquinone, to the preparation of the corresponding sulfenyl and sulfonyl derivatives. The highly regioselective monodeprotection of sulfur substituted quinone bisketals is also described.

Results and discussion

Racemic sulfinylquinones are readily available by oxidation (MCPBA) of the corresponding sulfides. However, reported results for the asymmetric oxidation[12] of sulfides are not yet as good as desired and depend crucially on both substrate and reagent. Therefore, we thought of introducing the quinone unit by anodic oxidation of a

chiral p-tolylsulfinylhydroquinone ether **3**, this method giving a general entry to protected quinone bisketals. This reaction has been already checked on (S)-2-p-tolylsulfinyl-1,4-dimethoxybenzene[9] (**3a**) which gave the expected quinone bisketal **1a**.

Anodic oxidation of derivatives **3** was carried out at constant current in a single cell using 2 % methanolic potassium hydroxide as both solvent and electrolyte, vessel (route 1 in Scheme 1). Thus, the dimethoxyderivative **3b** was electrochemically oxidized to **1b** in 71 % yield.

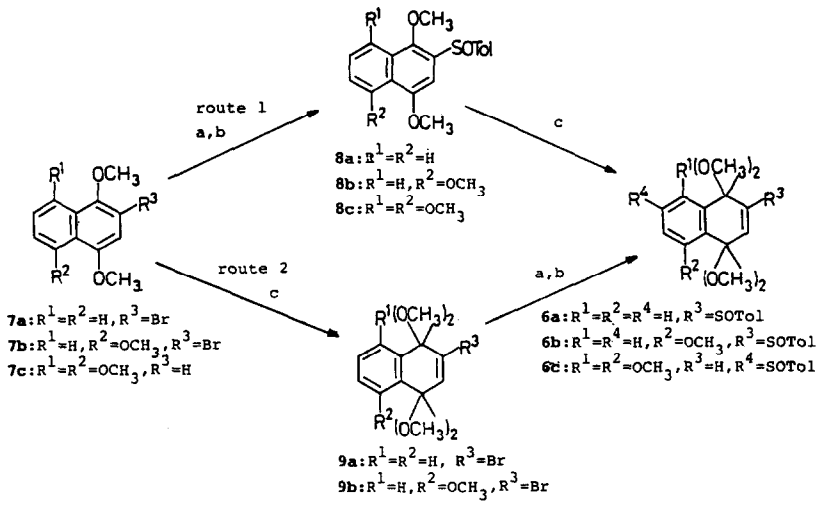


a) n-BuLi, b) (S)-p-TolSO$_2$Menthyl, c) (E), KOH, MeOH

Scheme 1

The sulfinyl hydroquinone ethers **3** were obtained by Andersen's synthesis,[13] from bromo dimethoxybenzene derivatives **4** which, upon metallation (n-BuLi), reacted with menthyl (S)-p-toluenesulfinate.[14] According to the well known stereochemistry of this process, the (S) configuration was assigned to the resulting chiral sulfoxides **3**. Inversion of the sequence metallation-sulfinylation/anodic oxidation, the latter in conditions similar to those described by Swenton,[15] also yielded compounds **1** (route 2 in Scheme 1). However, the isolation procedure gave rise to extensive decomposition in the case of **1b**.

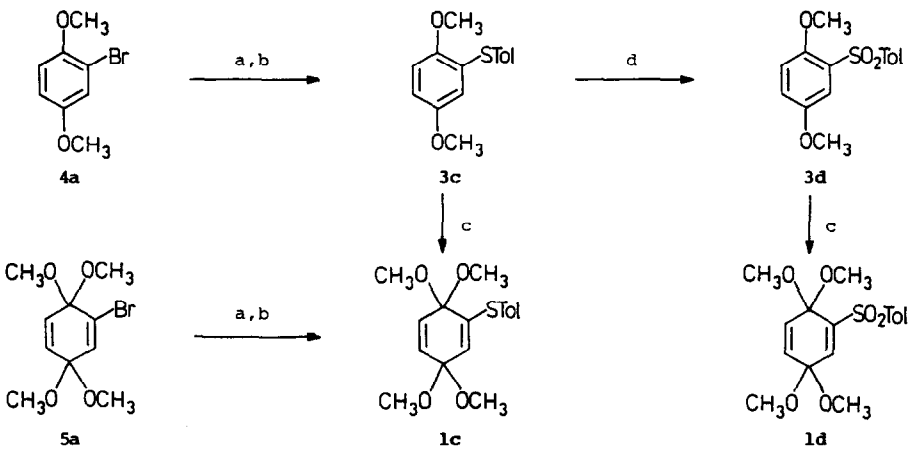
Reaction sequences of Scheme 1 were also applied to the corresponding 2-bromo-1,4-dimethoxynaphthalenes **7** (Scheme 2). Thus, **7a**[16] upon successive reaction with n-BuLi and menthyl (S)-p-toluenesulfinate gave (S)-2-p-tolylsulfinyl-1,4-dimethoxynaphthalene **8a** in 74 % isolated yield. Anodic oxidation of **8a** was carried out (route 1 in Scheme 2) as mentioned above at 25°C, affording **6a** (81 %). Inverting the sequence (route 2 in Scheme 2), **7a** gave **9a**[17] and **6a** (77 % yield). Starting from 2-bromo-1,4,5-trimethoxynaphthalene **7b**[18], route 1 gave sulfoxide **8b** (65%) and (S)-2-p-tolylsulfinyl juglone bisketal methyl ether **6b** (87%), whereas route 2 afforded **9b** (87% isolated) and **6b**. In the latter case, attempts to separate **6b** from menthol (flash chromatography) led to its extensive decomposition.



a) n-Buli, b) (S)-p-TolSO$_2$Menthyl, c) (E) , KOH, MeOH

Scheme 2

Naphthoquinone bisketal derivative **6c** was obtained from 1,4,5,8-tetramethoxynaphthalene **7c**[19] which was directly lithiated on C-2 (n-BuLi, 0°C) and further treated with menthyl (S)-p-toluenesulfinate yielding sulfoxide **8c** (58 %). Anodic oxidation of **8c** took place on the aromatic ring which does not bear the sulfinyl group, giving bisketal **6c** (86 %). This chemioselection was expected on the basis of the effect of electron withdrawing substituents on the oxidation potentials of alkoxy aromatic derivatives[20] and on the proposed mechanism for anodic oxidation of methoxylated naphthalenes[21] as well.



a) n-Buli, b) (p-Tol)$_2$S$_2$, c) (E) , KOH, MeOH, d) MCPBA

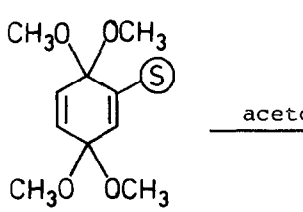
Scheme 3

The synthetic paths to 2-p-tolylsulfinylbenzoquinone bisketal have been extended to the corresponding sulfenyl derivative **1c** (Scheme 3). Thus, 2-bromo-1,4-dimethoxybenzene **4a** and bromo quinone bisketal **5a** were subsequently treated with n-BuLi and p-ditolyldisulfide to give compounds **3c** and **1c**, respectively, in high yield. Anodic oxidation of **3c** afforded 2-p-tolylsulfenyl-p-benzoquinone bisketal **1c** in 92 % yield. The synthesis of sulfonyl quinone bisketal **1d** was accomplished by electrochemical oxidation of 2-p-tolylsulfonyl-1,4-dimethoxybenzene **3d**, easily obtained by MCPBA oxidation of sulfide **3c**. The anodic oxidation rates of **3a**, **3c** and **3d** (sulfide > sulfoxide >> sulfone) are in agreement with the effect of the substituents already mentioned.[20] These kinetic observations reinforce the proposed mechanism of the reaction.[21]

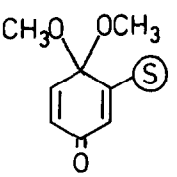
The partial hydrolysis of quinone bisketals has been described as a synthetic way to quinone monoketals[2]. However, the acidic aqueous media used in the reported methods could determine the easy evolution of monoketals to quinones. In the case of p-benzoquinone bisketals **1a,d** (Table 1) and naphthoquinone derivative **6a** (Table 2) we were able to obtain the corresponding monoketals using acetone in the presence of $CuSO_4$, avoiding further decomposition. Monoketal **12b** was sythesized starting from bisketal **6b** by partial deketalization in the presence of p-toluenesulfonic acid (Table 2). In the case of compound **6c** no acidic catalysis is necessary for monoketal **12c** formation.

The major monoketal resulted from reaction on the ketal group having no adjacent substituent. The regiochemistry was assigned on the basis of the ^{1}H-NMR spectra,[22] and was the expected on previously reported results related to monohydrolysis of 2-methylthio-p-benzoquinone bisketal and several monosubstituted naphthoquinone bisketals.[23] The high regioselectivity observed for **1c** and **6a-c**, must be a consequence of the steric effect of the sulfur substituent and/or the stabilizing effect of p-tolylthio group in **1c**, and aromatic ring in **6a-c** on the monohydrolysis intermediate.[2b,23] In the case of the sulfinyl **1a** and sulfonyl **1d** derivatives the steric and stereoelectronic effects are opposite resulting in a lower regioselectivity of deprotection.

Table 1.- Deprotection of p-benzoquinone bisketals **1**.



acetone



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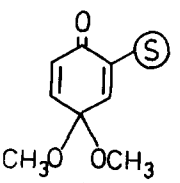

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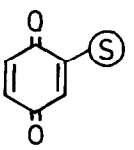

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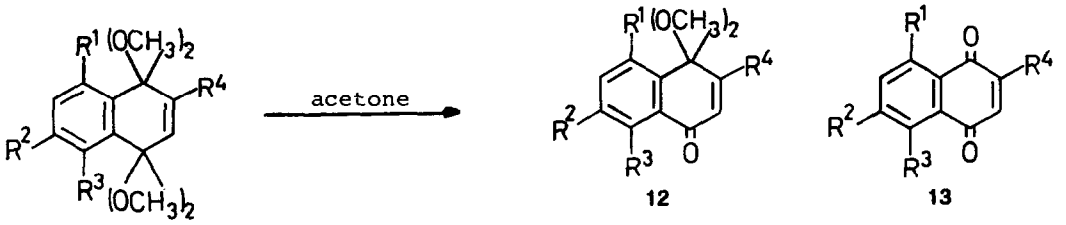
Compound	Reagent	Yield(%)	Yield(%)	Yield(%)
1a: (S) =SOTol	$CuSO_4$	60	10	0
"	p-TsOH	0	0	85
1c: (S) =STol	$CuSO_4$	84	0	0
"	p-TsOH	0	0	87
1d: (S) =SO_2Tol	$CuSO_4$	44	44	0

Table 2.- Deprotection of 1,4- naphthoquinone bisketals 6.



12 13

Compound	Reagent	Yield(%)	Yield(%)
6a:(R^1 =R^2=R^3=H;R^4=SOTol)	$CuSO_4$	82	0
6a: "	p-TsOH	0	75
6b:(R^1=R^2=H;R^3=OCH_3;R^4=SOTol)	p-TsOH[a]	90	0
6b: "	p-TsOH[b]	0	90
6c:(R^1=R^3=OCH_3;R^4=H;R^2=SOTol)	-	86	0
6c: "	p-TsOH	0	82

[a] Reaction time 1 h.; [b] Reaction time 24 h.

Treatment of bisketals **1a-c** and **6a-c** with p-toluenesulfonic acid afforded p-benzoquinones **2a-c** and naphthoquinones **13a-c**, which were isolated with the yields indicated on Tables 1 and 2. Synthesis of sulfonyl-p-benzoquinone was not possible due to decomposition of the product. The optical purity of the chiral sulfinyl derivatives was shown to be higher than 98 % by ^{1}H-NMR (Eu(thc)$_3$) in all the cases. Racemic compounds necessary for such a determination were synthetized following one of the routes described for each substrate by using methyl p-toluenesulfinate as sulfinylating agent.

The foregoing results confirm the utility of anodic oxidation of dialkoxyaromatic derivatives as a method to synthesize sulfur substituted quinone bisketals. The strategy described herein allowes the regioselective obtention of quinone monoketals and the synthesis of chiral sulfinyl quinones not available by other methods.

Experimental Section

Melting points were obtained in open capillary tubes and are uncorrected. Mass spectra were recorded at 70 eV. IR spectra are given in cm^{-1}. ^{1}H and ^{13}C NMR spectra were recorded at 200.1 and 50.3 MHz, in CDCl3. Thin layer chromatography was performed by using precoated sheets of silica gel 60 and flash column chromatography was performed with silica gel 60 (230-400 mesh) of Macherey-Nagel. Eluting solvents are indicated in the text. Dry THF was distilled from sodium/benzophenone ketyl. Apparatus for inert atmosphere experiments were dried by flaming in a stream of dry argon and all reactions were monitored by TLC.

General procedure for sulfinylation of bromo derivatives. Method A. To a solution of n-BuLi (9.9 mmol) in 20 ml of THF at -78°C was added dropwise the bromo derivative (9.9 mmol) in 50 ml of THF. The mixture was stirred for 1h. and then added through a cooled double tipped needle by means of argon pressure over a cooled (-78°C) solution of (S)-menthyl-p-toluenesulfinate (10.2 mmol) in 150 ml of THF with vigorous stirring. Hydrolysis was performed with 200 ml of water, and extraction with methylene chloride.The organic layer was separated, dried over anhydrous sodium sulfate and concentrated in vacuo.

(S)-1,4-Dimethoxy-2-*p*-tolylsulfinylbenzene (3a). Compound **3a** was obtained from **4a** by method A and purified by flash column chromatography (eluent 1:1 ethyl acetate-hexane) (62% yield) m.p. 83-85°C (from hexane) ^{1}H NMR δ 7.59 and 7.21 (AA'BB', tolyl system, 4H), 7.49 (d, 1H, J=3.1 Hz, H_3), 6.91 (dd, 1H, J=3.1 and 8.8 Hz, H_5), 6.78 (d, J=8.8 Hz, H_6), 3.80, 3.72 (s, 6H, CH_3O), 2.34 (s, 3H, CH_3Ar); ^{13}C NMR δ 154.4, 149.3, 142.1, 141.1, 133.8, 129.4, 125.1, 117.6, 112.4, 108.5, 55.9, 55.7, 21.1; IR (KBr) 1490, 1270, 1050, 810 ; MS m/z % 276 (M^+, 48), 259 (100), 228 (41), 213 (52), 198 (30), 153 (38), 125 (68), 123 (64), 105 (99); $[\alpha]_D$= -21° (c=1,$CHCl_3$).

(S)-1,5-Dimethoxy-2-p-tolylsulfinylbenzene (3b). Compound **3b** was obtained from **4b** by method A. Flash column chromatography of the reaction mixture (eluent 1:3 acetone-hexane) afforded pure **3b** (75% yield) m.p. 69-70°C (from hexane) ^{1}H NMR δ 7.75 (d, J=8.6 Hz, H_3), 7.56 and 7.23 (AA'BB' tolyl system, 4H), 6.64 (dd, J=2.3 and 8.6 Hz, H_4), 6.40 (d, J=2.3 Hz, H_6), 3.82 and 3.77 (s, 6H, CH_3O), 2.36 (s, 3H, CH_3Ar); ^{13}C NMR δ 162.9, 156.6, 142.2, 140.5, 129.0, 125.5, 124.5, 124.1, 105.1, 98.2, 55.1, 55.0, 20.8; IR (film) 1600, 1470, 1290, 1210, 1160, 1040, 820; MS m/z % 276 (M^+, 9), 259 (12), 228 (100), 213 (13), 185 (14), 153 (9), 127 (12), 105 (10); $[\alpha]_D$= -647° (c=1, $CHCl_3$).

1,4-Dimethoxy-2-p-tolylsulfenylbenzene (3c). Compound **3c** was obtained from **4a** by method A, using di-p-tolyldisulfide instead of menthyl p-toluenesulfinate. Purification by crystalization afforded pure **3c** (69% yield) m.p. 89-90°C (from hexane) ^{1}H NMR δ 7.35 and 7.16 (AA'BB' tolyl system, 4H), 6.80 (d, 1H, J= 8.8 Hz, H_6), 6.67 (dd, 1H, J= 3.1 and 8.8 Hz, H_5), 6.46 (dd, 1H, J= 3.1 Hz, H_3), 3.85 and 3.64 (s, 6H, CH_3O), 2.36 (s, 3H, CH_3O); ^{13}C NMR δ 153.7, 150.4, 137.7, 133.1, 129.9, 128.9, 127.1, 115.3, 111.2, 110.9, 56.0, 55.1, 20.8; IR 1600, 1490, 1280, 1220, 1050, 820 MS m/z % 260 (M^+, 100), 245 (33), 230 (45), 214 (24), 115 (10), Anal. Calcd. for $C_{15}H_{16}SO_2$: C, 69.26; H, 6.14; S, 12.30. Found: C, 69.50; H, 6.41; S, 12.13.

1,4-Dimethoxy-2-p-tolylsulfonylbenzene (3d). Over a solution of 1.3g (5mmol) of **3c** in 10ml of $CHCl_3$, 3g (11.6 mmol) of MCPBA dissolved in $CHCl_3$ were added. After 1h stirring, the resulting solution was treated with several portions of $NaHCO_3$ saturated solution. The organic layer was dried and the solvent eliminated, to yield 1.39 g (95%) of **3d** m.p. 113-114°C (from ether) ^{1}H NMR δ 7.85 and 7.28 (AA'BB' tolyl system, 4H), 7.68 (d, 1H, J=3.1 Hz, H_3), 7.06 (dd, 1H, J=3.1 and 8.8 Hz, H_5), 6.84 (d, 1H, J=8.8 Hz, H_6), 3.84 and 3.71 (s, 6H, CH_3O), 2.41 (s, 3H, CH_3Ar); IR (KBr) 1590, 1490, 1310, 1280, 1230, 1150; MS m/z % 292 (M^+, 100), 155 (6), 139 (22), 135 (22), 105 (14). Anal. Calcd. for $C_{15}H_{16}SO_4$: C, 61.64; H, 5.48. Found: C, 61.55; H, 5.35.

(S)-1,4-Dimethoxy-2-p-tolylsulfinylnaphthalene (8a). Compound **8a** was obtained from **7a** by method A. Flash column chromatography of the reaction mixture (eluent 1:3 acetone-hexane) afforded pure **8a** (74% yield) m.p. 98°C (from methanol) ^{1}H NMR δ 8.30-7.50 (m, 4H, Ar), 7.65-7.22 (AA'BB', tolyl system 4H), 7.19 (s, 1H, H_3), 4.03 and 4.01 (s, 6H, CH_3O), 2.31 (s, 3H, CH_3Ar); ^{13}C NMR 152.8, 146.2, 142.1, 140.6, 133.1, 129.2, 127.5, 126.8, 126.5, 124.1, 122.4, 121.5, 95.9, 55.3, 20.6; IR (KBr) 1590, 1465, 1370, 1115, 1055, 1000; MS m/z % 328 (7), 326 (M^+, 94), 310 (27), 309 (100), 263 (60), 175 (65), 129 (35), 105 (57); $[\alpha]_D$= -300° ($CHCl_3$, c=1). Anal. Calcd. for $C_{19}H_{18}SO_3$: C, 69.94; H, 5.52. Found: C, 69.80; H, 5.39.

(S)-1,4,5-Trimethoxy-2-p-tolylsulfinylnaphthalene (8b). Compound **8b** was obtained from **7b** by method A and purified by column chromatography (eluent 1:3 acetone-hexane) (65% yield) m.p. 117.5-118.5°C (from methanol/hexane) ^{1}H NMR δ 7.64 and 7.22 (AA'BB' tolyl system, 4H), 7.22 (s, 1H, H_3), 7.65-6.88 (m, 3H, Ar), 3.99, 3.98 and 3.92 (3s, 9H, CH_3O), 2.29 (s, 3H, CH_3O); IR (KBr) 1570, 1450, 1375, 1250, 1030; MS m/z % 356 (M^+, 100), 339 (41), 293 (35), 205 (47), 186 (31); $[\alpha]_D$= - 181° ($CHCl_3$, c=1). Anal. Calcd. for $C_{20}H_{20}SO_4$: C, 67.44; H, 5.62. Found: C,67.01; H, 5.31.

(S)-1,4,5,8-Tetramethoxy-2-p-tolylsulfinylnaphthalene (8c). Compound **8c** was obtained from **7c** by method A. The lithiated derivative was formed at 0°C. Flash column chromatography of the crude reaction mixture (eluent 1:3 acetone-hexane) afforded pure **8c** (58% yield) as a colorless oil. ^{1}H NMR δ 7.65 and 7.19 (AA'BB' tolyl system, 4H), 7.32 (s, 1H, H_3), 6.89 and 6.83 (AB system, 2H, J= 8.7 Hz, H_6 and H_7), 4.00, 3.90, 3.87 and 3.86 (4s, 12H, CH_3O), 2.29 (s, 3H, CH_3Ar); ^{13}C NMR δ 154.2, 150.9, 149.8, 146.2, 142.2, 140.5, 135.0, 129.2, 124.4, 121.8, 121.2, 109.6, 107.6, 99.0, 62.4, 57.0, 56.2, 55.9, 20.6; IR (film) 1570, 1250, 070, 1040, 810; MS m/z % 386 (M^+, 100), 369 (13), 323 (20), 263 (11), 235 (34), 232 (62), 217 (23); $[\alpha]_D$= -356° (c=1, $CHCl_3$).

General procedure for anodic oxidation of 1,4-dimethoxy aromatic derivatives. Method B. A solution of 1,4-dimethoxy aromatic derivative (2 mmol) dissolved in methanol (250ml) containing potassium hydroxyde (2.5 g) was stirred magnetically and subjected to constant current (1.0 A) electrolysis, provided by an AMEL model 549 potentiostat, on a circular platinum anode (60 cm^2) in an open vessel. The cathode was a 15 cm length of copper wire (diameter 0.7 cm) placed inside of the anode. Reaction time is indicated for each compound in brackets. The mixture was concentrated at reduced pressure and 20°C and the residue was dissolved in water and extracted with dichloromethane. The organic layer was dried over anhydrous sodium sulfate, and evaporated to dryness at 20°C. The crude material was purified by chromatography or crystallization, as indicated.

(S)-1,1,4,4-Tetramethoxy-2-*p*-tolylsulfinylcyclohexa-2,5-diene (1a). Compound **1a** was obtained from **5a** by method A (70% yield) being purified by flask chromatography (eluent 1:1 ethyl acetate-hexane) or from **3a** by method B (89% yield) at 0°C (3h). ^1H NMR δ 7.64 and 7.25 (AA'BB' tolyl system, 4H), 7.24 (d, 1H, J=2.7 Hz, H_2), 6.27 (dd, 1H, J=2.7 and 10.5 Hz, H_4), 5.87 (d, 1H, J=10.5 Hz, H_5), 3.39, 3.33, 3.32 and 2.50 (4s, 12H, CH_3O), 2.36 (s, 3H, CH_3Ar); ^{13}C NMR δ 147.8, 141.3, 140.3, 132.1, 130.6, 129.0, 128.6, 125.4, 96.1, 93.3, 50.8, 49.6, 49.6, 49.5, 21.0; IR (film) 1462, 1082, 969, 753; MS m/z % 338 (M^+, 3), 277 (76), 262 (69), 168 (32), 153 (50), 140 (39), 139 (35), 125 (100), 91 (36), 79 (43); $[\alpha]_D$= +254° (CHCl3, c=1).

(S)-1,3,3,6,6-Pentamethoxy-4-p-tolylsulfinylcyclohexa-1,4-diene (1b). Compound **1b** was obtained from **3b** by method B (71% yield) at 0°C, (8h) as a yellow oil ^1H NMR δ 7.66 and 7.27 (AA'BB' tolyl system, 4H), 7.11 (s, 1H, H_5), 4.85 (s, 1H, H_2), 3.70, 3.37, 3.34, 3.32 and 2.50 (5s, 15H, CH_3O), 2.39 (s, 3H, CH_3Ar); IR (film) 1080, 810, 760; MS m/z % 368 (M^+, 5), 337 (100), 307 (94), 258 (39), 228 (54), 198 (76), 183 (98), 155 (85), 139 (34), 105 (72); $[\alpha]_D$= +77° (c=1, $CHCl_3$).

3,3,6,6-Tetramethoxy-1-p-tolylsulfenylcyclohexa-1,4-diene (1c). Compound 1c was obtained from **5a** by method A (73% yield) using di-p-tolyldisulfide instead of menthyl p-toluene sulfinate or from **3c** by method B (92% yield) at r.t. (30 min) being purified by crystallization m.p. 81-83°C (from hexane) ^1H NMR δ 7.44 and 7.22 (AA'BB' tolyl system, 4H), 6.24 (dd, 1H, J=2.5 and 10.5 Hz, H_4) 5.99 (d, 1H, J=10.5 Hz, H_5), 5.35 (d, 1H, J=2.5 Hz, H_2), 3.32 and 3.16 (2s, 12H, CH_3O), 2.38 (s, 3H, CH_3Ar); ^{13}C NMR δ 143.8, 138.9, 135.4, 132.1, 130.0, 129.3, 125.6, 123.3, 95.7, 93.5, 50.6, 49.2, 20.7; IR (KBr) 1630, 1400, 1310, 1120, 1080, 960, 820; MS m/z % 322 (M^+, 8), 291 (24), 199 (24), 184 (10), 168 (100), 153 (31), 123 (18), 91 (15).

3,3,6,6-Tetramethoxy-1-p-tolylsulfonylcyclohexa-1,4-diene (1d). Compound **1d** was obtained pure from **3d** by method B (91% yield) at 0°C (8h) as a colorless oil ^1H NMR δ 7.84 and 7.29 (AA'BB' tolyl system, 4H), 7.53 (d, 1H, J=2.6 Hz, H_2), 6.23 (dd, 1H, J=2.6 and 10.4 Hz, H_4), 5.81 (d, 1H, J= 10.4 Hz, H_5), 3.36 and 2.97 (2s, 6H, CH_3O), 2.42 (s, 3H, CH_3Ar); IR (film) 1610, 1490, 1450, 1320, 1150, 1080, 810; MS m/z % 354 (M^+, 41), 323 (17), 293 (16), 229 (29), 199 (100), 183 (50), 168 (50), 155 (26).

(S)-1,1,4,4-Tetramethoxy-2-p-tolylsulfinyl-1,4-dihydronaphthalene (6a). Compound **6a** was obtained from **9a** by method A (77% yield) being purified by flask chromatography (eluent 1:5 acetone-hexane) or from **8a** by method B (81% yield) at r.t. (30min), being purified by crystallization m.p. 88-89°C (from ethyl ether). ^1H NMR δ 7.74 and 7.29 (AA'BB' tolyl system, 4H), 7.58 (s, 1H, H_3), 7.70-7.43 (m, 4H, Ar), 3.34, 3.26, 3.12 and 2,39 (4s, 12H, CH_3O), 2.06 (s, 3H, CH_3Ar); ^{13}C NMR δ 148.8, 141.8, 139.9, 137.3, 134.0, 132.9, 129.3, 126.1, 125.7, 125.5, 98.5, 95.2, 51.8, 51.0, 50.4, 21.3; IR (KBr) 1600, 1500, 1455, 1320, 1300, 1240, 1070, 1025; MS m/z % 388 (M^+, 7), 341 (21), 327 (43), 326 (40), 309 (40), 249 (35), 218 (41), 203 (100), 175 (37); $[\alpha]_D$= +154° ($CHCl_3$, c=1). Anal. calcd. for $C_{21}H_{24}SO_5$: C, 64.94; H, 6.23. Found : C, 64.26,; H, 5.96.

(S)-1,1,4,4,5-Pentamethoxy-2-p-tolylsulfinyl-1,4-dihydronaphthalene (6b). Compound **6b** was obtained from **9b** by method A (no isolation was posible) or from **8b** by method B (87% yield) at r.t. (30min), being purified by crystallization m.p. 172-173°C (from ethyl ether) ^1H NMR δ 7.74 and 6.98 (AA'BB' tolyl system, 4H), 7.45 (s, 1H, H_3), 7.70-7.10 (m, 3H, Ar), 3.91, 3.38, 3.23, 3.16 and 2.17 (5s, 15H, CH_3O), 2.38 (s, 3H, CH_3Ar); IR (KBr) 1665, 1590, 1473, 1270, 1080; $[\alpha]_D$= +178° ($CHCl_3$, c=1). Anal. Calcd. for $C_{22}H_{26}SO_6$: C, 63,16; H, 6.22. Found: C, 62.78; H, 5.83.

(S)-1,1,4,4,5,8-Hexamethoxy-6-p-ptolylsulfinyl-1,4-dihydronaphthalene (6c). Compound **6c** was obtained pure from **8c** by method B (86% yield) at r.t. (30 min) as a colorless oil ^{1}H NMR δ 7.62 and 7.20 (AA'BB', tolyl system, 4H), 7.56 (s, 1H, H_7), 6.20 and 6.15 (AB system, J= 11.0 Hz, H_2 and H_3), 4.00, 3.95, 3.38, 3.21 and 2.85 (5s, 18H, CH_3O), 2.33 (s, 3H, CH_3Ar);IR (film) 1460, 1300, 1210, 1080, 820, 740; $[\alpha]_D$= -64° (c=1, $CHCl_3$).

2-Bromo-1,1,4,4,5-pentamethoxy-1,4-dihydronaphthalene (9b). Compound **9b** was obtained from **7b** by method B (72% yield) at r.t., (2h) m.p. 130-132°C (from ethyl ether) ^{1}H NMR δ 7.45-6.97 (m, 3H, Ar), 6.81 (s, 1H, H_3), 3.92, 3.27 and 3.01 (3s, 15H, CH_3O); IR (KBr) 1675, 1600, 1480, 1280, 1100, 800; Anal. Calcd. for $C_{15}H_{19}BrO_5$: C, 50.14; H, 5.29. Found: C, 50.32; H, 5.26.

General procedure for preparation of quinone monoketals. Method C. Over a solution of quinone bisketal (1.2 mmol) in 25ml of acetone were added 10 mmol of anhydrous coppper (II) sulfate under an argon atmosphere. The resulting suspension was vigorously stirred. When all the starting material had been consumed (reaction times in brackets), the copper sulfate was separated by filtration. After solvent evaporation, the crude material was purified by chromathography or crystallization.

(S)-4,4-Dimethoxy-3-p-tolylsulfinylcyclohexa-2,5-dien-1-one (10a) and (S)-4,4-Dimethoxy-2-p-tolylsulfinylcyclohexa-2,5-dien-1-one (11a). Compounds **10a** and **11a** were obtained from **1a** by method C (3h) as a 5:1 mixture. **10a** was separated by flash chromatography (eluent 1:2 ethyl acetate-hexane). **10a**, 70% yield, m.p. 76-77°C (from hexane/ethyl ether) **10a** ^{1}H NMR δ 7.65 and 7.30 (AA'BB' tolyl system, 4H), 7.20 (d, 1H, J=2 Hz, H_2), 6.78 (d, 1H, J=10.2 Hz, H_5), 6.41 (dd, 1H, J=2.0 and 10.4 Hz, H_6), 3.42 and 2.59 (2s, 6H, CH_3O), 2.40 (s, 3H, CH_3Ar); ^{13}C NMR δ 183.2, 163.4, 143.0, 142.4, 131.6, 129.5, 128.2, 125.9, 125.7, 95.7, 51.5, 50.2, 21.3; IR (KBr) 1680, 1640, 1300, 1080, 1070, 840; MS m/z % 292 (M^+, 5), 262 (100), 247 (30), 213 (11), 153 (12), 139 (30), 125 (76), 107 (29), 91 (34), 79 (97), 65 (59), 53 (85); $[\alpha]_D$= +366° (c=1, $CHCl_3$). Anal. Calcd. for $C_{15}H_{16}SO_4$: C, 61.64; H, 5.48. Found: C, 61.43; H, 5.31. **11a** ^{1}H NMR δ 7.66 and 7.26 (AA'BB' tolyl system, 4H), 7.63 (d, 1H, J=3.2 Hz, H_3), 6.86 (dd, 1H, J=3.2 and 10.3 Hz, H_5), 6.17 (d, 1H, J=10.3 Hz, H_6), 3.45 and 3.40 (s, 6H, CH_3O), 2.37 (s, 3H, CH_3Ar).

4,4-Dimethoxy-2-p-tolylsulfenylcyclohexa-2,5-dien-1-one (10c). Compound **10c** was obtained from **1c** by method C (1h) as a yellow oil (84% yield) m.p. 80-82°C (from hexane) ^{1}H NMR δ 7.39 and 7.26 (AA'BB' tolyl system, 4H), 6.74 (d, 1H, J=8.2 Hz, H_5), 6.39 (dd, 1H, J=2.0 and 8.2 Hz, H_6), 5.65 (d, 1H, J=2.0 Hz, H_2), 3.36 (s, 6H, CH_3O), 2.40 (s, 3H, CH_3Ar); ^{13}C NMR δ 182.2, 164.4, 142.6, 140.7, 135.8, 132.4, 130.9, 123.6, 123.4, 95.8, 51.3 (2 C), 21.2; IR 1660, 1570, 1370, 1280, 1080, 820; MS m/z % 276 (M^+, 97), 261 (100), 230 (52), 201 (31), 147 (30), 128 (91), 99 (34), 83 (31).

4,4-Dimethoxy-3-p-tolylsulfonylcyclohexa-2,5-dien-1-one (10d) and 4,4-dimethoxy-2-p-tolylsulfonylcyclohexa-2,5-dien-1-one (11d). Compounds **10d** and **11d** were obtained from **1d** by method C (3h) as a 1:1 mixture (oil, 88% yield) ^{1}H NMR δ 8.30 and 7.30 (m, 10 H), 6.84 (dd, 1H, J=3.2 and 10.4 Hz, H_5-**11d**), 6.71 (d, 1H, J=10.3 Hz, H_5-**10d**), 6.42 (dd, 1H, J=3.1 and 10.3 Hz, H_6-**10d**), 6.17 (d, 1H, J=10.4 Hz, H_6-**11d**), 3.43 and 3.10 (2s, 12H, CH_3O), 2.45 and 2.42 (2s, 6H, CH_3Ar); ^{13} C NMR δ 184.0, 168.3, 153.6, 147.5, 145.2, 145.1, 144.7, 142.8, 140.2, 136.5, 135.9, 135.0, 130.7, 129.5, 129.4, 129.3, 129.2, 128.3, 99.0, 92.6, 51.3, 50.5, 21.7, 21.6; IR (film) 1740, 1680, 1600, 1460, 1320, 820.

(S)-4,4-Dimethoxy-3-p-tolylsulfinyl-1,4-dihydronaphthalene-1-one (12a). Compound **12a** was obtained from **6a** by method C (30min) as a yellow oil (82% yield) m.p. 110.5-112°C (from ethyl ether) ^{1}H NMR δ 8.13 (m, 1H, H_5), 7.76-7.31 (AA'BB' tolyl system, 4H), 7.8-7.5 (m, 3H, Ar), 7.57 (s, 1H, H_3), 3.20 and 2.40 (2s, 6H, CH_3O), 2.1 (s, 3H, CH_3Ar); ^{13}C NMR δ 181.5, 163.0, 142.3, 138.4, 138.3, 133.9, 132.0, 130.6, 129.7, 129.3, 126.3, 125.8, 125.7, 98.1, 51.8, 50.3, 21.1; IR (KBr) 1670, 1600, 1500, 1460, 1320, 1300, 1090, 1020; MS m/z % 342 (M^+, 5), 313 (21), 312 (100), 297 (72), 203 (37), 129 (39), 101 (40); $[\alpha]_D$= +127° ($CHCl_3$, c=1). Anal. calcd. for $C_{19}H_{18}SO_4$: C, 66,73; H, 5.3. Found: C,66.31; H,5.05.

(S)-4,4,8-Trimethoxy-3-p-tolylsulfinyl-1,4-dihydronaphthalen-1-one (12b). Compound **12b** was obtained from **6b** by method D (1h) as a yellow oil (90% yield) ^{1}H NMR δ 774 and 7.06 (AA'BB' tolyl system, 4H), 7.43 (s, 1H, H_3), 3.97, 3.19 and 2.07 (3s, 9H, CH_3O), 2.39 (s, 3H, CH_3Ar); ^{13}C NMR δ 181.6, 160.3, 158.9, 142.6, 141.7, 138.9, 135.4, 132.9, 129.7, 126.1, 121.4,

118.1, 113.1, 98.5, 56.2, 52.2, 50.6, 21.5; IR (film) 1655, 1580, 1460, 1255, 1080, 804; $[\alpha]_D$= +76° ($CHCl_3$, c=1).

(S)-4,4,5,8-Tetramethoxy-6-p-tolylsulfinyl-1,4-dihydronaphthalen-1-one (12c). A solution of 300 mg (0.67mmol) of **6c** in 10ml of acetone was stirred 5h. at r.t. After evaporation an orange solid was obtained (90% yield) m.p. 176-177°C (from methanol) ^1H NMR δ 7.71 (s, 1H, H_7), 7.62 and 7.22 (AA'BB' tolyl system, 4H), 6.66 and 6.47 (AB system, 2H, J=10.6 Hz, H_2 and H_3), 4.03, 4.00, 3.36 and 2.84 (4s, 12H, CH_3O), 2.36 (s, 3H, CH_3Ar); IR 1670, 1410, 1290, 1210, 1050, 820; MS m/z % 402 (M^+, 16), 385 (100), 371 (21), 354 (22), 293 (15), 217 (11), 139 (11); $[\alpha]_D$= -162° (c=1, $CHCl_3$).

General procedure for preparation of quinones. Method D. Over a solution of quinone bisketal (2 mmol) in 50 ml of acetone were added 4 mmol of dry p-toluenesulfonic acid under an argon atmosphere. The resulting solution was stirred for the time indicated in each case in brackets , concentrated, hydrolyzed with 50 ml of water and extracted with methylene chloride. The organic layer was dried and concentrated to dryness.

(S)-2-p-Tolylsulfinyl-1,4-benzoquinone (2a). Compound **2a**[9] was obtained from **1a** by method D IR (KBr) 1665, 1600, 1330, 1280, 1090, 1065; MS 246 (M^+, 24), 198 (27), 170 (16), 139 (79), 123 (17), 107 (20), 91 (33), 79 (39). Anal. Calcd. for $C_{13}H_{10}SO_3$: C, 63.41; H, 4.06; S,13.01. Found: C, 63.99; H, 4.42; S, 13.08.

2-p-tolylsulfenyl-1,4-benzoquinone (2c). Compound 2c was obtained from **1c** by method D (2h) as a red solid (87 %) m.p. 108-109°C (from methanol) (lit.[24] 107-109°C).

(S)-2-p-Tolylsulfinyl-1,4-naphthoquinone (13a). Compound **13a** was obtained from **6a** by method D (24h) as an orange solid (75% yield) m.p. 148-149.5°C (from ethanol) ^1H NMR δ 8.14-7.68 (m, 4H, Ar), 7.64 (s, 1H, H_3), 7.73-7.29 (AA'BB' tolyl system, 4H), 2.37 (s, 3H, CH_3Ar); ^{13}C NMR δ 182.6, 181.5, 157.1, 142.6, 138.5, 134.6, 134.1, 133.7, 132.0, 131.6, 130.1, 126.8, 126.4, 125.8, 21.3; IR (KBr) 1670, 1600, 1350, 1300, 1260, 1090, 1070, 1060; MS m/z % 298 (5), 297 (8), 296 (M^+, 31), 248 (35), 139 (80), 129 (44), 123 (46), 104 (39), 101 (100), 91 (67), 75 (67); $[\alpha]_D$= +214° (c=1, $CHCl_3$). Anal. Calcd. for $C_{17}H_{12}SO_3$: C, 68.92; H, 4.05. Found: C, 68.3; H, 4.45.

(S)-5-Methoxy-2-p-tolylsulfinyl-1,4-naphthoquinone (13b). Compound **13b** was obtained from **6b** by method D (24h) as a red solid (90% yield) m.p. 203-205°C (from ethanol) ^1H NMR δ 7.72 and 7.28 (AA'BB' tolyl system, 4H), 7.70-7.31 (m, 3H, Ar), 7.51 (s, 1H, H_3), 4.00 (s, 3H, CH_3O), 2.37 (s, 3H, CH_3Ar); IR (KBr) 1640, 1580, 1280, 1250, 1020, 780; $[\alpha]_D$= +84° (c=1, $CHCl_3$).

(S)-5,8-Dimethoxy-6-p-tolylsulfinyl-1,4-naphthoquinone (13c). Compound **13c** was obtained from **6c** by method D (2h) as a brown solid (82% yield) m.p. 170-172°C (from methanol) ^1H NMR δ 8.00 (s, 1H, H_7), 7.63 and 7.26 (AA'BB' tolyl system, 4H), 6.83 and 6.75 (AB system, 2H, J=10.3Hz, H_2 and H_3), 4.10 and 3.82 (2s, 6H, CH_3O), 2.36 (s, 3H, CH_3Ar); IR (KBr) 1660, 1550, 1460, 1240, 1050, 815; MS m/z % 356 (M^+, 25), 339 (100), 247 (34), 219 (17), 205 (13), 188 (34), 139 (22), 105 (37); $[\alpha]_D$= -140°C (c=0.1, $CHCl_3$).

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