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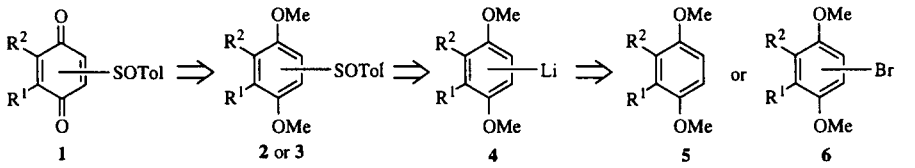
ortho-Directed metallation in the regiocontrolled synthesis of enantiopure 2- and/or 3-substituted (S)*S*-(*p*-tolylsulfinyl)-1,4-benzoquinones

M. Carmen Carreño*,* José L. García Ruano*, Miguel A. Toledo and Antonio Urbano
Departamento de Química Orgánica (C-I), Universidad Autónoma, Cantoblanco, 28049 Madrid, Spain

Abstract: Enantiomerically pure (S)*S*-(*p*-tolylsulfinyl)-1,4-benzoquinones with alkyl and methoxy substituents at C-2 and/or C-3 are synthesized by CAN oxidation of adequately substituted (S)*S*-(*p*-tolylsulfinyl)-1,4-dimethoxyaromatic precursors **2** or **3**. These compounds were obtained by *ortho*-directed metallation or bromo–metal exchange from the corresponding *p*-methoxyanisoles in a highly regiocontrolled manner. © 1997 Elsevier Science Ltd. All rights reserved.

Pursuing our interest in the Diels–Alder reactions of enantiomerically pure sulfinylbenzo-[1] and naphthoquinones,[2] we have pointed out two key features in the asymmetric synthesis of dihydronaphthoquinones and higher quinones. First, high asymmetric induction was always achieved in the cycloaddition process[1,2] and, second, the pyrolytic elimination of the sulfinyl group in the initially formed adduct took place spontaneously, giving access in a single operation to a new chiral quinonic system.[1c–d,2a,c] Several natural products such as diterpene quinones[3] could be synthesized by applying these tandem reactions, provided that adequately substituted sulfinyl-1,4-benzoquinones were accessible.

The method previously described by us[4] for the synthesis of simple (S)*S*-*p*-tolylsulfinylquinones relied on the controlled oxidation of aromatic sulfoxides **2** or **3** (Scheme 1) obtained by Andersen synthesis[5] using a lithium-1,4-dimethoxy derivative **4** and (S)*S*-menthyl-*p*-toluenesulfinate as sulfinylating agent. Lithium derivatives **4** are available both by direct hydrogen/metal interconversion of a dimethylhydroquinone **5** or by metal-exchange from a bromoderivative **6**. The presence of substituents R^1 and/or R^2 in **5** could determine the formation of two regioisomeric sulfoxides in the metallation/sulfinylation process. In order to achieve a regioselective synthesis, the controlled formation of the lithium derivative is essential. The regiocontrolled introduction of a bromine and the direct *ortho*-metallation of **5** might provide complementary procedures giving rise to both regioisomeric sulfoxides **2** or **3**, precursors of sulfinylquinones **1**.



Scheme 1.

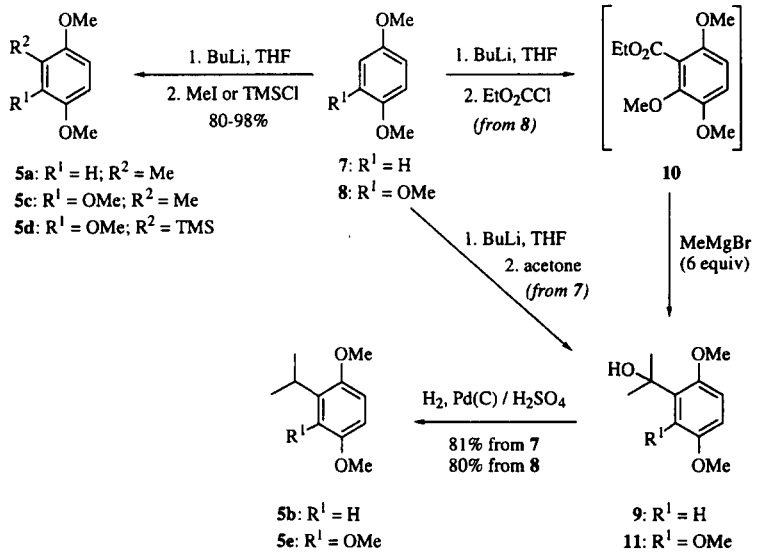
Although a large volume of data on aromatic *ortho*-metallation is available[6] no systematic reports dealing with 1,4-dimethoxybenzene derivatives bearing other substituents exist. The interest of this synthetic reaction was increased by the possibility of determining the effect of remote substituents on

* Corresponding author. Email: carmen.carrenno@uam.es

the regiochemistry of the metallation of *p*-dimethoxybenzene derivatives.[7–9] Several published studies devoted to the competition of substituents for site selectivity of metallation in substituted anisoles[10,11] revealed that regioselectivity was mainly controlled by the stronger *ortho*-directing neighboring group, although the nature of the reagent employed to effect the hydrogen–metal interconversion also influenced the site of metal introduction.[11] In the case of *p*-dimethoxybenzene derivatives, the *ortho*-directing power is the same and the differences observed could be due only to the presence of additional substituents. Although several findings have proved useful in controlling the site of metallation (use of different organometallic bases[12] or additives[7,13]), to our knowledge our study is the first where the effect of a remote substituent on *p*-methoxyanisole is pointed out. An essential piece of the work described herein establishes whether the substitution on the 1,4-dimethoxy aromatic system **5** could affect the regioselectivity of the *ortho*-metallation step. Additionally the syntheses of compounds **5** as well as the conditions used to obtain the quinones **1** are reported.

Results and discussion

The starting aromatic materials **5** required for the sulfinylation reactions are not easily accessible and were prepared from commercially available 1,4-dimethoxy and 1,2,4-trimethoxybenzenes, **7** and **8**, as depicted in Scheme 2.



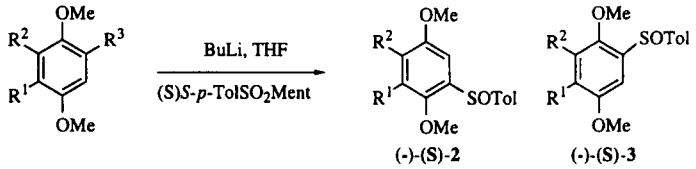
Scheme 2.

Thus, the sequential treatment of 1,4-dimethoxybenzene **7** with BuLi and MeI at rt afforded the 2-methyl derivative **5a**[14] in an almost quantitative yield. Similarly, when 1,2,4-trimethoxybenzene **8** was sequentially treated with BuLi and an electrophile (MeI or TMSCl) at room temperature, derivatives **5c**[15] and **5d**[7] were obtained in 95% and 80% yield respectively. As expected, metallation took place exclusively at the position mutually *ortho* to two methoxy groups.[7] The synthesis of the isopropyl derivative **5b** was achieved following a strategy previously described by Engler *et al.*[3a] for the analogous 1,3-dimethoxy substituted compound. Thus, when the lithiated intermediate derived from **7** was treated with acetone, the carbinol **9** was generated. After hydrogenation using 10% Pd on charcoal as catalyst in the presence of sulfuric acid, **9** was transformed into 2-isopropyl-1,4-dimethoxybenzene **5b**[16] in 81% yield.

A similar approach to 3-isopropyl-1,2,4-trimethoxybenzene **5e**[17] from **8** was unsuccessful. Thus, the sequence was modified by using ethylchloroformate instead of acetone giving rise to ester **10**,

which, without isolation, was treated with 6 equiv of MeMgBr affording the tertiary carbinol **11**. Compound **5e** could thus be obtained from **11** by hydrogenation in the presence of 10% Pd on charcoal and sulfuric acid in 80% overall yield from **8** (Scheme 2).

The corresponding bromoderivatives **6a–c** and **6e** (Scheme 3) had been cleanly obtained from aromatic compounds **5a–c** and **5e** respectively through a regioselective method recently reported by us,[18] using NBS in CH_3CN as brominating agent. Unfortunately, all attempts directed at obtaining the trimethylsilyl substituted derivative **6d** (R^1=TMS; R^2=OMe; R^3=Br) by this method resulted in the cleavage of the Ar–Si bond.



(-)-(S)-2 (-)-(S)-3

	R^1	R^2	R^3
5a:	H	Me	H
5b:	H	*i*-Pr	H
5c:	OMe	Me	H
5d:	OMe	TMS	H
5e:	OMe	*i*-Pr	H
6a:	Me	H	Br
6b:	*i*-Pr	H	Br
6c:	OMe	Me	Br
6e:	OMe	*i*-Pr	Br

	R^1	R^2
a:	H	Me
b:	H	*i*-Pr
c:	OMe	Me
d:	OMe	TMS
e:	OMe	*i*-Pr

Scheme 3.

With all aromatic precursors **5** and **6** in hand, we started the sulfinylation reactions to obtain the chiral aromatic sulfoxides **2** or **3**. The lithiations and subsequent reactions with (S)*S*-menthyl-*p*-toluenesulfinate were carried out under the experimental conditions collected in Scheme 3 and Table 1. The absolute configuration of the resulting substrates was assumed to be (S)*S* based on the well known stereochemical course of the Andersen-type reactions.[5]

Several aspects of the sulfinylation reactions presented in Table 1 are noteworthy. For all reactions of aromatic substrates bearing alkyl substituents (**5a–c** and **5e**) we used 2.5 equiv of BuLi because with

Table 1. Experimental conditions in sulfinylation of aromatic derivatives **5a–e**, **6a–c** and **6e**

Entry	Aromatic Compound	equiv BuLi	T (°C) (anion formation)	equiv *p*-$TolSO_2Ment$	T (°C) (*p*-$TolSO_2Ment$ addition)	Regioisomer Ratio **2** : **3**	Major Sulfoxide Isolated Yield (%)
1	**5a**[a]	2.5[c]	rt	2.5[f]	rt	[h]	---
2	**5b**[a]	2.5[c]	rt	2.5[f]	rt	85 : 15	**2b** (83)[i]
3	**5c**[a]	2.5[c,d]	rt	2.5[g]	-78	85 : 15	**2c** (55)
4	**5d**[a]	1.1[c]	rt	1.25[f]	rt	85 : 15	**2d** (78)
5	**5e**[a]	2.5[c]	rt	2.5[f]	rt	85 : 15	**2e** (75)
6	**6a**[b]	1.1[e]	-78	1.25[f]	rt	100 : 0	**2a** (60)
7	**6b**[b]	1.1[e]	-78	1.2[f]	rt	100 : 0	**2b** (68)
8	**6c**[b]	1.1[e]	-78	1.25[g]	-78	0 : 100	**3c** (73)
9	**6e**[b]	1.1[e]	-78	1.25[g]	-78	0 : 100	**3e** (66)

[a]0.70 M in THF; [b]0.25 M in THF; [c]BuLi/THF proportion: 1/1; [d]2.5 equiv of TMEDA; [e]BuLi/THFproportion: 1/3; [f]0.5 M in THF; [g]0.15 M in THF; [h]Mixture of **2a**:**3a**:**12**:**13**:**5a** (ratio 34:9:22:9:27); [i]65% of conversion by ^{1}H-NMR.

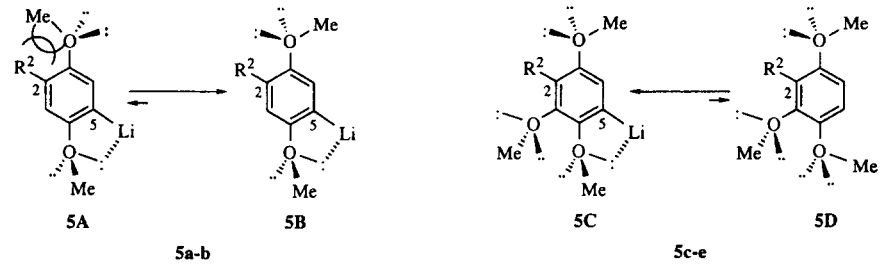


Figure 1.

stoichiometric amounts most of the starting material was recovered. Even with such excesses, reaction was not completed in the case of 2-methylhydroquinone dimethylether **5a**. After several experiments in different reaction conditions (changes of stoichiometry, temperature and concentration), the best results corresponded to those indicated in entry 1. Although the site selection was high (**2a/3a** 79:21), a complex crude mixture which included 25% of the starting material was formed. Moreover, a small amount of the product resulting from reaction on the mutually *ortho* position, 1,4-dimethoxy-2-methyl-3-*p*-tolylsulfinylbenzene **12** and from benzylic sulfinylation, 1,4-dimethoxy-2-(*p*-tolylsulfinylmethyl)-benzene **13**, were also detected. In the case of the isopropyl substituted derivative **5b** we obtained a 85:15 mixture of sulfoxides **2b** and **3b** with a 65% of conversion by ^{1}H-NMR (Table 1, entry 2). The yield of reaction with **5c** was increased up to 55% (Table 1, entry 3) by addition of 2.5 equiv of TMEDA.[7,13] The best results were achieved working in concentrated solutions from **5a–e** (0.7 M in THF) at room temperature. All substrates **5c–e** bearing a third methoxy substituent in the ring also evolved in a highly regioselective manner yielding a *ca.* 85:15 mixture of sulfoxides **2c–e** and **3c–e** (Table 1, entries 3–5) where the major component **2** could be separated pure by flash chromatography in 55–78% yield.

Sulfoxides **2a–b** were obtained as sole products starting from bromoderivatives **6a–b** (Table 1, entries 6–7). The sequence metal–halogen exchange and (S)*S*-menthyl-*p*-toluenesulfinate reaction of the resulting lithium anions prepared from 0.25 M solutions of **6a–b** in THF at −78°C, allowed the isolation of **2a–b** in 60 and 68% yields, respectively. The regioisomeric sulfoxides **3c** and **3e** were obtained from compounds **6c** and **6e** (Table 1, entries 8 and 9) in 73 and 66% yield respectively.

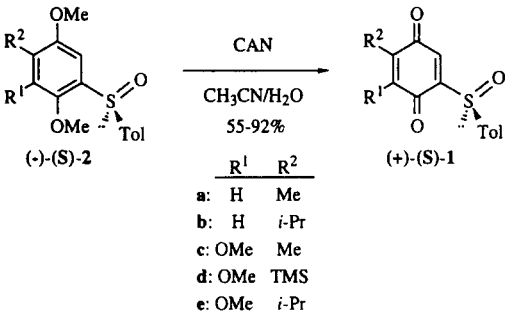
The structural assignment of both types of compounds **2** and **3** was based not only in their synthetic origin but in their ^{1}H-NMR parameters, mainly the chemical shifts of the hydrogen situated in the vicinal position to the sulfinyl group which appeared always slightly more shielded in isomers **2** due to the effect of the *p*-methoxy substituent (see the Experimental section).

The results obtained in the metallation of aromatic derivatives **5** deserve several comments. The regioselectivity observed for **5a–e** can be explained considering the influence of the remote alkyl group at C-2 on the anion formation. The minor *ortho*-lithiation at C-6[19] could be a consequence of the steric effect of R^2 which favors the conformation represented in Figure 1 as **5B**. In this major rotamer, the methyl group of the OMe at C-1 is hindering the coordination of the metal difficulting the lithiation at C-6 (major reaction at C-5).

Although the presence of a methoxy substituent at C-3 in **5c–e** could hinder the lithiation at C-5 in a similar fashion (see rotamer **5D**), the identical regioisomer ratio obtained (85:15, see Table 1) suggests that is not the case. Probably the gauche repulsive effects between both OMe groups at C-3 and C-4 are able to shift the conformational equilibrium toward rotamer **5C** where one of the lone electron pairs of the C-4 oxygen is more accesible for *ortho*-lithiation at C-5. Moreover, the acidic character of H-5 is enhanced by the −I effect[20] of the OMe group at C-3 and that of H-6 decreased by its +M effect.

The last step in our synthetic plan to enantiomerically pure substituted sulfinyl quinones corresponded to the controlled oxidative demethylation of the *p*-methoxyanisoles **2** and **3**. Thus, the oxidation

of sulfoxides **2a–e** was effectively carried out with cerium ammonium nitrate (CAN) to give the corresponding quinones **1a–e** in 55 to 90% yields (Scheme 4). Nevertheless, the same reaction on sulfoxides **3c** and **3e** bearing a methoxy substituent at the *para* position with respect to the sulfinyl group was unsuccessful giving rise to complex reaction mixtures. The use of other oxidizing agents such as AgO[21] in the reactions with **3c** and **3e** allowed the detection of the quinones in the ^{1}H-NMR spectrum of the crude reaction mixture but all attempts to isolate them pure were unsuccessful.



Scheme 4.

In conclusion, the results of this work allowed us to establish the ability of a remote substituent to direct the metallation of an asymmetrically substituted *p*-methoxyanisole. The sequence *ortho*-directed metallation/sulfinylation allowed the obtention of adequately substituted bis-aromatic sulfoxides en route to enantiomerically pure sulfinylquinones. The complementary route involved the bromination and sulfinylation of the same precursors.

Experimental section

Melting points were obtained in open capillary tubes and are uncorrected. IR spectra are given in cm^{-1}. ^{1}H- and ^{13}C-NMR spectra were recorded at 200.1 and 50.3 MHz in $CDCl_3$. All reactions were monitored by thin layer chromatography that 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. Apparatuses for inert atmosphere experiments were dried by flaming in a stream of dry argon. Dry THF was distilled from sodium/benzophenone ketyl. For routine workup, hydrolyses were carried out with H_2O, extractions with CH_2Cl_2, and solvent drying with Na_2SO_4.

General procedure for lithiations of hydroquinone dimethyl ethers. Method A

A solution of the aromatic compound **7** or **8** (25 mmol) in dry THF (20 mL) was added dropwise to a solution of BuLi 2.5 M (11 mL, 27.5 mmol) in dry THF (12 mL) at rt under argon and stirred for 1 h. The corresponding electrophile was added at the temperature required and after 1 h at rt the mixture was quenched with saturated aqueous NH_4Cl solution. After workup, the crude product was obtained and purified as indicated in each case.

General procedure for hydrogenation reactions. Method B

A mixture of the aromatic alcohol **9** or **11** (17.7 mmol), 10% palladium on charcoal (400 mg) and concentrated sulfuric acid (20 drops) in EtOAc (50 mL) was hydrogenated at 1 atm for 24 h. After that time, the reaction mixture was filtered through Celite, and the solvent evaporated. The residue was dissolved in ethyl ether and washed with saturated aqueous $NaHCO_3$ solution. After workup, the crude product was obtained.

General procedure for sulfinylation reactions. Method C

To a solution of BuLi 2.5 M in dry THF at the desired temperature (see Table 1 for reaction conditions) was added dropwise a solution of the aromatic compound **5** or **6** in dry THF under argon

and stirred for 1 h. The reaction mixture was added via cannula to a vigorously stirred solution of (S)*S*-menthyl-*p*-toluenesulfinate in dry THF. After 2 h, the mixture was hydrolyzed with saturated aqueous NH_4Cl solution. After workup, the crude product was obtained (see Table 1 for yields).

General procedure for oxidative demethylation with cerium ammonium nitrate. Method D

An aqueous solution (5 mL) of CAN (1.92 g, 3.5 mmol) was added to a solution of the corresponding aromatic sulfinyl compound **2** (1 mmol) in CH_3CN (5 mL) at rt. After stirring for 10 min CH_3CN was evaporated and the mixture extracted with CH_2Cl_2. After workup, the crude product was obtained.

1,4-Dimethoxy-2-methylbenzene ***5a***[14]

Compound **5a** was obtained from **7** following method A by adding MeI (6.23 mL, 100 mmol) via syringe at −78°C in nearly quantitative yield without further purification: ^{1}H-NMR δ 6.80–6.68 (3H, m), 3.83 and 3.79 (6H, 2s), 2.25 (3H, s).

1,4-Dimethoxy-2-isopropylbenzene ***5b***[16]

Compound **5b** was obtained from **7** following method A by adding a solution of acetone (7.34 mL, 100 mmol) in THF (27 mL) via cannula at rt. After workup the isolated alcohol **8** was treated by method B to give compound **5b** in 81% overall yield after flash chromatography (eluent EtOAc:hexane 1:80): ^{1}H-NMR δ 6.85 (1H, d, *J*=3.3 Hz), 6.82 (1H, d, *J*=8.9 Hz), 6.71 (1H, dd, *J*=3.0 and 8.8 Hz), 3.82 and 3.81 (6H, 2s), 3.34 (1H, sept, *J*=6.9 Hz), 1.24 (6H, d, *J*=6.8 Hz).

2-Methyl-1,3,4-trimethoxybenzene ***5c***[15]

Compound **5c** was obtained from **8** following method A by adding MeI (6.23 mL, 100 mmol) via syringe at −78°C in 95% yield without further purification: ^{1}H-NMR δ 6.69 and 6.53 (2H, AB system, *J*=8.9 Hz), 3.81, 3.79 and 3.77 (9H, 3s), 2.15 (3H, s).

(2,3,6-Trimethoxyphenyl)-trimethylsilane ***5d***

Compound **5d** was obtained as previously described:[7] ^{1}H-NMR δ 6.86 and 6.50 (2H, AB system, *J*=9.0 Hz), 3.77 and 3.70 (9H, 3s), 0.31 (9H, s).

2-Isopropyl-1,3,4-trimethoxybenzene ***5e***[17]

Compound **5e** was obtained from **8** following method A by addition of ethylchloroformate (2.87 mL, 30 mmol) in THF (10 mL) via cannula at 0°C. After stirring for 1 h at rt, a solution of MeMgBr 3.0 M in ether (50 mL, 150 mmol, 6 equiv) was added via syringe at 0°C. The mixture was allowed to reach rt, stirred for 1 h, and after workup the isolated alcohol **10** was treated by method B to give compound **5e** in an 80% overall yield after flash chromatography (eluent EtOAc:hexane 1:30): ^{1}H-NMR δ 6.69 and 6.55 (2H, AB system, *J*=9.0 Hz), 3.81, 3.80 and 3.76 (9H, 3s), 3.54 (1H, sept, *J*=7.1 Hz), 1.31 (6H, d, *J*=7.1 Hz).

*(S)S-1,4-Dimethoxy-2-methyl-5-*p*-tolylsulfinylbenzene* ***2a***

Compound **2a** was obtained from **6a** following method C after flash chromatography (eluent EtOAc:hexane 1:3): mp 107.5–108.5°C (hexane); $[\alpha]^{20}_D$=−28 (*c* 1, $CHCl_3$); IR ($CHCl_3$) 2960, 1485, 1465, 1385, 1375, 1040; ^{1}H-NMR δ 7.58 and 7.21 (4H, AA′ BB′ system), 7.38 (1H, s), 6.68 (1H, s), 3.87 and 3.72 (6H, 2s), 2.34 (3H, s), 2.22 (3H, s); ^{13}C-NMR δ 152.5, 149.0, 142.5, 141.0, 130.6, 130.2, 129.5, 125.1, 114.3, 105.3, 56.1, 55.9, 21.2, 16.4; Anal. Calcd. for $C_{16}H_{18}O_3S$: C, 66.18; H, 6.25; S, 11.04. Found: C, 66.08; H, 6.31; S, 11.36.

*(S)S-1,4-Dimethoxy-2-isopropyl-5-*p*-tolylsulfinylbenzene* ***2b***

Compound **2b** was obtained from **5b** or **6b** following method C after flash chromatography (eluent EtOAc:hexane 1:6): mp 99–100°C (hexane); $[\alpha]^{20}_D$=−41 (*c* 1, $CHCl_3$); IR ($CHCl_3$) 2960, 1485, 1460, 1180, 1035; ^{1}H-NMR δ 7.60 and 7.22 (4H, AA′ BB′ system), 7.39 (1H, s), 6.73 (1H, s), 3.87 and 3.75 (6H, 2s), 3.31 (1H, sept, *J*=6.9 Hz), 2.35 (3H, s), 1.19 and 1.17 (6H, 2d, *J*=6.9 Hz); ^{13}C-

NMR δ 151.6, 149.4, 142.5, 140.9, 130.0, 129.4 (2 C), 125.0, 109.9, 105.8, 56.0, 26.9, 22.4, 22.3, 21.2; Anal. Calcd. for $C_{18}H_{22}O_3S$: C, 67.89; H, 6.96; S, 10.07. Found: C, 67.85; H, 7.07; S, 10.55.

*(S)S-2-Methyl-5-*p*-tolylsulfinyl-1,3,4-trimethoxybenzene* **2c**

Compound **2c** was obtained from **5c** following method C after flash chromatography (eluent EtOAc:hexane 1:2): mp 56.5–57.5°C (hexane); $[\alpha]^{20}_D$=−37 (*c* 1, $CHCl_3$); IR ($CHCl_3$) 2940, 1465, 1400, 1130, 1035; ^{1}H-NMR δ 7.61 and 7.24 (4H, AA′ BB′ system), 7.14 (1H, s), 3.88, 3.76 and 3.63 (9H, 3s), 2.36 (3H, s), 2.13 (3H, s); ^{13}C-NMR δ 154.8, 151.4, 142.8, 142.7, 141.4, 135.3, 129.7, 125.5, 124.0, 100.0, 60.4, 60.2, 55.9, 21.3, 9.1; Anal. Calcd. for $C_{17}H_{20}O_4S$: C, 63.73; H, 6.29; S, 10.01. Found: C, 63.51; H, 6.33; S, 10.35.

*(S)S-5-*p*-Tolylsulfinyl-2-trimethylsilyl-1,3,4-trimethoxybenzene* **2d**

Compound **2d** was obtained from **5d** following method C after flash chromatography (eluent EtOAc:hexane 1:7): mp 60–61°C (hexane); $[\alpha]^{20}_D$=−9.1 (*c* 1.6, $CHCl_3$); IR ($CHCl_3$) 2940, 1465, 1400, 1130, 1035; ^{1}H-NMR δ 7.62 and 7.25 (4H, AA′ BB′ system), 7.09 (1H, s), 3.80, 3.72 and 3.59 (9H, 3s), 2.36 (3H, s), 0.28 (9H, s); ^{13}C-NMR δ 160.7, 157.7, 142.3, 142.2, 141.1, 140.5, 129.5, 125.2, 123.9, 99.8, 60.0, 59.6, 55.3, 21.0, 0.8.

*(S)S-2-Isopropyl-5-*p*-tolylsulfinyl-1,3,4-trimethoxybenzene* **2e**

Compound **2e** was obtained from **5e** following method C after flash chromatography (eluent EtOAc:hexane 1:3): $[\alpha]^{20}_D$=−11 (*c* 1.2, $CHCl_3$); IR ($CHCl_3$) 2940, 1455, 1400, 1345, 1125, 1020; ^{1}H-NMR δ 7.62 and 7.25 (4H, AA′ BB′ system), 7.10 (1H, s), 3.84, 3.76 and 3.64 (9H, 3s), 3.49 (1H, sept, *J*=7.1 Hz), 2.36 (3H, s), 1.27 (6H, d, *J*=7.1 Hz); ^{13}C-NMR δ 155.5, 143.2, 142.7, 141.4, 135.6, 133.6, 129.8, 125.5, 124.8, 101.1, 60.7, 60.3, 55.9, 25.3, 21.4, 20.8.

*(S)S-3-Methyl-5-*p*-tolylsulfinyl-1,2,4-trimethoxybenzene* **3c**

Compound **3c** was obtained from **6c** following method C after flash chromatography (eluent EtOAc:hexane 1:2): $[\alpha]^{20}_D$=−33 (*c* 1.1, $CHCl_3$); IR ($CHCl_3$) 2940, 1470, 1405, 1100, 1085, 1035, 1005; ^{1}H-NMR δ 7.60 and 7.24 (4H, AA′ BB′ system), 7.26 (1H, s), 3.89, 3.80 and 3.74 (9H, 3s). 2.35 (3H, s), 2.16 (3H, s); ^{13}C-NMR δ 150.1, 149.9, 148.5, 142.3, 141.1, 132.4, 129.5, 125.8, 124.8, 104.1, 61.0, 59.9, 55.8, 21.0, 9.1.

*(S)S-3-Isopropyl-5-*p*-tolylsulfinyl-1,2,4-trimethoxybenzene* **3e**

Compound **3e** was obtained from **6e** following method C after flash chromatography (eluent EtOAc:hexane 1:3): $[\alpha]^{20}_D$=−55 (*c* 0.9, $CHCl_3$); IR ($CHCl_3$) 2940, 1465, 1420, 1080, 1035; ^{1}H-NMR δ 7.59 and 7.24 (4H, AA′ BB′ system), 7.25 (1H, s), 3.87, 3.86 and 3.78 (9H, 3s), 3.31 (1H, sept, *J*=7.0 Hz) 2.36 (3H, s) 1.35 and 1.26 (6H, 2d, *J*=7.0 Hz); ^{13}C-NMR δ 151.2, 150.6, 148.0, 142.5, 141.0, 135.4, 132.6, 129.6, 124.8, 104.8, 62.5, 60.4, 55.7, 25.5, 21.4, 21.1.

*(S)S-2-Methyl-5-*p*-tolylsulfinyl-1,4-benzoquinone* **1a**

Compound **1a** was obtained from **2a** following method D in 92% crude yield: mp 145–146°C (ethyl ether); $[\alpha]^{20}_D$=+822 (*c* 1, $CHCl_3$); IR ($CHCl_3$) 2950, 1660, 1600, 1325, 1080, 1050; ^{1}H-NMR δ 7.66 and 7.29 (4H, AA′ BB′ system), 7.39 (1H, s), 6.55 (1H, q, *J*=1.6 Hz), 2.38 (3H, s), 2.06 (3H, d, *J*=1.6 Hz); ^{13}C-NMR δ 185.6, 183.6, 154.9, 147.9, 138.3, 133.1, 131.5, 130.1, 125.7, 21.4, 15.6; Anal. Calcd. for $C_{14}H_{12}O_3S$: C, 64.60; H, 4.65; S, 12.32. Found: C, 64.47; H, 4.84; S, 12.37.

*(S)S-2-Isopropyl-5-*p*-tolylsulfinyl-1,4-benzoquinone* **1b**

Compound **1b** was obtained from **2b** following method D in 90% crude yield: mp 113.5–114.5°C (hexane); $[\alpha]^{20}_D$=+718 (*c* 1, $CHCl_3$); IR ($CHCl_3$) 2965, 1655, 1595, 1330, 1080, 1055, 1030; ^{1}H-NMR δ 7.67 and 7.30 (4H, AA′ BB′ system), 7.37 (1H, s), 6.46 (1H, d, *J*=1.1 Hz), 3.04 (1H, d sept, *J*=1.1 and 6.8 Hz), 2.39 (3H, s), 1.13 and 1.11 (6H, 2d, *J*=6.8 Hz); ^{13}C-NMR δ 184.9, 184.0, 156.2,

154.2, 142.5, 138.3, 131.9, 130.2, 130.0, 125.6, 26.7, 21.3, 21.0; Anal. Calcd. for $C_{16}H_{16}O_3S$: C, 66.64; H, 5.59; S, 11.12. Found: C, 66.46; H, 5.77; S, 11.24.

*(S)S-3-Methoxy-2-methyl-5-*p*-tolylsulfinyl-1,4-benzoquinone* **1c**

Compound **1c** was obtained from **2c** following method D in 73% yield after flash chromatography (eluent EtOAc:hexane 1:4): mp 107.5–108.5°C (hexane); $[\alpha]^{20}_D$=+253 (*c* 0.35, $CHCl_3$); IR ($CHCl_3$) 2940, 1660, 1650, 1595, 1270, 1140; ^{1}H-NMR δ 7.66 and 7.29 (4H, AA′ BB′ system), 7.32 (1H, s), 3.93 (3H, s), 2.39 (3H, s), 1.94 (3H, s); ^{13}C-NMR δ 185.5, 179.7, 155.6, 153.3, 142.8, 141.4, 138.6, 131.9, 130.2, 125.7, 60.9, 21.4, 8.9; Anal. Calcd. for $C_{15}H_{14}O_4S$: C, 62.05; H, 4.88; S, 11.04. Found: C, 62.15; H, 5.13; S, 11.06.

*(S)S-3-Methoxy-5-*p*-tolylsulfinyl-2-trimethylsilyl-1,4-benzoquinone* **1d**

Compound **1d** was obtained from **2d** following method D in 55% yield after flash chromatography (eluent EtOAc:hexane 1:5): $[\alpha]^{20}_D$=+167 (*c* 0.6, $CHCl_3$); IR ($CHCl_3$) 2940, 1660, 1630, 1255, 1115, 845; ^{1}H-NMR δ 7.65 and 7.28 (4H, AA′ BB′ system), 7.26 (1H, s), 3.87 (3H, s), 2.37 (3H, s), 0.22 (9H, s); ^{13}C-NMR δ 189.4, 179.5, 164.5, 153.1, 142.8, 138.5, 133.9, 131.9, 130.2, 125.7, 61.0, 21.4, 0.4.

*(S)S-2-Isopropyl-3-methoxy-5-*p*-tolylsulfinyl-1,4-benzoquinone* **1e**

Compound **1e** was obtained from **2e** following method D in 70% yield after flash chromatography (eluent EtOAc:hexane 1:4): $[\alpha]^{20}_D$=+184 (*c* 0.4, $CHCl_3$); IR ($CHCl_3$) 2955, 1665, 1645, 1590, 1465, 1270; ^{1}H-NMR δ 7.67 and 7.30 (4H, AA′ BB′ system), 7.25 (1H, s), 3.89 (3H, s), 3.21 (1H, sept, *J*=7.0 Hz), 2.39 (3H, s), 1.19 and 1.18 (6H, 2d, *J*=7.0 Hz); ^{13}C-NMR δ 185.2, 180.2, 155.7, 152.6, 142.6, 138.8, 138.4, 132.3, 130.0, 125.5, 61.0, 24.7, 21.3, 20.1; Anal. Calcd. for $C_{17}H_{18}O_4S$: C, 64.13; H, 5.70; S, 10.05. Found: C, 63.91; H, 5.74; S, 10.09.

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