Chelation-assisted nucleophilic aromatic substitution of 2-sulfonyl-substituted 1-methoxynaphthalenes by Grignard reagents: factors determining the activating ability of the 2-sulfonyl substituents [1,2]

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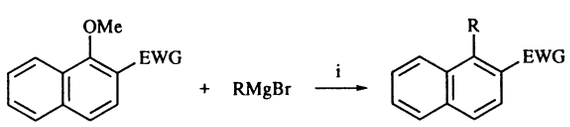
1-Methoxynaphthalenes 3–7 having sulfonyl substituents SO_2R (R = Me, Pr^i, Bu^t, OPh and $N[CH_2]_3CH_2$) at the 2-position undergo displacement of the 1-methoxy group on treatment with the Grignard reagents 8a–d by a chelation-assisted conjugate addition–elimination process. Activating ability of these sulfonyl groups for the apparent nucleophilic aromatic substitution is compared with that of an ester group, isopropoxycarbonyl, and a sulfinyl group, *tert*-butylsulfinyl, and found to fall roughly in the order $CO_2Pr^i > SO_2OPh > SO_2N[CH_2]_3CH_2 \geqslant SO_2Alkyl \gg SOBu^t$. The activation order is interpreted as being the outcome of a balance between the electron-withdrawing strength of the 2-substituents and the steric hindrance caused by the Grignard reagents 8a–d on approach to the substrates 1-methoxynaphthalenes 1–7. Asymmetric binaphthyl coupling by reaction of the chiral sulfamoyl-substituted naphthalene 20 with 1-naphthyl Grignard reagents 8d,e is also reported.

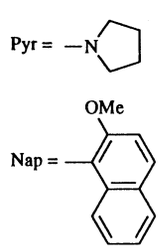
It is well-known that nucleophilic aromatic substitution (S_NAr) generally requires the presence of strong electron-withdrawing groups in positions *ortho* and/or *para* to a leaving group on the aromatic ring undergoing the reaction.[3,4] Of this class of displacement reactions, nucleophilic cleavage of an aryl–oxygen bond is particularly difficult because of the poor nucleofugacity of an alkoxy moiety as well as the resonance-stabilized partial double-bond character of the aryl–oxygen linkage.[5] In this context, the Meyers reaction is unique in that an oxazoline function, which would not be considered as strongly electron-withdrawing in the conventional S_NAr reaction, highly activates an *ortho*-alkoxy or fluoro group to undergo displacement by nucleophilic reagents that are possessed of metal ions capable of ligation to the oxazoline moiety.[6] This apparent S_NAr process has been considered to occur by strong coordination of the metal cations of the nucleophiles to the oxazolinyl nitrogen to facilitate a chelation-assisted conjugate addition of the anionic species to the *ipso*-carbon bearing the leaving group, followed by elimination of the metal alkoxide or fluoride.[6] The versatility of the Meyers reaction for regioselective as well as regiospecific introduction of a substituent into the relevant aromatic nucleus, particularly an aryl moiety for the construction of the biaryl structure, has been amply documented.[7,8]

On the other hand, we ourselves have demonstrated that an ester group can advantageously take the place of the oxazolinyl functionality to give a similar chelation-assisted S_NAr reaction;[9] the well-known 1,2-addition of the nucleophilic reagents to the ester carbonyl can essentially be suppressed by choice of an ester group of appropriate steric bulk.[10] Rational consideration of the mechanism of these unconventional S_NAr reactions has led us to use a diphenylphosphinoyl group as the activator for displacement of the 1-methoxy group from 2-diphenylphosphinoyl-1-methoxynaphthalene by *C*-, *N*- and *O*-centred nucleophiles.[11] As an extension of our efforts to develop other activating substituents, we considered the possibility of using oxygenated sulfur functional groups both because of the well-known ligating and electron-withdrawing ability of sulfinyl and sulfonyl groups as well as the potential importance in synthetic organic chemistry of such sulfur-containing functional groups.[12] In this respect, it should be mentioned here that sulfinyl and sulfonyl substituents have been reported to act as a nucleofuge in various types of S_NAr processes rather than as an activator for an *ortho*-alkoxy displacement.[3,12,13] Of particular interest in this respect are the quite recent reports by Baker and co-workers[14,15] dealing with the oxazoline- or ester-mediated displacement of sulfinyl groups from aryl sulfoxides by Grignard reagents and by Clayden *et al.*[16] dealing with the nickel-catalysed displacement of alkylsulfonyl groups by Grignard reagents. Herein, we report what we believe to be the first example of nucleophilic cleavage of the aryl–oxygen linkage of 1-methoxy-2-sulfonylnaphthalenes **3**–**7** by Grignard reagents **8a**–**d** (Scheme 1).[1,2]



1–7 **8** **9–15**

	EWG	8–15	R
1, 9	CO_2Pr^i	a	Bu
2, 10	$SOBu^t$	b	Pr^i
3, 11	SO_2Bu^t	c	Ph
4, 12	SO_2Pr^i	d	Nap
5, 13	SO_2Me		
6, 14	SO_2OPh		
7, 15	SO_2Pyr		



Scheme 1 *Reagents:* i, Et_2O–PhH

Results and discussion

Initially, the activating ability of an ester group, 2-isopropoxycarbonyl, was compared with that of a 2-sulfinyl or 2-sulfonyl substituent. Considering the high tendency for deprotonation of an α-hydrogen from these sulfur functional groups by a base (including organometallic reagents), the *tert*-butylsulfinyl and -sulfonyl groups were chosen as the 2-substituent of 1-methoxynaphthalene. Thus, the sulfinyl **2** and sulfonyl **3** sub-

Table 1 The S_NAr reaction of 2-EWG-substituted 1-methoxynaphthalenes **1**–**7** with Grignard reagent **8**

Entry	Substrate	Nucleophile (equiv.)	*t*/h	Product	Yield (%)
1	**1**	**8a** (1.4)	1[a]	**9a**	97
2	**1**	**8b** (1.4)	1[a]	**9b**	88
3	**1**	**8c** (1.4)	1[a]	**9c**	84[h]
4	**1**	**8d** (1.8)	3[a] ⟶ 2[b]	**9d**	87[i]
5	**2**	**8a** (2.0)	76[b]	**10a**	16
6	**2**	**8b** (2.0)	19[b]	**10b**	0
7	**2**	**8d** (2.0)	30[b]	**10d**	0
8	**2**	PhLi (2.0)	12[c]	**10c**	0
9	**3**	**8a** (2.0)	3[a]	**11a**	72
10	**3**	**8b** (2.0)	6.5[a]	**11b**	71
11	**3**	**8c** (2.0)	2[a]	**11c**	71
12	**3**	**8d** (2.0)	2[b]	**11d**	52
13	**3**	PhLi (2.0)	3[d]	**11c**	65
14	**4**	**8b** (2.0)	1[a]	**12b**[e]	91
15	**4**	**8c** (2.0)	1[a]	**12c**[e]	89
16	**4**	**8d** (2.0)	3[a]	**12d**[e]	26[j]
17	**5**	**8b** (2.0)	1[a]	[$^2H_1$]-**13b**[e,f]	79
18	**5**	**8c** (2.0)	1[a]	[$^2H_1$]-**13c**[e,g]	92
19	**5**	**8d** (2.0)	3[a]	**13d**[e]	0
20	**6**	**8a** (2.0)	2[a]	**14a**	92
21	**6**	**8b** (2.0)	1[a]	**14b**	97
22	**6**	**8c** (2.0)	3[a]	**14c**	95
23	**6**	**8d** (2.0)	6[a]	**14d**	76
24	**7**	**8a** (2.0)	3[a]	**15a**	80
25	**7**	**8b** (2.0)	1.5[a]	**15b**	99
26	**7**	**8c** (2.0)	5[a]	**15c**	83
27	**7**	**8d** (3.0)	36[a] ⟶ 6[b]	**15d**	42

[a] At room temp. [b] At reflux. [c] At room temp. in toluene. [d] At −46 °C in toluene. [e] Quenched with [$^2H_4$]acetic acid. [f] Deuteriated in 92 atom%. [g] Deuteriated in 91 atom%. [h] Data from ref. 10(*c*). [i] Data from ref. 9. [j] The substrate **4** was recovered in 53% yield.

strates were prepared from 1-methoxynaphthalene using conventional chemistry, which involved lithiation with butyllithium, reaction with di-*tert*-butyl disulfide, and then selective oxidation with hydrogen peroxide in acetic acid at room temperature and at an elevated temperature (90 °C), respectively.[16,17]

The 1-methoxynaphthalene substrates **1**–**3** were treated with Grignard reagents **8** (1.4–2.0 mol equiv.) in diethyl ether–benzene at room temperature or, if necessary, at reflux for the time indicated in Table 1. The 1-methoxy displacement products **9**–**11** were obtained after purification by column chromatography. Entries 1–13 in Table 1 compare the reactions of the sulfoxide **2** and the sulfone **3** with those of 2-isopropoxycarbonyl-1-methoxynaphthalene **1**. It can be seen that of the three, the ester function is the most effective activator; the ester **1** reacted quite readily with any of the four Grignard reagents **8a**–**d** of varying steric bulk affording the substitution products **9a**–**d** in excellent yields (entries 1–4). Comparison of the results in entries 1–13 indicates that on the basis of the yields of the substitution products **9**–**11** and the reaction conditions applied, the ester **1** is more reactive than the sulfone **3**; thus, the sterically undemanding Grignard reagents **8a**–**c** reacted smoothly with the sulfone **3** to give the displacement products **11a**–**c** in rather good yields (entries 9–11). However, in the reaction of the bulky Grignard reagent **8d**, it was necessary to heat the reaction mixture at reflux to induce 1-methoxy displacement from the sulfone **3** to give the product **11d** in a moderate yield (entry 12). Although it is known that a *tert*-butylsulfonyl group is an excellent director for *ortho*-lithiation by organolithium reagents,[18] phenyllithium could also displace the 1-methoxy group from the sulfone **3** in toluene at a low temperature (entry 13).

The tabulated results show that the sulfoxide **2** was far less reactive than the sulfone **3** to the Grignard nucleophiles **8a**–**d**, only the sterically small butylmagnesium bromide **8a** being able to induce displacement under rather forcing reaction conditions to give the product **10a** in poor yield (entry 5). No detectable amounts of the S_NAr products were found in the reactions of **2** with the Grignard reagents **8b**,**d** even after prolonged heating at reflux, while large quantities of unreacted **2** (entries 6 and 7) remained. Even phenyllithium failed to displace the 1-methoxy group from the sulfoxide **2** (entry 8). In this context, it should be noted that Pyne *et al.* reported successful generation of α-carbanions from 1-alkylsulfinyl-2-methoxynaphthalenes by treatment with butyllithium in tetrahydrofuran, without mentioning the displacement of the 2-methoxy substituent by the butyl carbanion.[19] From these observations a sulfinyl group seems, in general, to be insufficiently active to promote the S_NAr displacement of the *ortho*-alkoxy substituent by organomagnesium or -lithium nucleophiles, although it has been well-demonstrated that sulfoxides undergo many useful organometal-mediated transformations such as ligand coupling or ligand exchange,[13,20] directed *ortho*-metallation[21] and the like.[12]

The electron-withdrawing power of an ester, sulfinyl and sulfonyl moiety would be expected to be in the order $SO_2R \gg SOR > CO_2R$ taking into consideration the activating ability of the classical, so-called Meisenheimer-type S_NAr reactions and/or the Hammet σ values.[3,4] Therefore, it is obvious that electronic effects do not solely determine the reactivity order of the 2-substituted 1-methoxynaphthalenes to be **1** > **3** ≫ **2**. On the contrary, the sequence may be interpreted as indicating that 1-methoxy displacement from the sulfur compounds **2** and **3** also proceeds by a chelation-assisted addition–elimination mechanism similar to those proposed for the oxazoline- and ester-mediated reactions.[6,9] Based on this mechanism, steric effects are likely to play an important role in determining the reactivity of the substrate 1-methoxynaphthalenes **2** and **3**; a molecular modelling study indicates that the 2-*tert*-butylsulfonyl moiety of sulfone **3** imposes more severe steric hindrance than the ester **1** for the Grignard reagents **8** to coordinate to the sulfone **3** to form the chelated complex **17a** as illustrated in Fig. 1. As the steric bulk of the Grignard reagents **8** increases, the chelated complexes **17a** become more difficult to form and the 1-methoxy displacement reaction should be either slow or unable to occur. The importance of this kind of complexation between an organometallic nucleophile and substrate alkoxy arenes has been demonstrated by Meyers *et al.* in the oxazoline-mediated methoxy displace-

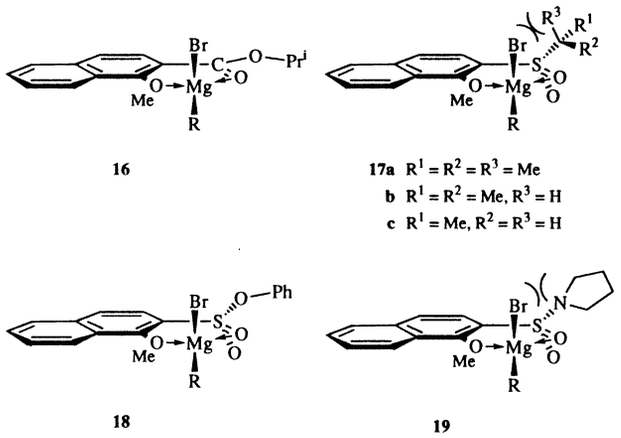


Fig. 1 Schematic views of chelated complexes derived from the substrates **1** and **3**–**7** with Grignard reagents

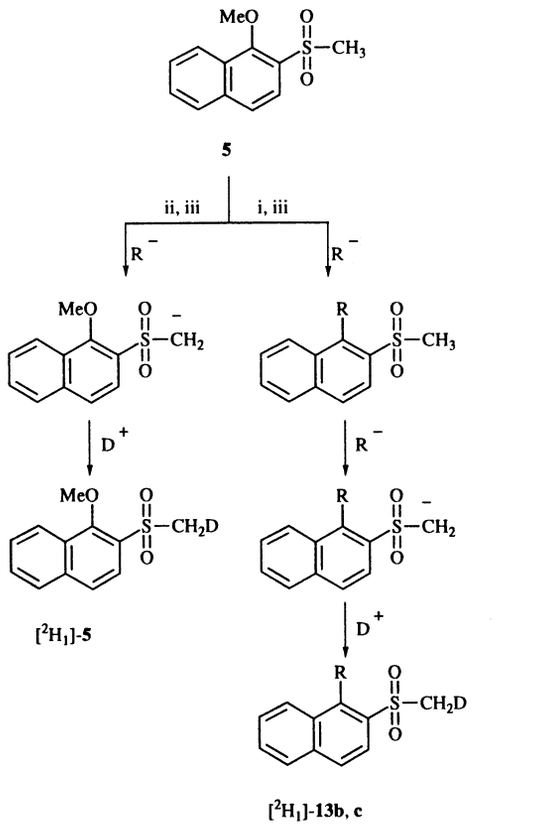
ment from *o*-(methoxy)aryloxazolines.[6] In fact, only a few organometallic reactions are found in the literature in which nucleophiles can displace an alkoxy group from alkoxyarenes without chelation assistance.[22]

Then, in the next series of reactions, the isopropyl **4** and methyl sulfones **5** were used instead of the *tert*-butyl sulfone **3** to examine how a reduction in steric bulk of the 2-substituent (entries 14–19) affects the influence which CPK-type molecular models of the chelated complexes **17a**–**c** (see Fig. 1) suggest it has. The reactions of the sulfones **4** and **5** with the Grignard reagents **8b**–**d** were terminated by addition of [$^2H_4$]acetic acid to check the occurrence of proton abstraction from the 2-sulfonyl substituents. It can be seen that the reactions of the isopropyl sulfone **4** with the sterically less demanding Grignards **8b**,**c** were greatly facilitated (entries 14 and 15) compared to those of the *tert*-butyl sulfone **3** (entries 10 and 11). The reaction of the sulfone **4** with the bulky Grignard **8d** also proceeded at room temperature to afford the substitution product **12d**, although somewhat sluggishly (entry 16). In these reactions, deuterium incorporation in the products **12b**–**d** was not detected by ^{1}H NMR spectroscopy.

The methyl sulfone **5** also reacted smoothly with the sterically undemanding Grignard reagents **8b**,**c**, and termination of these reactions by addition of [$^2H_4$]acetic acid afforded the substitution products [$^2H_1$]-**13b**,**c** in good yields with deuterium incorporation (entries 17 and 18). However, the reaction of the sulfone **5** with the bulky Grignard **8d** gave only the deuteriated sulfone [$^2H_1$]-**5**. This shows that the methyl sulfone **5** underwent deprotonation faster than the 1-methoxy displacement on treatment with the bulky Grignard reagent **8d**, and once the α-sulfonyl carbanion had formed, it greatly retarded the ability of the 1-methoxy group to undergo nucleophilic displacement because of the strong electron-donating tendency of the negative charge (Scheme 2).

In an alternative approach to reduce the steric hindrance imposed by the 2-sulfonyl activator with no α-hydrogen, a phenoxysulfonyl substituent was adopted to give the sulfonate **6** as the substrate. Although the electron-withdrawing ability of a 2-sulfonate substituent should be reduced to some extent compared to alkylsulfonyl substituents,[3] the sulfonate **6** reacted readily with the Grignard reagents **8a**–**d** to give the displacement products **14a**–**d** in good to excellent yields (entries 20–23). This means that the decreased steric hindrance of the sulfonate **6** compensated for the reduced electronic effect, again showing the importance of ligation of the 2-substituent to the metal centre of the nucleophiles which precedes the 1-methoxy substitution.

It was also found that a sulfamoyl substituent at the 2-position serves as an activator for the 1-methoxy displacement, as exemplified by the reaction of the 1-methoxy-2-pyrrolidinylnaphthalene **7** (entries 24–27), although the substitutions pro-

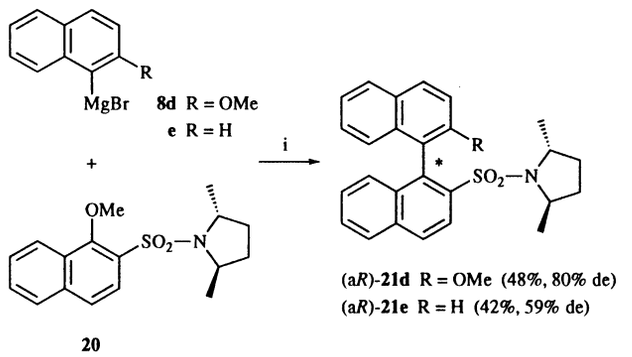


Scheme 2 *Reagent:* i, **8b** or **8c**, Et_2O–PhH; ii, **8d**, Et_2O–PhH; iii, CD_3CO_2D

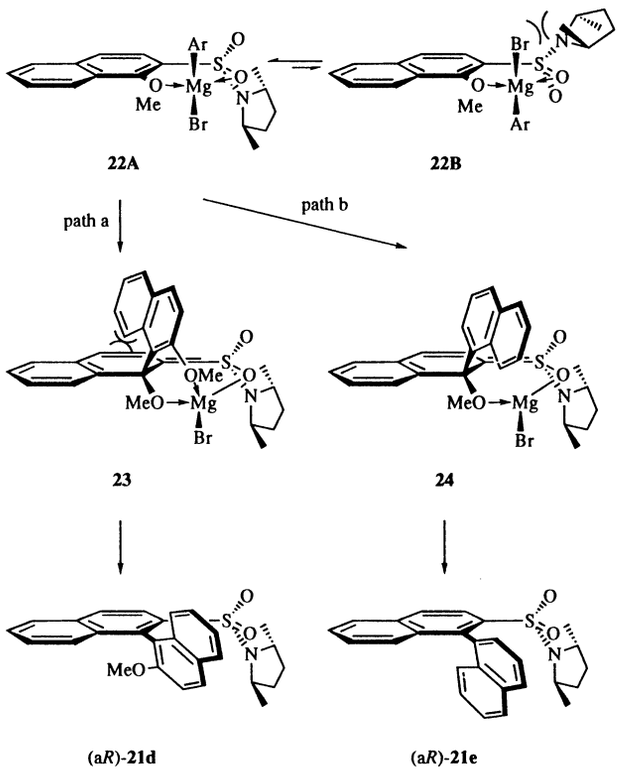
ceeded at a slightly reduced rate compared with those using the sulfate **6**; this reflected the decreased electron-withdrawing ability and seemingly increased steric hindrance of a sulfamoyl function compared with a sulfate (compare the complexes **18** and **19** in Fig. 1).

It is known that the displacement of a chiral alkoxy-[9] or sulfinyl-leaving group[14] can induce axial chirality in high optical yields in ester-mediated binaphthyl coupling reactions. However, the levels of asymmetric induction by use of chiral alkyl esters as chiral inducers are only poor to moderate due to the remote location of the chiral centre from the reaction site.[9] Taking into account that the amino sulfone **7**, rather than the ester **1**, will bring about more steric congestion on reaction with the Grignard reagents **8** (compare **16** and **19** in Fig. 1), a chiral sulfamoyl substituent seemed to induce axial chirality more efficiently than a chiral ester auxiliary. Accordingly, 2-[(2*R*,5*R*)-2,5-dimethylpyrrolidinylsulfonyl]-1-methoxynaphthalene **20** was prepared by reaction of 1-methoxy-2-naphthylsulfonyl chloride with (2*R*,5*R*)-2,5-dimethylpyrrolidine. Reaction of the chiral substrate **20** with 2-methoxy-1-naphthylmagnesium bromide **8d** in diethyl ether–benzene at room temperature for 36 h and then at reflux for 6 h afforded the atropisomeric 1,1′-binaphthyl (a*R*)-**21d** in 48% yield with 80% diastereoisomeric excess (de) (Scheme 3). The de was determined by ^{1}H NMR spectroscopy at 250 MHz in $CDCl_3$ solution and the absolute stereochemistry at the binaphthyl axis by chemical correlation to enantiomerically pure 2-amino-2′-methoxy-1,1′-binaphthyl of known configuration (see Experimental section). Similar treatment of the chiral sulfone **20** with the 1-naphthylmagnesium bromide **8e** resulted in the formation of the binaphthyl (a*R*)-**21e** in 42% yield with 59% de.

It should be noted that in **21d** and **21e** the direction of twist of the binaphthyl axis in each is the reverse of the other, although the two compounds have nominally the same a*R* chirality. The sense of asymmetric induction in these reactions may rationally be deduced from the previous mechanisms proposed for the asymmetric binaphthyl coupling mediated by



Scheme 3 *Reagents and conditions:* i, Et_2O–PhH, room temp., 36 h then reflux, 2.5–6 h



Scheme 4

chiral oxazolines[23] or esters[9,24] (see Scheme 4). Of the two possible conformers of the chelated complexes **22A**,**B** formed from the amino sulfone **20** and 1-naphthyl Grignard **8d**,**e**, the conformer **22A** may be favoured over the conformer **22B** to avoid non-bonding interactions between one of the two methyl substituents on the pyrrolidine ring and the Grignard moiety. For the conformer **22A** formed from the 2-methoxy-1-naphthyl Grignard **8d**, migration of the naphthyl carbanion to the *ipso*-carbon bearing the leaving methoxy group should occur from the β side in such a way that strong co-ordination of the 2-methoxy oxygen of the nucleophile to the magnesium centre overrides non-bonding steric repulsion between the *peri*-hydrogen of the naphthalene moiety derived from the nucleophile **8d** and the naphthalene plane undergoing the substitution to result in formation of a σ-bonded complex **23**. Elimination of MgBr(OMe) from the complex **23** would induce a*R* chirality in the resulting 1,1′-binaphthyl axis. On the other hand, for the conformer **22A** formed from the 1-naphthyl Grignard **8e**, the naphthyl carbanion migrates also from the β side to the *ipso*-carbon but in such a way that minimizes non-bonding repulsions between the two pertinent naphthalene moieties to afford the σ-bonded complex **24**. Elimination of MgBr(OMe) from complex **24** would induce a*R* chirality in the 1,1′-binaphthyl **21e**.

In conclusion, we have shown here that the presence of a 2-sulfonyl substituent in 1-methoxynaphthalene substantially activates the 1-methoxy group for nucleophilic displacement by Grignard reagents, which provides a convenient method for the synthesis of 1,1′-binaphthyls bearing a sulfur-functional group at the 2-position in a racemic or, if desired, in an atropisomeric form. It should be noted that asymmetric reactions by means of axially chiral biaryl sulfur compounds have recently been the subject of much interest.[25,26] The activating power of 2-*tert*-butyl-sulfinyl and -sulfonyl substituents as compared with that of a 2-isopropoxycarbonyl substituent falls roughly in the order $CO_2Pr^i > SO_2OPh > SO_2N\overline{[CH_2]_3}\overline{C}H_2 \geqslant SO_2alkyl \gg SOBu^t$ as a consequence of the balance between the electron-withdrawing power $SO_2Alkyl > SO_2OPh > SO_2N\overline{[CH_2]_3}\overline{C}H_2 > SOBu^t > CO_2Pr^i$ and the steric hindrance induced between the Grignard nucleophiles and the substrate 1-methoxynaphthalenes $SOBu^t > SO_2Alkyl > SO_2N\overline{[CH_2]_3}\overline{C}H_2 \geqslant SO_2OPh > CO_2Pr^i$.

Experimental

Mps were taken using a Yamato MP-21 or Mitamura Riken MP-P apparatus and are uncorrected. Optical rotations were measured on a JASCO DIP-100 polarimeter, and are given in units of 10^{-1} deg cm^2 g^{-1}. IR Spectra were recorded on a Shimadzu IR-460 spectrophotometer. ^{1}H NMR Spectra were recorded on a Bruker AC-250T or DPX-400 spectrometer using tetramethylsilane as the internal standard and $CDCl_3$ as the solvent. *J* Values are given in Hz. Microanalyses were carried out in the Microanalytical Laboratory of the Institute for Chemical Reaction Science, Tohoku University. Merck silica gel $60GF_{254}$ was used for analytical and preparative TLC (PLC). Silica gel columns were prepared by use of Merck silica gel 60 (63–200 μm). Water- and air-sensitive reactions were routinely carried out under nitrogen. Grignard reactions were performed by a similar procedure to that described in previous papers.[9,10b] Diethyl ether, benzene and toluene were distilled from sodium diphenylketyl just before use. Other solvents for experiments requiring anhydrous conditions were purified by the usual methods. Isopropyl 1-methoxy-2-naphthoate **1** was obtained as before.[9b] (2*R*,5*R*)-2,5-Dimethylpyrrolidine was prepared according to the literature procedure.[27]

General procedure for the preparation of 2-alkylsulfonyl-1-methoxynaphthalenes 3–5

To a mixture of 1-methoxynaphthalene (3.05 g, 19.3 mmol), *N*,*N*,*N*′,*N*′-tetramethylethane-1,2-diamine (TMEDA; 2.29 g, 19.7 mmol) and dry diethyl ether (20 cm^3) was added dropwise butyllithium (1.6 mol dm^{-3} in hexane; 12.3 cm^3, 19.7 mmol), and the mixture was stirred at room temperature for 2 h. It was then added to a solution of an appropriate dialkyl disulfide (19.7 mmol) in diethyl ether (20 cm^3) and the resulting mixture was stirred at room temperature for 30 min. After this the mixture was poured into 2 mol dm^{-3} hydrochloric acid (50 cm^3) and the two layers were separated. The aqueous layer was extracted with diethyl ether and the combined organic layer was washed successively with 2 mol dm^{-3} aq. NaOH and water, dried ($MgSO_4$) and evaporated. The residue was dried *in vacuo* to give crude 2-alkylthio-1-methoxynaphthalene. This sulfide was mixed with acetic acid (15 cm^3) and hydrogen peroxide (30% w/w in water; 10 cm^3) and the mixture was gradually heated to 90 °C to give a red solution. After the solution had been cooled to 0 °C, Na_2SO_3 was added to it until no more hydrogen peroxide was detected by KI-starch paper, when the mixture was neutralized by the addition of 5 mol dm^{-3} aq. NaOH. After warming to room temperature, the mixture was extracted with diethyl ether and the extracts were washed with water, dried ($MgSO_4$) and evaporated. The residue was chromatographed on a silica gel column using the indicated eluent.

Compound 3. Hexane–ethyl acetate (8:1) as the eluent;

crystals (3.17 g, 59%), mp 113 °C (Found: C, 64.45; H, 6.5. $C_{15}H_{18}O_3S$ requires C, 64.7; H, 6.5%); ν_{max}(KBr)/cm^{-1} 1292 (SO); δ_H(250 MHz) 1.38 (9 H, s, Bu^t), 4.15 (3 H, s, OMe) and 7.60–8.27 (6 H, m, ArH).

Compound 4. Hexane–ethyl acetate (5:1) as the eluent; an oil (3.11 g, 61%) (Found: C, 63.5; H, 6.1. $C_{14}H_{16}O_3S$ requires C, 63.6; H, 6.1%); ν_{max}(neat)/cm^{-1} 1301 (SO); δ_H(250 MHz) 1.29 (6 H, d, *J* 6.9, CH*Me*$_2$), 3.86 (1 H, septet, *J* 6.9, CH), 4.17 (3 H, s, OMe) and 7.60–8.22 (6 H, m, ArH).

Compound 5. Hexane–ethyl acetate (5:1) as the eluent; crystals (2.37 g, 52%), mp 89.0–90.0 °C (Found: C, 61.1; H, 5.2. $C_{12}H_{12}O_3S$ requires C, 61.0; H, 5.1%); ν_{max}(KBr)/cm^{-1} 1302 (SO); δ_H(250 MHz) 3.32 (3 H, s, Me), 4.20 (3 H, s, OMe) and 7.61–8.23 (6 H, m, ArH).

2-*tert*-Butylsulfinyl-1-methoxynaphthalene 2

This compound was prepared by a similar procedure to that used for the preparation of sulfones **3**–**5**. Crude 2-*tert*-butylthio-1-methoxynaphthalene, which had been prepared from 1-methoxynaphthalene (3.05 g, 19.3 mmol), was mixed with acetic acid (20 cm^3) and hydrogen peroxide (30% w/w in water; 10 cm^3). The mixture was stirred at room temperature for 1 h and then cooled to 0 °C. After a similar work-up to that described above, the crude product was chromatographed on a silica gel column with hexane–ethyl acetate (2:1 to 1:1) as eluent to give the sulfoxide **2** (2.58 g, 51%) as crystals, mp 134–135 °C (Found: C, 68.7; H, 7.0. $C_{15}H_{18}O_2S$ requires C, 68.7; H, 6.9%); ν_{max}(KBr)/cm^{-1} 1036 (SO); δ_H(250 MHz) 1.24 (9 H, s, Bu^t), 4.03 (3 H, s, OMe) and 7.58–8.15 (6 H, m, ArH).

1-Methoxynaphthalene-2-sulfonyl chloride

This compound was prepared according to the literature procedure.[17,28] To a mixture of 1-methoxynaphthalene (4.79 g, 30.3 mmol), TMEDA (3.56 g, 30.6 mmol) and dry diethyl ether (25 cm^3) was added dropwise butyllithium (1.6 mol dm^{-3} in hexane; 19.1 cm^3, 30.6 mmol), and the mixture was stirred at room temperature for 2 h. At the same time, sulfur dioxide gas, generated from $NaHSO_3$ (25 g) and conc. H_2SO_4 (25 cm^3), was passed through conc. H_2SO_4 and collected by liquefaction at −78 °C. The liquid sulfur dioxide was diluted with diethyl ether (20 cm^3) and the above-mentioned mixture was added dropwise to the cooled solution over 30 min. The resulting mixture was stirred at this temperature for 3 h to give a precipitate. After the mixture had warmed to room temperature, the precipitate was filtered off, washed with diethyl ether and then dried *in vacuo* to give crude lithium 1-methoxynaphthalene-2-sulfinate. To a suspension of the sulfinate in dry hexane (160 cm^3) was added a mixture of sulfuryl dichloride (3.0 cm^3) and hexane (40 cm^3) at 0 °C over 30 min. The mixture was stirred at this temperature for 1 h, after which it was allowed to warm to room temperature; the precipitate was then filtered off and the filtrate was evaporated to dryness. The residue was recrystallized from hexane–dichloromethane to give 1-methoxynaphthalene-2-sulfonyl chloride (3.26 g, 42%) as crystals, mp 66.0–67.0 °C (Found: C, 51.2; H, 3.5. $C_{11}H_9ClO_3S$ requires C, 51.5; H, 3.5%); ν_{max}(KBr)/cm^{-1} 1362 (SO); δ_H(250 MHz) 4.27 (3 H, s, OMe) and 7.66–8.30 (6 H, m, ArH).

Phenyl 1-methoxynaphthalene-2-sulfonate 6

A mixture of 1-methoxynaphthalene-2-sulfonyl chloride (2.93 g, 11.4 mmol), phenol (1.29 g, 13.7 mmol), 4-(dimethylamino)-pyridine (DMAP) (1.67 g, 13.7 mmol) and dry benzene (70 cm^3) was stirred at room temperature for 6 h. The mixture was poured into saturated NH_4Cl (100 cm^3) and the two layers were separated. The aqueous layer was extracted with diethyl ether and the extracts were washed with water, dried ($MgSO_4$) and evaporated. The residue was chromatographed on a silica gel column with hexane–ethyl acetate (10:1) as the eluent and then recrystallized from ethanol to give ester **6** (1.94 g, 54%) as crystals, mp 65.0–66.0 °C (Found: C, 65.15; H, 4.6. $C_{17}H_{14}O_4S$ requires C, 65.0; H, 4.5%); ν_{max}(KBr)/cm^{-1} 1385 (SO); δ_H(250 MHz) 4.23 (3 H, s, OMe), 7.08–7.27 (5 H, m, ArH) and 7.62–8.30 (6 H, m, ArH).

1-Methoxy-2-pyrrolidinylsulfonylnaphthalene 7

A mixture of 1-methoxynaphthalene-2-sulfonyl chloride (1.85 g, 7.21 mmol), pyrrolidine (624 mg, 8.77 mmol), DMAP (1.07 g, 8.76 mmol) and dry dichloromethane (25 cm^3) was stirred at room temperature for 5 h. The mixture was poured into 2 mol dm^{-3} hydrochloric acid (50 cm^3) and extracted with diethyl ether. The extracts were washed successively with 1 mol dm^{-3} aq. Na_2CO_3 and water, dried ($MgSO_4$) and evaporated. The residue was chromatographed on a silica gel column with hexane–ethyl acetate (7:1 to 5:1) as the eluent to give the amide **7** (2.02 g, 96%) as crystals, mp 79.6–81.1 °C (Found: C, 61.7; H, 5.6; N, 4.65. $C_{15}H_{17}NO_3S$ requires C, 61.8; H, 5.9; N, 4.8%); ν_{max}(KBr)/cm^{-1} 1331 (SO); δ_H(250 MHz) 1.75–1.82 (4 H, m, $NCH_2CH_2CH_2$), 3.39–3.46 (4 H, m, CH_2NCH_2), 4.15 (3 H, s, OMe) and 7.60–8.22 (6 H, m, ArH).

General procedure for the S_NAr reaction of 2-EWG-substituted 1-methoxynaphthalenes 1–7 with the Grignard reagent 8

To a solution of the substrate **1**–**7** (1.0 mmol) in dry benzene (3.5 cm^3) was added the Grignard reagent **8**, which had been prepared from the corresponding alkyl or aryl bromide (1.4–3.0 mmol) and an excess of magnesium turnings in dry diethyl ether (3.5 cm^3) with induction of dissolution by the addition of benzene (3.5 cm^3). In the reaction using the Grignard reagent **8d**, which was not sufficiently soluble in the above-mentioned volume of the mixed solvent, the Grignard reagent was prepared in diethyl ether (7.0 cm^3) and dissolved by the addition of benzene (7.0 cm^3); this solution was then added to a solution of the substrate in benzene (7.0 cm^3). After the mixture had been stirred at an appropriate temperature for 1–76 h it was worked up in the usual way. For the sulfones **4** and **5**, the reactions were quenched with [$^2H_4$]acetic acid (99.4 atom% deuteriated; 200 mm^3), and the resulting mixtures were diluted with water (30 cm^3) and extracted with diethyl ether. The extracts were washed successively with 1 mol dm^{-3} aq. Na_2CO_3 and water and dried ($MgSO_4$); see Table 1 for reaction conditions and the yield of the corresponding products **9**–**15**. Chromatography on a silica gel column was used for purification of the products using the indicated eluent, unless otherwise noted.

Compound 9a. The crude product was purified by PLC with hexane–ethyl acetate (9:1) as the eluent; an oil (Found: C, 80.05; H, 8.35. $C_{18}H_{22}O_2$ requires C, 80.0; H, 8.2%); ν_{max}(neat)/cm^{-1} 1715 (CO); δ_H(250 MHz) 1.00 [3 H, t, *J* 7.2, $(CH_2)_3Me$], 1.41 (6 H, d, *J* 6.1, CH*Me*$_2$), 1.47–1.61 [2 H, m, $(CH_2)_2CH_2$Me], 1.68–1.80 (2 H, m, CH_2CH_2Et), 3.31–3.38 (2 H, m, CH_2Pr), 5.32 (1 H, septet, *J* 6.1, CH) and 7.49–8.19 (6 H, m, ArH).

Compound 9b. The crude product was purified by PLC with hexane–ethyl acetate (19:1) as the eluent; an oil (Found: C, 79.6; H, 7.9. $C_{17}H_{20}O_2$ requires C, 79.65; H, 7.9%); ν_{max}(neat)/cm^{-1} 1719 (CO); δ_H(250 MHz) 1.44 (6 H, d, *J* 6.3, OCH*Me*$_2$), 1.63 (6 H, d, *J* 7.2, ArCH*Me*$_2$), 3.93 (1 H, septet, *J* 7.2, ArCH), 5.34 (1 H, septet, *J* 6.3, OCH) and 7.48–8.39 (6 H, m, ArH).

Compound 10a. Hexane–ethyl acetate (3:1 to 2:1) as the eluent; an oil (Found: C, 74.9; H, 8.3. $C_{18}H_{24}OS$ requires C, 75.0; H, 8.4%); δ_H(250 MHz) 0.96 [3 H, t, *J* 7.2, $(CH_2)_3Me$], 1.24 (9 H, s, Bu^t), 1.41–1.60 [2 H, m, $(CH_2)_2CH_2$Me], 1.65–1.77 (2 H, m, CH_2CH_2Et), 3.14–3.35 (2 H, m, CH_2Pr) and 7.53–8.11 (6 H, m, ArH).

Compound 11a. Hexane–ethyl acetate (10:1) to dichloromethane as the eluent; crystals, mp 89.0–90.0 °C (Found: C, 71.1; H, 8.0. $C_{18}H_{24}O_2S$ requires C, 71.0; H, 7.9%); ν_{max}(KBr)/cm^{-1} 1286 (SO); δ_H(250 MHz) 0.99 [3 H, t, *J* 7.2, $(CH_2)_3Me$], 1.37 (9 H, s, Bu^t), 1.51–1.65 [2 H, m, $(CH_2)_2CH_2$Me], 1.68–1.81 (2 H, m, CH_2CH_2Et), 3.57 (2 H, t, *J* 7.0, CH_2Pr) and 7.61–8.28 (6 H, m, ArH).

Compound 11b. Hexane–dichloromethane (1:3) to ethyl

acetate as the eluent; crystals, mp 149–150 °C (Found: C, 70.2; H, 7.8. $C_{17}H_{22}O_2S$ requires C, 70.3; H, 7.6%); ν_{max}(KBr)/cm^{-1} 1280 (SO); δ_H(250 MHz) 1.44 (9 H, s, Bu^t), 1.66 (6 H, d, *J* 7.3, CH*Me*$_2$), 4.91 (1 H, septet, *J* 7.3, CH) and 7.53–8.56 (6 H, m, ArH).

Compound 11c. Hexane–ethyl acetate (10:1) to dichloromethane as the eluent; crystals, mp 192–193 °C (Found: C, 74.2; H, 6.3. $C_{20}H_{20}O_2S$ requires C, 74.0; H, 6.2%); ν_{max}(KBr)/cm^{-1} 1300 (SO); δ_H(250 MHz) 1.28 (9 H, s, Bu^t) and 7.31–8.10 (11 H, m, ArH).

Compound 11d. Hexane–ethyl acetate (3:1) as the eluent; crystals, mp 227–228 °C (Found: C, 74.0; H, 6.1. $C_{25}H_{24}O_3S$ requires C, 74.2; H, 6.0%); ν_{max}(KBr)/cm^{-1} 1294 (SO); δ_H(250 MHz) 1.21 (9 H, s, Bu^t), 3.77 (3 H, s, OMe) and 6.93–8.18 (12 H, m, ArH).

Compound 12b. Hexane–ethyl acetate (5:1) as the eluent; crystals, mp 154–155 °C (Found: C, 69.3; H, 7.3. $C_{16}H_{20}O_2S$ requires C, 69.5; H, 7.3%); ν_{max}(KBr)/cm^{-1} 1284 (SO); δ_H(250 MHz) 1.35 (6 H, d, *J* 6.7, SO_2CHMe_2), 1.68 (6 H, d, *J* 7.3, ArCH*Me*$_2$), 3.39 (1 H, septet, *J* 6.7, SO_2CH), 4.62 (1 H, septet, *J* 7.3, ArCH) and 7.53–8.53 (6 H, m, ArH).

Compound 12c. Hexane–ethyl acetate (5:1) as the eluent; crystals, mp 102–104 °C (Found: C, 73.5; H, 5.8. $C_{19}H_{18}O_2S$ requires C, 73.5; H, 5.8%); ν_{max}(KBr)/cm^{-1} 1297 (SO); δ_H(250 MHz) 1.15 (6 H, d, *J* 6.8, CH*Me*$_2$), 2.77 (1 H, septet, *J* 6.8, CH) and 7.38–8.24 (11 H, m, ArH).

Compound 12d. Hexane–ethyl acetate (8:1 to 5:1) as the eluent; crystals, mp 89.2–91.4 °C (Found: C, 73.5; H, 5.4. $C_{24}H_{22}O_3S$ requires C, 73.8; H, 5.7%); ν_{max}(KBr)/cm^{-1} 1300 (SO); δ_H(400 MHz) 1.05 (3 H, d, *J* 6.8, CH*Me*$_2$), 1.07 (3 H, d, *J* 6.8, CH*Me*$_2$), 2.79 (1 H, septet, *J* 6.8, CH), 3.76 (3 H, s, OMe) and 6.85–8.28 (12 H, m, ArH).

Compound [^{2}H$_1$]-13b (92 atom% deuteriated). The crude product was purified by PLC with hexane–dichloromethane (1:3) as the eluent; crystals, mp 98.5–100 °C; ν_{max}(KBr)/cm^{-1} 1287 (SO); δ_H(400 MHz) 1.72 (6 H, d, *J* 7.2, CH*Me*$_2$), 3.19 (1.84 H, t, *J* 1.9, CH_2D), 3.20 (0.24 H, s, CH_3), 4.63 (1 H, septet, *J* 7.2, CH) and 7.56–8.52 (6 H, m, ArH).

Compound [^{2}H$_1$]-13c (91 atom% deuteriated). Hexane–ethyl acetate (3:1) as the eluent; crystals, mp 162–164 °C; ν_{max}(KBr)/cm^{-1} 1298 (SO); δ_H(400 MHz) 2.73 (1.82 H, t, *J* 1.8, CH_2D), 2.74 (0.27 H, s, CH_3) and 7.42–8.29 (11 H, m, ArH).

Compound 14a. Hexane–ethyl acetate (10:1) as the eluent; crystals, mp 89.0–89.6 °C (Found: C, 70.75; H, 6.0. $C_{20}H_{20}O_3S$ requires C, 70.6; H, 5.9%); ν_{max}(KBr)/cm^{-1} 1361 (SO); δ_H(400 MHz) 1.03 [3 H, t, *J* 7.3, $(CH_2)_3Me$], 1.59–1.68 [2 H, m, $(CH_2)_2CH_2$Me], 1.75–1.83 (2 H, m, CH_2CH_2Et), 3.61 (2 H, t, *J* 8.3, CH_2Pr), 6.98–7.26 (5 H, m, ArH) and 7.64–8.27 (6 H, m, ArH).

Compound 14b. Hexane–ethyl acetate (15:1) as the eluent; an oil (Found: C, 69.7; H, 5.6. $C_{19}H_{18}O_3S$ requires C, 69.9; H, 5.6%); ν_{max}(neat)/cm^{-1} 1374 (SO); δ_H (400 MHz) 1.74 (6 H, d, *J* 7.2, CH*Me*$_2$), 4.77 (1 H, septet, *J* 7.2, CH), 7.03–7.29 (5 H, m, ArH) and 7.60–8.58 (6 H, m, ArH).

Compound 14c. Hexane–dichloromethane (3:2 to 1:1) as the eluent; crystals, mp 174–175 °C (Found: C, 73.3; H, 4.5. $C_{22}H_{16}O_3S$ requires C, 73.3; H, 4.5%); ν_{max}(KBr)/cm^{-1} 1377 (SO); δ_H(250 MHz) 6.84–6.90 (2 H, m, ArH), 7.20–7.30 (5 H, m, ArH), 7.44–7.53 (5 H, m, ArH), 7.62–7.69 (1 H, m, ArH) and 7.95–8.13 (3 H, m, ArH).

Compound 14d. Hexane–ethyl acetate (7:1) as the eluent; crystals, mp 172–173 °C (Found: C, 73.8; H, 4.8. $C_{27}H_{20}O_4S$ requires C, 73.6; H, 4.6%); ν_{max}(KBr)/cm^{-1} 1369 (SO); δ_H(250 MHz) 3.70 (3 H, s, OMe) and 6.72–8.16 (17 H, m, ArH).

Compound 15a. Hexane–ethyl acetate (7:1) to ethyl acetate as the eluent; an oil (Found: C, 67.8; H, 7.2; N, 4.7; S, 10.4. $C_{18}H_{23}NO_2S$ requires C, 68.1; H, 7.3; N, 4.4; S, 10.1%); ν_{max}(neat)/cm^{-1} 1314 (SO); δ_H(250 MHz) 1.02 [3 H, t, *J* 7.1, $(CH_2)_3Me$], 1.53–1.78 [4 H, m, $CH_2(CH_2)_2$Me], 1.87–1.96 (4 H, m, $NCH_2CH_2CH_2$), 3.31–3.40 (4 H, m, CH_2NCH_2), 3.50–3.56 (2 H, m, CH_2Pr) and 7.58–8.23 (6 H, m, ArH).

Compound 15b. Hexane–ethyl acetate (10:1) as the eluent; an oil (Found: C, 67.25; H, 7.1; N, 4.8; S, 10.6. $C_{17}H_{21}NO_2S$ requires C, 67.3; H, 7.0; N, 4.6; S, 10.6%); ν_{max}(neat)/cm^{-1} 1319 (SO); δ_H(250 MHz) 1.64 (6 H, d, *J* 7.3, CH*Me*$_2$), 1.91–1.98 (4 H, m, $NCH_2CH_2CH_2$), 3.33–3.39 (4 H, m, CH_2NCH_2), 4.62 (1 H, septet, *J* 7.3, CH) and 7.51–8.52 (6 H, m, ArH).

Compound 15c. Hexane–ethyl acetate (15:1) to ethyl acetate as the eluent; crystals, mp 165–166 °C (Found: C, 71.3; H, 5.7; N, 4.4. $C_{20}H_{19}NO_2S$ requires C, 71.2; H, 5.7; N, 4.2%); ν_{max}(KBr)/cm^{-1} 1315 (SO); δ_H(250 MHz) 1.66–1.74 (4 H, m, $NCH_2CH_2CH_2$), 2.82–2.89 (4 H, m, CH_2NCH_2) and 7.34–8.23 (11 H, m, ArH).

Compound 15d. Hexane–ethyl acetate (5:1) as the eluent; crystals, mp 183–184 °C (Found: C, 71.8; H, 5.45; N, 3.3. $C_{25}H_{23}NO_3S$ requires C, 71.9; H, 5.6; N, 3.4%); ν_{max}(KBr)/cm^{-1} 1318 (SO); δ_H(250 MHz) 1.17–1.43 (4 H, m, $NCH_2CH_2CH_2$), 2.41–2.49 (2 H, m, NCH_2), 2.75–2.84 (2 H, m, NCH_2), 3.81 (3 H, s, OMe) and 6.79–8.34 (12 H, m, ArH).

Attempted reaction of sulfoxide 2 with phenyllithium

To a solution of the sulfoxide **2** (263 mg, 1.00 mmol) in dry toluene (7.0 cm^3) was added dropwise phenyllithium (1.01 mol dm^{-3} in cyclohexane–diethyl ether; 2.0 cm^3, 2.02 mmol) at −46 °C. The mixture was stirred at room temperature for 12 h and then quenched with 2 mol dm^{-3} hydrochloric acid (20 cm^3). The mixture was extracted with diethyl ether and the extracts were washed successively with 1 mol dm^{-3} aq. Na_2CO_3 and water, dried ($MgSO_4$) and evaporated. The residue was chromatographed on a silica gel column eluting with hexane–ethyl acetate (2:1) to give recovery of the sulfoxide **2** (240 mg, 91%).

Reaction of sulfone 3 with phenyllithium

The reaction procedure was similar to that for the reaction of the sulfoxide **2** with phenyllithium. To a solution of the sulfone **3** (279 mg, 1.00 mmol) in dry toluene (7.0 cm^3) was added dropwise phenyllithium (1.01 mol dm^{-3} in cyclohexane–diethyl ether; 2.0 cm^3, 2.02 mmol) at −46 °C. The mixture was stirred at this temperature for 3 h and then quenched with 2 mol dm^{-3} hydrochloric acid (20 cm^3). After work-up similar to that described above, the crude product was chromatographed on a silica gel column with hexane–ethyl acetate (10:1) to dichloromethane as the eluent to give substituted product **11c** (211 mg, 65%) as crystals, the spectral data of which were identical with those of compound **11c** obtained from the reaction of the sulfone **3** with phenylmagnesium bromide.

2-[(2*R*,5*R*)-2,5-Dimethylpyrrolidinylsulfonyl]-1-methoxynaphthalene 20

A mixture of 1-methoxynaphthalene-2-sulfonyl chloride (963 mg, 3.75 mmol), (2*R*,5*R*)-2,5-dimethylpyrrolidine (410 mg, 4.13 mmol), DMAP (505 mg, 4.13 mmol) and dry dichloromethane (15 cm^3) was stirred at room temperature for 36 h. After a similar work-up to that described for the preparation of amide **7**, chromatography on a silica gel column with hexane–ethyl acetate (6:1) as the eluent gave amide **20** (647 mg, 54%) as crystals, mp 84.6–85.5 °C (Found: C, 64.0; H, 6.6; N, 4.45. $C_{17}H_{21}NO_3S$ requires C, 63.9; H, 6.6; N, 4.4%); $[\alpha]_D^{20}$ +50.6 (*c* 1.00, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 1328 (SO); δ_H(250 MHz) 1.11 (6 H, d, *J* 6.4, Me), 1.47–1.55 (2 H, m, CH_2), 2.14–2.23 (2 H, m, CH_2), 4.30–4.40 (2 H, m, NCH) and 7.56–8.23 (6 H, m, ArH).

2-[(2*R*,5*R*)-2,5-Dimethylpyrrolidinylsulfonyl]-2′-methoxy-1,1′-binaphthyl 21d

To a solution of the sulfonamide **20** (252 mg, 0.789 mmol) in dry benzene (5.0 cm^3) was added Grignard reagent **8d** which had been prepared from 1-bromo-2-methoxynaphthalene (560 mg, 2.36 mmol) and magnesium turnings (100 mg) in dry diethyl ether (5.0 cm^3), dissolution being achieved by the add-

ition of benzene (5.0 cm^3). The mixture was stirred at room temperature for 36 h and then refluxed for 6 h. After work-up, chromatography on a silica gel column with hexane–ethyl acetate (6:1) as the eluent afforded the binaphthyl **21d** (168 mg, 48%) as crystals; δ_H(250 MHz) 0.87, 0.91 [6 H: d, *J* 6.4, Me (a*R*); d, *J* 6.4, Me (a*S*)], 0.84–2.02 (4 H, m, CH_2CH_2), 3.00–3.11, 3.49–3.59 [2 H: m, NCH (a*S*); m, NCH (a*R*)], 3.76, 3.83 [3 H: s, OMe (a*R*); s, OMe (a*S*)] and 6.85–8.32 (12 H, m, ArH).

^{1}H NMR Analysis of the sample differentiated well the 2′-methoxy signal of the (a*S*)- and (a*R*)-diastereoisomers. Thus, the axial chirality of the coupling product was determined to be a*R* (80% de) by comparison of its ^{1}H NMR spectrum with that of an authentic sample which had been prepared as follows. A mixture of (a*S*)-2-chlorosulfonyl-2′-methoxy-1,1′-binaphthyl[29] (47.6 mg, 124 μmol), (2*R*,5*R*)-2,5-dimethylpyrrolidine (44.9 mg, 453 μmol), dry pyridine (1.0 cm^3) and dry benzene (3.0 cm^3) was heated at 60 °C for 3 h. After cooling, the mixture was poured into 2 mol dm^{-3} hydrochloric acid (5.0 cm^3) and extracted with diethyl ether. The extracts were washed successively with 1 mol dm^{-3} aq. Na_2CO_3 and water, dried ($MgSO_4$) and evaporated. The residue was purified by PLC with hexane–ethyl acetate (2:1) as the eluent to give an authentic sample of (a*S*)-**21d** (24.4 mg, 44%) as crystals, mp 217–218 °C (Found: C, 72.9; H, 6.3; N, 3.0. $C_{27}H_{27}NO_3S$ requires C, 72.8; H, 6.1; N, 3.1%); $[\alpha]_D^{20}$ +92.3 (*c* 1.00, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 1323 (SO); δ_H(250 MHz) 0.91 (6 H, d, *J* 6.4, Me), 0.84–1.33 (4 H, m, CH_2CH_2), 3.00–3.11 (2 H, m, CHNCH), 3.83 (3 H, s, OMe) and 6.85–8.32 (12 H, m, ArH).

2-[(2*R*,5*R*)-Dimethylpyrrolidinylsulfonyl]-1,1′-binaphthyl 21e

To a solution of the sulfonamide **20** (252 mg, 0.789 mmol) in dry benzene (5.0 cm^3) was added Grignard reagent **8e** which had been prepared from 1-bromonaphthalene (491 mg, 2.37 mmol) and magnesium turnings (100 mg) in dry diethyl ether (5.0 cm^3), dissolution being achieved by the addition of benzene (5.0 cm^3). The mixture was stirred at room temperatue for 36 h and then refluxed for 2.5 h. After usual work-up, PLC with hexane–dichloromethane (2:1) as the eluent afforded the binaphthyl **21e** (138 mg, 42%) as crystals; δ_H(250 MHz) 0.89, 0.90 [6 H: d, *J* 6.3, Me (a*R*); d, *J* 6.3, Me (a*S*)], 0.73–2.12 (4 H, m, CH_2CH_2), 2.83–2.93, 3.48–3.58 [2 H, m, CHNCH (a*R*); m, CHNCH (a*S*)] and 7.03–8.39 (13 H, m, ArH).

The ^{1}H NMR spectrum of compound **21e** revealed the presence of two diastereoisomers with 2 H due to the methine protons adjacent to the pyrrolidinyl nitrogen. Thus, the axial chirality of the coupling product was determined to be a*R* (59% de) by comparison of its ^{1}H NMR spectrum with that of an authentic sample which had been prepared as follows. A mixture of (a*S*)-2-chlorosulfonyl-1,1′-binaphthyl[29] (19.3 mg, 54.7 μmol), (2*R*,5*R*)-2,5-dimethylpyrrolidine (13.6 mg, 137 μmol), DMAP (16.8 mg, 138 μmol) and dry dichloromethane (2.0 cm^3) was stirred at room temperature for 5 h. After a work-up similar to that described for the preparation of an authentic sample of (a*S*)-**21d**, PLC with hexane–ethyl acetate (5:1) as the eluent gave (a*S*)-**21e** (12.3 mg, 54%) as crystals (Found: C, 75.3; H, 6.0; N, 3.4. $C_{26}H_{25}NO_2S$ requires C, 75.2; H, 6.1; N, 3.4%); $[\alpha]_D^{19}$ +8.54 (*c* 0.75, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 1319 (SO); δ_H(250 MHz) 0.90 (6 H, d, *J* 6.3, Me), 1.34–2.12 (4 H, m, CH_2CH_2), 3.48–3.58 (2 H, m, CHNCH) and 7.08–8.29 (13 H, m, ArH).

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29 Synthesis and resolution of 2-amino-1,1′-binaphthyls and their stereospecific transformation to 2-chlorosulfonyl-1,1′-binaphthyls will be published elsewhere.

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