Directed Metalation of Benzenesulfinamides. A Novel Route to Meta-Substituted Aromatic Compounds

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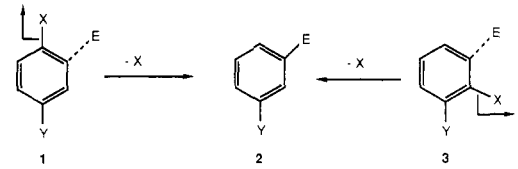
Directed lithiation ortho to the sulfinamide group of readily available ortho- and para-substituted *N*-phenylbenzenesulfinamides (**5a–d**) and reaction with a variety of electrophiles followed by mercuridesulfination ($HgCl_2$) or dehydrodesulfination (Ra/Ni) constitutes a novel route to meta-substituted benzenes.

The introduction of a substituent at the meta-position to an ortho/para-directing group is a classical problem of organic chemistry.[1] An old solution is nitration ortho/para to the existing group, followed by reduction, substitution ortho/para to the now dominating amino group, and elimination of the amino group.[2] Other methods include: (i) the temporary introduction of sulfonic acid groups as directing and/or blocking substituents, followed by desulfonation;[3] (ii) the reversible modification of the ortho/para-directing group into a meta-directing group, the amino group is an example, since, although the free base form is highly ortho/para-directing, the conjugated acid is deactivated, and, therefore, meta-directing;[4] (iii) recently, arenechromium tricarbonyl complexes have been used as directing and/or blocking groups followed by addition with a nucleophile and removal of chromium tricarbonyl by oxidation.[5]

All these methods suffer from disadvantages such as (i) the number of substituents introduced is limited by the nature of the directing group;[2-5] (ii) the substitution reactions are frequently not regiospecific, and side reactions compete simultaneously;[4,5] (iii) removal of the directing and/or blocking group is strongly influenced by the other substituents and can be insufficiently facile.[2-4] In view of this, we have devised an alternative which now allows the preparation of a wide variety of meta-substituents via a directed lithiation technique.

Directed ortho-metalation reactions have evolved as an important strategy in aromatic and heterocyclic synthesis.[6] Substituents which direct the lithium atom to the ortho position of an aromatic system on metalation with organolithium reagents (e.g. n-BuLi, sec-BuLi, t-BuLi, LDA) include NMe_2,[7] CH_2NMe_2,[8] $CH_2CH_2NMe_2$,[9] OMe,[10] OCH_2OCH_3,[11] $CONR_2$,[12] SO_2NR_2,[13] SO_2R,[14] CF_3,[15] F,[16] 2-oxazoline,[17] $CSNR_2$,[18] and SO_3H.[19] Our strategy focused on the identification of a new ortho-directing group which, after enabling regiospecific metalation at the ortho position, could be removed easily under mild conditions. It was envisaged that this concept could form the basis of a useful synthetic method for the regiospecific construction of diversely functionalized meta-substituted aromatics from immediate precursors consisting of aromatics substituted in the para or ortho position with such a directing group. The concept is illustrated in Scheme I, where **2** is obtained either from an aromatic, **1**, initially substituted in its para-position with such a directing group, or from an aromatic, **3**, initially substituted in its ortho-position.

Scheme I[a]



1 2 3

[a] E, new substituent introduced; X, directing substituent subsequently eliminated.

If the directing group chosen can itself be introduced easily into the ortho or para position of a monosubstituted benzene, then this, in combination with the above sequence, clearly enables the conversion of a monosubstituted into a meta-disubstituted benzene. We now report

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Table I. Reaction of Dilithiated Sulfinamides 5a–d with Electrophiles

starting sulfinamide	lithiation[a] condition	electrophile	product	solvent	recryst yield, % (isolated)	mp, °C
5a	A	$(C_6H_5)_2CO$	**7a** (11)	$CHCl_3$–hexane	81	125–126
5a	A	CH_3I	**7b**	$CHCl_3$–hexane	76	105–109
5a	A	$(CH_3)_3CNCO$	**7c**	$CHCl_3$–hexane	87	158–160
5a	A	$(C_6H_5S)_2$	**7d**	$CHCl_3$–hexane	72	148–150
5b	B	D_2O	**8a**	$CHCl_3$–petroleum ether	100[b]	158–159
5b	B	$(C_6H_5)_2CO$	**8b** (12)	$CHCl_3$–hexane	87	160–162
5b	B	C_6H_5CHO	**8c** (13)	ether–hexane	83	136–138
5b	B	$(C_6H_5S)_2$	**8d**	$CHCl_3$–hexane	78	168–169
5b	B	CH_3I	**8e**	$CHCl_3$–petroleum ether	89	129–130
5b	B	I_2	**8f**	benzene–petroleum ether	75	145–147
5b	B	$(CH_3)_3CNCO$	**8g**	EtOAc	68	195–197
5c	C	D_2O	**9a**	$CHCl_3$–hexane	72[b]	136–137
5c	C	$(C_6H_5S)_2$	**9b**		61[c]	120–122
5c	C	$(C_6H_5)_2CO$	**9c** (14)	ether–hexane	60	152–154[e]
5d	D	$(C_6H_5)_2CO$	**10a** (15)	ether–hexane	53[d]	138–140

[a] A: −20 °C for 3 h and then 0 °C for 1 h. B: −78 °C for 20 min and then −20 °C for 10 min. C: −78 °C for 3 h and then −10 °C for 1 h. D: −40 °C for 45 min and then −20 °C for 15 min. [b] NMR yield. [c] Purified by column chromatography using $CHCl_3$–hexane (5:2) as eluate. [d] Synthesized by one-pot procedure. [e] This compound first melts at 152–154 °C and then solidifies further to melt at 182–184 °C.

that the use of sulfinamides has led to the successful realization of this strategy. The final desulfination is a general, readily occurring reaction and achieves rapid access to meta-substituted aromatics according to Scheme I.

A somewhat similar strategy was proposed earlier by Martin,[19] who found that lithium arenesulfonates could be selectively ortho-lithiated, the *o*-lithium replaced by an electrophile, and the sulfonic acid group removed by hydrolysis. However, our method offers many advantages over this previous route, which has not been tested for scope and generality and which suffers from the low solubility of lithium sulfonates in organic solvents, the difficulty of separation of the sulfonic acid intermediates, and less easily available starting materials.

Sulfinamides have been generally prepared by the treatment of sulfinyl chlorides with amines[20] or by the treatment of thionylamines with appropriate Grignard reagents.[21] We conveniently prepared *N*-phenylarenesulfinamides using the appropriate aryl Grignard or aryllithium with readily available[22] thionylaniline. Sulfinamides **5a–d** were obtained (70–90% yield) by this method.

Sulfinamides have been known for many years,[23] but few of their reactions have been studied in any depth.[24] In general, sulfinamides are much less stable than sulfonamides; they hydrolyze readily in aqueous acid or base to give the corresponding sulfinic acids and amines.[20] Sulfinamides react readily with nucleophiles at sulfur, as evidenced by this easy hydrolysis and also by the reaction of *N,N*-dimethyl-*p*-toluenesulfinamide with methyllithium to form methyl *p*-tolyl sulfoxide.[25] However, in a mono-N-substituted arylsulfinamide, nucleophilic attack at sulfur should be discouraged by anion formation, and the strong coordinating and electron-withdrawing properties[26] of sulfinamide groups suggested that treatment with an appropriate lithiating agent might provide access to stabilized dianions by ortho-lithiation in the aryl ring.[27]

We found that the dilithiation of *N*-phenylbenzenesulfinamides (**5a–d**) is indeed readily accomplished by the addition of 2.1 equiv of *n*-BuLi in tetrahydrofuran at low temperatures as indicated in Table I. Examination of the crude product of a D_2O quench of the dilithiated **5b** (*n*-BuLi/THF, −78 °C then −20 °C) shows quantitative ortho-lithiation, as evidenced by the integrals and by the coupling patterns in the 200-MHz ^1H NMR spectra. Sulfinamide **5b** exhibited an ^1H NMR spectrum having a well-resolved AA′BB′ pattern in the δ 7.60–7.76 ppm region. The downfield proton resonance was assigned to the protons situated ortho to the sulfinamide substitution due to its deshielding effect.[26] After the quench with D_2O, the product showed clean attenuation of the downfield proton signal and broadening of the upfield signal, indicating deuterium incorporation ortho to the sulfinamide substituent. The integral of the downfield proton resonance is equal to one proton and the integral of the upfield proton resonance is equal to two protons.

Treatment of **5c** with *n*-BuLi at −78 °C and then aging at −10 °C for 4 h (compare with **5b**) gave a bright reddish-orange solution of the dianion. After quenching with D_2O, the ^1H NMR spectrum of the product showed attenuation of the downfield proton signal and broadening of the upfield proton signal of the AA′BB′ system. The downfield portion was equivalent to 1.28 protons and the upfield portion to 2.00 protons. This result corresponded to 72% metalation ortho to the sulfinamide substituent.

Addition of appropriate electrophiles to the solutions of the dilithiated species, **6**, provided a variety of derivatives substituted ortho to the sulfinamide group in moderate to good yields, as indicated in Table I (Scheme II). In the general procedure, the reaction mixture was stirred at −78 °C for 2 h and then allowed to warm up to 25 °C overnight. The workup was accomplished by quenching with 10% aqueous HCl or water followed by extraction with ether. After evaporation of the solvent, the residue was purified by recrystallization or by chromatography on silica gel.

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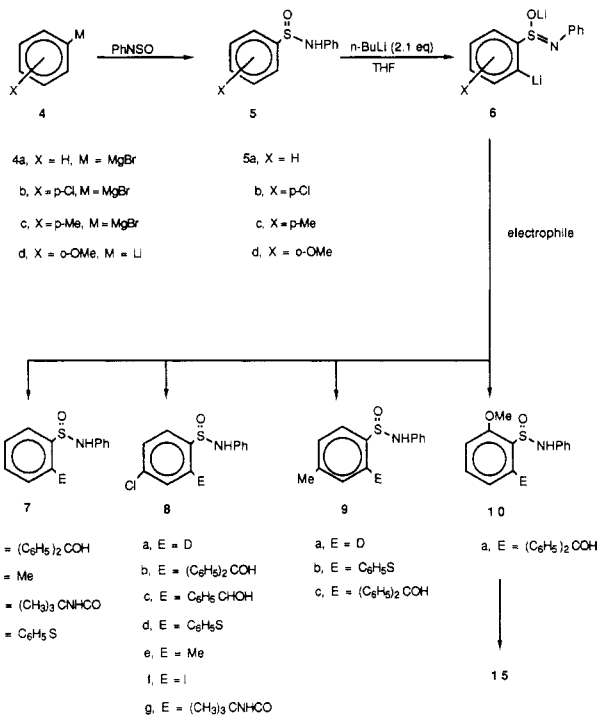
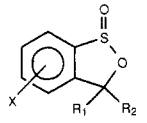
Scheme II



The ortho-substituted sulfinamides **7a**, **8b**, **8c**, **9c**, and **10a** produced by reactions with ketones or aldehydes as electrophiles undergo hydrolysis and cyclization during the aqueous workup to give the novel sultines **11**, **12**, **13**, **14**, and **15**.[28] The conversion of **9c** → **14** proves unequivocally that no metalation occurred at the (quite acidic) CH_3 site in **9c**. Furthermore, these sultine formations preclude metalation ortho to the aniline nitrogen atom.



11, X = H, $R_1 = R_2 = C_6H_5$
12, X = p-Cl, $R_1 = R_2 = C_6H_5$
13, X = p-Cl, R_1 = H, $R_2 = C_6H_5$
14, X = p-Me, $R_1 = R_2 = C_6H_5$
15, X = o-OMe, $R_1 = R_2 = C_6H_5$

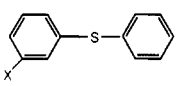
In suitable cases, a mono-substituted benzene can be converted in a one-pot sequence into the trisubstituted derivative **6**. Thus, compound **10a** (**15**) was synthesized without isolation of intermediates from anisole, which was directly treated with *n*-BuLi in refluxing ether to give *o*-lithioanisole. After the successive addition of thionylaniline and of *t*-BuLi, the dianion species **6** reacted with benzophenone to give compound **10a** (**15**) in an overall yield of 53%. Analogous to the results of the lithiation of *o*-methoxybenzamide,[12] metalation of the *o*-methoxy sulfinamide occurred ortho to the sulfinamide function, and no evidence for byproduct formation was found.

As summarized in Table I, the effects of the para substituents on the ease of metalation are clearly seen on both the time and the temperature of the metalation and on the yield of product. A chloro substituent accelerates the rate of metalation substantially as shown by comparison with hydrogen and methyl substituents, a result in agreement with observations made with benzamides[12] and thiobenzamides.[18]

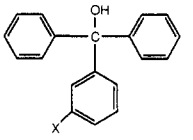
Table II. Desulfination of Ortho-Substituted Benzenesulfinamides (Sultines)

entry	sulfinamide (sultine)	method	product (yield, %)
1	**8d**	A	**16** (81)
2	**12**	A	**17** (72)
3	**9b**	A	**18** (85)
4	**14**	B	**19** (87)
5	**15**	B	**20** (78)

Desulfination was readily accomplished by either of two known procedures. (i) An easy hydrolysis, followed by mercuridesulfination,[29] an effective method for the removal of sulfinic acid groups. Thus, compound **8d** was refluxed in dilute NaOH solution (0.25 N) to give the sodium sulfinate, which (without isolation) was treated with mercuric chloride in acidic solution, to yield compound **16** (81%). Desulfination of sultines can also be accomplished by mercuridesulfination. Thus compound **12** was desulfinated with mercuric chloride in a refluxing hydrochloric acid–ethanol solution, leading to corresponding carbinol **17** in 72% yield. (ii) Desulfination of sultines was also carried out by reductive desulfination using Raney Ni in refluxing ethanol.[30] A representative example was desulfination of compound **9c**: it was dissolved in ethanolic NaOH (pH = 10) and refluxed with Raney Ni overnight to give carbinol **19** in 87% yield. The chloro substituent in **12** does not survive under the Ra/Ni conditions for desulfination, so method i was used.



16, X = Cl
18, X = Me



17, X = Cl
19, X = Me
20, X = OMe

Table II lists the results of desulfinations using both methods. All the products were characterized by comparison with literature data, ^1H and ^{13}C NMR spectra, and mass spectra.

In view of the easy attachment and removal of sulfinamide groups, the expanding scope of ortho-directed metalation, and the increasing number of directing groups, the method reported herein should have broad synthetic utility for aromatic transformations involving the introduction of a meta substituent. The high yields, easy manipulation, and relatively mild conditions further demonstrate the accessibility and the utility of the present method.

Experimental Section

Column chromatography was carried out by using MBS silica gel (230–400 mesh). Melting points of the products were measured in a Thomas-Hoover melting point apparatus and are uncorrected. ^1H NMR (200 MHz) spectra were recorded on a Varian XL200 (FT mode) spectrometer using Me_4Si as an internal standard. The following abbreviations are used: (b) broad, (w) weak, (ex) exchangeable with D_2O, (s) singlet, (d) doublet, (t) triplet, (q) quartet, (m) multiplet. ^{13}C NMR (50 MHz) were recorded on a Varian

(28) An attempt to avoid hydrolysis during the workup by quenching with water at low temperature was unsuccessful: a mixture was isolated containing both cyclic and uncyclic compounds which was not easy to separate.

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XL200 (FT mode) spectrometer. Mass spectra were recorded on a AEI MS 30 mass spectrometer. Exact mass measurements were performed on a KRATOS MS-80-RFA double-focusing spectrometer using the peak matching technique at nominal resolution of 5000 (10% valley definition).

Compounds **5a–d** were prepared according to literature procedures:[21b] **5a**, mp 113–114 °C (lit.[21b] mp 113–114 °C); **5b**, mp 158–159 °C; **5c**, mp 135–136 °C (lit.[21b] mp 137–138 °C); **5d**, mp 123–125 °C.

Electrophiles were purified by standard methods before use.

Preparation of Substituted Benzenesulfinamides (7a–d). General Procedure. Benzenesulfinamide (5 mmol) was dissolved in 45 mL of tetrahydrofuran (dried over sodium/benzophenone and freshly distilled) in a two-necked Schlenk type reactor under an argon atmosphere and cooled to −20 °C. *n*-BuLi (4.2 mL, 2.5 M in hexane) was added dropwise. The reaction mixture was stirred at −20 °C for 3 h and then allowed to warm to 0 °C and stirred at 0 °C for 10–45 min. The reaction mixture was recooled to −78 °C, and the electrophile (10 mmol) in tetrahydrofuran (5 mL) was added slowly. The reaction mixture was kept at −78 °C for a few hours and allowed to warm to room temperature overnight. Aqueous hydrochloric acid (10%) or water was added to quench the reaction, and the solution was extracted with ether. The combined ether extracts were washed with brine and dried over Na_2SO_4. After the solvent had been removed under vacuum, the residue was purified by recrystallization or by column chromatography. The melting points of the products, recrystallization solvents, and column chromatography eluates are presented in Table I.

3,3-Diphenyl-3*H*-2,1-benzoxathiole 1-oxide (11): ^{1}H NMR ($CDCl_3$) δ 7.18–7.69 (m, 14 H); ^{13}C NMR ($CDCl_3$) δ 104.6 (CO), 124.1, 125.5, 127.5, 127.6, 128.3, 128.4, 128.7, 129.7, 132.2, 142.1, 142.5, 143.1, 146.5.

Anal. Calcd for $C_{19}H_{14}O_2S$: C, 74.48; H, 4.60. Found: C, 74.69; H, 4.61.

2-Methylbenzenesulfinanilide (7b): ^{1}H NMR ($CDCl_3$) δ 2.23 (s, 3 H), 6.58 (s, 1 H, NH), 6.94–8.07 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 18.4 (CH_3), 118.1, 123.0, 123.8, 126.4, 129.2, 130.8, 131.1, 135.7, 141.0, 142.0.

Anal. Calcd for $C_{13}H_{13}NOS$: C, 67.50; H, 5.66; N, 6.06. Found: C, 67.59; H, 5.32; N, 5.66.

2-(*tert*-Butylcarbamoyl)benzenesulfinanilide (7c): ^{1}H NMR (DMSO-d_6) δ 1.46 (s, 9 H), 7.05–8.36 (m, 10 H), 9.08 (s, 1 H, NH); ^{13}C NMR (DMSO-d_6) δ 28.4 (CH_3), 51.0 ($C(CH_3)_3$), 117.2, 121.7, 124.7, 128.4, 129.0, 129.8, 130.6, 136.3, 142.8, 143.1, 166.0 (CONH).

Anal. Calcd for $C_{17}H_{20}N_2O_2S$: C, 64.53; H, 6.37; N, 8.85. Found: C, 64.71; H, 6.31; N, 8.61.

2-(Phenylthio)benzenesulfinanilide (7d): ^{1}H NMR ($CDCl_3$) δ 4.78 (s, 1 H, NH), 6.91–8.12 (m, 14 H); ^{13}C NMR ($CDCl_3$) δ 117.9, 122.5, 125.0, 126.8, 127.5, 128.8, 129.0, 131.2, 131.5, 131.6, 133.6, 135.0, 140.9, 143.6.

Anal. Calcd for $C_{18}H_{15}NOS_2$: C, 66.43; H, 4.65; N, 4.30. Found: C, 66.76; H, 4.55; N, 4.19.

Preparation of Substituted Benzenesulfinamides (8a–g). General Procedure. Similar procedure as the preparation of sulfinamides (**7a–d**), except the lithiation temperature and time are different (see Table I). The following compounds were prepared by the procedure.

4-Chloro-2-deuteriobenzenesulfinanilide (8a): ^{1}H NMR (DMSO-d_6) δ 6.92–7.35 (m, 5 H), 7.58–7.82 (m, 3 H), 9.39 (s, 1 H, NH, ex); ^{13}C NMR (DMSO-d_6) δ 117.9, 122.3, 127.5, 128.9, 129.0, 129.1, 135.8, 141.5, 143.4; MS (HR) for $C_{12}H_9DClNOS$ calcd 252.0234, found 252.0226.

5-Chloro-3,3-diphenyl-3*H*-2,1-benzoxathiole 1-oxide (12): ^{1}H NMR ($CDCl_3$) δ 7.18–7.79 (m, 13 H); ^{13}C NMR ($CDCl_3$) δ 104.4 (CO), 125.3, 125.7, 127.5, 127.6, 128.5, 128.6, 129.0, 130.3, 138.8, 141.5, 141.9, 145.1, 145.4; MS (HR) for $C_{19}H_{13}ClO_2S$ calcd 340.0325, found 340.0326.

Anal. Calcd for $C_{19}H_{13}ClO_2S$: C, 66.96; H, 3.84. Found: C, 66.75; H, 3.91.

5-Chloro-3-phenyl-3*H*-2,1-benzoxathiole 1-oxide (13): ^{1}H NMR ($CDCl_3$) δ 6.56 (s, 1 H), 7.08–7.61 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 91.8 (CHO), 124.0, 124.5, 127.9, 129.1, 129.2, 129.9, 135.8, 138.9, 143.5, 146.1; MS (HR) for $C_{13}H_9ClO_2S$ calcd 264.0012, found 264.0024.

Anal. Calcd for $C_{13}H_9ClO_2S$: C, 58.98; H, 3.43. Found: C, 58.92; H, 3.34.

4-Chloro-2-(phenylthio)benzenesulfinanilide (8d): ^{1}H NMR (DMSO-d_6) δ 6.75–7.90 (m, 13 H), 9.20 (s, 1 H, NH, ex); ^{13}C NMR (DMSO-d_6) δ 117.3, 122.2, 127.0, 127.4, 129.0, 129.2, 129.3, 130.0, 131.9, 132.9, 136.4, 137.6, 141.7, 142.1.

Anal. Calcd for $C_{18}H_{14}ClNOS_2$: C, 60.07; H, 3.92; N, 3.89. Found: C, 59.65; H, 3.92; N, 3.81.

4-Chloro-2-methylbenzenesulfinanilide (8e): ^{1}H NMR ($CDCl_3$) δ 2.38 (s, 3 H), 6.81 (s, 1 H, NH, ex), 6.98–7.85 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 18.2 (CH_3), 118.3, 123.3, 125.6, 126.5, 129.3, 130.7, 137.2, 137.6, 140.5, 140.7.

Anal. Calcd for $C_{13}H_{12}ClNOS$: C, 58.75; H, 4.55; N, 5.27. Found: C, 58.67; H, 4.48; N, 5.25.

4-Chloro-2-iodobenzenesulfinanilide (8f): ^{1}H NMR (DMSO-d_6) δ 6.92–8.01 (m, 8 H), 8.23 (b s, 1 H, NH); ^{13}C NMR (DMSO-d_6) δ 95.7, 117.1, 122.2, 128.0, 128.6, 129.3, 136.5, 138.4, 142.0, 145.3; MS (HR) for $C_{12}H_9ClINOS$ calcd 376.9138, found 376.9156.

4-Chloro-2-(*tert*-butylcarbamoyl)benzenesulfinanilide (8g): ^{1}H NMR (DMSO-d_6) δ 1.39 (s, 9 H), 7.39–8.32 (m, 8 H), 9.16 (s, 1 H, NH); ^{13}C NMR (DMSO-d_6) δ 28.3 (CH_3), 51.2 ($C(CH_3)_3$), 117.3, 121.9, 127.0, 128.2, 129.0, 129.6, 135.4, 137.8, 142.3, 142.5, 164.4 (CONH).

Anal. Calcd for $C_{17}H_{19}ClN_2O_2S$: C, 58.20; H, 5.46; N, 7.98. Found: C, 58.38; H, 5.37; N, 7.65.

Preparation of Substituted Benzenesulfinamides (9a–c). General Procedure. Similar procedure as the preparation of sulfinamides (**7a–d**), except the lithiation temperature and time are different (see Table I). The following compounds were prepared by the procedure.

4-Methyl-2-deuteriobenzenesulfinanilide (9a): ^{1}H NMR ($CDCl_3$) δ 2.41 (s, 3 H), 6.63 (s, 1 H, NH, ex), 6.95–7.39 (m, 7 H), 7.42 (d, 1 H); ^{13}C NMR ($CDCl_3$) δ 21.4 (CH_3), 118.8, 123.4, 125.5, 129.4, 129.6, 129.7, 140.8, 141.5, 141.7; MS (HR) for $C_{13}H_{12}DNOS$ calcd 232.0780, found 232.0775.

4-Methyl-2-(phenylthio)benzenesulfinanilide (9b): ^{1}H NMR ($CDCl_3$) δ 2.38 (s, 3 H), 6.45 (s, 1 H, NH), 6.87–7.98 (m, 13 H); ^{13}C NMR ($CDCl_3$) δ 21.3 (CH_3), 118.7, 123.2, 125.6, 127.6, 128.5, 129.2, 129.3, 129.6, 131.5, 133.2, 140.9, 141.0, 141.4, 141.6.

Anal. Calcd for $C_{19}H_{17}NOS_2$: C, 67.23; H, 5.05; N, 4.13. Found: C, 67.19; H, 5.44; N, 4.31.

5-Methyl-3,3-diphenyl-3*H*-2,1-benzoxathiole 1-oxide (14): ^{1}H NMR ($CDCl_3$) δ 2.42 (s, 3 H), 7.19–7.73 (m, 13 H); ^{13}C NMR ($CDCl_3$) δ 21.8 (CH_3), 104.2 (CO), 123.8, 125.8, 127.6, 127.7, 128.2, 128.3, 128.4, 128.6, 130.8, 142.3, 142.6, 143.1, 143.6, 144.0.

Anal. Calcd for $C_{20}H_{16}O_2S$: C, 74.97; H, 5.03. Found: C, 74.95; H, 5.00.

Preparation of 7-Methoxy-3,3-diphenyl-3*H*-2,1-benzoxathiole 1-Oxide (15). One-Pot Procedure. Anisole (1.08 g, 10 mmol) was dissolved in 20 mL of dry ethyl ether (dried over sodium/benzophenone, freshly distilled) in a two-necked Schlenk reactor, and *n*-BuLi (4.0 mL, 10 mmol, 2.5 M in hexane) was added dropwise at 25 °C. The mixture was refluxed for 14 h. The reaction mixture was cooled to −78 °C, and thionylaniline (1.39 g, 10 mmol) was added slowly to give a yellow suspension. The mixture was stirred at 25 °C for 30 min and cooled to −40 °C, *t*-BuLi (5.9 mL, 10 mmol, 1.7 M in pentane) was added dropwise. The solution turned red-orange, and the precipitate gradually dissolved. The mixture was stirred at −40 °C for a few minutes, allowed to warm to −20 °C, and stirred at this temperature for 1 h. The reaction mixture was recooled to −78 °C, and benzophenone (1.84 g, 10 mmol) in 5 mL of ethyl ether was added slowly. The reaction mixture was stirred at −78 °C for a few hours and then warmed to room temperature overnight. The reaction was quenched with aqueous HCl (10%), extracted with ether (3 × 30 mL), washed with brine, and dried over Na_2SO_4. After evaporation of the solvent an oily residue was obtained. The residue was diluted with ether and hexane to give a white solid, which was recrystallized from ether–hexane to give 1.78 g (53%) of compound **15**: mp 138–140 °C; ^{1}H NMR ($CDCl_3$) δ 3.92 (s, 3 H), 6.87–7.50

(m, 13 H); ^{13}C NMR ($CDCl_3$) δ 55.3 (CH_3O), 104.1 (CO), 110.4, 116.4, 126.9, 127.5, 127.6, 127.8, 133.8, 141.5, 141.7, 144.9, 155.8.

Anal. Calcd for $C_{20}H_{16}O_3S$: C, 71.41; H, 4.80. Found: C, 71.63; H, 4.55.

Desulfination of Substituted Benzenesulfinamides (Sultines). Mercuridesulfination (Method A). General Procedure. Sulfinamide (250 mg) was dissolved in a mixture of 10 mL of NaOH (0.25 N) and 10 mL of ethanol. The mixture was refluxed for a few hours and acidified with acetic acid. Mercuric chloride (0.4 g) was added, and the mixture was refluxed for 1 h to give a precipitate. The precipitate was collected and suspended in a mixture of 10 mL of concentrated hydrochloric acid and 10 mL of ethanol. The mixture was refluxed for a few hours until the suspension dissolved. The mixture was diluted with water, extracted with benzene (3 × 25 mL), and dried over Na_2SO_4. Evaporation of the solvent gave the crude product, which was purified by recrystallization or chromatography on silica gel. Compounds (**16**–**18**) were prepared by this procedure.

***m*-Chlorophenyl phenyl sulfide (16)**: an oil from chromatography on silica gel (Et_2O–hexane) (lit.[31] bp 186 °C (30mm)); ^1H NMR ($CDCl_3$) δ 7.08–7.48 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 126.6, 127.8, 127.9, 128.3, 129.3, 129.9, 132.2, 133.8, 134.8, 138.8; MS *m/e* 220 (M^+, 100); MS (HR) for $C_{12}H_9ClS$ calcd 220.0113, found 220.0016.

(*m*-Chlorophenyl)diphenylcarbinol (17): oil (lit.[32] mp 53–55 °C); ^1H NMR ($CDCl_3$) δ 3.28 (b s, 1 H, ex), 6.85–7.36 (m, 14 H); ^{13}C NMR ($CDCl_3$) δ 81.6 (COH), 126.5, 127.5, 127.6, 127.8, 128.0, 128.4, 129.3, 129.5, 143.0, 145.9; MS (HR) for $C_{19}H_{15}ClNO$ calcd 294.0812, found 294.0815.

***m*-Tolyl phenyl sulfide (18)**: an oil from chromatography on silica gel (Et_2O–hexane); bp 309–310 °C (760 mm) (lit.[33] bp 309.5 °C (760 mm)); ^1H NMR ($CDCl_3$) δ 2.24 (s, 3 H), 7.15–7.58 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 21.2 (CH_3), 126.8, 127.9, 128.3, 128.9, 129.1, 130.7, 131.8, 135.2, 136.1, 138.9.

Desulfination of Substituted Benzenesulfinamides (Sultines). Hydrodesulfination (Method B). General Procedure. The sulfinamide (sultine) (250 mg) was dissolved in a mixture of 20 mL of NaOH (0.25 N) and 20 mL of ethanol and refluxed for a few hours with Raney Ni (5 g). The alkaline solution was filtered, acidified with 5% HCl, and extracted with chloroform. The extract was dried over Na_2SO_4 and evaporated to give the crude product, which was purified by recrystallization or chromatography on silica gel. Compounds **19** and **20** were prepared by the procedure described above.

***m*-Tolyldiphenylcarbinol (19)**: after recrystallization from benzene–petroleum ether, mp 65–67 °C (lit.[34] mp 62–65 °C); ^1H NMR ($CDCl_3$) δ 2.18 (s, 3 H), 2.78 (b s, 1 H, ex), 6.82–7.24 (m, 14 H); ^{13}C NMR ($CDCl_3$) δ 21.5 (CH_3), 81.9 (COH), 125.2, 125.5, 127.1, 127.7, 127.8, 127.9, 128.4, 135.7, 137.5, 146.9.

(*m*-Methoxyphenyl)diphenylcarbinol (20): after recrystallization from ethyl ether, mp 88–89 °C (lit.[34] mp 87–89 °C); ^1H NMR ($CDCl_3$) δ 2.89 (b s, 1 H, ex), 3.74 (s, 3 H), 6.84–7.52 (m, 14 H); ^{13}C NMR ($CDCl_3$) δ 54.9 (OCH_3), 81.8 (COH), 120.5, 127.1, 127.6, 127.8, 127.9, 128.7, 128.6, 146.7, 148.4, 159.1.

Registry No. **5a**, 14933-97-2; **5b**, 14934-01-1; **5c**, 6873-54-7; **5d**, 21532-54-7; **7a**, 123858-12-8; **7b**, 123858-13-9; **7c**, 123858-14-0; **7d**, 123880-76-2; **8a**, 123858-15-1; **8b**, 123858-16-2; **8c**, 123858-17-3; **8d**, 123858-18-4; **8e**, 123858-19-5; **8f**, 123858-20-8; **8g**, 123858-21-9; **9a**, 123858-22-0; **9b**, 123858-23-1; **9c**, 123858-24-2; **10a**, 123858-25-3; **11**, 66820-99-3; **12**, 123858-26-4; **13**, 123858-27-5; **14**, 123858-28-6; **15**, 123858-29-7; **16**, 38700-88-8; **17**, 29647-82-3; **18**, 13865-48-0; **19**, 6922-90-3; **20**, 78238-98-9; $(C_6H_5)_2CO$, 119-61-9; anisole, 100-66-3; thionylaniline, 1122-83-4.

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In Situ Generation of ^{17}O-Labeled Carbonyl Anion Radical Systems

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Strong well-resolved ESR spectra of ^{17}O-labeled anion radicals of ketones, quinones, and semidiones can be obtained via the simple addition of microliter amounts of 20% ^{17}O-labeled water to 0.5–1 mL of the unlabeled anion radical solutions in either hexamethylphosphoramide or in liquid ammonia. Compared to the standard procedure of synthesizing the labeled carbonyl compounds prior to the ESR study, this technique represents a very simple alternative procedure for the study of ^{17}O coupling constants and spin densities.

Introduction

The lack of a radioactive isotope of oxygen has been the source of frustration of life scientists interested in the aerobic process. On the other hand, ^{17}O does have a nuclear spin of 5/2 and can be studied in living systems via magnetic resonance techniques. Both in vivo and in vitro studies involving the direct observation of either the ESR or NMR ^{17}O coupling are hindered by the low natural abundance of ^{17}O (0.037%) and the difficulty in incorporating it into the systems of interest. However, the presence of ^{17}O-enriched water in biological systems can be observed indirectly via its effect upon water proton relaxation rates ($1/T_2$).[1] Of possible clinical value is the fact that the rate at which $1/T_2$ varies with the concentration of $H_2{}^{17}O$ is dependent upon the physiological and pathological state of the tissue.[1] The change in T_2 resulting from $H_2{}^{17}O$ enrichment is a function of the ^{17}O residence time, and it can even be used to study proton transfer rates.[2]

In contrast to the indirect effects of ^{17}O upon magnetic resonance parameters, the direct ESR observation of ^{17}O requires incorporation of this isotope of oxygen directly into the radical of interest. Besides radicals of biological interest, ^{17}O-enriched systems are needed for oxygen spin density,[3] ion association,[4] and hydrogen bonding[5] studies.

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