

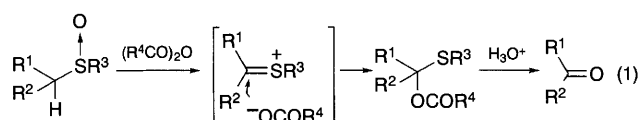
# An Efficient Synthesis of *p*-Quinones utilizing a Novel Pummerer-type Rearrangement of *p*-Sulfinylphenols

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Treatment of the *p*-sulfinylphenol derivatives **1** and **5** with trifluoroacetic anhydride causes a Pummerer-type rearrangement on aromatic rings and concomitant desulfurization to give 1:1 mixtures of the corresponding *p*-quinones and *p*-dihydroquinones, which are subjected to mild oxidation to provide high yields of *p*-quinones **3** and **7**.

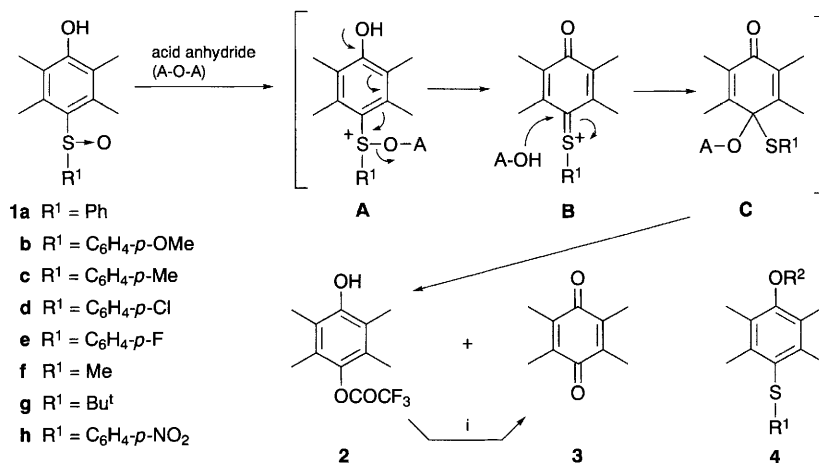
The treatment of aliphatic sulfoxides with acid anhydrides causes the Pummerer rearrangement which produces  $\alpha$ -acyloxy sulfides. Since these products can be readily hydrolysed to carbonyl compounds, the overall reaction provides a convenient method for the transformation of sulfinyl groups into carbonyl groups [eqn. (1)].<sup>1,2</sup> If similar sequential reactions occur in



*p*-sulfinylphenols, this could prove to be an effective method for the preparation of *p*-quinones. However, the possibility of such a reaction has never been elucidated. Only two related examples have been reported, for the reactions of *p*-(methylsulfinyl)-<sup>3</sup> and *o*-(phenylsulfinyl)-phenol.<sup>4</sup> These aromatic sulfoxides were reacted with acid anhydrides to give the sulfonium ions, to

which nucleophiles were added at the  $\gamma$ -carbon of the sulfinyl group, giving the corresponding nucleophile-substituted sulfinylphenols. We report here the first Pummerer-type rearrangement of *p*-sulfinylphenols **1** and **5**, which gave the corresponding *p*-quinones **3** and **7** in high yields.

In order to examine the possibility of a Pummerer-type rearrangement on aromatic rings, we first examined the reaction of 2,3,5,6-tetramethyl-*p*-(phenylsulfinyl)phenol **1a** with several acid anhydrides. We assumed that the reaction of **1a** with an acid anhydride would cause similar sequential reactions to the usual Pummerer rearrangement,<sup>1</sup> giving the  $\alpha$ -acyloxy sulfide **C** through intermediates **A** and **B**, in which the electron-donating hydroxy group at the *para*-position would strongly accelerate both the first *O*-acylation of **1** and the second S–O bond fission in **A**. Therefore, the appropriate hydrolysis of **C** would give the desired quinone (Scheme 1). Although the reaction of **1a** with 10 equiv. acetic anhydride in refluxing 1,2-dichloroethane did not proceed at all (run 1 in Table 1), reaction of **1a** with 10 equiv. trifluoroacetic anhydride in methylene chloride occurred immediately at 0°C. A 1:1



Scheme 1 Reagents and conditions: i, aq. NaHCO<sub>3</sub>, MeOH, room temp., 1 h

Table 1 Conversion of the *p*-sulfinylphenols **1a–h** to the quinone **3**

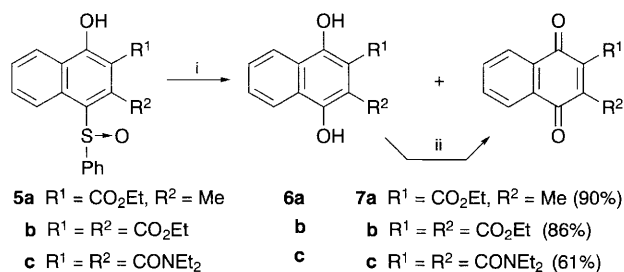
Run	1	Reaction conditions	Product yield, (%)	
			3	4
1	a	Ac <sub>2</sub> O (10 equiv.), ClCH <sub>2</sub> CH <sub>2</sub> Cl, reflux, 2 h	— <sup>a</sup>	—
2	a	(CF <sub>3</sub> CO) <sub>2</sub> O (10 equiv.), CH <sub>2</sub> Cl <sub>2</sub> , 0°C, 5 min	84 <sup>b</sup>	—
3	a	(CF <sub>3</sub> SO <sub>2</sub> ) <sub>2</sub> O (10 equiv.), CH <sub>2</sub> Cl <sub>2</sub> , 0°C, 5 min	64 <sup>b</sup>	29 (R <sup>1</sup> = Ph, R <sup>2</sup> = H)
4	a	(CF <sub>3</sub> SO <sub>2</sub> ) <sub>2</sub> O (10 equiv.), AcONa (10 equiv.), MeCN, 0°C, 5 min	60 <sup>b</sup>	31 (R <sup>1</sup> = Ph, R <sup>2</sup> = Ac)
5	b	(CF <sub>3</sub> CO) <sub>2</sub> O (10 equiv.), CH <sub>2</sub> Cl <sub>2</sub> , 0°C, 5 min	73 <sup>b</sup>	—
6	c	(CF <sub>3</sub> CO) <sub>2</sub> O (10 equiv.), CH <sub>2</sub> Cl <sub>2</sub> , 0°C, 5 min	68 <sup>b</sup>	—
7	d	(CF <sub>3</sub> CO) <sub>2</sub> O (10 equiv.), CH <sub>2</sub> Cl <sub>2</sub> , 0°C, 5 min	74 <sup>b</sup>	19 (R <sup>1</sup> = C <sub>6</sub> H <sub>4</sub> - <i>p</i> -Cl, R <sup>2</sup> = H)
8	e	(CF <sub>3</sub> CO) <sub>2</sub> O (10 equiv.), CH <sub>2</sub> Cl <sub>2</sub> , 0°C, 5 min	70 <sup>b</sup>	—
9	f	(CF <sub>3</sub> CO) <sub>2</sub> O (10 equiv.), CH <sub>2</sub> Cl <sub>2</sub> , 0°C, 15 min	76	—
10	g	(CF <sub>3</sub> CO) <sub>2</sub> O (10 equiv.), CH <sub>2</sub> Cl <sub>2</sub> , 0°C, 5 min	61	—
11	h	(CF <sub>3</sub> CO) <sub>2</sub> O (10 equiv.), CH <sub>2</sub> Cl <sub>2</sub> , 0°C, 5 min	10	—

<sup>a</sup> **1a** was recovered almost quantitatively. <sup>b</sup> Corresponding disulfide was isolated in 96 (run 2), 58 (run 3), 60 (run 4), 86 (run 5), 97 (run 6), 65 (run 7) and 63% yield (run 8), respectively.

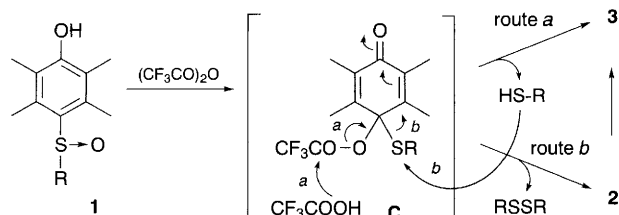
mixture of the dihydroquinone mono(trifluoroacetate) **2** and the benzoquinone **3** was obtained directly and almost quantitatively. Treatment of this mixture with aqueous  $\text{NaHCO}_3$  in MeOH at room temperature for 1 h caused hydrolysis of the trifluoroacetate **2** and subsequent auto-oxidation to give **3** in 84% yield (run 2). A similar reaction of **1a** with trifluoromethanesulfonic anhydride (10 equiv.) with or without sodium acetate (10 equiv.) also provided **3** in lower yields (60–64%) along with formation of the sulfide **4** ( $\text{R}^2 = \text{H}$  or Ac) in 29–31% yields (runs 3 and 4). In runs 2–4, 58–96% yields of diphenyl disulfide were formed as a by-product, which were comparable to the yields of **3**. Thus, reactive acid anhydrides, particularly trifluoroacetic anhydride, were found to cause very quickly the Pummerer-type rearrangement of the *p*-sulfinylphenol **1a** and the concomitant desulfurization leading to the oxygen-substituted products **2** and **3**.

As summarized in Table 1, substitution of the  $\text{R}^1$  group of **1a** by *p*-methoxy- **1b**, *p*-methyl- **1c**, *p*-chloro- **1d** and *p*-fluorophenyl groups **1e** had little effect on the reactivity and gave similar yields (68–74%) of **3** (runs 5–8). The reactions of two alkylsulfinyl derivatives **1f** and **1g** also gave **3** in 76% and 61% yields, respectively (runs 9 and 10). However, the *p*-nitrophenyl derivative **1h** provided only a 10% yield of **3** (run 11). These results reveal that various aryl- and alkyl-sulfinylphenols are readily converted into the quinone **3** in good to high yields and that among them, the *p*-(phenylsulfinyl)phenol **1a** was the most suitable substrate for this Pummerer-type rearrangement in terms of its yield, cost and ready availability.†

The present method is also applicable to the sulfoxides **5a–c** having one or two electron-withdrawing ester and amide groups. Their treatment with trifluoroacetic anhydride from  $-30^\circ\text{C}$  to room temperature gave 1:1 mixtures of the dihydroquinones **6a–c** and the quinones **7a–c**, which were subjected to mild oxidation by  $\text{MnO}_2$  to provide **7a–c** in 61–90% yields (Scheme 2). The structures of the products **3** and **7a–c** were unambiguously established by IR,  $^1\text{H}$  NMR and HRMS data.



**Scheme 2** Reagents and conditions: i,  $(\text{CF}_3\text{CO})_2\text{O}$ ,  $\text{CH}_2\text{Cl}_2$ ,  $-30^\circ\text{C}$ , 10 min (for **5a, b**), or  $-30^\circ\text{C} \rightarrow$  room temp., 1 h (for **5c**); ii,  $\text{MnO}_2$ ,  $\text{CH}_2\text{Cl}_2$ , room temp., 1 d



**Scheme 3** Proposed reaction mechanism

Considering the fact that a 1 : 1 mixture of the quinone and the dihydroquinone was usually and directly obtained in this reaction, along with formation of the disulfide, the reaction mechanism is proposed as illustrated in Scheme 3; as we expected, the reaction of **1** with trifluoroacetic anhydride must give the  $\alpha$ -acyloxy sulfide **C**. Then half of **C** was hydrolysed to give the quinone **3** that released the thiol (route *a*). This thiol reacted with the other half of **C** to give the dihydroquinone mono(trifluoroacetate) **2** and the disulfide (route *b*).

The preparation of the sulfoxides **1** and **5** was readily achieved from the corresponding phenols.† A recent paper<sup>6</sup> also presented an effective preparation of fused phenol derivatives having *p*-sulfenyl groups by the anionic [4 + 2]-cycloaddition of thiophthalides to enones. Therefore, the present method will open a novel and alternative method for the preparation of quinone moieties. That is, the oxidation of phenols to quinones are carried out using appropriate oxidizing reagents,<sup>7</sup> while our method does not need such oxidants. This method also features: (i) a simple operation; (ii) mild reaction conditions (the reactions were completed below room temperature within 1 h); (iii) compatibility with electron-withdrawing groups, and (iv) an unprecedented transformation of sulfinyl groups into oxygen functional groups on aromatic rings. Further extension of the present method to other substrates and natural product synthesis is in progress.

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## Footnote

† The sulfoxides **1a–h** and **5a–c** were readily prepared from the corresponding *p*-unsubstituted phenols by (a) direct arylsulfonylation;<sup>8</sup> (b) arylsulfonylation<sup>9</sup> and oxidation with *m*-chloroperbenzoic acid or (c) thiocyanation,<sup>10</sup> reaction with Grignard reagent and oxidation.

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