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PREPARATION OF (PHENYLSULFINYL)PHENOLS FROM ARYL PHENYLSULFINATES: 'THIA-FRIES REARRANGEMENT'

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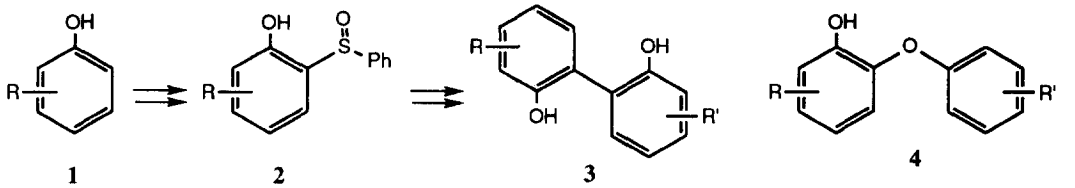
Summary: Treatment of aryl phenylsulfinates **5** (prepared from phenols **1** by reaction with phenylsulfinyl chloride) with $AlCl_3$ at 25 °C furnishes good yields of the (phenylsulfinyl)phenols **2** via a 'thia-Fries rearrangement.'

The Fries rearrangement is useful for the preparation of acylphenols from phenols via Lewis acid catalyzed rearrangement of phenyl esters.[2] The normal products of electrophilic aromatic substitution, namely the *o*- and *p*-acylphenols, are formed. For the synthesis of biphenols **3** and *o*-aryloxyphenols **4**,[3] we needed to prepare the corresponding phenylsulfinyl phenols **2**. Although these compounds can be prepared by a Friedel-Crafts-type electrophilic aromatic substitution of the phenols **1** (phenylsulfinyl chloride and $AlCl_3$), we wanted to investigate the possibility of a reaction analogous to the Fries rearrangement. We report here the successful preparation of *o*- and *p*-(phenylsulfinyl) phenols from phenyl sulfinates via a "thia-Fries rearrangement."

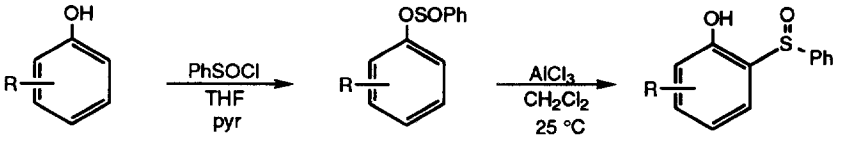


1 **2** **3** **4**

Alkyl sulfinates can be prepared by reaction of primary and secondary alcohols with an alkyl or aryl sulfinyl chloride in the presence of base[4] The same procedure works well for phenols. Thus treatment of the phenols **1a-e** with phenylsulfinyl chloride in THF with an equivalent of pyridine afforded the desired aryl phenylsulfinates **5a-e** in good yields (87-92% based on recovered starting material) (Table). Several reaction conditions were attempted for the rearrangement, with the following proving to be the best. Addition of 2 equivalents of $AlCl_3$ in one batch to a solution of the aryl phenylsulfinates **5a-e** in dichloromethane and stirring for 1 h at 25°C afforded, after aqueous workup and recrystallization of the products, the (phenylsulfinyl)phenols **2a-e**. The yields varied from 72-87%. With the 4-substituted substrates **5ab**, only 2-(phenylsulfinyl) phenols **2ab** were obtained. The 3-chloro substrate **5e** gave only the 6-(phenylsulfinyl) isomer **2c** (substitution para to the chlorine). The 3-methyl substrate **5d** furnished a 3.5:1 ratio of the 6- and 4-isomers. Recrystallization allowed isolation of the 6-isomer [5-methyl-2-(phenylsulfinyl)phenol] in 53% yield. Finally rearrangement of the 2-methyl substrate **5e** gave a 2.5:1 ratio of the 4- and 6-isomers. The structures of the products were determined by comparison to authentic samples and/or high field proton NMR spectroscopy. In the spectra of all of the *o*-(phenylsulfinyl)phenols, the phenolic proton resonates at very low field compared to the corresponding proton in the *p*-isomers.

As far as we can tell, there are no examples of this type of rearrangement in the literature. The closest analogy is the rearrangement of aryl sulfonates to give aryl sulfones.[5] However, these rearrangements required drastic conditions ($AlCl_3$ neat at 120-60°C or in refluxing nitrobenzene) and produced very low yields (generally <20%) of the desired products. By comparison, the thia-Fries rearrangement of **5** to give **2** requires quite mild conditions and proceeds in very good yields. A typical experimental procedure is given below. The further reactions of the (phenylsulfinyl)phenols will be given in due course.[6]

Table. Preparation and Thia-Fries Rearrangement of Aryl Phenylsulfinates



1	5	2
Phenol	Yield of 5[a]	Rearrangement Product (Yield)
1a R = 4-Me	87%	2-SOPh (77%)
1b R = 4-OMe	92%	2-SOPh (87%)
1c R = 3-Cl	91%	6-SOPh (72%)
1d R = 3-Me	89%	3.5 : 1 6-SOPh : 4-SOPh (77%)[b]
1e R = 2-Me	90%	2.5 : 1 4-SOPh : 6-SOPh (80%)

a) Based on recovered starting material, Conversions are 60-70%. b) The major product [5-methyl-2-(phenylsulfinyl)phenol] was isolated in 53% yield by recrystallization.

Preparation of Aryl Phenylsulfinates: To a round bottom flask under nitrogen are added 0.7 g (5.64 mmol) of 4-methoxyphenol **1b**, 0.548 ml (6.77 mmol) pyridine, and 16 ml dry THF. The solution is cooled to -78°C and 1.09 g (6.77 mmol) phenylsulfinyl chloride in 2 ml THF is added dropwise. A white precipitate is observed immediately upon addition. The reaction is stirred at -78°C for 5-6 h (or until no further cleavage is observed by TLC and/or ^{1}H NMR). The reaction is then diluted with diethyl ether and water and the phases separated. The organic phase is washed with 5% aq. citric acid, saturated $NaHCO_3$, and brine and then dried over $MgSO_4$. The unreacted phenol **1b** (182 mg) is extracted with 0.5 N NaOH and recovered after acidification with 1N HCl. Evaporation of the solvent afforded 0.952 g of 4-methoxyphenyl phenylsulfinate **5b** as a transparent colorless oil (68%, 92% based on recovered starting material).

Thia-Fries Rearrangement of Aryl Phenylsulfinates: In a round bottom of flask is placed 0.3 g (1.2 mmol) 4-methoxyphenyl phenylsulfinate **5b** in 5 ml dichloromethane under nitrogen. Aluminum trichloride (0.323 g, 2.42 mmol) is added in one batch. The solution becomes somewhat green in color and begins to reflux. The reaction is stirred for 1 h at 25°C. The reaction is diluted with dichloromethane and water is added dropwise. The organic phase is washed with water, saturated $NaHCO_3$, and brine and dried over $MgSO_4$. If an emulsion is observed during workup, the combined aqueous washes are extracted several times with dichloromethane and added to the organic phase. The crude product (after removal of solvent) is recrystallized from acetonitrile to give 0.2603 g (87% yield) of 4-methoxy-2-(phenylsulfinyl)phenol **2b** as pinkish -white crystals.

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References and Notes

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