

# Occurrence of Ligand Coupling in the Reaction of the 2-Thienyl Sulfoxides with Organometallic Compounds

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## ABSTRACT

*Treatment of 2-pyridyl 2-thienyl sulfoxide with 2-thienyllithium was found to give both 2-(2-pyridyl)thiophene 2 and 2,5-(di-2-pyridyl)thiophene 3. The reaction between 2-thienyllithium and thionyl chloride was found to give 2,2'-bithienyl 8, a coupling product, which is also formed by the reaction between di-2-thienyl sulfoxide 7 and 2-thienyllithium.*

## INTRODUCTION

Although much more work remains to be done on ligand coupling within sulfurane intermediates, the concept has been introduced [1], and numerous studies of ligand coupling reactions have been carried out [2]. From an early period, the occurrence of the coupling seems to be associated with the electronic state of the coupling carbon atom of the coupling ligands, while the electronic state of the carbon ligands is considered to be diagnosed roughly on the basis of  $^{13}\text{C}$  NMR chemical shifts. Indeed, this working hypothesis has led to many interesting findings. The sulfoxides which can undergo ligand coupling on treatment with benzyl, vinyl, or similar organometallic reagents carry an aromatic group whose  $\alpha$ -carbon chemical shift

ranges from  $\delta = 150$  to  $175.5$  [3]. Although *p*-(phenylsulfonyl)phenyl ( $\delta = 151.8$ ) 2-pyridyl sulfoxide undergoes both ligand coupling and exchange in the reaction with a Grignard reagent [4], the phenyl ( $\delta = 146.3$ ) sulfoxide undergoes only ligand exchange [5]. Since the resonance of the 2-carbon of 2-thienyl sulfoxide appears at  $\delta = 150.3$ , it would be of interest to see how the 2-thienyl group would behave in the reactions of 2-thienyl sulfoxides with typical organometallic reagents.

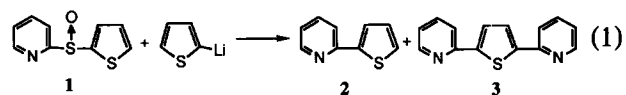
2-Pyridyl 2-thienyl sulfoxide was reported to couple with 2-thienyllithium in an earlier communication, resulting in the formation of 2-(2-pyridyl)thiophene 2 and 2,5-(di-2-pyridyl)thiophene 3 [6].

This preliminary work has now been more thoroughly investigated, and we have discovered a new and facile coupling between two 2-thienyl groups in the treatment of 2-thienyllithium with thionyl chloride. This article describes the details of these reactions.

## RESULTS AND DISCUSSION

### Formation of 2-(2-Pyridyl)thiophene 2

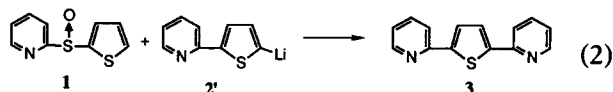
The first reaction examined was that between 2-pyridyl 2-thienyl sulfoxide 1 with 2-thienyllithium, which gave both 2-(2-pyridyl)thiophene 2 and 2,5-(di-2-pyridyl)thiophene 3, as shown below.



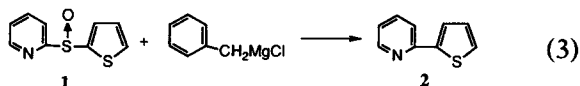
Dedicated to Prof. James Cullen Martin on the occasion of his sixty-fifth birthday.

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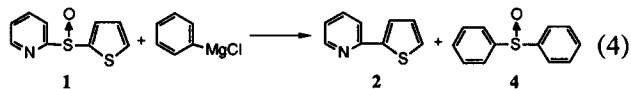
The latter compound was undoubtedly formed by a second coupling between 2-pyridyl 2-thienyl sulfoxide **1** and 2-[5-(2-pyridyl)thiophenyl]lithium **2'**, formed *in situ* from **2**. In a separate experiment, it was found that the reaction indeed proceeds as shown below.



When benzylmagnesium chloride was treated in the same manner, however, no benzylated thiophene or pyridine was obtained but 2-(2-pyridyl)thiophene **2** was obtained in a good yield, as shown below, unlike the results of the reaction between other 2-pyridyl sulfoxides with benzylmagnesium chloride, in which 2-benzylpyridine was obtained [7].



This indicates clearly that ligand exchange proceeds prior to the ligand coupling, as in the following reaction between 2-pyridyl 2-thienyl sulfoxide **1** and phenylmagnesium bromide, in which ligand exchange proceeded prior to the minor coupling that gave only a meager amount (6%) of 2-(2-pyridyl)thiophene **2** and mainly diphenyl sulfoxide **4**, a ligand exchange product.

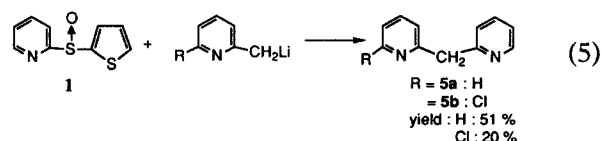


The above reaction is considered to involve ligand exchange to form 2-pyridylmagnesium bromide and then 2-thienylmagnesium bromide. The latter ligand exchange product, 2-thienylmagnesium bromide, in a subsequent step, attacks the original sulfoxide **1** to give the ligand coupling product **2**.

Since pyridine was obtained in quantitative yield, various 2-pyridyllithium compounds were allowed to react with 2-pyridyl 2-thienyl sulfoxide **1** under various conditions, as described in the Experimental section; however, none of the 2-pyridyllithium compounds were found to react with the sulfoxide, unlike the reaction of 2-pyridyllithium with methyl 2-pyridyl sulfoxide [8]. Apparently not much exchange is taking place under these conditions, since the recovery of the starting material, especially 2-pyridyl 2-thienyl sulfoxide **1**, is nearly

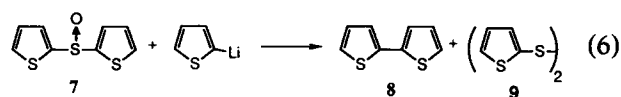
quantitative. Both starting materials were quite soluble in THF, and yet there was no apparent reaction. This is rather strange.

Apparently the 2-thienyl group of 2-thienyllithium is a much better ligand than 2-pyridyl to couple, while the 2-thienyl group of 2-thienyllithium is a better coupling reagent than the benzyl group to couple with the 2-thienyl ligand. However, 2-pyridylmethyl lithium compounds prefer to couple with the 2-pyridyl ligands rather than with the 2-thienyl group. Thus, the following coupling reaction was observed. Obviously, an electron-withdrawing 2-pyridylmethyl group, although similar to a benzylic group, prefers to couple with a pyridyl group.

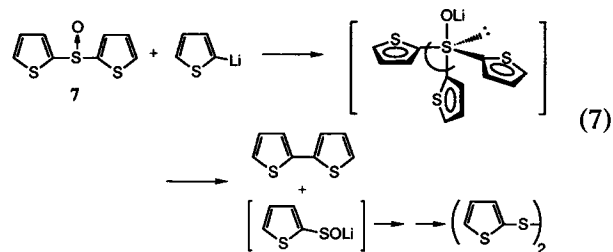


### B. Reaction between Di-2-thienyl Sulfoxide **7** with 2-Thienyllithium

Since 2-pyridyl 2-thienyl sulfoxide **1** readily reacted with 2-thienyllithium which furnishes a better coupling reagent than the benzyl group, the reaction between di-2-thienyl sulfoxide **7** and 2-thienyllithium was carried out similarly, as shown below. Then a facile coupling of two thienyl groups was found to take place. Here, again, the remaining product was di-2-thienyl disulfide **9**.



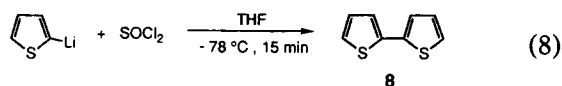
Obviously, the reaction would be expected to proceed through ligand coupling within the hypervalent species, as shown below.



### C. Reaction between 2-Thienyllithium and Thionyl Chloride

Earlier, the reaction between 2-benzothiazyl lithium and phosphorus trichloride was found to proceed through ligand coupling to afford 2,2'-bi-benzothiazyl as a major product [9]. Similarly, when 2-thienyllithium was treated with thionyl

chloride, the reaction product formed in a good yield was found to be 2,2'-bithienyl **8**.



In a separate experiment, it had already been shown that, in the reaction between di-2-thienyl sulfoxide **7** with 2-thienyllithium, the same product **8** was obtained. Although more work would be necessary to elucidate the mechanism, the reaction would be expected to involve another ligand coupling.

## EXPERIMENTAL

### General

All the melting points were uncorrected and were taken on a Yanagimoto melting-point apparatus. The IR spectra were obtained on a Jasco-IRA-202 and Perkin-Elmer FT-IR 1760X spectrometer. The NMR spectra were obtained on a JEOL-JNM-PMX60<sub>SI</sub> or a JEOL-GSX-270 FT-NMR spectrometer in CDCl<sub>3</sub> using TMS as an internal standard.

All the reactions were monitored by TLC (Merck, Kieselgel 60 F254), GLC (Hitachi 163 and 663-30, using a 3% silicone OV-17 chromosorb W of 60–80 mesh, a 30% silicone gum SE-30 of 60–80 mesh, or a 30% polyethylene glycol 20 M of 60–80 mesh in the column), HPLC (Shimadzu SPD-6A, OD-ST 5 μm in the column). The silica gel used for column chromatography was Wakogel C-200 and C-300. Mass spectra were taken with a Shimadzu GCMS-QP1000(A) mass spectrometer. Elemental analyses were carried out at the Elemental Analysis Center in Wako Pure Chemical Industries Ltd.

### Materials

All reagents were obtained from Wako Pure Chemical Industries Ltd., Tokyo Kasei Co., and Aldrich Chemical Co through Wako in Osaka. The reagents used and reaction solvents were further purified by general methods. Starting disulfides were prepared by oxidation of the corresponding thiols with KI<sub>3</sub>; sulfides were prepared by the treatment of the corresponding disulfides with organolithium compounds; and sulfoxides were prepared by oxidation of the corresponding sulfides with *m*-chloroperbenzoic acid, according to previously reported procedures [10–12].

### Reaction of Sulfoxide **1** with 2-Thienyllithium

A typical experimental procedure is as follows. A solution of 2-thienyllithium was prepared by adding 3.74 mmol of *n*-BuLi (as a 1.47 M solution in

*n*-hexane) to a solution of 2-bromothiophene (0.52 mL, 5.00 mmol) in THF (20 mL). The solution was added to a stirred solution of **1** (1.05 g, 5.00 mmol) in THF (30 mL) at –30°C under a nitrogen atmosphere. The solution turned red. After 1 hour reaction at –30°C, water was added to the reaction mixture. The product was extracted with ether three times. The combined ether layer was washed with water and dried over anhyd MgSO<sub>4</sub>. After the solvent had been evaporated, the residue was purified by silicagel column chromatography. The yields of 2-(2-pyridyl)thiophene **2** and 2,5-(di-2-dipyridyl)thiophene **3** were 48% and 10%, respectively, based on determination of the amounts of **2** [13] and **3** [14] isolated.

### Reaction of Sulfoxide **1** with 2-[5-(2-Pyridyl)thiophenyl]lithium **2'**

A similar procedure to that described earlier was followed with 1.31 M *n*-BuLi (2.28 mL, 2.99 mmol), 2-(2-pyridyl)thiophene (0.48 g, 2.99 mmol) in THF (20 mL), and **1** (0.57 g, 2.74 mmol) in THF (30 mL) to give **3**. The yield of **3** was 10%, which was determined by isolation, while 2-(2-pyridyl)thiophene used as a nucleophilic reagent was recovered in a yield of 79%.

### Reaction of Sulfoxide **1** with Benzylmagnesium Chloride

A similar procedure to that described previously was followed with benzylmagnesium chloride (2.20 mL, 2.20 mmol), **1** (0.42 g, 2.00 mmol), and THF (30 mL) to give **2**. The yield of **2** was 71%, which was determined by isolation.

### Reaction of Sulfoxide **1** with Phenylmagnesium Bromide

A similar procedure to that described earlier was followed with phenylmagnesium bromide (3.94 mL, 2.6 mmol), **1** (0.50 g, 2.40 mmol), and THF (30 mL) to give **2** and **4**. The yields of **2** and **4** were 6% and 21%, respectively, which were determined by isolation, while pyridine was detected quantitatively by HPLC analysis.

### Reaction of Sulfoxide **1** with 2-Pyridylmethylolithium

A similar procedure to that described earlier was followed with 1.44 M *n*-BuLi (0.69 mL, 1.00 mmol), 2-picoline (0.10 mL, 0.96 mmol) in THF (20 mL), and **1** (0.20 g, 0.96 mmol) in THF (30 mL) to give **5a**. The yield of **5a** was 51%, which was determined by isolation, while sulfoxide **1** used as a starting material was recovered in a yield of 31%.

### Reaction of Sulfoxide 1 with 6-Chloro-2-pyridylmethylithium

A similar procedure to that described earlier was followed with 1.39 M *n*-BuLi (0.79 mL, 1.10 mmol), 6-chloro-2-picoline (0.12 mL, 1.10 mmol) in THF (5 mL), and **1** (0.21 g, 1.00 mmol) in THF (10 mL) to give **5b**. The yield of **5b** was 20%, which was determined by isolation, while sulfoxide **1** used as a starting material was recovered in a yield of 52%.

**6-Chloro-2,2'-Dipyridylmethane 5b.** Oil, MS (*m/z*); ( $M^+$ ) 204,  $^1\text{H NMR}$  ( $\delta$ ); 4.21 (s,  $\text{CH}_2$ , 2H), 7.00–7.10 (m, 4Py, 4'Py, 5Py, 3H), 7.48 (d, 5Py, 1H), 7.51 (d, 3'Py, 1H), 7.53 (d, 5'Py, 1H), 8.43 (d, 6Py, 1H).

### Reaction of Sulfoxide 1 with 2-Pyridyllithium

A similar procedure to that described earlier was followed with 1.47 M *n*-BuLi (1.70 mL, 2.50 mmol), 2-bromopyridine (0.24 mL, 2.50 mmol) in THF (5 mL), and **1** (0.52 g, 2.50 mmol) in THF (10 mL). The reaction temperature was maintained at  $-30^\circ\text{C}$ . The conversion of **1** was determined by HPLC analysis, while sulfoxide **1** used as a starting material was recovered quantitatively. Even in the presence of 15-crown-5 (500  $\mu\text{L}$ ) at  $-30^\circ\text{C}$ ,  $25^\circ\text{C}$ , and  $66^\circ\text{C}$ , the reaction did not proceed and only sulfoxide **1** was recovered nearly quantitatively.

### Reaction of Sulfoxide 1 with 6-Bromo-2-pyridyllithium

A similar procedure to that described earlier was followed with 1.47 M *n*-BuLi (0.37 mL, 0.55 mmol), 2,6-dibromopyridine (0.10 g, 0.50 mmol) in THF (5 mL), and **1** (0.10 g, 0.50 mmol) in THF (10 mL). The reaction temperature was maintained at  $-30^\circ\text{C}$  or  $-30^\circ\text{C}$ ,  $25^\circ\text{C}$ , and  $66^\circ\text{C}$  in the presence of 15-crown-5 (500  $\mu\text{L}$ ). The conversion of **1** was determined by HPLC analysis, while sulfoxide **1** used as a starting material was recovered quantitatively.

### Reaction of Sulfoxide 1 with 6-Methyl-2-pyridyllithium

A similar procedure to that described earlier was followed with 1.47 M *n*-BuLi (0.37 mL, 0.55 mmol), 6-bromo-2-picoline (86.0 mg, 0.55 mmol) in THF (5 mL), and **1** (0.10 g, 0.50 mmol) in THF (10 mL). The reaction temperature was maintained at  $-30^\circ\text{C}$  or  $-30^\circ\text{C}$ ,  $25^\circ\text{C}$ , and  $66^\circ\text{C}$  in the presence of 15-crown-5 (500  $\mu\text{L}$ ). The conversion of **1** was determined by HPLC analysis, while sulfoxide **1** used as a starting material was recovered quantitatively.

### Reaction of Sulfoxide 7 with 2-Thienyllithium

A similar procedure to that described previously was followed with 1.61 M *n*-BuLi (0.68 mL, 1.10

mmol), 2-bromothiophene (0.10 mL, 1.00 mmol) in THF (5 mL), and **7** (0.21 g, 1.00 mmol) in THF (10 mL) to give **8** and **9**. The yields of **8** and **9** were 43% and 20%, respectively, while sulfoxide **7** was recovered in a yield of 40%.

### Reaction of Thionyl Chloride with 2-Thienyllithium

A similar procedure to that described earlier was followed with 1.86 M *n*-BuLi (10.75 mL, 0.02 mol), 2-bromothiophene (1.45 mL, 0.02 mol) in THF (10 mL), and thionyl chloride (4.38 mL, 0.06 mol) in THF (30 mL) to give **8**. The yield of **8** was 30% upon determination of the amount isolated based on the amount of thionyl chloride used.

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