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# Synthesis and reactivity of (1-fluorovinyl) phenyl sulfoxide as a dienophile

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## Abstract

(1-Fluorovinyl) phenyl sulfoxide **2** was prepared in two steps from (1-fluorovinyl)methyldiphenylsilane. Although the sulfoxide **2** underwent Diels-Alder reaction with very reactive diene, 1,3-diphenylisobenzofuran, to give the corresponding fluorinated-naphthalene derivative in one step, it did not afford cycloadducts with other dienes employed.

*Keywords:* (1-Fluorovinyl) phenyl sulfoxide; Diels-Alder reaction; Mono-fluorinated building block; 1,3-Diphenylisobenzofuran

## 1. Introduction

The Diels-Alder cycloaddition is a fundamental tool for the construction of a six-membered ring. The application of this reaction using suitable fluorinated dienophiles would selectively provide fluorinated cyclohexenes that serve as versatile synthetic intermediates for the construction of complex-fluorinated compounds [1]. Despite their importance, the successful [4 + 2] cycloaddition reactions of fluorinated dienophiles are scarce [2]. Accordingly, the development of mono-fluorinated dienophiles [3–9] as well as di- or tri-fluorinated dienophiles is limited [10–15]. The reason seemed to be the difficulty with introduction of fluorine(s) to olefins. We have been interested in new methodologies for the incorporation of the mono-fluorovinylic moiety and have recently reported useful mono-fluorinated building blocks [16–19]. We have expected the title compound as a convenient equivalent of fluoroacetylene that is not easy to handle for the [4 + 2] cycloaddition reactions. This report describes the first preparation and reactions of (1-fluorovinyl) phenyl sulfoxide.

## 2. Results and discussion

Our synthetic route for the preparation of the sulfoxide **2** is depicted in Scheme 1. Since we have reported the preparation of (1-fluorovinyl)methyldiphenylsilane as a useful reagent for the introduction of a 1-fluorovinyl group into organic compounds [16,18], this method was applied to the synthesis of the (1-fluorovinyl) phenyl sulfide **1** as a precursor for **2**. The cesium fluoride-initiated cross-coupling reaction of (1-fluorovinyl)methyldiphenylsilane with *S*-phenyl benzenethiosulfonate in DMF at 80 °C afforded the corresponding sulfide **1** in 93% yield. The sulfide **1** is volatile and easily susceptible to oxidation reactions. The second step for the preparation of **2** required the selective oxidation of the sulfide **1**. Inspection of literature sources revealed the system of aqueous 30% $H_2O_2$ in hexafluoro-2-propanol (HFIP) for the selective oxidation of sulfide to sulfoxide [20]. Although we applied this method to the sulfide **1**, we obtained the mixture of **1**, the desired sulfoxide **2**, and the overoxidized sulfone **3** [9,21]. The difficulty of the separation of these three compounds impelled us to examine other selective oxidation methods. After many attempts we obtained the sulfoxide **2** using mCPBA at 0 °C in 80% yield.

We have examined the use of **2** as a potential reagent for a mono-fluorinated dienophile. Haufe and co-workers described the successful Diels-Alder reaction of 1,3-diphenylisobenzofuran **4** and fluorostyrenes [3,6]. This prompted us to use **4** as a promising diene for this Diels-Alder reaction. We examined some reaction conditions for the Diels-Alder reaction, and the results are shown in Table 1. We obtained not the corresponding *endo*-and *exo*-cycloadducts **6**, but 2-fluoro-1,4-diphenylnaphthalene **5** as the aromatized product in moderate yield (Table 1). Its $^1$H NMR spectrum and its

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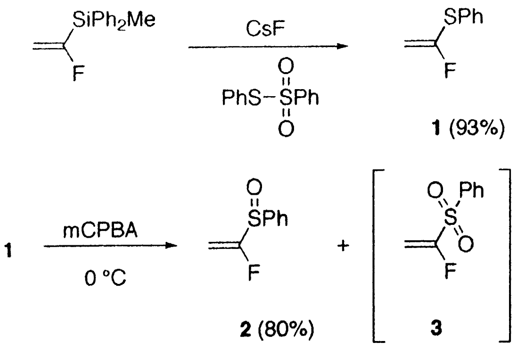


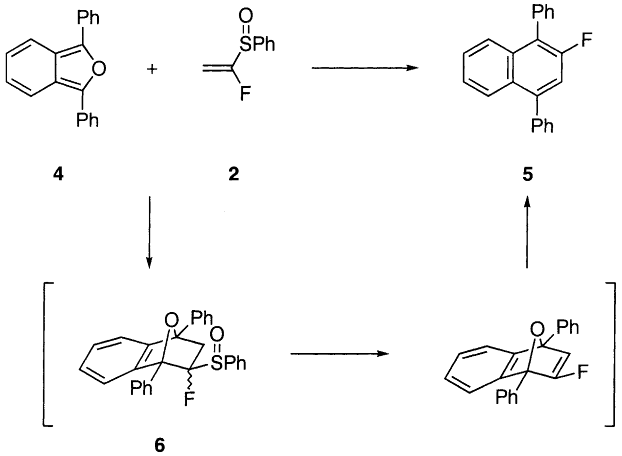
Scheme 1.

$^{13}$C NMR spectrum cleanly characterized the product **5**. The values of the chemical shifts and coupling constants of $^{13}$C–$^{19}$F are in good agreement with those of 2-fluoronaphthalene as a similar compound [22]. These findings are suggested that the sulfoxide **2** has lower reactivity than 1-fluorostyrene on the contrary of our expectation. We have not examined the reaction mechanism in detail; however, the reaction proceeded via in situ thermal elimination of benzenesulfenic acid followed by deoxygenation.

Since phenyl vinyl sulfoxide **7** has so far been shown to react with various dienes at high temperature [23–28], we next examined the reaction of **2** with an excess of other dienes such as cyclopentadiene, 2,3-dimethyl-1,3-butadiene, anthracene, 1,4-diphenyl-1,3-butadiene under various conditions. Unfortunately, these dienes afforded no cycloadduct along with the recovery of **2**. Furthermore, the reaction of **2** with *o*-quinodimethane as a more reactive diene also failed [29].

In order to obtain information about the lower reactivity of **2** compared to **7**, the orbital energies of **2** and phenyl vinyl sulfoxide **7** were calculated on the ab initio level (6-31G). To our surprise, they have nearly the same value (3.977 eV for **2** and 4.000 eV for **7**) with respect to the LUMO energies. We are afraid that it is not so easy to explain the lower reactivity of **2**.

Table 1
Diels-Alder reaction of (1-fluorovinyl) phenyl sulfoxide and 1,3-diphenylisobenzofuran



| Entry | Solvent | Additive | Temperature (°C) | Yield (%)[a] |
|---|---|---|---|---|
| **1** | Toluene | None | 110 | 12 |
| **2** | Toluene | $ZnCl_2$ | 100 | Trace |
| **3** | Tetraglyme | None | 180 | 33 |
| **4** | Ethylene glycol | None | 100 | 49 |
| **5** | Neat | None | 80 | 40 |
| **6** | Neat | None | 100 | 47 |
| **7** | Neat | None | 120 | 39 |

[a] Isolated yield.

## 3. Conclusion

We have demonstrated the first preparation of (1-fluorovinyl) phenyl sulfoxide **2** from (1-fluorovinyl)methyldiphenylsilane in two steps in good overall yields and the successful Diels-Alder reaction of **2** with 1,3-diphenylisobenzofuran **4**. We have shown that the sulfoxide **2** functioned as a fluoroacetylene synthon albeit only one example.

## 4. Experimental

Melting points were measured with a Yanagimoto micro melting point apparatus MP-S3 and are uncorrected. Infrared (IR) spectra were recorded on Perkin-Elmer Spectrum 2000. $^{1}$H NMR spectra were measured on JEOL JNM-GX270. $^{13}$C NMR spectra were measured on JEOL JNM-EX400 at the Institute for Fundamental Research of Organic Chemistry, Kyushu University. Chemical shifts were given by $\delta$ relative to that of an internal $Me_4Si$ (TMS). GC-mass spectra were obtained with JEOL JMS-AMII15. Elemental analyses were accomplished at the service center of the elementary analysis of organic compounds, Kyushu University. Analytical thin layer chromatography (TLC) was performed on a silica gel plate (Merck, Kieselgel 60 F254, 20 cm × 20 cm, 0.25 mm). DMF, toluene, tetraglyme and $CH_2Cl_2$ were used as a reaction solvent after distillation from $CaH_2$.

### 4.1. (1-Fluorovinyl) phenyl sulfide (1)

To a solution of (1-fluorovinyl)methyldiphenylsilane (1.00 g, 4.13 mmol) and *S*-phenyl benzenethiosulfonate (1.35 g, 5.39 mmol) in DMF (30 ml) was added cesium fluoride (0.95 g, 6.25 mmol) at room temperature under argon. The solution was heated at 80 °C for 12 h. After cooling to room temperature, water was added to the resulting solution. The mixture was twice extracted with hexane/ether = 3/1, and the combined organic layer was dried over $Na_2SO_4$. The solution was concentrated in vacuo, and the residue was purified by chromatography on silica gel (hexane) to give the desired sulfide **1** as a colorless oil (0.59 g, 93%): IR (neat) $\nu$ 3063, 1629, 1584, 1479, 1442, 1162, 1086, 1024, 1000, 923, 867, 743, 689 $cm^{-1}$; $^1H$ NMR (270 MHz, $CDCl_3$) $\delta$ 4.97 (1H, dd, $J = 42.7$, 2.9 Hz), 5.12 (1H, dd, $J = 10.7$, 2.9 Hz), 7.24–7.47 (5H, m); GC-MS 70 eV, *m/z* (rel int): 154 ($M^+$, 99), 153 (60), 134 (36), 109 (86), 91 (100), 77 (44), 65 (30), 51 (67), 50 (33); Anal. Calcd. for $C_8H_7FS$: C, 62.31; H, 4.58. Found: C, 62.07; H, 4.57.

### 4.2. *(1-Fluorovinyl) phenyl sulfoxide* (**2**)

mCPBA (0.92 g, 5.33 mmol) was slowly added to a solution of (1-fluorovinyl) phenyl sulfide (0.69 g, 4.47 mmol) in $CH_2Cl_2$ (4 ml) at 0 °C. The resulting mixture was stirred for 5 h at 0 °C, and then the reaction was quenched with saturated sodium hydrogen sulfite. The organic layer was separated and the aqueous layer was extracted with $CH_2Cl_2$. After the combined organic layer was dried over anhydrous sodium sulfate and concentrated, the residue was purified by column chromatography (silica gel, hexane/ethyl acetate = 20/1) to give the desired sulfoxide **2** as a colorless oil (0.61 g, 80%): IR (neat) $\nu$ 3121, 3037, 1651, 1476, 1446, 1180, 1087, 1057, 920, 878, 751, 689 $cm^{-1}$; $^1H$ NMR (270 MHz, $CDCl_3$) $\delta$ 5.32 (1H, dd, $J = 13.7$, 4.9 Hz), 5.56 (1H, dd, $J = 44.7$, 4.9 Hz), 7.26–7.76 (5H, m); GC-MS 70 eV, *m/z* (rel int): 170 ($M^+$, 5), 125 (32), 122 (100), 109 (79), 97 (30), 77 (70), 65 (27), 51 (58), 50 (28); Anal. Calcd. for $C_8H_7FOS$: C, 56.46; H, 4.15. Found: C, 56.63; H, 4.35.

### 4.3. *2-Fluoro-1,4-diphenylnaphthalene* (**5**)

To a mixture of (1-fluorovinyl) phenyl sulfoxide (29.6 mg, 0.174 mmol) and ethylene glycol (0.5 ml) in a sealed tube was added 1,3-diphenylisobenzofuran (81.5 mg, 0.301 mmol). The mixture was heated at 100 °C for 8 h. After cooling to room temperature, the reaction mixture was diluted with hexane-ether = 3/1 and $H_2O$. The organic layer was separated and the aqueous layer was extracted with hexane-ether = 3/1. After the combined organic layer was dried over anhydrous sodium sulfate and concentrated, the residue was purified by chromatography on silica gel (hexane) to give 2-fluoro-1,4-diphenylnaphthalene **5** as a white solid (25.5 mg, 49%): mp 115.0–115.8 °C; IR (KBr) $\nu$ 3057, 2926, 1588, 1574, 1516, 1496, 1456, 1444, 1373, 1352, 1188, 1150, 1072, 1030, 1006, 946, 913, 871, 771, 747, 701, 682, 658 $cm^{-1}$; $^1H$ NMR (270 MHz, $CDCl_3$) $\delta$ 7.30–7.93 (15H, m); $^{13}C$ NMR (100.6 MHz, $CDCl_3$) $\delta$ 156.2 ($J = 244.5$ Hz), 142.3 ($J = 9.2$ Hz), 139.6, 133.9 ($J = 3.6$ Hz), 133.5, 130.9, 129.9, 129.0, 128.4, 127.9, 127.8, 126.7, 126.4, 126.0 ($J = 7.4$ Hz), 124.9, 123.2 ($J = 16.5$ Hz), 116.9 ($J = 27.6$ Hz); GC-MS 70 eV, *m/z* (rel int): 299 ($M^+ + 1$, 16), 298 ($M^+$, 87), 297 (100), 296 (34), 295 (13), 294 (15), 276 (18), 221 (27), 220 (36), 219 (14); Anal. Calcd. for $C_{22}H_{15}F$: C, 88.57; H, 5.07. Found: C, 88.29; H, 5.27.

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