

HIGHLY DIASTEREOSELECTIVE OXIDATION OF 1-ALKYLSULFINYL-9-(ALKYLTHIO)DIBENZOTHIOPHENE WITH MCPBA IN THE PRESENCE OF TRIFLUOROBORAN ETHERATE

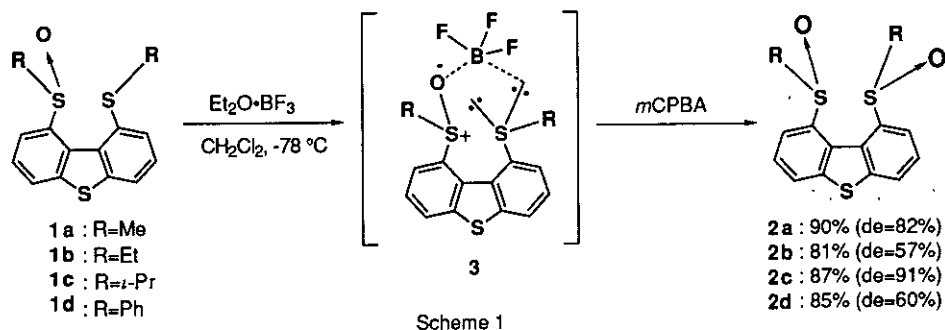
Takeshi Kimura, Hidetaka Nakayama, and Naomichi Furukawa*

Department of Chemistry, University of Tsukuba, Tsukuba, Ibaraki 305, Japan

Abstract - 1-Alkylsulfinyl-9-(alkylthio)dibenzothiophene was oxidized readily by *m*CPBA/Et₂O·BF₃ in CH₂Cl₂ at -78 °C to give one diastereomeric isomer of 1,9-bis(alkylsulfinyl)dibenzothiophene in high yield.

Preparation of optically active sulfoxides by asymmetric induction has been an important subject of research in organic synthesis.^{1,2} Recently, we have reported that optically active 1-(*S*-methylsulfinyl)-9-(methylthio)-dibenzothiophene (**1a**) was prepared by oxidation of 1,9-bis(methylthio)dibenzothiophene with bromine and pyridine in the presence of *l*-menthol.³ The diastereoselective oxidation of sulfides to the corresponding sulfoxides was performed with the assistance of a hydroxyl group in a neighboring interaction.^{4,5} Meanwhile, *R*- α -methylthiomethyl *p*-tolyl sulfoxide which has one optically active sulfinyl group as a chiral auxiliary was oxidized with hydrogen peroxide in acetic acid to give the corresponding bissulfoxides in low diastereomeric excess.⁶ Oxidation of 1,9-bis(alkylthio)dibenzothiophene with two equivalents of *m*-chloroperbenzoic acid (*m*CPBA) produced the corresponding bissulfoxides as two diastereomeric mixtures of (*RR* and *SS* configurations) and (*RS* and *SR* configurations). Interestingly, the oxidation of 1-alkylsulfinyl-9-(alkylthio)dibenzothiophene (**1**) was performed with *m*CPBA in the presence of Et₂O·BF₃ to give predominantly one diastereomeric mixture in high yield. This oxidation reaction of compound (**1**) may proceed *via* the coordination of BF₃ to the sulfinyl group of the starting sulfoxide (**1**) in the solution. Furthermore, the configuration of the optically pure bissulfoxide was determined by X-ray crystallographic analysis with Cu-K α radiation. This communication describes the diastereoselective oxidation of compound (**1**) bearing one sulfinyl group and one sulfenyl group in close proximity at 1, 9 positions with *m*CPBA in the presence of Et₂O·BF₃ to give a diastereomeric mixture of 1,9-bis(alkylsulfinyl)dibenzothiophene (**2**) in high yield.

This paper is dedicated to the memory of the late Dr. Yoshio Ban.



Typically, 1-(*i*-propylsulfinyl)-9-(*i*-propylthio)dibenzothiophene (**1c**) (5.9 mg, 0.017 mmol, in 2.0 ml CH₂Cl₂) was treated with *m*CPBA (9.88 M in CH₂Cl₂, 0.189 ml, 0.0186 mmol, assay >99%) in the presence of Et₂O·BF₃ (0.164 M in CH₂Cl₂, 0.31 ml, 0.050 mmol) at -78 °C under argon for 12 h. After usual work-up, a mixture of diastereomeric 1,9-bis(*i*-propylsulfinyl)dibenzothiophenes ('**2c** and **2c'**') was obtained by separation from the starting **1c** with column chromatography (silica gel, CH₂Cl₂ : EtOH=1:1) in 87% yield (5.3 mg). Then the diastereomeric excess of the major diastereomer (**2c**) was determined by the ¹H-nmr spectrum to be 91% (Scheme 1). The oxidation of 1-ethylsulfinyl-9-(ethylthio)dibenzothiophene (**1b**) and 1-phenylsulfinyl-9-(phenylthio)dibenzothiophene (**1d**) was performed by the identical procedure as described above to give predominantly the corresponding one diastereomer such as 1,9-bis(ethylsulfinyl)dibenzothiophene (**2b**) and 1,9-bis(phenylsulfinyl)dibenzothiophene (**2d**), respectively (Scheme 1). Furthermore, optically pure **1a** which has an *S* configuration at the sulfinyl sulfur atom⁷ was oxidized identically to produce 1,9-bis(methylsulfinyl)dibenzothiophene (**2a**) in 90 % yield (*de*=82%). The bisulfoxide (**2a**) was separated easily from its diastereomer by column chromatography (silica gel, CH₂Cl₂ : EtOH=1:1) and then was further purified by recrystallization (CH₂Cl₂ : EtOH=1:1), [α]_D²³=-476° (c=0.10, CHCl₃), *de*=100%. On the other hand, when the oxidation of **1a** was carried out at -20 °C or without Et₂O·BF₃ at -78 °C, the diastereomeric excess of **2a** decreased to *de*=45% (yield: 83%) and *de*=39% (yield: 83%), respectively, suggesting that this oxidation reaction essentially requires low temperature and Et₂O·BF₃ to attain the high diastereoselectivity.

It is important to verify the absolute configuration of the optically pure **2a** obtained by this oxidation. Therefore, X-ray crystallographic analysis of the optically pure **2a** was carried out with Cu-Kα radiation to determine the configuration of the sulfinyl sulfur atoms at 1, 9-positions (Figure 1). As shown in Figure 1, the bisulfoxide (**2a**) belongs to the point group C₂ symmetry and has an *S* configuration at the two sulfinyl sulfur atoms, respectively. The configuration of optically pure **2a** containing the *S* configuration at both of the two sulfinyl sulfur atoms is a correct choice, and its enantiomeric structure bearing an *R'* configuration at the two sulfinyl groups could be rejected at the 0.005 significance level by the Hamilton test.⁸ These results reveal clearly that the optically pure **2a** has an *S* configuration at the two sulfinyl sulfur atoms, respectively, and this asymmetric

oxidation of the methylsulfenyl group using the optically pure sulfinyl group as a chiral auxiliary produced one more optically active sulfinyl group bearing the same configuration as that of the starting sulfoxide predominantly. Accordingly, the configurations of the major diastereomers (**2b-d**) obtained by this oxidation should consist of *RR* and *SS* configurations.

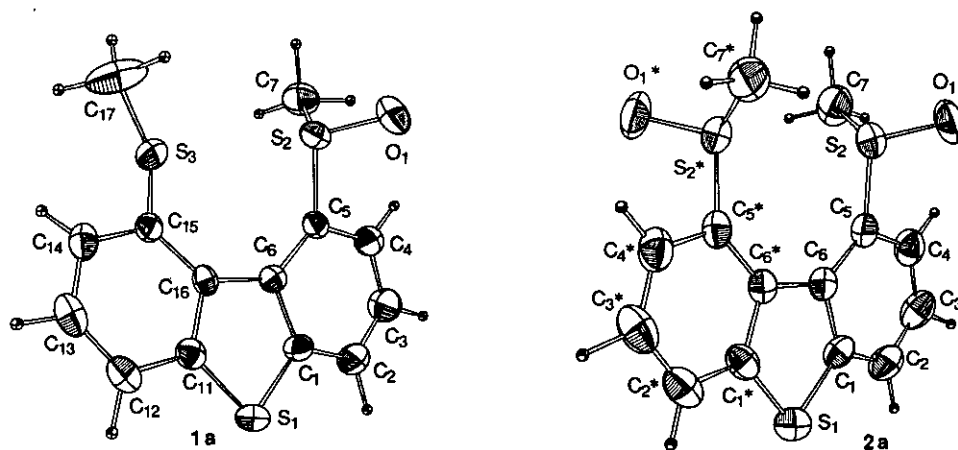


Figure 1. The ORTEP Drawing of **1a** and **2a**.

In order to determine the role of $\text{Et}_2\text{O}\cdot\text{BF}_3$ in this diastereoselective oxidation, the ^1H -nmr of **1a** was measured in the presence of $\text{Et}_2\text{O}\cdot\text{BF}_3$ in CDCl_3 at -20°C . Interestingly, while the signal of the methylsulfinyl proton at the 1 position of **1a** was found to shift largely from 2.78 ppm to 3.46 ppm by addition of $\text{Et}_2\text{O}\cdot\text{BF}_3$, the chemical shift of the methylsulfonyl proton at the 9 position changed slightly from 2.34 ppm to 2.52 ppm in the spectrum. These downfield shifts of methyl protons in the ^1H -nmr spectrum by addition of $\text{Et}_2\text{O}\cdot\text{BF}_3$ should be brought about by coordination of BF_3 to **1a**, which may exhibit increase in the positive charge on the sulfinyl sulfur atom of **1a**. On the other hand, the ^1H -nmr spectrum of **1a** in the presence of $\text{Et}_2\text{O}\cdot\text{BF}_3$ was analogous to that of ethoxysulfonium salt of 1,9-bis(methylthio)dibenzothiophene which was prepared by treatment of 1-methylsulfinyl-9-(methylthio)dibenzothiophene with $\text{Et}_3\text{O}\cdot\text{BF}_4$ in CH_2Cl_2 at 25°C under argon in 70% yield.¹¹ The two signals of the methylsulfonio and methylsulfonyl groups at the 1, 9-position of dibenzothiophene were found in the ^1H -nmr spectra to be 4.05 ppm and 2.83 ppm in ethoxysulfonium salt and 4.05 ppm and 2.69 ppm in *l*-menthoxy sulfonium salt.³ Furthermore, the methyl protons of dithia dication of 1,9-bis(methylthio)dibenzothiophene have been reported to be observed at 3.37 ppm in ^1H -nmr spectrum of its BF_4 salt in CD_3CN .¹² These results of the ^1H -nmr spectra suggested that BF_3 coordinates strongly to the sulfinyl oxygen at the 1 position of **1a** and interacts weakly to one lone pair electrons of the sulfur atom at the 9 position at -20°C . Therefore, the sulfoxide (**1a**) produced initially an intermediate such as **3** similar to alkoxy sulfonium salt by treatment with $\text{Et}_2\text{O}\cdot\text{BF}_3$ in CH_2Cl_2 at -78°C , and then the lone pair electrons in the sulfur atom at the 9 position may react with *m*CPBA avoiding the BF_3 complexation site to give predominantly one diastereomer (Scheme 1).

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7. The configuration of optically pure **1a** was determined as an *S* configuration at the sulfinyl sulfur atom by the X-ray crystallographic analysis not only with Mo-K α radiation³ but also with Cu-K α radiation. The crystal data for **1a**; orthorhombic, P2₁2₁2₁, a=8.839 (1) Å, b=17.333 (1) Å, c=8.445 (3) Å, v=1293.9 Å³, Z=4, ρ =1.50 g/cm³, μ (Cu-K α)=50.3 cm⁻¹, R=0.04018 (R_w=0.04327). The R values of the enantiomeric structure of **1a** are R=0.04765 (R_w=0.05022). Therefore, the *S* configuration of optically pure sulfoxide **1a** is correct, and its enantiomeric structure could be rejected at the 0.005 significance level.⁸
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9. **2a**: mp 238-242 °C; ¹H-nmr (270 MHz, CDCl₃) δ 2.91 (s, 6H), 7.84 (t, J=7.5 Hz, 2H), 8.11 (dd, J=7.5, 1.1 Hz, 2H), 8.41 (dd, J=7.5, 1.1 Hz, 2H); ms (m/z) 308 (M⁺); Anal. Calcd for C₁₄H₁₂O₂S₃•2H₂O: C, 48.82; H, 4.68. Found: C, 48.67; H, 4.67; the crystal data: C₁₄H₁₂O₂S₃•2H₂O, orthorhombic, C222₁, a=13.629 (0), b=15.881 (1), c=7.025 (0) Å, v=1520.6 Å³, Z=4, ρ =1.50 g/cm³, μ (Cu-K α)=43.5 cm⁻¹, R=0.03927 (R_w=0.04271); the R values of the enantiomeric structure of **2a**: R=0.04790 (R_w=0.05099).
10. ¹H-Nmr of sulfoxide **1a** in the presence of Et₂O•BF₃ at -20 °C (270 MHz, CDCl₃) δ 2.52 (s, 3H, SCH₃), 3.46 (s, 3H, SOCH₃), 7.58 (t, J=8.1 Hz, 1H), 7.79 (d, J=8.1 Hz, 1H), 7.82 (t, J=8.1 Hz, 1H), 7.91 (d, J=8.1 Hz, 1H), 8.15 (d, J=8.1 Hz, 1H), 8.36 (d, J=8.1 Hz, 1H).
11. Ethoxysulfonium salt: mp 141-144 °C; ¹H-nmr (270 MHz, CDCl₃) δ 1.18 (t, J=7.0 Hz, 3H, CH₃), 2.83 (s, 3H, SCH₃), 3.76 (dq, J=7.0, 2.4 Hz, 1H, CH₂), 4.05 (s, 3H, SOCH₃), 4.28 (dq, J=7.0, 2.4 Hz, 1H, CH₂), 7.63 (t, J=7.8 Hz, 1H), 7.72 (d, J=7.8 Hz, 1H), 7.89 (t, J=7.8 Hz, 1H), 7.91 (d, J=7.8 Hz, 1H), 8.21 (d, J=7.8 Hz, 1H), 8.23 (d, J=7.8 Hz, 1H); FABms (m/z) 321 (M-BF₄)⁺; Anal. Calcd for C₁₆H₁₇OBF₄S₃: C, 47.06; H, 4.19. Found: C, 46.86; H, 4.19.
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