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

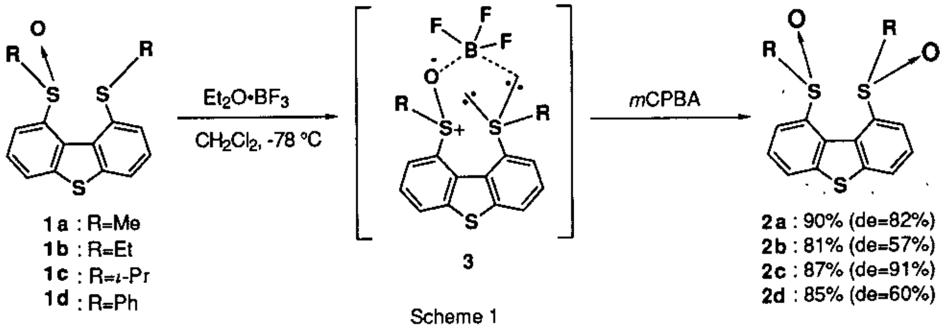
Takeshi Kimura, Hidetaka Nakayama, and Naomichi Furukawa*

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

Abstract - 1-Alkylsulfinyl-9-(alkylthio)dibenzothiophene was oxidized readily by *m*CPBA/$Et_2O{\bullet}BF_3$ in CH_2Cl_2 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 $Et_2O{\cdot}BF_3$ to give predominantly one diastereomeric mixture in high yield. This oxidation reaction of compound (**1**) may proceed *via* the coordination of BF_3 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-Kα 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 $Et_2O{\cdot}BF_3$ 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.



1a : R=Me
1b : R=Et
1c : R=*i*-Pr
1d : R=Ph

3

2a : 90% (de=82%)
2b : 81% (de=57%)
2c : 87% (de=91%)
2d : 85% (de=60%)

Scheme 1

Typically, 1-(*i*-propylsulfinyl)-9-(*i*-propylthio)dibenzothiophene (**1c**) (5.9 mg, 0.017 mmol, in 2.0 ml CH_2Cl_2) was treated with *m*CPBA (9.88 M in CH_2Cl_2, 0.189 ml, 0.0186 mmol, assay >99%) in the presence of $Et_2O{\cdot}BF_3$ (0.164 M in CH_2Cl_2, 0.31ml, 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, CH_2Cl_2 : EtOH=1:1) in 87% yield (5.3 mg). Then the diastereomeric excess of the major diastereomer (**2c**) was determined by the ^{1}H-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 diastereo isomer 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 atom[7] was oxidized identically to produce 1,9-bis(methylsulfinyl)-dibenzothiophene (**2a**) in 90 % yield (*de*=82%). The bissulfoxide (**2a**) was separated easily from its diastereo isomer by column chromatograpy (silica gel, CH_2Cl_2 : EtOH=1:1) and then was further purified by recrystallization (CH_2Cl_2 : EtOH=1:1), $[\alpha]_D^{23}$=-476° (c=0.10, $CHCl_3$), *de*=100%. On the other hand, when the oxidation of **1a** was carried out at -20 °C or without $Et_2O{\cdot}BF_3$ 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 $Et_2O{\cdot}BF_3$ 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 bissulfoxide (**2a**) belongs to the point group C_2 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.

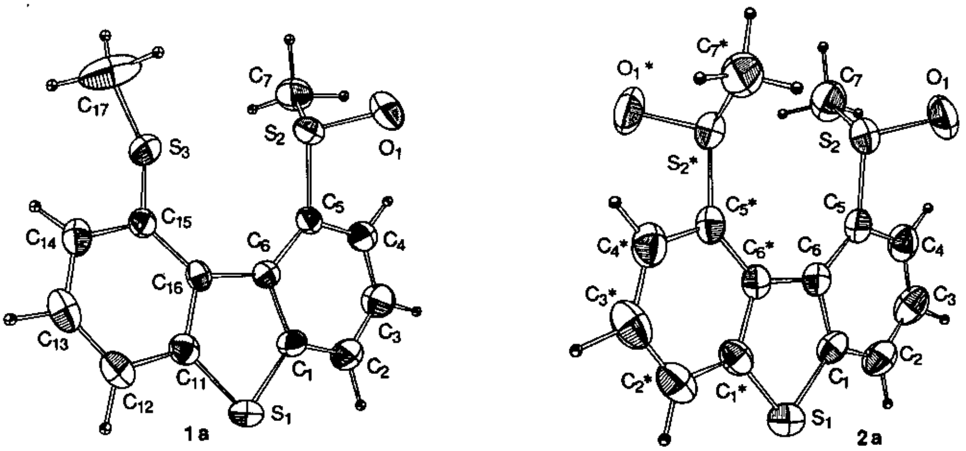


Figure 1. The ORTEP Drawing of **1a** and **2a**.

In order to determine the role of $Et_2O•BF_3$ in this diastereoselective oxidation, the ^{1}H-nmr of **1a** was measured in the presence of $Et_2O•BF_3$ 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 $Et_2O•BF_3$, the chemical shift of the methylsulfenyl 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 ^{1}H-nmr spectrum by addition of $Et_2O•BF_3$ 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 ^{1}H-nmr spectrum of **1a** in the presence of $Et_2O•BF_3$ 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 $Et_3O•BF_4$ in CH_2Cl_2 at 25 °C under argon in 70% yield.[11] The two signals of the methylsulfonio and methylsulfenyl groups at the 1, 9-position of dibenzothiophene were found in the ^{1}H-nmr spectra to be 4.05 ppm and 2.83 ppm in ethoxysulfonium salt and 4.05 ppm and 2.69 ppm in *l*-menthoxysulfonium 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 ^{1}H-nmr spectrum of its BF_4 salt in CD_3CN.[12] These results of the ^{1}H-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 alkoxysulfonium salt by treatment with $Et_2O•BF_3$ in CH_2Cl_2 at -78 °C, and then the lone pare 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).

ACKNOWLEDGMENT

This work was supported by a Special Grant from the University of Tsukuba (the *TARA* project).

REFERENCES

1. For reviews, see: A. J. Walker, *Tetrahedron Asymmetry*, 1992, **3**, 961; J. Drabowicz, P. Kielbasinski, and M. Mikolajczyk, *'The Chemistry of Sulfones and Sulfoxides'*, ed by S. Patai, Z. Rappoport, and C. Stirling, John Wiley & Sons, New York, 1988, pp. 233-378; M. Madesclaire, *Tetrahedron*, 1986, **42**, 5459.
2. T. Shibutani, H. Fujihara, and N. Furukawa, *Tetrahedron Lett.*, 1991, **32**, 2947.
3. T. Kimura, H. Nakayama, and N. Furukawa, *Chem. Lett.*, 1994, 27.
4. R. S. Glass, W. N. Setzer, U. D. G. Prabhu, and G. S. Wilson, *Tetrahedron Lett.*, 1982, **23**, 2335; R. S. Glass, A. Petsom, and G. S. Wilson, *J. Org. Chem.*, 1987, **52**, 3537.
5. O. De Lucchi, V. Lucchini, C. Marchioro, G. Valle, and G. Modena, *J. Org. Chem.*, 1986, **51**, 1457.
6. N. Kunieda, J. Nokami, and M. Kinoshita, *Chem. Lett.*, 1973, 871; N. Kunieda, J. Nokami, and M. Kinoshita, *Bull. Chem. Soc. Jpn.*, 1976, **49**, 256.
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-Kα radiation[3] but also with Cu-Kα radiation. The crystal data for **1a**; orthorhombic, $P2_12_12_1$, a=8.839 (1) Å, b=17.333 (1) Å, c=8.445 (3) Å, v=1293.9 Å^3, Z=4, ρ=1.50 g/cm^3, μ(Cu-Kα)=50.3 cm^{-1}, R=0.04018 (Rw=0.04327). The R values of the enantiomeric structure of **1a** are R=0.04765 (Rw=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]
8. W. C. Hamilton, *Acta Crystallogr.*, 1965, **18**, 502; W. C. Hamilton, *'International Tables for X-Ray Crystallography, Vol IV'*; ed by J. A. Ibers and W. C. Hamilton, Kynoch Press, Birmingham, 1973, pp. 285-310.
9. **2a** : mp 238-242 °C; ^{1}H-nmr (270 MHz, $CDCl_3$) 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 $C_{14}H_{12}O_2S_3 \cdot 2H_2O$: C, 48.82; H, 4.68. Found: C, 48.67; H, 4.67; the crystal data: $C_{14}H_{12}O_2S_3 \cdot 2H_2O$, orthorhombic, $C222_1$, a=13.629 (0), b=15.881 (1), c=7.025 (0) Å, v=1520.6 Å^3, Z=4, ρ=1.50 g/cm^3, μ(Cu-Kα)=43.5 cm^{-1}, R=0.03927 (R_w=0.04271); the R values of the enantiomeric structure of **2a**: R=0.04790 (Rw=0.05099).
10. ^{1}H-Nmr of sulfoxide **1a** in the presence of $Et_2O \cdot BF_3$ at -20 °C (270 MHz, $CDCl_3$) δ 2.52 (s, 3H, SCH_3), 3.46 (s, 3H, $SOCH_3$), 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; ^{1}H-nmr (270 MHz, $CDCl_3$) δ 1.18 (t, J=7.0 Hz, 3H, CH_3), 2.83 (s, 3H, SCH_3), 3.76 (dq, J=7.0, 2.4 Hz, 1H, CH_2), 4.05 (s, 3H, $SOCH_3$), 4.28 (dq, J=7.0, 2.4 Hz, 1H, CH_2), 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 $(M-BF_4)^+$; Anal. Calcd for $C_{16}H_{17}OBF_4S_3$: C, 47.06; H, 4.19. Found: C, 46.86; H, 4.19.
12. N. Furukawa, T. Kimura, Y. Horie, S. Ogawa, and H. Fujihara, *Tetrahedron Lett.*, 1992, **33**, 1489.

Received, 9th March, 1995