

Published on Web 07/04/2003

The Thiosulfinyl Group Serves as a Stereogenic Center and Shows Diamagnetic Anisotropy Similar to That of the Sulfinyl Group

Sanae Tanaka, Yoshiaki Sugihara, Akira Sakamoto, Akihiko Ishii, and Juzo Nakayama*

Department of Chemistry, Faculty of Science, Saitama University, Sakura-ku, Saitama, Saitama 338-8570, Japan

Received May 1, 2003; E-mail: nakaj@post.saitama-u.ac.jp

The chemistry of compounds having the general structure of R₂S=S has attracted much attention because of the expected intriguing properties of the thiosulfinyl group.¹ Although thiosulfoxides (R = alkyl or aryl for R₂S=S) have long been proposed as transient intermediates, they still elude even detection by spectroscopies.¹ On the other hand, thionosulfites [(RO)₂S=S] are more stable than thiosulfoxides because of electronic stabilization by the oxygen atoms.^{2,3} Thus, Harpp et al. succeeded in the synthesis and X-ray single-crystal structure analysis of the thionosulfite 1.^{3a} Here, we report the synthesis, X-ray crystallographic analysis, and chemical and spectroscopic properties of a pair of isolable, diastereomeric thionosulfites **4a** and **4b**.

Initially, we obtained sulfite **5** as a mixture of diastereomers **5a** and **5b**,⁴ as the precursor to **4**, by condensation of *cis*-3,4-di-*tert*butylthiolane-3,4-diol (**2**)⁵ with SOCl₂.⁶ Disappointingly, however, attempted conversion of **5** to **4** by treatment with Lawesson's reagent was unsuccessful. We then applied the Harpp method to obtain **4** from **2** directly.^{3a} Thus, **2** was treated with 4 molar amounts of 1,1'-thiobisbenzimidazole (**3**)⁷ in MeCN for 72 h at room temperature. The expected reaction took place to give a diastereomeric mixture of thionosulfites **4a** and **4b** in the ratio 82:18 (Scheme 1). Separation of the diastereomers could be satisfactorily performed by HPLC to afford **4a** and **4b** in 45% and 10% isolated yields, respectively.⁸



Scheme 1. Synthesis of 4a and 4b



The stereochemistry of **4a** and **4b** was established by X-ray crystallographic analyses. Molecular structures of **4a** and **4b** are shown in Figure 1. Figure 2 shows the bond angles and bond lengths around the S=S group of **4a** and the S=O group of **5a**.⁶ The sum of the two O-S-S bond angles and the one O-S-O bond angle of **4a** is 311.5° and comparable to that of **5a** (309.5°), while it is smaller than the sum of the three H-C-H bond angles of methane (328.5°). Thus, the pseudotetrahedral geometry of the thiosulfinyl sulfur atom of **4a** is deeper than that of methane. Incidentally, the sum of the corresponding angles for **4b** is 310.4° . The S=S bond lengths of **4a** and **4b** are 1.9154(6) and 1.8964(13) Å, respectively,

and are comparable with that of **1** (1.901(2) Å). The two *tert*-butyl groups of **4a** and **4b** are twisted with dihedral angles of $43.7(2)^{\circ}$ and $38.0(3)^{\circ}$, respectively, to reduce the steric repulsion. The optimized molecular structures of **4a** and **4b** (Figure 3), predicted by density functional theory (DFT) calculations (B3LYP/6-31G* level), are in good agreement with the experimental structures.⁹



Figure 1. Molecular structures of 4a and 4b.



Figure 2. Bond angles and bond lengths around the S=S group of 4a and the S=O group of 5a.



Figure 3. Optimized structures of 4a and 4b.

No thermal isomerization was observed between **4a** and **4b**, even when each isomer was heated at 120 °C in toluene- d_8 , indicating that the pseudotetrahedral geometry around the thiosulfinyl group is rigid enough to serve as a stereogenic center.¹⁰ However, decomposition of **4** took place instead; **4a** gave **6**, **7**,⁵ and **4a** in the ratio 39:13:48 after heating for 96 h, while **4b** decomposed completely to produce **6** and **7** in the ratio 6:94 after heating for 24 h (Scheme 2). The experimental ratio of **4a** and **4b**, 82:18, is therefore kinetically controlled. The DFT calculations predicted that **4a** is more stable than **4b** by 1.69 kcal/mol. **4a** and **4b** are susceptible to alkaline hydrolysis. Thus, **4a** was hydrolyzed to give the diol **2** in 93% yield in the presence of NaHCO₃ in a 1:1 mixture of H_2O and THF, whereas it remained unchanged in the absence of NaHCO₃ for several days. Oxidation of **4a** with 1.1 molar amounts of MCPBA gave **8** and **9** in the ratio 94:6 (**8** was isolated in 77% yield), while oxidation with 3.3 molar amounts of MCPBA furnished **9** and **10** in the ratio 90:10. The structure of **8** was determined by X-ray crystallographic analysis, while **9** and **10** agreed with the authentic samples prepared by oxidation of **5b**.⁶ These results reveal that the S=S group is more resistant toward oxidation than the sulfide sulfur atom, and interestingly the S=S group is converted to the S=O group with inversion of the configuration.

Scheme 2. Reactions of 4a



As to the diamagnetic anisotropy of the S=S group, no data information has been available. Figure 4 shows the chemical shift data of the methylene protons of **4a** and **4b** and those of **5a** and **5b**; each methylene proton appeared as a doublet with J = 13-14Hz due to geminal coupling.⁶ The assignments were based on NOE experiments. The inspection of these data reveals that the shielding and deshielding zones of the S=S group are similar to those of the S=O group. Therefore, the shielding and deshielding zones of the S=S group are assigned as depicted in Figure 5 by analogy of the well-documented corresponding zones of the S=O group.¹¹



Figure 4. Chemical shift data of 4a,b and 5a,b.



Figure 5. Shielding (+) and deshielding (-) zones of the S=S group.

The strong infrared absorption and Raman bands were observed for **4a** at 653 and 650 cm⁻¹, respectively. The DFT calculations of **4a** predicted the appearance of the strong infrared absorption band and the medium-sized Raman band mainly due to the contribution of the S=S stretching vibration at 639 cm⁻¹. Therefore, these strong infrared and Raman bands at about 650 cm⁻¹ can be assigned to the S=S stretching vibration. Similarly, the strong Raman band assignable to the S=S stretching vibration was observed at 666 cm^{-1} for **4b**. The corresponding infrared absorption band was observed at 665 cm^{-1} as a shoulder of the strong 670 cm^{-1} band. The DFT calculations of 4b predicted the medium-sized infrared absorption band and the strong Raman band at 647 cm⁻¹, which are assigned to the S=S stretching vibration. The observed S=S stretching infrared and Raman bands at about 650 cm⁻¹ for 4a and at about 666 cm⁻¹ for **4b** are in good agreement with the observed infrared and Raman bands for 1 at about 650 cm⁻¹.^{3b} The UV/vis spectrum of 4a showed the two absorption maxima at 253 ($\epsilon =$ 2790) and 324 (142) nm, while the time-dependent DFT calculations predicted the appearance of two strong absorptions at 249 and 263 nm and a weak absorption at 361 nm. Similarly, 4b showed the two absorption maxima at 245 ($\epsilon = 3060$) and 313 (203) nm, although the calculation predicted the appearance of the two strong absorptions at 241 and 262 nm and the weak absorption at 351 nm. Also for 1, the strong absorption at 250 nm and the weak absorption at 311 nm were reported.3b

Supporting Information Available: Procedures for the preparation of **4** and other reactions, plausible mechanisms of the formation of **4** and other reactions, X-ray crystallographic data of **4a**, **4b**, and **8**, and calculated structural and spectral data of **4a** and **4b** (PDF, CIF, TIF). This material is available free of charge via the Internet at http:// pubs.acs.org.

References

- (1) For a leading review, see: Kutney, G. W.; Turnbull, K. *Chem. Rev.* **1982**, 82, 333.
- (2) (a) Thompson, Q. E.; Crutchfield, M. M.; Dietrich, M. W. J. Org. Chem. 1965, 30, 2696. (b) Abdullaev, G. K.; Mamedov, I. A.; Mamedov, M. M. Azerb. Khim. Zh. 1973, 5–6, 43.
- (3) (a) Harpp, D. N.; Steliou, K.; Cheer, C. J. J. Chem. Soc., Chem. Commun. 1980, 825. (b) Snyder, J. P.; Nevins, N.; Tardif, S. L.; Harpp, D. N. J. Am. Chem. Soc. 1997, 119, 12685.
- (4) For a review on five-membered cyclic sulfites: Mitchell, G. In Comprehensive Heterocyclic Chemistry II; Storr, R. C., Ed.; Pergamon Press: Oxford, U. K., 1996; Vol. 4, Chapter 4.15.
- (5) (a) Nakayama, J.; Yamaoka, S.; Hoshino, M. *Tetrahedron Lett.* **1988**, *29*, 1161.
 (b) Nakayama, J.; Hasemi, R.; Yoshimura, K.; Sugihara, Y.; Yamaoka, S. *J. Org. Chem.* **1998**, *63*, 4912.
- (6) Tanaka, S.; Sugihara, Y.; Sakamoto, A.; Ishii, A.; Nakayama, J. *Heteroat. Chem.*, in press (to appear in number 7, 2003). The structural assignment of 5a and 5b was performed by X-ray diffraction analyses.
- (7) Harpp, D. N.; Steliou, K.; Chan, T. H. J. Am. Chem. Soc. 1978, 100, 1222.
- (8) The use of other solvents, such as CH₂Cl₂, C₆H₆, THF, and DMSO, resulted either in no reaction or in the formation of 4a and 4b in decreased yields. The use of 1,1'-dithiobisbenzimidazole gave 4a and 4b in very low yield.
- (9) (a) The calculations have been performed by using the Gaussian 98 (revision A.7) program on personal computers running RedHat Linux 6.0. (b) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian* 98; Gaussian, Inc.: Pittsburgh, PA, 1998.
- (10) The inversion energy of (MeO)₂S=S was calculated to be 32.3 kcal/mol (see Supporting Information of ref 3b).
- (11) (a) Green, C. H.; Hellier, D. G. J. Chem. Soc., Perkin Trans. 2 1972, 458. (b) Green, C. H.; Hellier, D. G. J. Chem. Soc., Perkin Trans. 2 1973, 243. (c) Pritchard, J. G.; Lauterbur, P. C. J. Am. Chem. Soc. 1961, 83, 2105. (d) Buchanan, G. W.; Hellier, D. G. Can. J. Chem. 1976, 54, 1428. (e) Green, C. H.; Hellier, D. G. J. Chem. Soc., Perkin Trans. 2 1975, 190.

JA035892S