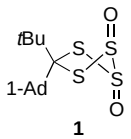
A Convenient Method for the Generation of a Disulfur Monoxide Equivalent and Its Reaction with Diazoalkanes to Yield Dithiirane 1-Oxides**

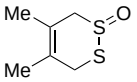
Akihiko Ishii,* Tetsuhiko Kawai, Kentaro Tekura, Hideaki Oshida, and Juzo Nakayama*

Dedicated to Professor Rolf Huisgen on the occasion of his 80th birthday

Recently we found that thermal decomposition of tetrathiolane 2,3-dioxide **1** (1-Ad = 1-adamamtyl) generates disulfur monoxide S_2O, which was trapped with 2,3-dimethyl-1,3-butadiene to give the 3,6-dihydro-1,2-dithiin 1-oxide **2** in high



1



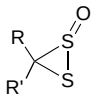
2

yield (ca. 90%).[1] Up to now, the use of S_2O in organic chemistry has been limited to reactions with a few 1,3-butadienes.[2] One reason for this is probably the troublesome methods for its generation; for example, pyrolysis of ethylene episulfoxide,[2] electronic discharge of SO_2,[3] and reactions of heavy metal oxides or sulfides with elemental sulfur at 250–400 °C or with gaseous $SOCl_2$ at 160 °C and 0.5 Torr.[3]

Decomposition of oxides of elemental sulfur (S_8) is expected to be an alternative way to generate S_2O. Steudel et al. reported that S_nO ($n = 6-8$) are isolable but decompose to SO_2 and sulfur in solution or to S_2O and S_{n-2} in vacuo.[4–6] Here we report a convenient and inexpensive method for the generation of S_2O[7] and its reaction with typical 1,3-dipoles, namely, diazoalkanes. To our knowledge, there is no precedent for the reaction of diazoalkanes with S_2O, although reactions with SO_2,[8] SO,[9] and thioketone *S*-oxides (sulfines) have been investigated.[10] The reaction of diazoalkanes with SO_2 was claimed to give thioketone *S*,*S*-dioxides (sulfenes) **3**.[8] If the reaction of diazoalkanes with S_2O takes place in a similar fashion, the formation of thiosulfenes **4** or their cyclic isomers, dithiirane 1-oxides **5**, is expected.

3

4

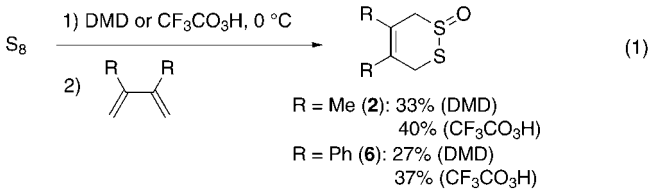


5

[*] Assoc. Prof. Dr. A. Ishii, Prof. Dr. J. Nakayama, T. Kawai, K. Tekura, H. Oshida
Department of Chemistry
Faculty of Science, Saitama University
Urawa, Saitama 338-8570 (Japan)
Fax: (+81) 48-858-3700
E-mail: ishiiaki@chem.saitama-u.ac.jp
nakaj@post.chem.saitama-u.ac.jp

[**] This work was supported by a Grant-in-Aid for Scientific Research (No. 90193242) from the Ministry of Education, Science, Sports, and Culture, Japan.

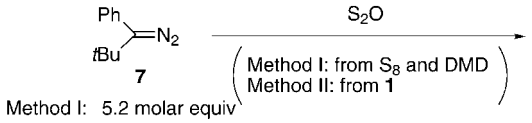
An equimolar amount of dimethyldioxirane (DMD)[11] was added to a solution of elemental sulfur (S_8) in CH_2Cl_2/benzene at 0 °C, and the solution was stirred for 1 h. The mixture contains S_8O as an S_2O precursor.[7] Then, 2,3-dimethyl- or 2,3-diphenyl-1,3-butadiene (11 and 3 molar equiv, respectively) was added, and the mixture was warmed to room temperature. Workup gave the adducts **2** and **6**[2] in 33 and 27% yield, respectively [Eq. (1)]. The use of excess DMD

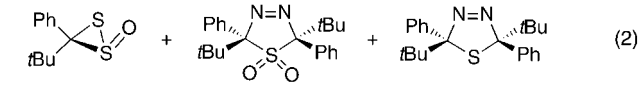


(1)

did not improve the yields of the adducts because of the instability of higher oxides of S_8.[4d] When trifluoroperoxyacetic acid was employed as the oxidant in CH_2Cl_2,[4b] the yields of **2** and **6** improved to 40 and 37%, respectively. The above results indicate that 0.3–0.4 molar equiv of S_2O is available from equimolar amounts of S_8 and an oxidizing agent under these conditions.

We next examined reactions of diazoalkanes with S_2O generated in situ. Two methods were investigated: in method I, S_2O was generated from one molar equivalent of S_8 and DMD in CH_2Cl_2/benzene or in CH_2Cl_2, and in method II, from **1** in CH_2Cl_2.[1] The efficiency of the generation of S_2O by method I is 30%, as mentioned above, and by method II, nearly 90%.[1] The reaction of *tert*-butyl(phenyl)diazomethane **7** (5.2 molar equiv) with S_2O [Eq. (2); method I] gave





(2)

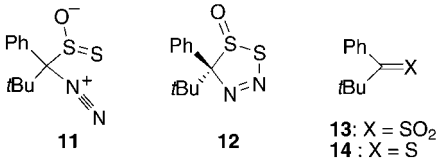
8 **9** **10**

I	0.22 molar equiv	0.12 molar equiv	0.51 molar equiv
II	0.59 molar equiv	0.068 molar equiv	0.10 molar equiv

the expected dithiirane 1-oxide **8** (0.22 molar equiv based on S_8 and DMD) along with 1,3,4-thiadiazoline 1,1-dioxide **9**[12] (0.12 molar equiv) and 1,3,4-thiadiazoline **10**[12] (0.51 molar equiv). The configuration of **8** was determined to be 1*R**,3*S** from ^{1}H NMR spectroscopic data, and no other stereoisomer was obtained. The reaction of **7** (5.9 mol equiv) with S_2O by method II gave **8** in higher yield (0.59 molar equiv based on **1**) along with **9** and **10** in lower yields (0.068 and 0.10 molar equiv, respectively).

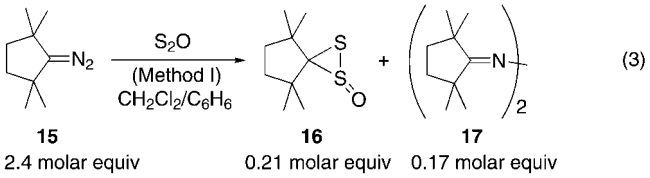
In the proposed mechanism for the reaction of Equation (2), three reactions take place independently. By analogy with reactions of diazoalkanes with SO_2,[8] the reaction of **7** with S_2O would give an initial adduct **11** or **12**, although we

  0044-8249/01/11310-1978 $ 17.50+.50/0



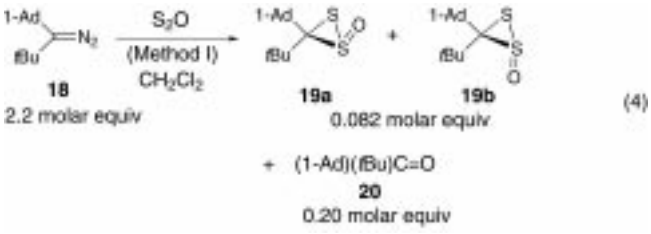
have no direct evidence for its formation. The extrusion of N_2 from the intermediate yields the dithiirane 1-oxide **8**. The formation of the 1,3,4-thiadiazoline 1,1-dioxide **9** implies the generation of sulfene **13** by reaction of **7** with SO_2, which undergoes a cycloaddition with **7** to give **9**.[8] The SO_2 would be supplied by decomposition of higher oxides of S_8[4d] or disproportionation of S_2O.[1, 13] The 1,3,4-thiadiazoline **10** is a cycloadduct of the thioketone **14** and **7**.[14] In fact, the thioketone **14**, prepared by a reported method,[15] reacted with **7** quickly to give **10** in high yield. Since a separate experiment revealed that the reaction of **7** and elemental sulfur (S_8), which gives **14**, is sluggish under similar conditions,[16] sulfur allotropes S_n that are more reactive than S_8 should be responsible for the formation of **14**.

The reaction of a diazocyclopentane **15**[17] (2.4 molar equiv) with S_2O (method I) yielded the spirodithiirane 1-oxide **16** (0.21 molar equiv) along with azine **17**[17] (0.17 molar equiv) [Eq. (3)]. The formation of azines by reaction of diazoalkanes



(3)

with SO_2 is known.[8, 18] The reaction of 1-adamantyl-*tert*-butyldiazomethane **18** with S_2O (method I) gave two stereoisomeric 1-oxides **19a** and **19b**,[19] albeit in a low combined yield (0.082 molar equiv), probably for steric reasons, together with ketone **20** as the main product [Eq. (4)]. In these cases, products corresponding to **9** and **10** were not obtained.



(4)

Diphenyldiazomethane and monoaryl diazomathane **21** failed to react with S_2O (method I): diphenyldiazomethane gave a complex mixture, whereas **21** gave an alkene[8, 18] ((*E*)- and (*Z*)-MesCH=CHMes,[20] 5:1) together with an azine[8, 18] ((MesCH=N)$_2$[21]).

21 (Mes = 2,4,6-$Me_3C_6H_2$)

In summary, we have developed a convenient method for the generation of an S_2O equivalent by treatment of elemental sulfur with an oxidizing agent. The efficiency of generation was 30–40%. We also investigated the reaction of S_2O with diazoalkanes, which provides an alternative method for the preparation of dithiirane derivatives.[22]

Experimental Section

Materials: elemental sulfur (S_8) was recrystallized from CS_2 before use. Dimethyldioxirane (DMD) was prepared as a solution in acetone.[11]

General procedure for the generation of S_2O (method I) and the trapping reaction: DMD (0.10 M in acetone) was added to a solution of S_8 (80 mg, 0.31 mmol) in dichloromethane (10 mL) and benzene (2 mL) at 0 °C. After stirring at 0 °C for 1 h, a solution of a trapping reagent in dichloromethane was added. The mixture was warmed to room temperature, stirred for 1 h, and evaporated to dryness under reduced pressure. The yields of **2** and **6** were determined from ^{1}H NMR integral ratios with 9-acetylanthracene as internal standard.

Reaction of **7** with S_2O: Method I: 1) A solution of S_8 (32 mg, 0.124 mmol) in dichloromethane/benzene was treated with DMD (0.123 mmol), followed by addition of a solution of **7** (112 mg, 0.64 mmol, 5.2 equiv) in dichloromethane. Yields of **8**, **9**, and **10** were determined to be 0.027 (22% based on DMD), 0.0144, and 0.0624 mmol, respectively, by the ^{1}H NMR integral-ratio method with thioanisole as internal standard. 2) A solution of S_8 (70 mg, 0.27 mmol) in dichloromethane/benzene was treated with DMD (0.27 mmol), followed by addition of a solution of **7** (246 mg, 1.34 mmol, 4.9 equiv) in dichloromethane. The mixture was subjected to medium-pressure liquid chromatography (SiO_2, hexane/Et_2O 4/1) to give **8** (11 mg, 0.047 mmol, 17% based on DMD), **9** (71 mg, 0.185 mmol), and **10** (26 mg, 0.073 mmol). Method II: A solution of 5-(1-adamantyl)-5-(*tert*-butyl)tetrathiolane (**22**)[1, 23] (33 mg, 0.10 mmol) in dichloromethane (8 mL) was treated with DMD (0.40 mmol) at −20 °C. The mixture was stirred for 1.5 h at −20 °C and then the solvent was removed under reduced pressure. The residue was dissolved in a solution of **7** (106 mg, 0.595 mmol, 5.9 equiv) in dichloromethane (10 mL) at −20 °C, and then the mixture was warmed to room temperature. Yields of **8**, **9**, and **10** were determined to be 0.059 (59% based on **22**), 0.0068, and 0.0101 mmol, respectively, from the ^{1}H NMR integral ratios with thioanisole as internal standard.

8: Colorless crystals, m.p. 62–64 °C (dichloromethane/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.02$ (s, 9H), 7.37–7.50 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 28.1$, 38.4, 86.2, 127.8, 128.8, 133.2, 133.3; IR (KBr): $\tilde{\nu} = 1118$ cm^{-1} (S=O); elemental analysis (%) calcd for $C_{11}H_{14}OS_2$: C 58.36, H 6.23; found: C 58.16, H 6.26.

9: Pale yellow crystals, m.p. 189–192 °C (hexane). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.06$ (s, 18H), 7.31–7.47 (m, 6H), 7.54–7.56 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 26.9$, 42.1, 127.2, 127.5, 127.9, 128.6, 129.8, 133.4 (the signal of the thiadiazoline C atom seems to be superimposed on a signal for an sp^2 C atom); IR (KBr): $\tilde{\nu} = 1304$, 1136 cm^{-1} (SO_2); elemental analysis (%) calcd for $C_{22}H_{28}N_2O_2S$: C 68.72, H 7.34, N 7.29; found: C 68.69, H 7.39, N, 7.33.

10: Colorless needles, m.p. 157–158 °C decomp (hexane). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.81$ (s, 18H), 7.22–7.32 (m, 6H), 7.60 (br d, J = 7.4 Hz, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 26.8$ (CH_3), 41.3 (C), 124.4 (C), 127.06 (CH), 127.10 (CH), 128.2 (CH), 142.0 (C); elemental analysis (%) calcd for $C_{22}H_{28}N_2S$: C 74.95, H 8.01, N 7.95; found: C 75.32, H 8.06, N 8.04.

Reaction of **15** with S_2O (method I): A solution of S_8 (32.6 mg, 0.127 mmol) in dichloromethane/benzene was treated with DMD (0.111 mmol), followed by addition of a solution of **15** (40 mg, 0.265 mmol) in dichloromethane. The mixture was subjected to medium-pressure liquid chromatography (SiO_2, hexane/Et_2O 4/1) to give **16** (4.8 mg, 0.0235 mmol, 21% based on DMD) and **17** (5.4 mg, 0.195 mmol).

16: m.p. 81 – 83 °C (hexane). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.72$ (s, 3H), 1.04 (s, 3H), 1.18 (s, 3H), 1.56 (s, 3H), 1.70 – 1.90 (m, 3H), 2.04 – 2.11 (m, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 23.1$, 28.5, 29.3, 30.9, 39.2, 41.7, 44.2, 48.0, 90.0; IR (KBr): $\tilde{\nu} = 1123\ cm^{-1}$ (S=O); elemental analysis (%) calcd for $C_9H_{16}OS_2$: C 52.90, H 7.89; found: C 53.51, H 8.00.

Received: September 25, 2000
Revised: February 8, 2001 [Z15850]

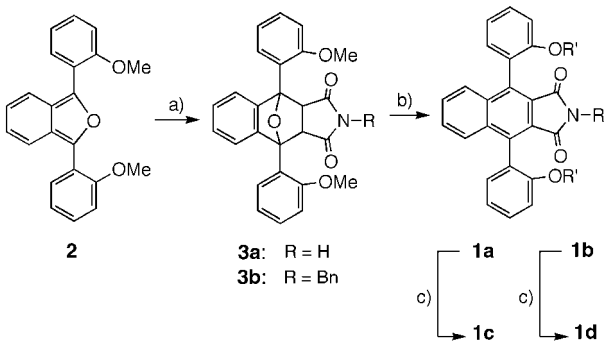
[1] A. Ishii, M. Nakabayashi, J. Nakayama, *J. Am. Chem. Soc.* **1999**, *121*, 7959 – 7960.
[2] R. M. Dodson, V. Srinivasan, K. S. Sharma, R. F. Sauers, *J. Org. Chem.* **1972**, *37*, 2367 – 2372.
[3] Review: A. R. V. Murthy, T. R. N. Kutty, D. K. Sharma, *Int. J. Sulfur Chem. B* **1971**, *6*, 161 – 175.
[4] a) R. Steudel, M. Rebsch, *Angew. Chem.* **1972**, *84*, 344 – 345; *Angew. Chem. Int. Ed. Engl.* **1972**, *11*, 302 – 303; b) R. Steudel, J. Latte, *Angew. Chem.* **1974**, *86*, 648; *Angew. Chem. Int. Ed. Engl.* **1974**, *13*, 603 – 604; c) R. Steudel, P. Luger, H. Bradaczek, M. Rebsch, *Angew. Chem.* **1973**, *85*, 452 – 453; *Angew. Chem. Int. Ed. Engl.* **1973**, *12*, 423 – 424; d) R. Steudel, T. Sandow, *Angew. Chem.* **1978**, *90*, 644 – 645; *Angew. Chem. Int. Ed. Engl.* **1978**, *17*, 611 – 612.
[5] R. Steudel, T. Sandow, *Angew. Chem.* **1976**, *88*, 854 – 855; *Angew. Chem. Int. Ed. Engl.* **1976**, *15*, 772 – 773; R. Steudel, R. Reinhardt, T. Sandow, *Angew. Chem.* **1977**, *89*, 757 – 758; *Angew. Chem. Int. Ed. Engl.* **1977**, *16*, 716.
[6] R. Steudel, J. Steidel, *Angew. Chem.* **1978**, *90*, 134 – 135; *Angew. Chem. Int. Ed. Engl.* **1978**, *17*, 134 – 135.
[7] A referee proposed that we examine the reaction of S_8O with trapping reagents, with regard to the mechanism of the reactions reported here. The reaction of S_8O, prepared by a reported method,[4b] with 2,3-dimethyl-1,3-butadiene in dichloromethane at room temperature for 1 h gave **2** in only 1.4% yield, while that carried out under reflux gave **2** in 25% yield. At present we do not have direct evidence for the existence of free S_2O in solution, so that "S_2O" should be read as "S_2O equivalent" throughout this paper.
[8] For a review, see: G. Opitz, *Angew. Chem.* **1967**, *79*, 161 – 177; *Angew. Chem. Int. Ed. Engl.* **1967**, *6*, 107 – 123.
[9] B. F. Bonini, G. Maccagnani, G. Mazzanti, *J. Chem. Soc. Chem. Commun.* **1976**, 431.
[10] B. F. Bonini, A. Cappelli, G. Maccagnani, G. Mazzanti, *Gazz. Chim. Ital.* **1975**, *105*, 827 – 839; B. F. Bonini, G. Maccagnani, *Tetrahedron Lett.* **1973**, 3585 – 3588; B. F. Bonini, G. Maccagnani, A. Wagenaar, L. Thijs, B. Zwanenburg, *J. Chem. Soc. Perkin Trans. 1* **1972**, 2490 – 2493; L. Thijs, A. Wagenaar, E. M. M. van Rens, B. Zwanenburg, *Tetrahedron Lett.* **1973**, 3589 – 3592; C. G. Venier, C. G. Gibbs, *Tetrahedron Lett.* **1972**, 2293 – 2296.
[11] W. Adam, J. Bialas, L. Hadjiarapoglou, *Chem. Ber.* **1991**, *124*, 2377; W. Adam, L. Hadjiarapoglou, A. Smerz, *Chem. Ber.* **1991**, *124*, 227 – 232.
[12] The *trans* stereochemistry of **9** and **10** was determined by X-ray crystallography and will be reported elsewhere.
[13] S.-Y. Tang, C. W. Brown, *Inorg. Chem.* **1975**, *14*, 2856 – 2858; A. G. Hopkins, S.-Y. Tang, C. W. Brown, *J. Am. Chem. Soc.* **1973**, *95*, 3486 – 3490.
[14] D. H. R. Barton, F. S. Guziec, Jr., I. Shahak, *J. Chem. Soc. Perkin Trans. 1* **1974**, 1794 – 1799, and references therein.
[15] R. Ahmed, W. Lwowsi, *Tetrahedron Lett.* **1969**, 3611 – 3612.
[16] M. Sander, *Chem. Rev.* **1966**, *66*, 297 – 339; N. Latif, I. Fathy, N. Mishriky, B. Haggag, *Can. J. Chem.* **1966**, *44*, 629 – 632.
[17] F. S. Guziec, Jr., C. J. Murphy, E. R. Cullen, *J. Chem. Soc. Perkin Trans. 1* **1985**, 107 – 113.
[18] L. v. Vargha, E. Kovács, *Chem. Ber.* **1942**, *75*, 794 – 802; N. Tokura, T. Nagai, S. Matsumura, *J. Org. Chem.* **1966**, *31*, 349 – 350.
[19] Y.-N. Jin, A. Ishii, Y. Sugihara, J. Nakayama, *Tetrahedron Lett.* **1998**, *39*, 3525 – 3528.
[20] K. A. Muszkat, E. Fischer, *J. Chem. Soc. B* **1967**, 662 – 678.
[21] H. Nozaki, R. Noyori, K. Sisido, *Tetrahedron* **1964**, *20*, 1125 – 1132.
[22] J. Nakayama, A. Ishii, *Adv. Heterocycl. Chem.* **2000**, *77*, 221 – 284.
[23] A. Ishii, Y. Jin, Y. Sugihara, J. Nakayama, *J. Chem. Soc. Chem. Commun.* **1996**, 2681 – 2682.

Solid-State Isomerization of Atropodiastereomers: Effective Diastereoselection through Polymorphic Transformations**

Cathy Einhorn, André Durif, Marie-Thérèse Averbuch, and Jacques Einhorn*

Polymorphism is a fascinating phenomenon accompanied by a lot of strange manifestations.[1] It is generally defined as the existence of a given compound in more than one crystalline form. In conformational polymorphs,[2] a given molecular compound adopts different conformations in different polymorphs. But, at a molecular level, conformational changes may involve quite high energy barriers, allowing in some cases the isolation of separate stereoisomers (atropisomers) which do not interconvert rapidly in solution at room temperature, but do so if enough energy is supplied. Herein we report solid-state thermal isomerizations of compounds **1**, which present such a type of atropisomerism. These isomerizations have features reminiscent of polymorphic transformations, although not involving polymorphs in the usual sense of the word.[3]

As depicted in Scheme 1, the synthesis of **1** has been achieved by Diels – Alder reactions between isobenzofuran **2** and maleimide or *N*-benzylmaleimide, giving adducts **3a** or **3b** in good yields. Their aromatization under strongly acidic conditions furnished **1a** and **1b** quantitatively. Demethylation of **1a** and **1b** gave diphenols **1c** and **1d** in high yields.



Scheme 1. Reagents, conditions, and yields: a) for **3a**: 1 equiv maleimide, toluene, RT, 6 h, 96%; for **3b**: 1 equiv *N*-benzylmaleimide, toluene, RT, 6 h, 81%; b) 6 equiv $MeSO_3H$, CH_2Cl_2, RT, 12 h, >99% for **1a**, >99% for **1b**; c) 3 equiv BBr_3, CH_2Cl_2, −78 °C to RT, 15 h, 98% for **1c**, 99% for **1d**. Full details can be found in the Supporting Information. RT = room temperature.

[*] Dr. J. Einhorn, Dr. C. Einhorn, Dr. A. Durif, Dr. M.-T. Averbuch
Laboratoire d'Etudes Dynamiques et Structurales de la Sélectivité
UMR 5616
Université Joseph Fourier
BP 53, 38041 Grenoble Cedex 9 (France)
Fax: (+33) 4-76-51-48-36
E-mail: Jacques.Einhorn@ujf-grenoble.fr

[**] Prof. Jean-Louis Pierre and Prof. Jacques Reisse are gratefully acknowledged for fruitful discussions, as well as Dr. Christian Philouze for assistance with the X-ray crystallographic studies. We would also like to thank one of the referees for valuable suggestions. We thank Université Joseph Fourier and CNRS for financial support.

Supporting information for this article is available on the WWW under http://www.angewandte.com or from the author.

  0044-8249/01/11310-1980 $ 17.50+.50/0