

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

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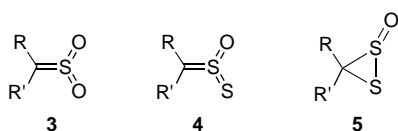
Dedicated to Professor Rolf Huisgen on the occasion of his 80th birthday

Recently we found that thermal decomposition of tetra-thiolane 2,3-dioxide **1** (1-Ad = 1-adamantyl) generates disulfur monoxide S₂O, which was trapped with 2,3-dimethyl-1,3-butadiene to give the 3,6-dihydro-1,2-dithiin 1-oxide **2** in high

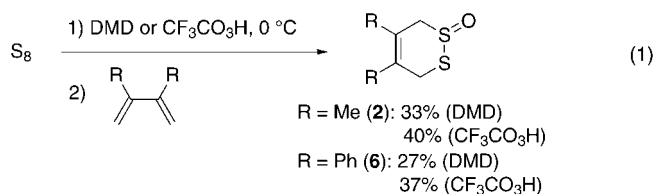


yield (ca. 90%).^[1] Up to now, the use of S₂O in organic chemistry has been limited to reactions with a few 1,3-butadienes.^[2] One reason for this is probably the troublesome methods for its generation; for example, pyrolysis of ethylene episulfide,^[2] electronic discharge of SO₂,^[3] and reactions of heavy metal oxides or sulfides with elemental sulfur at 250–400 °C or with gaseous SOCl₂ at 160 °C and 0.5 Torr.^[3]

Decomposition of oxides of elemental sulfur (S₈) is expected to be an alternative way to generate S₂O. Steudel et al. reported that S_nO (*n* = 6–8) are isolable but decompose to SO₂ and sulfur in solution or to S₂O and S_{*n*-2} in vacuo.^[4–6] Here we report a convenient and inexpensive method for the generation of S₂O^[7] and its reaction with typical 1,3-dipoles, namely, diazoalkanes. To our knowledge, there is no precedent for the reaction of diazoalkanes with S₂O, although reactions with SO₂,^[8] SO,^[9] and thioketone *S*-oxides (sulfines) have been investigated.^[10] The reaction of diazoalkanes with SO₂ was claimed to give thioketone *S,S*-dioxides (sulfenes) **3**.^[8] If the reaction of diazoalkanes with S₂O takes place in a similar fashion, the formation of thiosulfenes **4** or their cyclic isomers, dithiirane 1-oxides **5**, is expected.

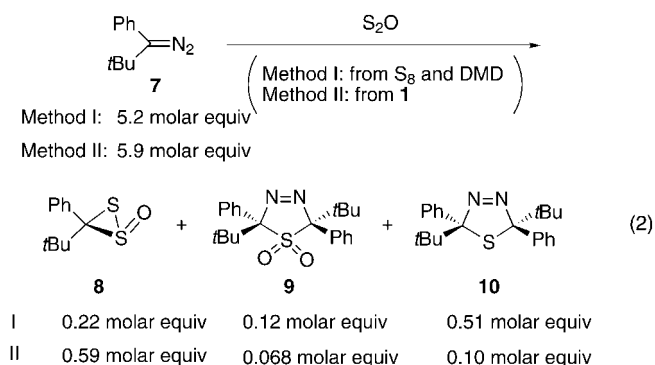


An equimolar amount of dimethyldioxirane (DMD)^[11] was added to a solution of elemental sulfur (S₈) in CH₂Cl₂/benzene at 0 °C, and the solution was stirred for 1 h. The mixture contains S₈O as an S₂O precursor.^[7] Then, 2,3-dimethyl- or 2,3-diphenyl-1,3-butadiene (**11** and **3** molar equiv, respectively) 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



did not improve the yields of the adducts because of the instability of higher oxides of S₈.^[4d] When trifluoroperoxyacetic acid was employed as the oxidant in CH₂Cl₂,^[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 S₂O is available from equimolar amounts of S₈ and an oxidizing agent under these conditions.

We next examined reactions of diazoalkanes with S₂O generated in situ. Two methods were investigated: in method I, S₂O was generated from one molar equivalent of S₈ and DMD in CH₂Cl₂/benzene or in CH₂Cl₂, and in method II, from **1** in CH₂Cl₂.^[1] The efficiency of the generation of S₂O 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 S₂O [Eq. (2); method I] gave

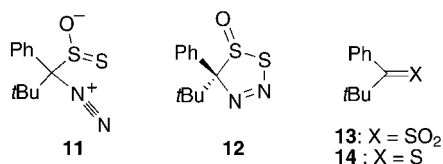


the expected dithiirane 1-oxide **8** (0.22 molar equiv based on S₈ and DMD) along with 1,3,4-thiadiazoline 1,1-dioxide **9**^[12] (0.12 molar equiv) and 1,3,4-thiadiazoline **10**^[12] (0.51 molar equiv). The configuration of **8** was determined to be 1*R**,3*S** from ¹H NMR spectroscopic data, and no other stereoisomer was obtained. The reaction of **7** (5.9 mol equiv) with S₂O 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 SO₂,^[8] the reaction of **7** with S₂O would give an initial adduct **11** or **12**, although we

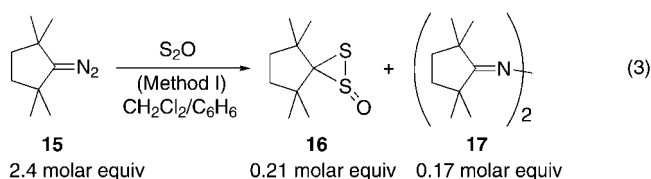
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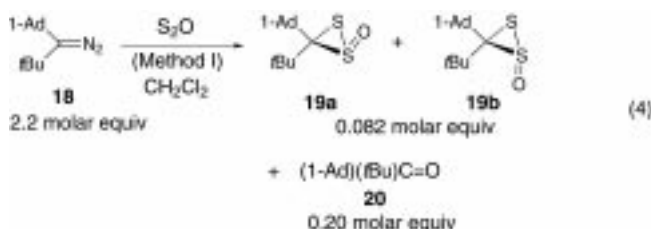


have no direct evidence for its formation. The extrusion of N₂ from the intermediate yields the dithiirane 1-oxide **8**. The formation of the 1,3,4-thiadiazoline 1,1-dioxide **9** implies the generation of sulfene **13** by reaction of **7** with SO₂, which undergoes a cycloaddition with **7** to give **9**.^[8] The SO₂ would be supplied by decomposition of higher oxides of S₈^[4d] or disproportionation of S₂O.^[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 (S₈), which gives **14**, is sluggish under similar conditions,^[16] sulfur allotropes S_n that are more reactive than S₈ should be responsible for the formation of **14**.

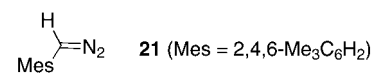
The reaction of a diazocyclopentane **15**^[17] (2.4 molar equiv) with S₂O (method I) yielded the spirodithiirane 1-oxide **16** (0.21 molar equiv) along with azine **17**^[17] (0.17 molar equiv) [Eq. (3)]. The formation of azines by reaction of diazoalkanes



with SO₂ is known.^[8, 18] The reaction of 1-adamantyl-*tert*-butyldiazomethane **18** with S₂O (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.



Diphenyldiazomethane and monoaryl diazomethane **21** failed to react with S₂O (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].



In summary, we have developed a convenient method for the generation of an S₂O equivalent by treatment of elemental sulfur with an oxidizing agent. The efficiency of generation was 30–40%. We also investigated the reaction of S₂O with diazoalkanes, which provides an alternative method for the preparation of dithiirane derivatives.^[22]

Experimental Section

Materials: elemental sulfur (S₈) was recrystallized from CS₂ before use. Dimethyldioxirane (DMD) was prepared as a solution in acetone.^[11]

General procedure for the generation of S₂O (method I) and the trapping reaction: DMD (0.10 M in acetone) was added to a solution of S₈ (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 ¹H NMR integral ratios with 9-acetylanthracene as internal standard.

Reaction of **7** with S₂O: Method I: 1) A solution of S₈ (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 ¹H NMR integral-ratio method with thioanisole as internal standard. 2) A solution of S₈ (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 (SiO₂, hexane/Et₂O 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)tetra-thiolane (**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 ¹H NMR integral ratios with thioanisole as internal standard.

8: Colorless crystals, m.p. 62–64 °C (dichloromethane/hexane). ¹H NMR (400 MHz, CDCl₃): δ = 1.02 (s, 9H), 7.37–7.50 (m, 5H); ¹³C NMR (100.6 MHz, CDCl₃): δ = 28.1, 38.4, 86.2, 127.8, 128.8, 133.2, 133.3; IR (KBr): ν̄ = 1118 cm^{–1} (S=O); elemental analysis (%) calcd for C₁₁H₁₄OS₂: C 58.36, H 6.23; found: C 58.16, H 6.26.

9: Pale yellow crystals, m.p. 189–192 °C (hexane). ¹H NMR (400 MHz, CDCl₃): δ = 1.06 (s, 18H), 7.31–7.47 (m, 6H), 7.54–7.56 (m, 4H); ¹³C NMR (100.6 MHz, CDCl₃): δ = 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 sp² C atom); IR (KBr): ν̄ = 1304, 1136 cm^{–1} (SO₂); elemental analysis (%) calcd for C₂₂H₂₈N₂O₂S: 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). ¹H NMR (400 MHz, CDCl₃): δ = 0.81 (s, 18H), 7.22–7.32 (m, 6H), 7.60 (brd, *J* = 7.4 Hz, 4H); ¹³C NMR (100.6 MHz, CDCl₃): δ = 26.8 (CH₃), 41.3 (C), 124.4 (C), 127.06 (CH), 127.10 (CH), 128.2 (CH), 142.0 (C); elemental analysis (%) calcd for C₂₂H₂₈N₂S: C 74.95, H 8.01, N 7.95; found: C 75.32, H 8.06, N 8.04.

Reaction of **15** with S₂O (method I): A solution of S₈ (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 (SiO₂, hexane/Et₂O 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). ¹H NMR (400 MHz, CDCl₃): δ = 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); ¹³C NMR (100.6 MHz, CDCl₃): δ = 23.1, 28.5, 29.3, 30.9, 39.2, 41.7, 44.2, 48.0, 90.0; IR (KBr): ν̄ = 1123 cm⁻¹ (S=O); elemental analysis (%) calcd for C₉H₁₆OS₂: C 52.90, H 7.89; found: C 53.51, H 8.00.

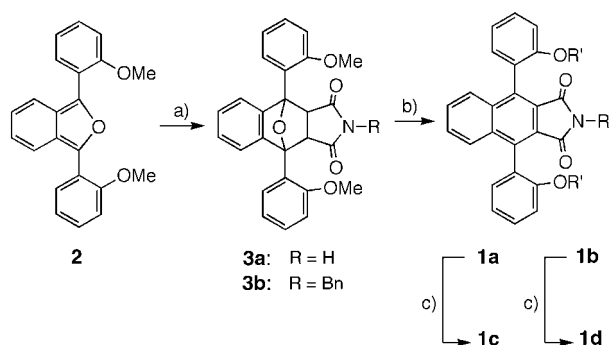
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Solid-State Isomerization of Atropodiastereomers: Effective Diastereoselection through Polymorphic Transformations**

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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 MeSO₃H, CH₂Cl₂, RT, 12 h, > 99% for **1a**, > 99% for **1b**; c) 3 equiv BBr₃, CH₂Cl₂, –78 °C to RT, 15 h, 98% for **1c**, 99% for **1d**. Full details can be found in the Supporting Information. RT = room temperature.

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

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