A Mild, High-Yield Conversion of Thiols into Disulfides Using Disulfide Dication Salt: A New Redox System

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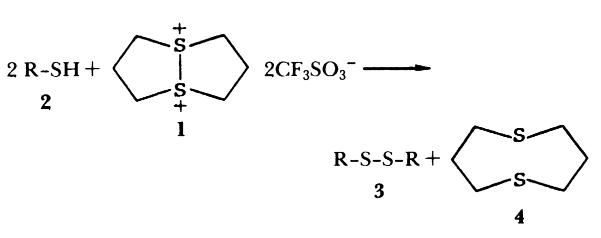
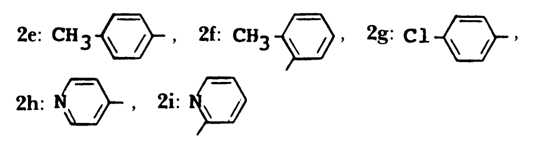
Synopsis. A new redox reaction of thiols with disulfide dication salt, 1,5-dithioniabicyclo[3.3.0]octane bis(trifluoromethanesulfonate), under mild conditions gave the corresponding disulfides in good yields together with 1,5-dithiacyclooctane.

The conversion of thiols into disulfides is an important phenomenon in chemical and biological redox reactions.[1,2] Numerous procedures are available for the oxidation of thiols to disulfides.[1] Meanwhile, the formation and the isolation of a few disulfide dications have been reported.[3,4] However, reactions using disulfide dication have not been well explored because of difficulties to obtain stable compounds. Recently, we succeeded in the preparation of the disulfide dication, 1,5-dithioniabicyclo[3.3.0]octane bis(trifluoromethanesulfonate) (**1**), as a remarkably stable crystalline salt which was first characterized by X-ray diffraction.[5] We found that the disulfide dication **1** acts both as an oxidizing agent and as an electrophile toward aromatics.[6] No synthetic application of this attractive organosulfur compound has been reported. We present here a new type of redox reaction of thiols with the disulfide dication salt **1** under mild conditions.



2a: *n*-C_4H_9, **2b**: *cyclo*-C_6H_{11}, **2c**: *t*-C_4H_9, **2d**: C_6H_5,



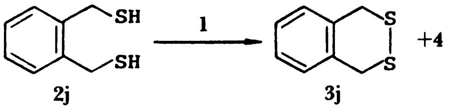
The disulfide dication salt **1** is a remarkably stable compound under dry conditions and can be easily prepared by the reaction of 1,5-dithiacyclooctane 1-oxide with trifluoromethanesulfonic anhydride. A redox reaction was carried out simply by stirring anhydrous acetonitrile solution of thiols (**2a**—**i**) and dication salt **1** under an Ar atmosphere at room temperature. Disulfides were completely consumed within a few hours, as determined by GLC or TLC. After the usual work-up procedure, the residue was purified by column chromatography to give the corresponding symmetrical disulfides (**3a**—**i**) in good yields, together with 1,5-dithiacyclooctane (**4**) as a reduction product. The results are summarized in Table 1. This method can be applied to the oxidation of a variety of alkane- (**2a**—**c**), arene- (**2d**—**g**), and heteroarenethiols (**2h** and **2i**).

Table 1. Oxidation of Thiols with Dication **1**[a)]

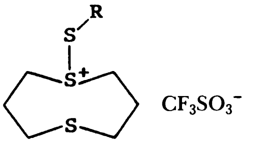
R-SH	Yield/%		Mp or Bp/°C/mmHg[b)] (lit)
	3	**4**	**3**
2a[c)]	80	86	228—230/760(226/760)[8)]
2b	82	95	120—123/0.6(138—141/1)[9)]
2c	35	42	82—84/18(83—86/18)[9)]
2d	86	84	60—61(61—62)[10)]
2e	78	60	46(44—46)[10)]
2f	73	83	36(36—38)[11)]
2g	80	86	72(72—73)[12)]
2h	86	80	d)
2i	83	84	57—58(57)[13)]
2j	44	77	80(80—81)[14)]

a) Time, 5 h. b) 1 mmHg≈133.322 Pa. c) At 0 °C.
d) Determined by NMR with authentic compound.

2-Methyl-2-propanethiol (**2c**) can be oxidized to the corresponding disulfide in comparatively low yield, though in general the oxidation of **2c** is difficult. The oxidative cyclization of 1,2-bis(mercaptomethyl)benzene (**2j**) was performed using a high-dilution method and gave the corresponding cyclic disulfide **3j** and **4** (see Table 1). These were obtained together with polymeric products, due to an intermolecular oxidation of **2j**.



These results demonstrate that the disulfide dication **1** employed acts as an oxidant toward thiols. This redox reaction may proceed through an electron-transfer process between thiols and the dication **1**, since the oxidation potential of thiols is relatively lower than that of **4** as a precursor of **1**.[6)] Another possibility, that involves the thiasulfonium cation intermediate, such as **5**, is also conceivable in the present reaction.



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Thus, a new organosulfur compound, disulfide dication **1**, can be used for the oxidation of several thiols under mild conditions.

Experimental

The IR spectra were obtained on a JASCO A-3 spectrometer. ^1H NMR spectra were measured on a Hitachi R-600 FT-NMR spectrometer. All of the reactions were monitored by gas chromatography (GLC) [Hitachi 163, using a 2% Silicon OV-1 Chromosorb W on SiO_2 (80—100 mesh) column] or thin-layer chromatography (TLC) [Wakogel B-5F].

Thiols, as shown in Table 1, were obtained from Wako Pure Chemicals. 1,2-Bis(mercaptomethyl)benzene was prepared from 1,2-bis(bromomethyl)benzene by a standard procedure.[7] 1,5-Dithiacyclooctane 1-oxide was prepared by a method given in the literature.[4] Other chemicals were of reagent grade.

Preparation of Disulfide Dication 1. To a stirred solution of 1,5-dithiacyclooctane 1-oxide (3.2 g, 19.5 mmol) in anhydrous dichloromethane (160 mL) was added dropwise a solution of trifluoromethanesulfonic anhydride (5.5 g, 19.5 mmol) in anhydrous dichloromethane (160 mL) at −20 °C. After the addition was complete, the mixture was stirred for 3 h, and the white precipitates were filtered and washed with anhydrous dichloromethane, giving salts **1** in 80% yield: mp 100—102 °C; ^{1}H NMR (CD_3CN) δ=2.2—2.7 (br s, 4H, CH_2) and 2.9—3.6 (br s, 8H, $^+SCH_2$). Calcd for $C_8H_{12}F_6O_6S_4$: C, 21.52; H, 2.70%. Found: C, 21.42; H, 2.71%.

Oxidation of Thiols with Dication 1. In a typical run, to a stirred solution of disulfide dication **1** (240 mg, 0.54 mmol) in anhydrous acetonitrile (5 mL) was added a solution of benzenethiol (118 mg, 1.08 mmol) in anhydrous acetonitrile (3 mL) under an Ar atmosphere at room temperature. The mixture was stirred at room temperature and the reaction was monitored by GLC. After the reaction was complete, the reaction mixture was treated with aqueous sodium hydrogencarbonate solution. The mixture was extracted with dichloromethane (5X20 mL). The extracts were dried with magnesium sulfate, and the solvent was evaporated under reduced pressure. The residue was purified with column chromatography on silica gel (eluent: hexane) to afford diphenyl disulfide. The oxidations of the other thiols were confirmed by the similar procedure. The yields of disulfides obtained are listed in Table 1. The purity of the isolated product was confirmed by GLC analysis: the IR and NMR spectra, and bp or mp, were in satisfactory agreement with values found in the literature.

Oxidation of 1,2-Bis(mercaptomethyl)benzene (2j). A solution of dication **1** (240 mg, 1.54 mmol) in anhydrous acetonitrile (20 mL) and 1,2-bis(mercaptomethyl)benzene (**2j**) (92 mg, 1.54 mmol) in anhydrous acetonitrile (20 mL) was added separately and simultaneously over 2 h to a vigorously stirred solution of anhydrous acetonitrile (10 mL). The mixture was stirred at room temperature for 8 h under an Ar atmosphere. The mixture was then treated as described above. Cyclic disulfide **3j** was obtained in 44% yield.

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