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Reactions of *p*-Toluenesulfinic Acid with Dialkoxy or Diamino Sulfides and Disulfides

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The reactions of *p*-toluenesulfinic acid (**1**) with dialkoxy disulfides (**2**), dialkoxy sulfides (**6**), diamino disulfides (**8**), diamino sulfides (**9**), and diamino sulfoxides (**15**) were examined and found to give di-*p*-toluenesulfonyl disulfide (**3**), di-*p*-toluenesulfonyl sulfide (**4**), amino *p*-toluenesulfonyl disulfides (**10**), amino *p*-toluenesulfonyl sulfides (**13**), and *p*-toluenesulfinamides (**16**), respectively.

Keywords——sulfinate S-nucleophile; intermolecular reaction; dialkoxy disulfide; dialkoxy sulfide; diamino disulfide; diamino sulfide; diamino sulfoxide; amino sulfonyl disulfide; amino sulfonyl sulfide

Although dialkoxy disulfides[1] were initially prepared in 1895, little attention has been paid to their reactivity except for a few investigations on the reactions with sodium alcoholate,[1c,2] alkyllithium,[1d] and β-diketone.[1d] In these reactions, nucleophilic attack on the sulfur results in cleavage of the sulfur–sulfur or sulfur–oxygen bond. Recently, Motoki has found that thiocarboxylic acids, thiols, and amines readily displace an alcohol moiety to give acyl alkoxy trisulfides,[3] alkoxy alkyl trisulfides,[4] and alkoxy amino disulfides,[4] respectively.

We are interested in studying the reactivity of sulfinic acids toward dialkoxy disulfides and related classes of compounds, such as dialkoxy sulfides,[5] diamino disulfides,[4] diamino sulfides,[6] diamino sulfoxides,[7] and diamino sulfones.[8]

Reactions of *p*-Toluenesulfinic Acid with Dialkoxy Disulfides and Dialkoxy Sulfides

When dialkoxy disulfides (**2**) were allowed to react with two molar equivalents of *p*-toluenesulfinic acid (**1**) in dichloromethane at room temperature for 2 h, di-*p*-toluenesulfonyl disulfide (**3**) was obtained in 68—75% yield. The same reaction in boiling dichloromethane for 1 h gave di-*p*-toluenesulfonyl sulfide (**4**) and di-*p*-toluenesulfonyl trisulfide (**5**) in yields of about 30% each. The formation of **4** and **5** is presumed to proceed through disproportionation of intermediately formed **3**. In practice, when **3** was heated in dichloromethane under boiling, **4** and **5** were obtained in 36 and 33% yields, respectively.

The reaction of **1** with dialkoxy sulfides (**6**) was analogously achieved in dichloromethane at room temperature to provide **4** in 65—73% yield. The yields of **3** and **4** in these reactions are summarized in Table I.

The structures of **3**, **4**, and **5** were established by analysis of the spectral and analytical data, and by comparison with authentic samples prepared by alternative methods.[9]

In the vast majority of reactions, sulfinic acid behaves as an ambident anion, which shows S- and O-nucleophilicities. The reaction of **1** with **2** or **6** is presumed to be initiated by nucleophilic attack of *p*-toluenesulfinate S-nucleophile on the sulfur atom of protonated **2** or **6**, resulting in cleavage of the O–S bond. However, no trace of the monosulfonated

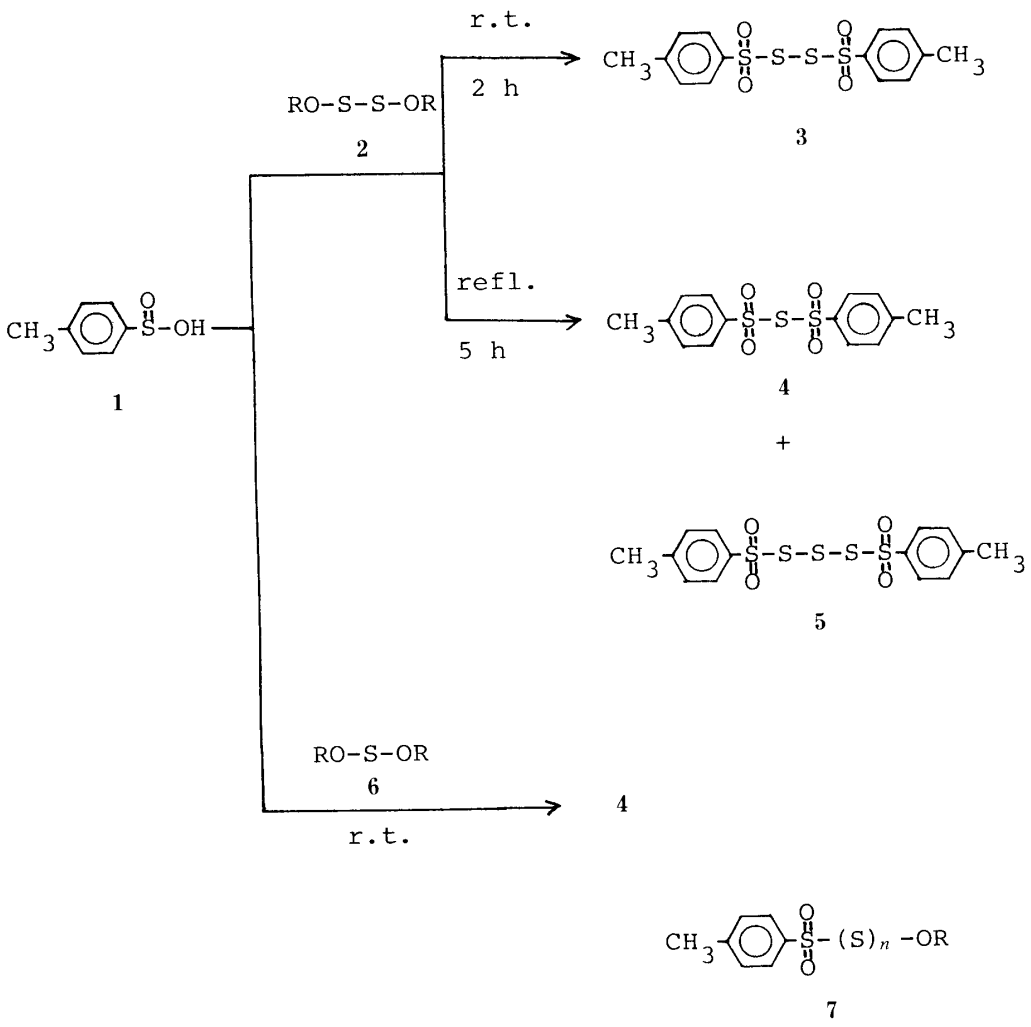


Chart 1

TABLE I. Reactions of Dialkoxy Disulfides (**2**) and Dialkoxy Sulfides (**6**) with *p*-Toluenesulfinic Acid (**1**)

R	Reactant	Product yield (%) **3** or **4**
C_2H_5O–	**2a**	72 —
	6a	— 69
$(CH_3)_2CHO$–	**2b**	70 —
	6b	— 73
–O–	**2c**	75 —
	6c	— 71
$-CH_2O-$	**2d**	68 —
	6d	— 65

intermediate (**7**) was detected by thin layer chromatography.

Reactions of *p*-Toluenesulfinic Acid with Diamino Disulfides and Diamino Sulfides

In the reactions of diamino disulfides (**8**) and diamino sulfides (**9**) with **1**, the monosulfonated compounds may be isolated. Generally, sulfenamides are known to be more stable than sulfenic esters.

When dimorpholino and dipiperidino disulfides (**8a** and **8b**) were treated with two molar

equivalents of **1** in dichloromethane at room temperature for 2 h, the corresponding morpholino and piperidino *p*-toluenesulfonyl disulfides (**10a** and **10b**)[10] were obtained in 62% and 32% yields, respectively, along with a good yield of *p*-toluenethiosulfonate (**11**).[11] On the other hand, the same reactions in boiling dichloromethane gave **4** and **5** along with a small amount of *p*-toluenesulfonamides (**12**),[12] no trace of **10** being isolated.

Analogously, the reactions of **1** with dimorpholino and dipiperidino sulfides (**9a** and **9b**) in dichloromethane at room temperature afforded morpholino and piperidino *p*-toluenesulfonyl sulfides (**13a** and **13b**) in 60% and 25% yields, respectively, with a small amount of **4**. The same reactions under reflux provided **4** in 61—66% yield, though no trace of **13** was isolated. The yields of these products are summarized in Table II. The formations of **10** and **13** are presumed to proceed through initial attack of the *p*-toluenesulfinate S-nucleophile on the sulfur atoms of protonated **8** and **9** with heterolytic cleavage of the N–S bonds. The

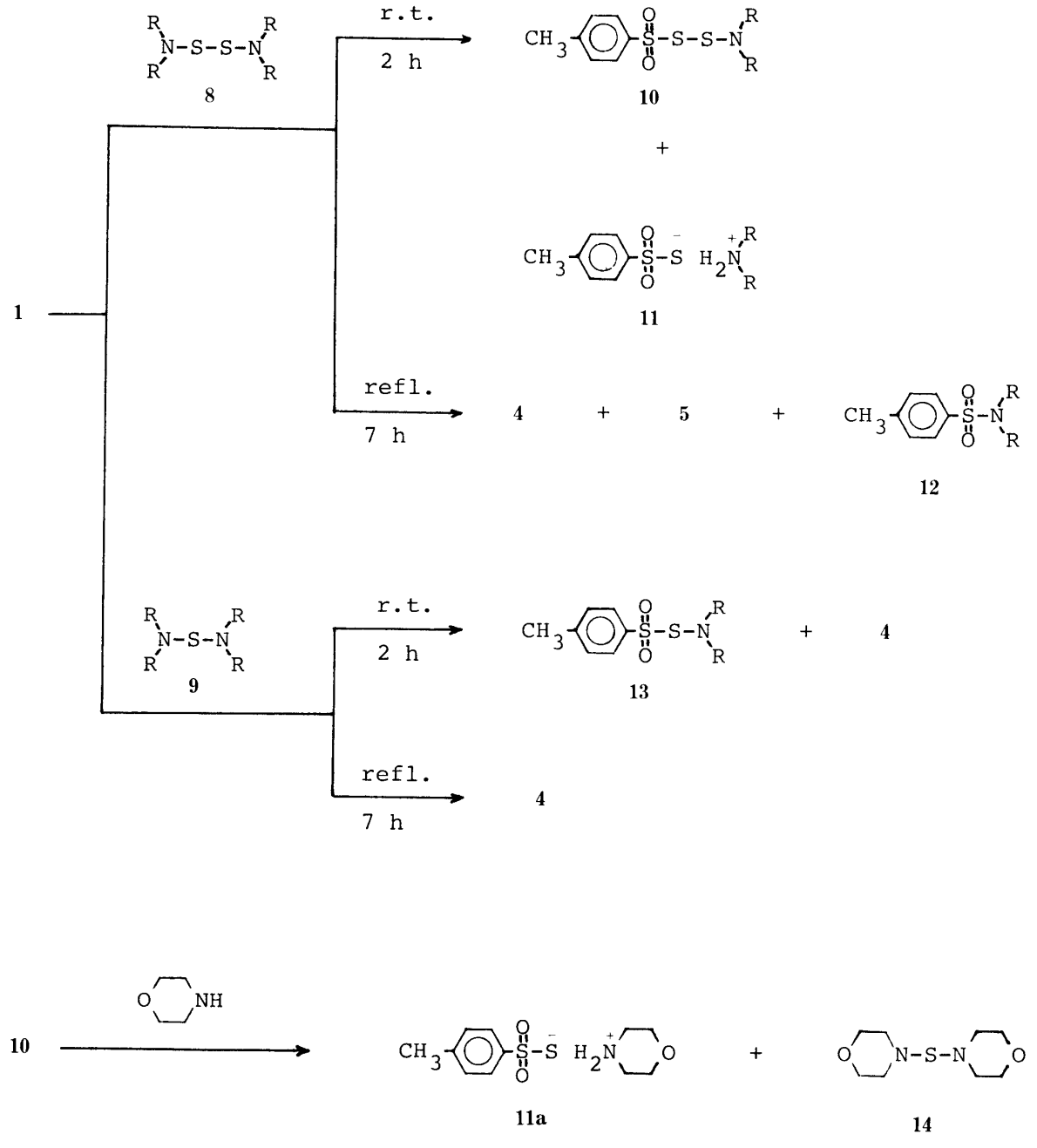
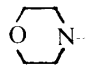
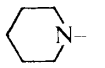
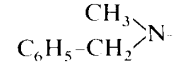
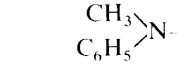
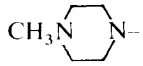


Chart 2

TABLE II. Main Products in the Reactions of Diamino Disulfides (**8**) and Diamino Sulfides (**9**) with *p*-Toluenesulfinic Acid (**1**)

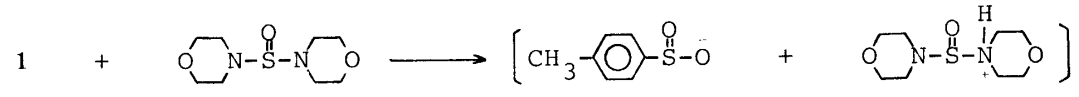
R	Reactant	Product yield (%)					
		10	r.t. or	**13**	**4**	refl. and	**5**
	**8a**	62		—	40		27
	9a	—		60	64		—
	**8b**	32		—	34		26
	9b	—		25	63		—
	**8c**	0		-	35		19
	9c	—		0	61		—
	**8d**	0		—	42		21
	9d	—		0	61		—
	**8e**	0		—	46		20
	9e	—		0	67		—

formation of **12** is assumed to be due to thermal decomposition of **10**. As expected, heating of **10a** in dichloromethane under reflux afforded **12a** in 12% yield. This decomposition was influenced by the boiling point and polarity of the solvent, and the yield of **12a** was increased to 32% or 43% by using chloroform or toluene, respectively. The decomposition presumably proceeds through an ionic pathway. Moreover, the formation of **12a** was not observed in the decomposition after dilution with the same solvent. Some intermolecular interaction may be involved in the reaction mechanism, though no evidence is yet available.

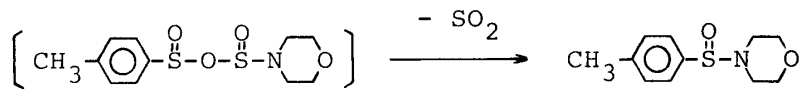
The structures of compounds **10** and **13** were assigned on the basis of the spectral and analytical data. Further support for the structure of **10** was provided by the reaction with morpholine. The reaction was carried out in dichloromethane at room temperature to give dimorpholino sulfide (**14**) and ammonium *p*-toluenethiosulfonate (**11a**) in 20% and 64% yields, respectively. The formation of **14** presumably occurs by nucleophilic attack of the amine on the sulfur atom adjacent to the nitrogen atom in **10** with elimination of thiosulfonic acid.

Reaction of *p*-Toluenesulfinic Acid with Dimorpholino Sulfoxide

Treatment of **15** with two molar equivalents of **1** under similar conditions gave *p*-toluenesulfinylmorpholide (**16**) in 49% yield, with evolution of sulfur dioxide. In this case, if the sulfinate anion reacts as the S-nucleophile as in the reaction with **9a**, sulfonamide would be formed. This is not the case, however. The finding that the product is sulfinamide (**16**) suggests



15



17 **16**

Chart 3

that the sulfinate anion behaves as an O-nucleophile to give intermediate **17**, followed by elimination of sulfur dioxide.

Such a difference in chemical behavior of **15** from **9** toward **1** can be explained in terms of the hard and soft acids and bases (HSAB) principle.[13] The soft sulfenyl sulfur atom of **9** may easily react with the soft sulfinate S-nucleophile rather than the hard sulfinate O-anion, whereas the hard sulfinyl sulfur atom of **15** would react preferentially with the hard nucleophilic site of ambident sulfinate.

Contrary to expectation, the similar reaction of **1** with diamino sulfones did not proceed, resulting in quantitative recovery of the starting materials. This is presumed to be due to the strength of the N–SO_2 bond, as well as to the steric hindrance and electric repulsion of the sulfonyl oxygen atom, preventing approach of the sulfinate anion.

Experimental

All melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. Infrared (IR) spectra were recorded with a JASCO IRA-1 grating infrared spectrometer. Proton nuclear magnetic resonance (^{1}H-NMR) spectra were determined with a JEOL C-60H high-resolution NMR instrument. Mass spectra (MS) were measured with a JEOL-01SG mass spectrometer.

General Procedure for Reaction of *p*-Toluenesulfinic Acid (1) with Dialkoxy Disulfides (2)——A solution of **1** (20 mmol) and **2** (10 mmol) in dichloromethane (50 ml) was stirred for 2 h at room temperature. The mixture was washed with H_2O (50 ml) three times, dried over anhyd. Na_2SO_4, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (benzene) to give di-*p*-toluenesulfonyl disulfide (**3**)[9] melting at 114—115 °C. IR ν_{max}^{KBr} cm^{-1}: 1145, 1330 (SO_2). MS *m/z*: 155 (*p*-$MeC_6H_4SO_2^+$). *Anal.* Calcd for $C_{14}H_{14}O_4S_4$: C, 44.87; H, 3.76. Found: C, 44.65; H, 3.78. The same reaction in boiling CH_2Cl_2 for 7 h gave di-*p*-toluenesulfonyl sulfide (**4**) and di-*p*-toluenesulfonyl trisulfide (**5**). These results are summarized in Table I.

General Procedure for Reaction of *p*-Toluenesulfinic Acid (1) with Dialkoxy Sulfides (6)——A solution of **1** (20 mmol) and **6** (10 mmol) in CH_2Cl_2 (50 ml) was stirred for 2 h at room temperature. The mixture was then worked up in the same manner as described for compound **3** to give di-*p*-toluenesulfonyl sulfide (**4**) melting at 136—137 °C. The yields are listed in Table I. IR ν_{max}^{KBr} cm^{-1}: 1155, 1350 (SO_2).

Procedure for Reaction of *p*-Toluenesulfinic Acid (1) with Diamino Disulfides (8)——Compound **1** (100 mmol) was added to a stirred solution of a diamino disulfide (**8**) (50 mmol) in CH_2Cl_2 (100 ml) at room temperature, and stirring was continued for 2 h. The mixture was washed successively with H_2O (100 ml), 0.5 M HCl (50 ml), and H_2O (2 × 100 ml), then dried over anhyd. Na_2SO_4, and evaporated to dryness under reduced pressure. The residue was washed with cold EtOH (20 ml) and recrystallized from *n*-hexane to give amino *p*-toluenesulfonyl disulfide (**10**). Attempted purification by column chromatography using silica gel resulted in decomposition. Evaporation of the washings gave ammonium *p*-toluenethiosulfonate (**11**).[11]

Morpholino *p*-Toluenesulfonyl Disulfide (**10a**): mp 78—79 °C. Yield 62%. IR ν_{max}^{KBr} cm^{-1}: 1140, 1330 (SO_2). ^{1}H-NMR ($CDCl_3$) δ: 2.40 (3H, s, CH_3), 2.85—3.20 (4H, m, CH_2–N–CH_2), 3.40—3.97 (4H, m, CH_2–O–CH_2), 7.33, 7.83 (4H, dd, J=9 Hz, –C_6H_4–). MS *m/z*: 305 (M^+). *Anal.* Calcd for $C_{11}H_{15}NO_3S_3$: C, 43.29; H, 4.92; N, 4.60. Found: C, 43.08; H, 4.83; N, 4.43.

Piperidino *p*-Toluenesulfonyl Disulfide (**10b**): mp 77—78 °C. Yield 32%. IR ν_{max}^{KBr} cm^{-1}: 1145, 1330 (SO_2). ^{1}H-NMR ($CDCl_3$) δ: 1.15—1.95 (6H, m, $CH_2CH_2CH_2$), 2.45 (3H, s, CH_3), 2.85—3.20 (4H, m, CH_2–N–CH_2), 7.32, 7.82 (4H, dd, J=8 Hz, –C_6H_4–). MS *m/z*: 303 (M^+). *Anal.* Calcd for $C_{12}H_{17}NO_2S_3$: C, 47.52; H, 5.61; N, 4.56. Found: C, 47.52; H, 5.68; N, 4.56.

Morpholinium *p*-Toluenethiosulfonate (**11a**): mp 156—158 °C. Yield 64%. IR ν_{max}^{KBr} cm^{-1}: 1115, 1205 (SO_2). *Anal.* Calcd for $C_{11}H_{17}NO_3S_2$: C, 47.98; H, 6.22; N, 5.09. Found: C, 47.77; H, 6.35; N, 4.93.

Piperidinium *p*-Toluenethiosulfonate (**11b**): mp 102—104 °C. Yield 37%. IR ν_{max}^{KBr} cm^{-1}: 1115, 1210 (SO_2). *Anal.* Calcd for $C_{12}H_{19}NO_2S_2$: C, 52.72; H, 7.00; N, 5.12. Found: C, 52.56; H, 7.07; N, 5.34.

In the reaction of **1** with **8** in boiling CH_2Cl_2, **4**, **5**, and a small amount of *p*-toluenesulfonamide (**12**) were obtained.

Procedure for Reaction of *p*-Toluenesulfinic Acid (1) with Diamino Sulfides (9)——The reaction mixture of **1** with **9** was worked up in the same manner as described for compound **10** to give amino *p*-toluenesulfonyl sulfide (**13**). Evaporation of the washings gave a small amount of di-*p*-toluenesulfonyl sulfide (**4**), mp 136—137 °C.

Morpholino *p*-Toluenesulfonyl Sulfide (**13a**): mp 104—105 °C. Yield 60%. IR ν_{max}^{KBr} cm^{-1}: 1135, 1300 (SO_2). ^{1}H-NMR ($CDCl_3$) δ: 2.46 (3H, s, CH_3), 3.15—3.50 (4H, m, CH_2–N–CH_2), 3.50—3.85 (4H, m, CH_2–O–CH_2), 7.31, 7.81 (4H, dd, J=9 Hz, –C_6H_4–). MS *m/z*: 273 (M^+). *Anal.* Calcd for $C_{11}H_{15}NO_3S_2$: C, 48.33; H, 5.42; N, 5.12. Found: C, 47.80; H, 5.37; N, 5.20.

Piperidino *p*-Toluenesulfonyl Sulfide (**13b**): mp 65—67 °C. Yield 25%. IR ν_{max}^{KBr} cm^{-1}: 1130, 1300 (SO_2). ^{1}H-NMR ($CDCl_3$) δ: 1.15—1.85 (6H, m, $CH_2CH_2CH_2$), 2.45 (3H, s, CH_3), 3.10—3.60 (4H, m, CH_2–N–CH_2), 7.30, 7.80 (4H, dd, J=8 Hz, –C_6H_4–). MS *m/z*: 271 (M^+). *Anal.* Calcd for $C_{12}H_{17}NO_2S_2$: C, 53.13; H, 6.27; N, 5.16. Found: C, 53.81; H, 6.36; N, 5.43.

The reaction of **1** with **9** at boiling temperature gave **4** as the sole product.

Thermal Decomposition of Di-*p*-toluenesulfonyl Disulfide (3)——A solution of **3** (5 mmol) in CH_2Cl_2 (20 ml) was heated with stirring for 1 h under reflux. The solvent was distilled off, and the residue was dissolved in cold acetone. The insoluble part was collected by filtration and recrystallized from benzene to give **4** (36%). The filtrate was evaporated, and the residue was recrystallized from EtOH to give **5** (33%).

Thermal Decomposition of Morpholino *p*-Toluenesulfonyl Disulfide (10a)——A solution of **10a** (6 mmol) in CH_2Cl_2 (20 ml) was heated with stirring for 7 h under reflux, and the solvent was distilled off under reduced pressure. The residue was extracted with EtOH (10 ml) and the extract was concentrated to give *p*-toluenesulfonylmorpholide (**11a**) (12%), mp 145—147 °C. IR ν_{max}^{KBr} cm^{-1}: 1170, 1350 (SO_2).

Reaction of Morpholino *p*-Toluenesulfonyl Disulfide (10a) with Morpholine——Morpholine (10 mmol) was added to a stirred solution of **10a** (5 mmol) in CH_2Cl_2 (30 ml) at room temperature and stirring was continued for 2 h. The solution was concentrated under reduced pressure, and the residue was extracted with cold benzene. The insoluble part was collected by filtration and recrystallized from benzene to give morpholinium *p*-toluenethiosulfonate (**11a**) (64%). The filtrate was evaporated, and the residue was washed with cold EtOH then recrystallized from MeOH to give dimorpholino sulfide (**14**) (26%).

Procedure for Reaction of *p*-Toluenesulfinic Acid (1) with Dimorpholino Sulfoxide (15)——Compound **1** (10 mmol) was added to a stirred solution of **15** (5 mmol) in CH_2Cl_2 (30 ml) at room temperature, and stirring was continued for 3 h. The solvent was distilled off, and the residue was extracted with cold benzene. The insoluble part was collected and recrystallized from benzene to give morpholinium *p*-toluenesulfinate (76%). The filtrate was washed with H_2O, dried over $MgSO_4$, and evaporated. The residue was recrystallized from *n*-hexane to give *p*-toluenesulfinylmorpholide (**16**) (63%), mp 122—123 °C. IR ν_{max}^{KBr} cm^{-1}: 1065 (SO). ^{1}H-NMR ($CDCl_3$) δ: 2.43 (3H, s, CH_3), 3.10 (4H, t, J=5 Hz, CH_2–N–CH_2), 3.72 (4H, t, J=5 Hz, CH_2–O–CH_2), 7.28, 7.56 (4H, dd, J=8 Hz, –C_6H_4–). MS *m/z*: 225 (M^+). *Anal.* Calcd for $C_{11}H_{15}NO_2S$: C, 58.66; H, 6.66; N, 6.21. Found: C, 59.06; H, 6.84; N, 6.33.

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