A Catalytic Effect of Amines on the Reaction of Arenesulfinic Acids with *N*,*N*′-Thiodiphthalimide[1)]

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In the presence of catalytic amounts of several amines, *N*,*N*′-thiodiphthalimide has been allowed to react with one or two equiv. of arenesulfinic acids in dichloromethane, thus giving *N*-(arylsulfonylthio)phthalimides or bis(arenesulfonyl) sulfides respectively in good yields. The arenesulfinate anion seems to be a better nucleophile against *N*,*N*′-thiodiphthalimide than arenesulfinic acid. The mechanism of the catalytic reaction will be discussed.

N,*N*′-Thiodiphthalimide (**1**) has been known to be a useful sulfur-transfer reagent, giving symmetrical trisulfides[2)] and *N*,*N*′-thiodiamines[3)] by reactions with two equiv. of thiols and secondary amines respectively. Unsymmetrical trisulfides and *N*-(alkyldithio- or aryldithio)amines are prepared by the reactions of the intermediates derived from **1** with one equiv. of thiols and amines respectively.[3)] It has previously been reported that **1** reacts with one equiv. of arenesulfinic acids (**2**) to give *N*-(arylsulfonylthio)phthalimides (**3**) and with two equiv. of **2** to give bis(arenesulfonyl) sulfides (**4**).[4)] In a preceding paper,[5)] it was shown that catalytic amounts of amines accelerate the reaction of α-toluenethiol with **1** in benzene or dichloromethane.

We wish now to report our examination to confirm that amines and their ammonium salts catalyze the reaction of **1** with **2** in dichloromethane, and to elucidate the mechanism of the catalyzed reaction. In addition, we will show the IR characteristic absorptions of the S–N bond in the compounds **3a**—**g** produced in the present reaction.

Results and Discussion

The reaction of **1** with **2** in the presence of catalytic amounts of amines was performed in dichloromethane at the boiling point for 1 h. Representative authentic arenesulfinic acids are stable at the same temperature for several hours in the same solvent. The product **3** was isolated from the reaction mixture by fractional dissolution in benzene and ethanol, and **4**, by column chromatography using silica gel. Preliminary work indicated that Compound **4** was recovered quantitatively from the column; Compound **3** was recovered in a 60—70% yield, but Compound **4** was not detected in the remaining eluate. These experiments suggest that **3** do not give **4** through the column.

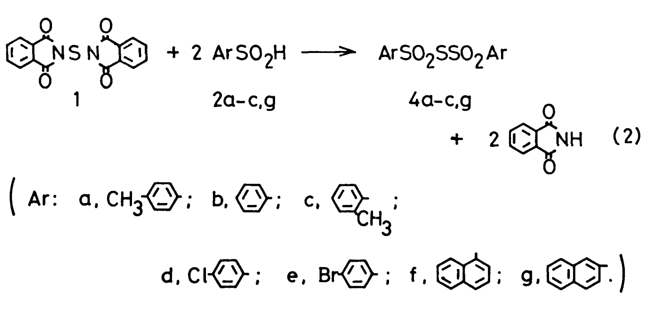
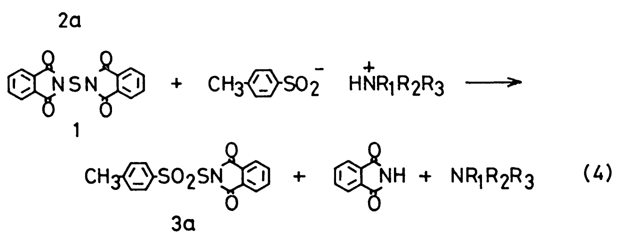


Table 1. Effects of amines on the reaction of **1** with **2a**[a)]

Entry	Amine	pK_a	Yield of products 3a(%)	4a(%)
1	None		24	2
2	Aniline	4.60	91	0
3	*N*-Methylaniline	4.85	84	0
4	*p*-Toluidine	5.12	75	1
5	Pyridine	5.17	70	4
6	2,6-Lutidine	6.75	80	2
7	2,4-Lutidine	6.79	79	6
8	Imidazole	6.95	84	0
9	*N*-Methylmorpholine	7.41	78	4
10	Morpholine	8.36	88	3
11	Butylamine	10.60	81	2
12	Triethylamine	10.67	88	2
13	Tributylamine	10.87	77	6
14	Piperidine	11.22	81	7
15	DBU		59	1

a) All the reactions were performed by the use of **1** (5 mmol), **2** (5 mmol), and an amine (0.5 mmol) in dichloromethane (100 ml) at the boiling point for 1 h.

*The Reaction of **1** with One Equiv. of **2**.* Regardless of the functional group (*i.e.*, primary, secondary, or tertiary), all the amines used here accelerated the reaction of **1** with *p*-toluenesulfinic acid (**2a**). The results of the reactions are summarized in Table 1. The yield of *N*-(*p*-tolylsulfonylthio)phthalimide (**3a**) did not vary significantly with the amine. Previously, the catalytic ability of amine in the reaction of **1** with α-toluenethiol was explained by the S–H–N-type hydrogen bonding.[5)] It is more reasonable, however, to expect that the catalytib ability of amine in the present reaction is due to the formation of the corresponding ammonium sulfinate from amine and arenesulfinic acid, since the arenesulfinate anion is generally more nucleophilic to the sulfur atom than the arenesulfinic acid is. The fact that the yield of **3a** increases upon the addition of amine, independent of the pK_a value, compared with that in the reaction without amine, suggests that amine forms a salt with **2a** in dichloromethane. Therefore, a reaction mechanism in which amine revives as a catalyst is



described by Eqs. 3 and 4. When DBU was used, the yield of **3a** was not so good as those with other amines, indicating that DBU would form a very tight salt with **2a**, thus, the migration of the sulfinate anion would be restrained.

To confirm the mechanism proposed above, ammonium salts were first examined as catalysts. When each 0.1 equiv. of pyridinium, imidazolium, or piperidinium *p*-toluenesulfinate was added to the reaction system, **3a** was obtained in yields of 69, 81, and 70% respectively. Comparing the yields with those of the corresponding amines in Table 1, it is clear that the two results are not significantly different.

Second, we examined the catalytic effect of amine hydrochloride and tetraalkylammonium halides, the anions of which are exchangeable. When 0.1 equivalents of each of these salts were used, **3a** was formed in yields of 85% (triethylammonium hydrochloride), 60% (tetraethylammonium chloride), 63% (tetraethylammonium bromide), and 78% (tetraethylammonium iodide). The halide anion is expected to form a hydrogen bonding with the acidic hydrogen atom of arenesulfinic acid and, consequently, to activate the acid in a manner similar to the condensation reactions of a number of organic compounds with alkyl halides in the presence of potassium fluoride.[6] As may be seen in the results with the three tetraethylammonium halides, however, the chloride anion which is more electron-rich and nucleophilic[7] has less catalytic activity than the iodide anion. In other words, the salt with a weaker ionic bonding force has a larger catalytic ability. This fact also suggests that the catalytic ability is due to the formation of a sulfinate anion *via* anion exchange rather than to the activation by hydrogen bonding between a halide anion and sulfinic acid.

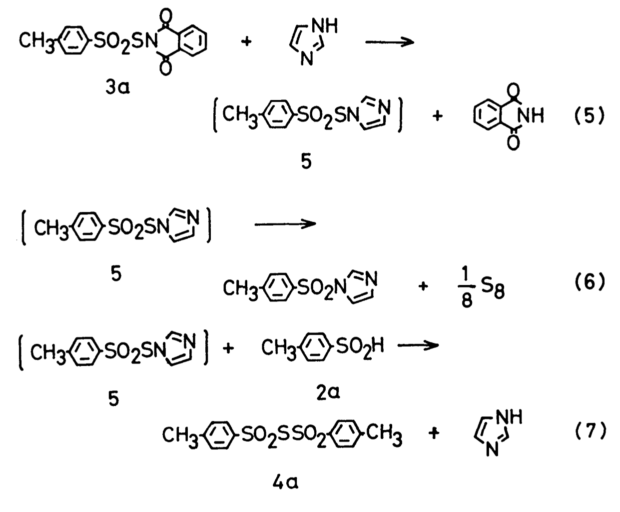
The reaction of aqueous sodium *p*-toluenesulfinate with **1** in dichloromethane was performed with the aid of a phase-transfer reagent. Unfortunately, the yield of **3a** was very poor. The decrease in the yield may be a result of the decomposition of the product, **3a**. Therefore, the stability of **3a** was examined; **3a** was recovered quantitatively after having been boiled for 1 h in a mixture of water and dichloromethane, but it was found to be unstable in an alkaline solution. Since slightly basic sodium phthalimide should be formed by the reaction of sodium *p*-toluenesulfinate with **1**, the product, **3a**, had to decompose. Accordingly, it seems hard to prepare **3** from an aqueous solution of the sulfinate.

Table 2. Effects of the amount of imidazole or triethylamine[a)]

Entry	Amine	Ratio[b)]	Yield of **3a** (%)
1	None	0	24
2	Imidazole	0.05	78
3	Imidazole	0.1	84
4	Imidazole	0.2	28
5	Imidazole	1	0[c)]
6	Triethylamine	0.05	85
7	Triethylamine	0.1	88
8	Triethylamine	0.2	73
9	Triethylamine	1	62

a) All the reactions were performed by the use of **1** (5 mmol), and **2a** (5 mmol) in dichloromethane (100 ml) at the boiling point for 1 h. b) Molar ratio of amine to **1**. c) 1-(*p*-Tolylsulfonyl)imidazole and elemental sulfur were isolated.

The relationship between the amount of imidazole or triethylamine and the yield of **3a** was examined for the reaction of **1** with one equiv. of **2a**; the results are summarized in Table 2. In the case of triethylamine, **3a** was isolated in a considerable yield even if the ratio of triethylamine to **1** was 1. The yield of **3a**, however, decreased with the addition of a 0.2 equiv. of imidazole. With the addition of one equiv. of imidazole, **3a** was not isolated from the reaction mixture, but 1-(*p*-tolylsulfonyl)imidazole and elemental sulfur were isolated. It has been reported that *N*-(alkyldithio)phthalimides react with secondary amine[3] and that the S–N bond of 1,1′-thiodiimidazole is very reactive.[8] The reactivity of the S–N bonds seems to indicate that **3a** reacted with imidazole to give the undesirable products by the course shown by Eqs. 5—7. Equation 5 shows that imidazole reacted with **3a** to give 1-(*p*-tolylsulfonylthio)imidazole (**5**), which is an unstable intermediate. The acid, **2a**, still remaining in the reaction mixture would react with it to give **4a** and regenerate imidazole (Eq. 7). However, in the absence of **2a** in the reaction mixture, **5** must be desulfurated to give stable 1-(*p*-tolylsulfonyl)imidazole (Eq. 6). When authentic **3a** was treated with one equiv. of imidazole, 1-(*p*-tolylsulfonyl)imidazole was isolated in a 51% yield.



Taking into account the results obtained above, a series of **3** were prepared by the reactions of **1** with

Table 3. Preparation$^{\text{a)}}$ and IR spectra of *N*-(arylsulfonylthio)phthalimides (**3**)

Substance	Aryl group in **3**	Yield/%	Mp/°C	IR (cm^{-1}) $\nu_{C=O}$	ν_{SO_2}	ν_{SN}
3a	*p*-Tolyl	83	166—167	1756,	1341, 1143,	870
3b	Phenyl	69	171—172	1750,	1327, 1147,	870
3c	*o*-Tolyl	79	165—166	1755,	1321, 1125,	867
3d	*p*-Chlorophenyl	73	168—169	1754,	1335, 1142,	868
3e	*p*-Bromophenyl	57	166—169	1743,	1341, 1144,	867
3f	1-Naphthyl	82	201—202	1752,	1344, 1153,	866
3g	2-Naphthyl	75	222—223	1751,	1326, 1127,	866
1				1760		866

a) All the reactions were performed by the use of **1** (5 mmol), **2** (5 mmol), and imidazole (0.5 mmol) in dichloromethane (100 ml) at the boiling point for 1 h.

Table 4. Effects of amines on the reaction of **1** with 2 equivalents of **2a**$^{\text{a)}}$

Entry	Amine	pK_a	Yield/% **4a**	Phthalimide
1	None		46$^{\text{b)}}$	—
2	Aniline	4.60	88	93
3	Pyridine	5.17	85	86
4	Imidazole	6.95	81	93
5	*N*-Methylmorpholine	7.41	90	87
6	Morpholine	8.36	89	93
7	Triethylamine	10.67	86	92
8	Tributylamine	10.87	84	91
9	DBU		77	92

a) All the reactions were performed by the use of **1** (2.5 mmol), **2** (5 mmol), and an amine (0.5 mmol) in dichloromethane (50 ml) at the boiling point for 1 h. b) This value is cited from Ref. 4, and the reaction was performed for 24 h.

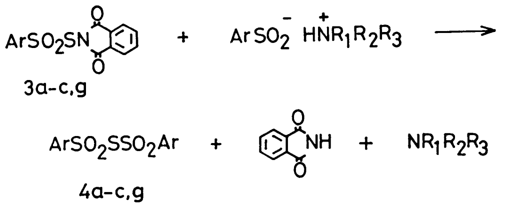
Table 5. Bis(arenesulfonyl) sulfides (**4**)$^{\text{a)}}$

Substance	Aryl group in **4**	Reaction time/h	Yield/%	Mp (lit, mp)
4a	*p*-Tolyl	3	76	135—136(131)[9)]
4b	Phenyl	3	73	132—133(133)[9)]
4c	*o*-Tolyl	1	80	136—137 (138—139)[10)]
4d	*p*-Chlorophenyl	3	0$^{\text{b)}}$	
4e	*p*-Bromophenyl	3	0$^{\text{c)}}$	
4f	1-Naphthyl	3	0$^{\text{d)}}$	
4g	2-Naphthyl	1	63	158—159(153)[10)]

a) All the reactions were performed by the use of **1** (2.5 mmol), **2** (5 mmol), and imidazole (0.5 mmol) in dichloromethane (50 ml) at the boiling point. b) Bis(*p*-chlorobenzenesulfonyl)disulfide was isolated in a 39% yield; mp 153—154 °C. c) Bis(*p*-bromobenzenesulfonyl) disulfide was isolated in a 47% yield; mp 175 °C. d) **3f** was isolated in a 95% yield.

several arenesulfinic acids in the presence of catalytic amounts of imidazole, which was chosen as a catalyst because of its convenience. The results are summarized in Table 3. The yields of **3** were improved significantly compared with those in reactions without any catalysts.[4)]

*The Reaction of **1** with Two Equiv. of **2**.* The reaction of **1** with two equiv. of **2a** in the presence of 0.2 equiv. of amines was performed in dichloromethane at the boiling point for 1 h. Only **4a** was produced, no **3a**. All the amines also accelerated the reaction. The results are summarized in Table 4. The yield of **4a** increased by the use of amine compared with that in the reaction without amine. This trend is similar to that of the yield of **3a** in Table 1; it implies that, at an early stage of the reaction, **3a** had appeared as an intermediate in the mechanism mentioned above, but reacted quickly with the ammonium salt of the excess **2a** to give **4a** (Eq. 8). A series of **4** were prepared by the



(8)

reaction of **1** with two equiv. of some arenesulfinic acids in the presence of imidazole. The results are summarized in Table 5. The yields of **4** were improved significantly,[4)] but **2d**—**f** did not give **4**. In the case of **2f**, **3f** was isolated in a 95% yield, but no **4f** was. On the other hand, the desired **4g** was obtained in a moderate yield. The difference in the results could be due to the difference in the steric factor of the naphthyl groups. When **2d** or **2e** was used in the reaction, no **4** was formed, but the corresponding bis(arenesulfonyl) disulfide was obtained in a yield of less than 50%. Two possible explanations for the formation of the compound are as follows: (1) the arenethiosulfonate anion, which could be formed by the reaction of the arenesulfinate anion with elemental sulfur in the reaction mixture, reacted with the corresponding **3** to give bis(arenesulfonyl) disulfide, or (2) the arylsulfonylthio group dimerized after the scission of the S–N bond in **3d** or **3e**. In order to confirm these processes, a solution of **3d** or **3e** in dichloromethane was refluxed for 3 h in the presence of imidazole. The compounds, **3d** and **3e**, were stable under these conditions and were recovered quantitatively from the solution. When a solution of **3d** and one equiv. of **2d** in dichloromethane was refluxed for 3 h in the presence of imidazole, **4d** was not formed, but the starting **3d** was recovered from the mixture. The real mechanism for the formation of the bis-

Table 6. Reactions of **3** with **2** in the presence of imidazole[a]

Entry	Aryl group in **3** and **4**	Reaction time/h	Yield of **4** %
1	Phenyl	2	71
2	*p*-Tolyl	2	94
3	*o*-Tolyl	3	80
4	*p*-Chlorophenyl	3	0[b]

a) All the reactions were performed by the use of **2** (5 mmol), **3** (5 mmol), and imidazole (0.1 mmol) in dichloromethane (50 ml) at the boiling point. b) The starting material, **3d**, was recovered quantitatively.

(arenesulfonyl) disulfide remains mysterious.

Four authentic **3** were allowed to react with each equiv. of the corresponding **2** to give **4**; the results are summarized in Table 6.

IR Spectra. The IR spectra of **3a**—**g** showed the characteristic bands at 1750±7 cm^{-1} (C=O stretching) and 1139±15 and 1332±12 cm^{-1} (SO_2 stretching), as may be seen in Table 3. Although a few observations have been made on the IR spectra of several organic sulfonamides and sulfenamides near 900 cm^{-1} [11a] and at 900—985 cm^{-1},[11b] which are assigned to the S–N stretching, no one has yet reported on the S–N stretching assignment in the IR spectra of *N*-(alkylthio and arylthio)imides. The IR spectra of **1** and **3** showed no conspicuous band in the region of 900—1000 cm^{-1}. Although, the nitrogen atom of organic sulfenamides is able to give its unpaired electron to the vacant *d* orbital of the adjacent sulfur atom, thus forming a stable $\overset{-}{S}=\overset{+}{N}$ canonical structure, the unpaired electrons of the nitrogen atoms of **1** and **3**, which are withdrawn by the two adjacent carbonyl groups, seem not to interact with the *d* orbital of the sulfur atom. Therefore, the S–N absorptions in **3a**—**g** and **1** shift to lower frequencies compared with those of the sulfenamide and sulfonamide; a sharp band at 868±2 cm^{-1} in the IR spectra of those compounds can be assigned to the S–N group.

Experimental

The *N,N'*-thiodiphthalimide (**1**) was prepared according to a previously reported method.[12] The arenesulfinic acids, **2**, were prepared from the corresponding arenesulfonyl chloride by either of two methods reported in the literature.[13] The benzene was purified by distillation before use. The other chemical reagents were obtained from commercial sources and were used directly. The IR spectra were recorded on a JASCO-701G grating spectrometer with KBr disks. The elemental analyses were performed by microanalytical laboratories of this Institute and the Osaka Chemical Analytical Center, Sakai, Osaka.

(1) Reaction of 1 with One Equiv. of 2. General Procedure: A solution of **1** (1.62 g, 5 mmol), **2** (5 mmol), and amine or ammonium salt (0.5 mmol) in dichloromethane (100 ml) was refluxed for 1 h. The solution was then evaporated under reduced pressure, and the residue was washed with water and dried. To the residue, 100 ml of benzene was added. After the mixture had stood for 30 min, the remaining solids were removed by filtration . The benzene filtrate was evaporated on a rotary evaporator, and the residue was washed with 50 ml of ethanol to give **3** as white crystals, which were later recrystallized from ethanol or benzene.

The analytical data of the compounds newly obtained here, except for **3a**, **b**, **d**, **e**,[4] will be presented below:

N-*(*o*-Tolylsulfonylthio)phthalimide (3c)*: Found: C, 54.22; H, 3.19; N, 4.17; S, 18.92%. Calcd for $C_{15}H_{11}NO_4S_2$: C, 54.04; H, 3.33; N, 4.20; S, 19.24%.

N-*(1-Naphthylsulfonylthio)phthalimide (3f)*: Found: C, 58.55; H, 2.84; N, 3.60; S, 17.05%. Calcd for $C_{18}H_{11}NO_4S_2$: C, 58.53; H, 3.00; N, 3.79; S, 17.36%.

N-*(2-Naphthylsulfonylthio)phthalimide (3g)*: Found: C, 58.93; H, 2.79; N, 3.55; S, 16.80%. Calcd for $C_{18}H_{11}NO_4S_2$: C, 58.53; H, 3.00; N, 3.79; S, 17.36%. The ethanol washings were evaporated, and the residue was chromatographed on silica gel (Wakogel C-200, eluent: benzene). The first fraction gave **4**.

Procedure for a Heterogeneous Reaction: A mixture of **1** (0.811 g, 2.5 mmol), sodium *p*-toluenesulfinate (0.536 g, 2.5 mmol), benzyltriethylammonium chloride (0.144 g, 0.5 mmol), water (50 ml), and dichloromethane (50 ml) was refluxed for 1 h. The mixture was evapotated to remove the dichloromethane under reduced pressure. The aqueous mixture was then filtered, and the residue was washed with water and treated as has been described above, giving **3a** in an 18% yield.

Stability of 3a: A mixture of **3a** (0.834 g, 2.5 mmol), benzyltriethylammonium chloride (0.144 g, 0.5 mmol), water (50 ml), and dichloromethane (50 ml) was refluxed for 1 h. The mixture was treated as has been described above, giving **3a** in a 94% yield.

A mixture of **3a** (0.834 g, 2.5 mmol), potassium phthalimide (0.338 g, 2.5 mmol), benzyltriethylammonium chloride (0.114 g, 0.5 mmol), water (50 ml), and dichloromethane (50 ml) was refluxed for 1 h. The mixture was treated as has been described above, giving **3a** in a 76% yield.

Reaction of 1 with One Equiv. of 2a and Imidazole: A solution of **1** (6.5 g, 20 mmol), **2a** (3.1 g, 20 mmol), and imidazole (1.3 g, 20 mmol) in dichloromethane (100 ml) was refluxed for 2 h. The mixture was then filtered to give 5.3 g (90%) of phthalimide. The filtrate was evaporated under reduced pressure, and the residue was washed with acetone to give 0.4 g (65%) of elemental sulfur. The acetone solution was evaporated, and the residue was washed with water and dried. The residue was extracted with ethanol. The extract was then evaporated to give 1.8 g crude 1-(*p*-tolylsulfonyl)-imidazole (mp 75—95 °C). Recrystallization from hexane gave 1.7 g (39%) of a pure sample (mp 76—78 °C).

Reaction of 3a with Imidazole. A solution of **3a** (1.67 g, 5 mmol) and imidazole (0.34 g, 5 mmol) in dichloromethane (50 ml) was refluxed for 1 h. The solution was then evaporated, and the residue was extracted with benzene to give 0.66 g (90%) of phthalimide. The benzene extract was chromatographed on silica gel (eluent: benzene). The first fraction gave elemental sulfur (0.083 g, 52%). The polar substances remaining in the column were eluted with methanol. The eluate was evaoprated, and the residue was recrystallized from petroleum ether, giving 0.56 g (51%) of 1-(*p*-tolylsulfonyl)-imidazole.

(2) Reaction of 1 with Two Equiv. of 2. A solution of **1** (0.81 g, 2.5 mmol), **2** (5 mmol), and amine (0.5 mmol) in dichloromethane (50 ml) was refluxed for 1—3 h. The solution was treated as the same way described in the reaction of **1** with one equiv. of **2**. The products thus obtained, **4a**—**c**, **g**, were identified by means of their mixed melting points.[9,10] The analytical data of bis(arenesulfonyl) disulfides obtained unexpectedly are shown below.

*Bis(*p*-chlorobenzenesulfonyl) Didulfide.* Found: C, 34.30;

H, 1.76; S, 30.8; Cl, 16.8%. Calcd for $C_{12}H_8Cl_2O_4S_4$: C, 34.70; H, 2.08; S, 30.88; Cl, 17.07%.

*Bis(*p*-Bromobenzenesulfonyl) Disulfide.* Found: C, 28.67; H, 1.61; S, 24.4; Br, 31.1%. Calcd for $C_{12}H_8Br_2O_4S_4$: C, 28.59; H, 1.60; S, 25.43; Br, 31.69%.

*Reaction of **3** with **2**.* A solution of **3** (5 mmol), the corresponding **2** (5 mmol), and imidazole (0.068 g, 1 mmol) in dichloromethane (50 ml) was refluxed for 2—3 h. The solution was then treated as has been described in the reaction of **1** with one equiv. of **2**.

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