Thermal and Acid-catalyzed Decomposition of 3,6-Diphenyl-1,4-bis(phenylsulfonyl)-1,4-dihydro-1,2,4,5-tetrazine[1]

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Thermolysis of the title dihydrotetrazine in boiling toluene gives benzenesulfonic anhydride, *S*-phenyl benzenethiosulfonate, and small amounts of diphenyl disulfide and a rearrangement product, 3,6-diphenyl-1,2-bis(phenylsulfonyl)-1,2-dihydro-1,2,4,5-tetrazine, together with 3,6-diphenyl-1,2,4,5-tetrazine. On the other hand, the treatment with concentrated sulfuric acid affords 3,6-diphenyl-1,4-dihydro-1,2,4,5-tetrazine in good yield. On the basis of the kinetic parameters obtained for the thermolysis, the mechanism was discussed.

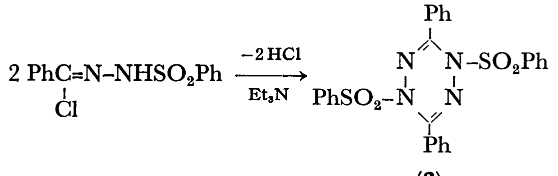
3,6-Diphenyl-1,4-bis(*p*-tolylsulfonyl)-1,4-dihydro-1,2,4,5-tetrazine (**1**), obtained by the reaction of 5-phenyltetrazole with *p*-toluenesulfonyl chloride, yields 3,6-diphenyl-1,2,4,5-tetrazine (**2**) when heated at its melting point or treated with ethanolic potassium hydroxide at room temperature, and *p*-toluenesulfonic acid alone was isolated as a by product.[2)]

The thermal decomposition of 2-*p*-tolylsulfonyl-5-phenyltetrazole[3)] was also reported:[4)] this reaction gave traces of **2** together with other products and should not proceed *via* **1** as an intermediate, and further details are unavailable for the decomposition reaction of **1** and its homologs.

The present paper deals with the thermolysis and the acid-catalyzed dephenylsulfonylation of 3,6-diphenyl-1,4-bis(phenylsulfonyl)-1,4-dihydro-1,2,4,5-tetrazine (**3**).

Results and Discussion

Preparation and Thermolysis of Dihydrotetrazine. Dihydrotetrazine (**3**) was obtained in good yields by treating *N*-(phenylsulfonyl)benzohydrazonoyl chloride with triethylamine in THF[4,5)] (Scheme 1).



(**3**)

Scheme 1.

In the IR spectra, dihydrotetrazine **3** exhibits a characteristic peak at 1320 cm^{-1} (strong) which should be assigned to the 1,4-dihydrotetrazine ring vibration. Compound **3** is thermolabile and melt with decomposition to give tetrazine **2**; a partial decomposition is also observed below the melting point. Furthermore, **3** altered gradually to **2** at room temperature when dissolved in a polar solvent such as DMF or DMSO.

The thermolysis of **3** was carried out in the following two procedures: (A) Keeping at 150—155 °C for 30 min in a sealed tube without solvent; (B) refluxing a toluene solution for 20 h. The IR spectrum of the resulting dark red solid from Procedure A showed the formation of benzenesulfonic anhydride (**4**), a portion of which could be isolated as a sparingly soluble part in benzene.

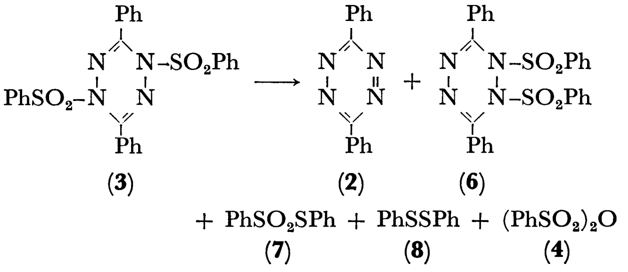
The precipitation of anilinium benzenesulfonate (**5**) was observed when aniline was added to the chloroform solution of the product from Procedure A or the reaction mixture in toluene from Procedure B. Work-up gave 3,6-diphenyl-1,2-bis(phenylsulfonyl)-1,2-dihydro-1,2,4,5-tetrazine (**6**), *S*-phenyl benzenethiosulfonate (**7**), diphenyl disulfide (**8**), and benzenesulfonanilide (**9**) along with 3,6-diphenyl-1,2,4,5-tetrazine (**2**) and anilinium benzenesulfonate (**5**). The results are summarized in Table 1.[6)]

Table 1. Thermolysis of dihydrotetrazine **3**

Reaction condition[a)]	Yield (%) of product[b)]					
	2	**6**	**7**	**8**	**9**	**5**
A	98	0	24	6	62	70
B	88	3	26	3	58	52

a) A: Kept at 150—155 °C for 30 min in a sealed tube without solvent with subsequent treatment with aniline. B: Refluxed in toluene for 20 h with subsequent treatment with aniline. b) Yield as mole per cent based on **3**.

When ethanol was added to the primary reaction mixture from Procedure A or B, ethyl benzenesulfonate was obtained. Compounds **5** and **9** or ethyl benzenesulfonate should be derived from **4** formed in the reaction. Thus, the thermal decomposition reaction may be formulated as follows (Scheme 2).



Scheme 2.

Compound **6** decomposed when heated at its melting point, giving the same products as those obtained from **3**. No promotion of reaction was observed when benzoyl peroxide was added in the thermolysis of **3** in toluene

Kinetics and Mechanism. In order to obtain some kinetic data, the thermolysis of **3** in toluene was conducted in Pyrex tubes under nitrogen atmosphere at 110,

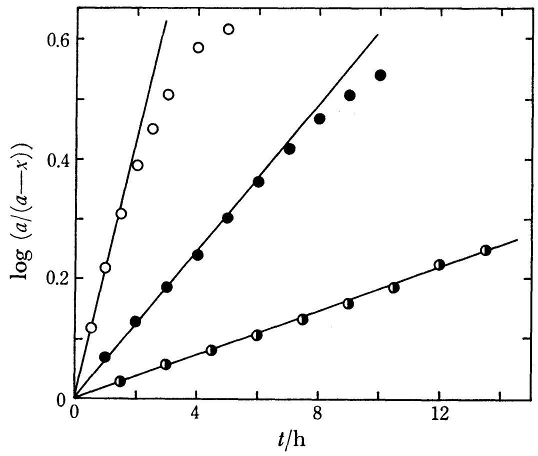


Fig. 1. First order plots for the thermolysis of dihydro tetrazine **3** in toluene.

○: 130 °C, ●: 120 °C, ◑: 110 °C; $[\mathbf{3}]_0$=1.95 mmol·l^{-1}.

120, and 130 °C. The course of decomposition was followed by measuring the tetrazine absorption at 550 nm.

Since the reaction is not simple as has been shown above, the integral method cannot be employed for the kinetic determination: thus any good linear relationship may be hardly found in the first order plots (Fig. 1) and also in the second order ones for the reaction.

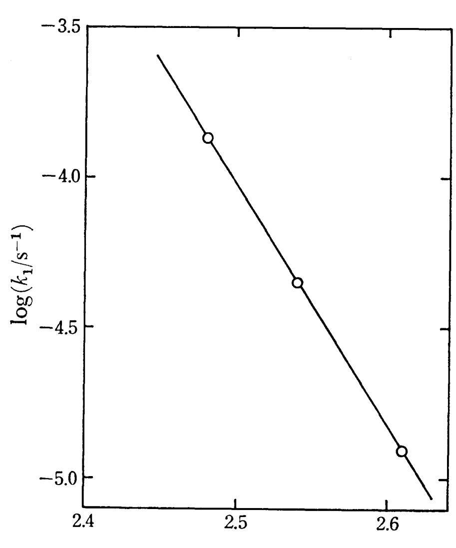


Fig. 2. Arrhenius plots for the thermolysis of dihydrotetrazine **3** in toluene.

The decomposition reaction of **3** to **2** was analyzed by the initial rate method, which showed the reaction to obey good first order kinetics and gave k_1(h^{-1})= 0.493(130 °C); 0.162(120 °C); 0.0447(110 °C). The plots of log k_1 *vs.* $1/T$ are given in Fig. 2, from which the Arrhenius parameters, E_a(=154 kJ/mol) and $\Delta S^{\neq}$(= 61 J/(K mol)), were obtained.

When the solvent toluene was replaced by DMSO, plots of yield of tetrazine *vs.* time gave a curve with an inflection point (Fig. 3, Curve II), but almost no difference in the reaction rate at the initial period between DMSO and toluene could be detected.

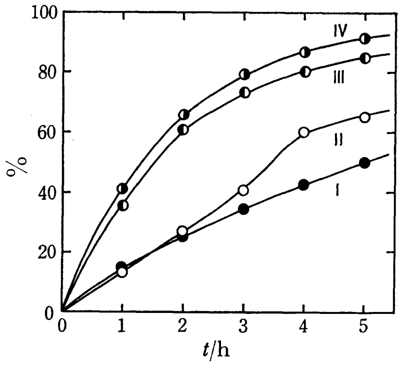
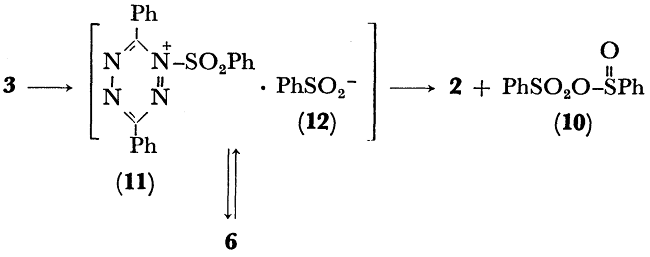


Fig. 3. Plots of yield of tetrazine **2** *vs.* time for the thermolysis of dihydrotetrazine **3**.

●: In toluene/N_2, ○: in DMSO/N_2, ◐: in DMSO with TosOH/N_2, ◑: in DMSO with TosOH/O_2; $[\mathbf{3}]_0$ =1.95 mmol l^{-1}, [TosOH]=2.0 mmol l^{-1}; temp: 120 °C.

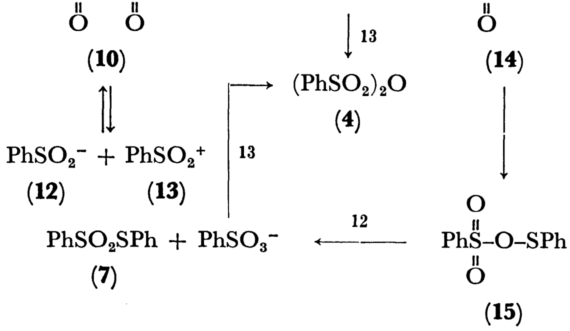
In view of the fact that the reaction is not promoted by a radical initiator and that the $\Delta S^{\neq}$ value is positive, the following route can be given as a possible mechanism for the thermolysis of **3**, in which benzenesulfonic benzenesulfinic anhydride (**10**) is postulated as an intermediate for **4** and **7**.



Scheme 3.

Since, as has been described, little difference in the rate at the initial reaction period is found between DMSO (polar) and toluene (less polar), the intermediate, [**11**·**12**], should exist as an intimate ion pair.8) The formation of **6** can be explained by the recombination of **11** and **12** (internal return).

The thermolability of **3** is possibly due to the nonaromaticity of eight-electron dihydrotetrazine system,



Scheme 4.

which alters to a stable aromatic six-electron one by releasing **12**.[9] Mass spectroscopic data (*vide post*) may be consistent with the collapse of **3** to **11** and **12**.

The formation of *S*-phenyl benzenethiosulfonate (**7**) and benzenesulfonic anhydride (**4**) can be well interpreted by the intermediacy of benzenesulfonic benzenesulfinic anhydride (**10**) (Scheme 4).

p-Toluenesulfonic *p*-toluenesulfinic anhydride has been postulated as the primary intermediate in the reaction of *p*-toluenesulfonyl chloride with sodium *p*-toluenesulfinate, from which *S*-*p*-tolyl *p*-toluenethiosulfonate and sodium *p*-toluenesulfonate are formed.[10] Anhydride **10** corresponds to carboxylic *p*-toluenesulfinic anhydride which has been proposed as an intermediate for the formation of carboxylic anhydride and *S*-*p*-tolyl *p*-toluenethiosulfonate in the reaction of sodium *p*-toluenesulfinate with acyl chloride.[11]

The intermediacy of sulfinyl sulfone **14** and sulfenic sulfonic anhydride **15** and the rearrangement **14** to **15** have been also proposed for the formation of *S*-*p*-tolyl *p*-toluenethiosulfonate in the disproportionation of *p*-toluenesulfinic acid under acidic conditions.[12]

From Scheme 4, the following stoichiometric formula can be obtained:

$$3[PhSO_2^+ + PhSO_2^-] \longrightarrow \underset{(\mathbf{4})}{2(PhSO_2)_2O} + \underset{(\mathbf{7})}{PhSO_2SPh}$$

This formula is consistent with that of the disproportionation of *p*-toluenesulfinic acid,[12] and in agreement with the experimental results obtained (Table 1). The formation of diphenyl disulfide (**8**) can be explained in terms of the air oxidation of benzenethiolate ion[13] generated by the hydrolysis of thiosulfonate **7**.[12]

The characteristic feature of Curve II shown in Fig. 3 suggests that the reaction in DMSO may involves an autocatalyzed process as a parallel one,[14] which may be due to benzenesulfonic acid formed from traces of moisture and **4**. In the initial presence of *p*-toluenesulfonic acid a pronounced catalysis took place (Fig. 3, Curve III), and a further promotion of reaction was observed under oxygen atmosphere (Curve IV).

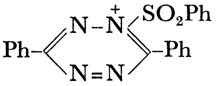
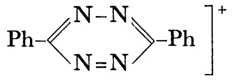
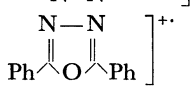
In general, DMSO accelerates ionic processes and can also function as an oxidizing agent itself, thus the primary product of the acid-catalyzed reaction in DMSO may be dephenylsulfonylated dihydrotetrazine, which would be oxidized to **2** by DMSO.[15] The acid-catalyzed dephenylsulfonylation will be discussed later.

An acceleration of reaction was observed also when a small amount of *p*-toluenesulfonic acid was added in the thermolysis of **3** in toluene, but this effect of acid was less remarkable than when DMSO was used as the solvent.

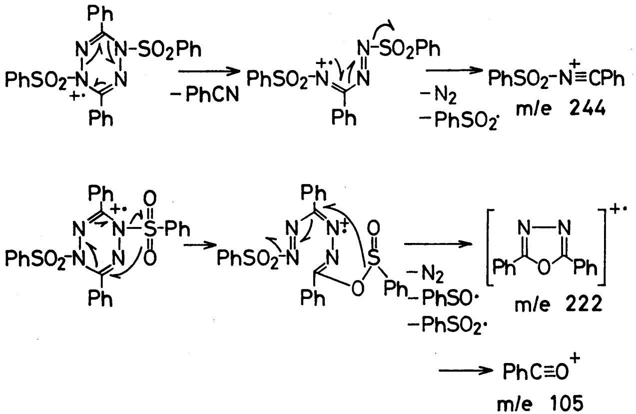
*Structure Assignment of **6**.* Compound **6** also decomposes somewhat higher temperature, giving the same products as those of **3**. The IR spectrum of **6** is simpler than that of **3**, and shows a medium peak at 1284 cm^{-1} (νSO_2: 1370, 1171 cm^{-1}) and none at near 1320 cm^{-1}. The peak at 1284 cm^{-1} might be attributed to the 1,2-dihydrotetrazine ring vibration.

The mass spectrum of **6** also differs from that of **3** in some respects: it is particularly characteristic that the peaks of *m/e* 105, 222, and 244 of **6** are far weaker than those of **3** in intensity (Table 2). The fragment ions of *m/e* 105, 222, and 244 as assigned in Table 2 may be produced from the 1,4-dihydrotetrazine structure as shown in Scheme 5. In conclusion, compound **6** must be a structural isomer of **3**, thus **6** can be assigned to be 3,6-diphenyl-1,2-bis(phenylsulfonyl)-1,2-dihydro-1,2,4,5-tetrazine. The peak of *m/e* 250 is possibly the parent peak of *S*-phenyl benzenethiosulfonate (**7**) formed by the partial thermolysis of **3** and **6** in the ionization chamber, which may be supported by the appearance of its fragment ions, *m/e* 125, 109, and 65.[16,17]

TABLE 2. MASS SPECTRAL DATA OF DIHYDROTETRAZINES **3** AND **6** (MAJOR PEAKS)

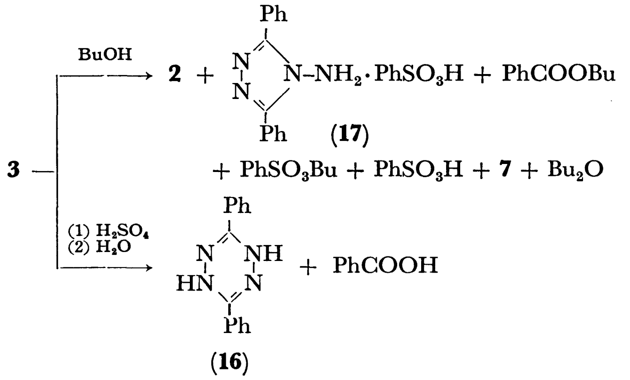
m/e	Assignment	Relative abundance[a)] **3**	Relative abundance[a)] **6**
516	M$^+$	0.8	0.3
375		47	83
250	$[PhSO_2\text{–}S\text{–}Ph]^+$	2.1	4.5
244	$Ph\text{–}C^+N\text{–}SO_2Ph$	15	0.2
234		8.0	19
222		3.8	0.3
141	$PhSO_2^+$	69	71
125	PhSO$^+$	9.3	9.4
109	PhS$^+$	3.4	5.7
105	PhC≡O$^+$	23	2.0
103	PhC≡N$^+$	56	93
77	Ph$^+$	100	100
65	$C_5H_5^+$	3.0	4.3
51	$C_4H_3^+$	19	26

a) Ionizing energy: 75 eV.



Scheme 5.

*Acid-catalyzed Decomposition of **3**.* When **3** was treated with concentrated sulfuric acid at room temperature, 3,6-diphenyl-1,4-dihydro-1,2,4,5-tetrazine (**16**: 86%) and benzoic acid (12%) were obtained. Treatment of **3** with refluxing 1-butanol gave 4-amino-3,5-diphenyl-1,2,4-triazole (as benzenesulfonate, **17**: 54%), butyl benzoate (42%), and **2** (24%) together with small amounts of butyl benzenesulfonate, benzenesulfonic acid, and **7**. The formation of dibutyl ether was also confirmed (Scheme 6).



Scheme 6.

The formation of **16** can be interpreted in terms of the *N*-protonation of **3** followed by the removal of benzenesulfonyl ion. The reaction in refluxing 1-butanol is explained as follows: the thermal decomposition of **3** takes place in part to give **2** and benzenesulfonic anhydride (**4**), and acid catalysis by benzenesulfonic acid generated from **4** leads to the formation of **16** as an intermediate The acid-catalyzed rearrangement[18] and hydrolysis[19] of the intermediate **16** should afford **17** and benzoic acid, respectively. A part of **2** obtained here may be derived from **16** by air-oxidation.

Experimental

Melting points were determined with a Yanagimoto micromelting point apparatus Model MP-S3 and are uncorrected. The microanalysis was performed on a Perkin-Elmer elemental analyzer Model 240. The IR, VIS, and MS spectra were recorded with a JASCO DS-301, a Hitachi EPU-2A, and a JEOL JMS-013G-2 spectrometer, respectively. *N*-(Phenylsulfonyl)benzohydrazonoyl chloride was prepared by the method reported.[20]

*Preparation of **3**.* A solution of triethylamine (5.5 g, 54 mmol) in THF (20 ml) was added dropwise to a solution of *N*-(phenylsulfonyl)benzohydrazonoyl chloride (14.8 g, 50 mmol) in THF (60 ml) under cooling (ice water) and stirring. The reaction mixture was stirred additionally for 1 h at room temperature. After removal of the separated triethylamine hydrochloride by filtration, the THF solution was concentrated and washed with aqueous ethanol to give fairly pure dihydrotetrazine **3** as yellow solids. The product was purrified by crystallization from benzene–hexane (Yield: 11.6 g, 22 mmol, 45 mol %).

Mp 151—156 °C (dec), IR (KBr, cm^{-1}): 1320 (Ring); 1367, 1183 (νSO$_2$). Found: C, 60.21; H, 3.93; N, 10.81%; M$^+$, 516. Calcd for $C_{26}H_{20}N_4O_4S_2$: C, 60.44; H, 3.90; N, 10.84%; M, 516.

*Thermolysis of **3**.* *Procedure A*: Dihydrotetrazine **3** (2.58 g, 5 mmol) was heated in a sealed tube at 150—155 °C for 30 min. The resulting dark red mass was dissolved in chloroform (50 ml). To the chloroform solution, aniline (2 g) was added and the mixture was allowed to stand for a few hours. The separated precipitates (anilinium benzenesulfonate, **5**: 0.89 g, 3.5 mmol) were filtered, and the filtrate was washed with 10% sodium hydroxide solution followed by dilute hydrochloric acid and dried. After removal of the solvent, the residue was dissolved in hot ethanol. Diphenyltetrazine **2** (1.11 g, 4.7 mmol) separated upon cooling was filtered, and the filtrate was concentrated and then chromatographed on a silica gel (15 g) column, using hexane and benzene as the eluents, to give diphenyl disulfide (**8**: 0.06 g, 0.3 mmol), **2** (0.05 g, 0.2 mmol), and *S*-phenyl benzenethiosulfonate (**7**: 0.30 g, 1.2 mmol). Benzenesulfonanilide (**9**: 0.72 g, 3.1 mmol) was isolated by acidification from the aqueous sodium hydroxide washings above obtained. Treatment of the primary product (dark red mass) with benzene gave a small amount of benzenesulfonic anhydride (**4**) as a sparingly soluble matter.

All the products obtained were identified by comparison with authentic specimens.

Procedure B: A solution of **3** (2.58 g) in 15 ml of toluene dried over sodium wire was refluxed for 20 h. Addition of a solution of aniline (2 g) in toluene (5 ml) to the red reaction mixture led to the precipitation of **5** (0.64 g, 2.6 mmol), which was filtered from the hot toluene solution. Removal of the solvent from the toluene filtrate followed by treatment with chloroform gave pale cream-colored precipitates (**6**: 0.07 g, 0.14 mmol) which after recrystallization from DMF–ethanol melted at 168—171 °C with decomposition.

IR (KBr, cm^{-1}): 1284 (Ring); 1370, 1171 (νSO$_2$). Found: C, 60.45; H, 3.92; N, 11.00%; M$^+$, 516. Calcd for $C_{26}H_{20}N_4O_4S_2$: C, 60.44; H, 3.90; N, 10.84%; M, 516.

The chloroform filtrate was worked up in the same manner that used in Procedure A. **2**: 1.04 g (4.4 mmol); **7**: 0.32 g (1.3 mmol); **8**: 0.03 g (0.14 mmol); **9**: 0.68 g (2.9 mmol).

The results of thermolysis are summarized in Table 1.

*Thermolysis of **6**.* Compound **6** (0.52 g, 1 mmol) was heated in a sealed tube at 170—173 °C for 20 min. The resulting dark red mass was treated in the same manner that used in the thermolysis of **3** (Procedure A). **2**: 0.21 g (0.90 mmol); **5**: 0.18 g (0.72 mmol); **7**: 0.04 g (0.16 mmol); **8**: trace; **9**: 0.14 g (0.60 mmol).

Kinetic Measurement. Rates for the formation of **2** in toluene (and in DMSO[21]) were determined spectrophotometrically by the usual sealed-ampoule technique. In a typical experiment, 10 ampoules each containing *ca.* 6.5 ml of solution of **3** in dry toluene were prepared. They were sealed after being flashed with dry nitrogen. The reaction mixture was taken out from each ampoule after quenching by cooling, and the absorbance of the mixture was determined at 550 nm. The rate constants were obtained by means of the initial rate method.

*Reaction of **3** with Sulfuric Acid.* A solution of **3** (2.58 g, 5 mmol) in chloroform (15 ml) was stirred vigorously with concentrated sulfuric acid (10 ml) for 1 h at room temperature. The sulfuric acid layer was poured into water to give light fine needles, which were filtered and identified to be 3,6-diphenyl-1,4-dihydro-1,2,4,5-tetrazine (**16**). Yield: 1.01 g (4.3 mmol); mp 194—195 °C (lit,[22] mp 191—193 °C).

From the aqueous filtrate, salting-out with sodium sulfate followed by extraction with ether gave benzoic acid (0.07 g, 0.6 mmol).

*Reaction of **3** with Boiling Butanol.* A solution of **3** (2.58 g) and 1-butanol (15 ml) was refluxed for 15 h. Dibutyl ether was detected from the reaction mixture by means of GLC. Addition of ethanol (15 ml) followed by cooling the solution led to the precipitation of **2** (0.28 g, 1.2mmol). Removal of the solvent from the alcohol filtrate gave a residue, which was treated with ether and filtered. The solids (**17**: 1.07 g; 2.7 mmol) obtained were confirmed to be fairly pure by IR spectroscopy, and melted at 193—195 °C after recrystallization from ethanol.

IR (KBr, cm^{-1}): 3240 (brd)(νNH$_3^+$); 1240, 1158, 1120 (νSO$_2$). Found: C, 60.68; H, 4.56; N, 14.41%. Calcd for

$C_{20}H_{18}N_4O_3S$: C, 60.90; H, 4.60; N, 14.20%. Dissolution of this product in pyridine followed by dilution with water gave 4-amino-3,5-diphenyl-1,2,4-triazole, mp 260—262 °C. (lit,[18] mp 263 °C).

Benzenesulfonic acid was removed by washing with water from the ether filtrate above obtained; butyl benzoate (0.37 g, 2.1 mmol), butyl benzenesulfonate (0.02 g, 0.09 mmol), **7** (0.04 g, 0.16 mmol), and **2** (trace) were determined by means of gas or liquid (column) chromatography.

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1) Presented in part at the 37th National Meeting of the Chemical Society of Japan, Yokohama, April 1978.

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5) S. Ito, Y. Tanaka, and K. Yoshida, Abstracts of the Meeting of the Tokai Branch of the Chemical Society of Japan, Matsumoto, November 1972, p. 1; Abstracts of the 28th National Meeting of the Chemical Society of Japan, Tokyo, April 1973, Vol. III, p. 1371.

6) The original presence of aniline in the reaction in boiling toluene gave a similar result: phenyl *p*-aminophenyl sulfide and/or sulfoxide, which would form by the reaction of benzenesulfinic acid with aniline,[7] could not be found.

7) O. Hinsberg, *Ber.*, **36**, 113 (1903).

8) E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt and Co., New York (1960), p. 580.

9) The release of **12** from **3** in the first step of reaction may be supported by the fact that 3,6-di(*p*-nitrophenyl)- and 3,6-di(*p*-cyanophenyl)-1,4-bis(phenylsulfonyl)-1,4-dihydro-1,2,4,5-tetrazine prepared from the corresponding hydrazonoyl chlorides are stable thermally as compared with **3**.[5]

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12) J. L. Kice and K. W. Bowers, *J. Am. Chem. Soc.*, **84**, 605 (1962).

13) D. S. Tarbell, in "Organic Sulfur Compounds," ed by N. Kharasch, Pergamon Press, London (1961), Vol. 1, Chap. 10, p. 97.

14) T. Kagiya, "Kagaku-hanno no Sokudoron-teki Kenkyuho," Kagaku-dojin, Kyoto (1970), p. 218.

15) Dihydrotetrazine **16** is known to be oxidized to tetrazine **2** by air. When **16** was warmed in DMSO under nitrogen atmosphere, the fast formation of **2** was observed.

16) The mass spectrum of *S*-phenyl benzenethiosulfonate has appeared: S. Kozuka, H. Takahashi, and S. Oae, *Bull. Chem. Soc. Jpn.*, **43**, 129 (1970).

17) The fragment ion of *m/e* 65 should be assigned to be $C_5H_5^+$ generated from PhS^+ by the loss of C=S.

18) A. Pinner, *Ber.*, **27**, 1004 (1894); "Beilsteins Handbuch der Organischen Chmie," Bd 26, Hauptwerke (1937), p. 83.

19) Water should be furnished by the acid-catalyzed dehydration of butanol.

20) S. Ito, Y. Tanaka, and A. Kakehi, *Bull. Chem. Soc. Jpn.*, **49**, 762 (1976).

21) Commercial reagent-grade DMSO was used without purification.

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