Chemistry of *N*-Thiosulfinylanilines. IV.[1] Reactions of *N*-Thiosulfinylanilines with Electrophilic Reagents

Yoshio INAGAKI, Renji OKAZAKI, and Naoki INAMOTO*

Department of Chemistry, Faculty of Science, The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113

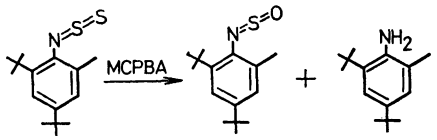
(Received May 24, 1979)

Reaction of 2,4-di-*t*-butyl-6-methyl-*N*-thiosulfinylaniline (**1**) with *m*-chloroperbenzoic acid (MCPBA) afforded the corresponding aniline and *N*-sulfinylaniline. Reaction of MCPBA with 2,4,6-tri-*t*-butyl-7,8-dithia-9-azabicyclo-[4.3.0]nona-2,4,9-triene equilibrated with 2,4,6-tri-*t*-butyl-*N*-thiosulfinylaniline gave 2,4,*r*-6-tri-*t*-butyl-7,8-dithia-9-azabicyclo[4.3.0]nona-2,4,9-triene *t*-7-oxide (**12**), 4,6-di-*t*-butyl-3*H*-1,2,3-benzodithiazole 2-oxide (**13**), and 2,4,6-tri-*t*-butyl-*N*-sulfinylaniline (**14**). The oxide **13** was considered to be produced *via* a primary product 2,4,*r*-6-tri-*t*-butyl-7,8-dithia-9-azabicyclo[4.3.0]nona-2,4,9-triene *t*-8-oxide which was found to be unstable above −30 °C. Thermolysis of **12** affording **13**, **14**, and 2,4,6-tri-*t*-butylaniline demonstrated oxygen or sulfur migration in the thiosulfinate type compound. Bromine reacted with **1** to give bis(2,4-di-*t*-butyl-6-methylphenyl)sulfur diimide probably *via* a thionitroso intermediate. Neither trimethyloxonium tetrafluoroborate nor trimethylsilyl chloride reacted with **1**.

The synthesis of stable thiosulfinylamino compounds containing a new functional group (–N=S=S) has recently been reported by Barton's group[2] and us,[3] and the thermal[2,3] and photochemical behavior[3] has been delineated. Since the reactivity of thiosulfinylamino group towards electrophilic reagents has not been explored except for acid hydrolysis,[2] we investigated the reaction of stable *N*-thiosulfinylanilines with *m*-chloroperbenzoic acid, bromine, and other electrophiles, which is the subject of this paper.[4]

Results and Discussion

Reaction with m-*Chloroperbenzoic Acid (MCPBA).* Reaction of 2,4-di-*t*-butyl-6-methyl-*N*-thiosulfinylaniline (**1**) with an equimolar amount of MCPBA afforded 2,4-di-*t*-butyl-6-methyl-*N*-sulfinylaniline (**2**) and 2,4-di-*t*-butyl-6-methylaniline (**3**) in 30.8 and 41.3% yields, respectively, along with recovered **1** (14.9%).

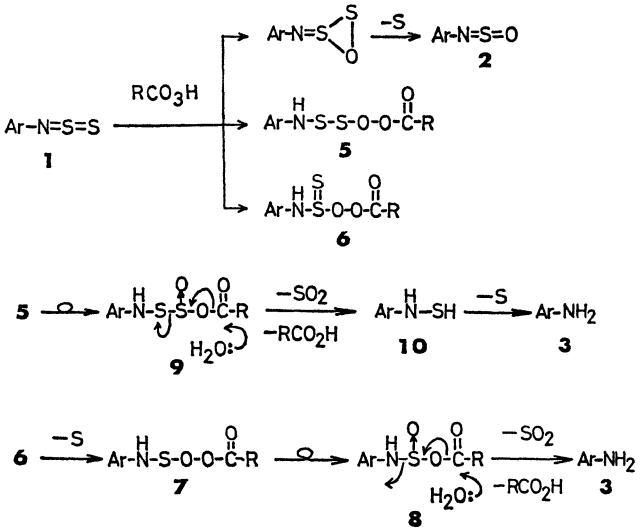


1 **2** **3**

Probable mechanism of formation of **2** and **3** is depicted in Scheme 1.

The reaction of aniline **3** with MCPBA has been reported to give 2,4-di-*t*-butyl-6-methylnitrosobenzene (**4**).[5] Therefore, the absence of **4** in the products suggests that **3** did not exist in the reaction mixture but was produced during the work-up procedure (probably hydrolysis of **8** or **9** with aqueous sodium hydrogencarbonate, see Experimental). The sulfinylaniline (**2**) was stable under the work-up conditions not to be hydrolyzed to the aniline (**3**).

Since a peroxy acid is known to attack sulfur atom of a thioketone,[6] the initial formation of **5** seems probable. The intermediate **5** would rearrange into **9**, which is considered to be hydrolyzed to give thiohydroxylamine (**10**), sulfur dioxide, and *m*-chlorobenzoic acid in analogy to acid hydrolysis of an acid anhydride. As

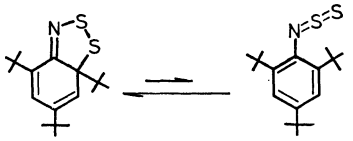


Ar=2,4-di-*t*-butyl-6-methylphenyl
R =*m*-chlorophenyl

Scheme 1.

thiohydroxylamine (**10**) has been reported to be unstable to give the corresponding amine and sulfur,[7] **10** would produce **3** as a final product. Since a peroxycarboxylic acid is a relatively strong nucleophile as to add to organic isocyanate,[8] nucleophilic attack on **1** to give **6** seems also reasonable. The intermediate **6** would lose one sulfur atom to give **7**.[9] Here also **7** probably rearranges into **8**, whose hydrolysis would give **3**, sulfur dioxide, and *m*-chlorobenzoic acid. We think that both mechanisms are plausible and have no experimental evidence at present to determine which is correct.

As the compound **11a** exists as a tautomeric mixture with *N*-thiosulfinylaniline (**11b**) as the minor component,[3] products arising from **11b** as well as **11a** are expected to be obtained in this case.

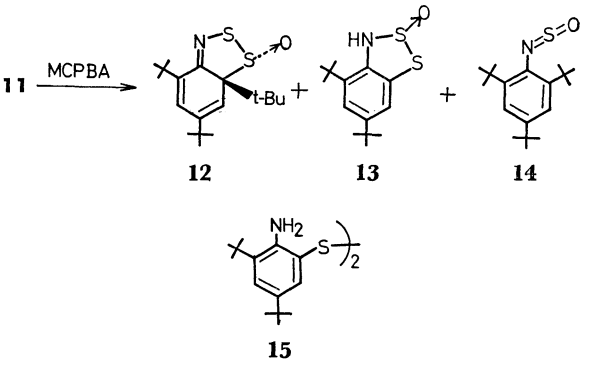


11a **11b**

TABLE 1. YIELDS OF THE PRODUCTS

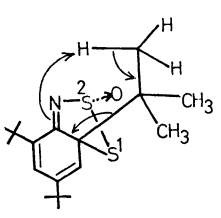
Temp °C	Time min	Conversion %	Yield/% 12	13	14	13/12
39	3	92	44.8	43.9	1.3	0.98
22	30	91	36.3	44.0	5.8	1.21
0	20	98.5	34.3	42.9	6.2	1.25
−23	20	99.5	36.7	50.6	5.8	1.38
−78	40	94.3	20.6	62.2	2.9	3.02

Treatment of the dithiazole (**11**) with slightly deficient amount of MCPBA in dichloromethane gave **12**, **13**, and **14**. Yields and reaction conditions are shown in Table 1.



The structure of a new type of thiosulfinate (**12**) was determined by X-ray crystallographic analysis,[10] because conclusive evidence for that could not be obtained by spectroscopic and chemical behavior. The identity of **13** was established by the spectral data and by alkaline hydrolysis affording **15**.[11,14] The *N*-sulfinylaniline (**14**) was identified by comparison of the spectral data with those of an authentic sample obtained by the reaction of 2,4,6-tri-*t*-butylaniline with thionyl chloride. Formation of **14** is most likely attributable to the oxidation of **11b** because **1** was found to be oxidized by MCPBA under similar conditions to give the corresponding *N*-sulfinylaniline (*vide supra*). The major products **12** and **13** obviously result from the oxidation of the cyclized form **11a**. Although **11a** is the major component in the tautomeric mixture (*e.g.*, [**11a**]/[**11b**]=14.2 in CD_2Cl_2 at 35 °C),[3] much higher yields of **12** and **13** than that of **14** suggest that the reactivity of *N*-thiosulfinylaniline (**11b**) towards MCPBA is lower than that of **11a**.

As the compound **12** is stable in refluxing dichloromethane even in the presence of *m*-chlorobenzoic acid, **13** cannot be formed *via* **12** under the reaction conditions. Since the peroxy acid would attack **11a** also on the sulfur S^2 to give **16**, it is likely that **13** was produced *via* **16** which was unstable under the reaction conditions towards fast retro-ene type decomposition. Direct evidence for intermediacy of **16** was provided by monitoring the reaction spectroscopically: NMR spectrum of a mixture of **11** and MCPBA in CD_2Cl_2 at −50——40 °C showed a set of signals which seemed to be due to **16**[12] [δ 0.87 (s, 9H), 1.20 (s, 9H), 1.42 (s, 9H), 6.11 (d, J=2 Hz, 1H), and 6.98 (d, J=2 Hz, 1H)] besides two sets of signals due to **11** and **12** (the molar ratio; **11**:**12**:**16**=1:0.67:0.8). Upon raising the temperature, decomposition of **16** into **13** and 2-methylpropene started at −30 °C, and the intensity of the NMR signals due to **16** gradually decreased with concomitant increase in intensity of the signals due to **13** and 2-methylpropene. Finally, at 34 °C, the signals of **16** were completely replaced by those of **13** and 2-methylpropene.

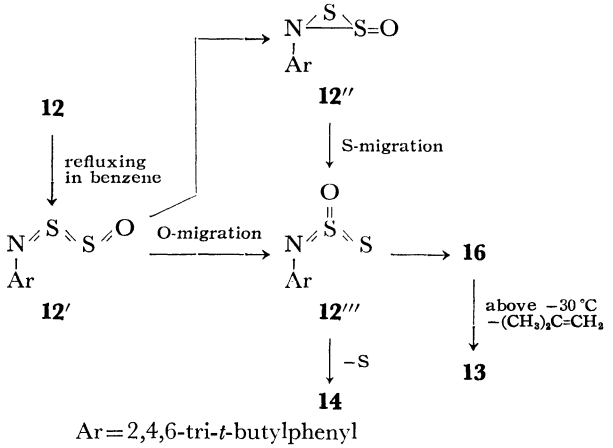


16

This unusual instability of **16** with respect to retro-ene reaction is in marked contrast with the stability exhibited by related compounds **11** and **12**.[13]

Under forced conditions (in refluxing benzene for 3.5 h), **12** gave **13** (11.6%), **14** (24.4%), and 2,4,6-tri-*t*-butylaniline (28.7%) along with recovered **12** (14.1%). Formation of **13** and **14** is noteworthy, because it indicates the occurrence of oxygen migration from S^1 to S^2 during the thermolysis. Thermal behavior of a thiosulfinate has recently attracted considerable attention because of its intriguing decomposition mode and the conclusion has been drawn from Block's extensive studies that *S*-alkyl thiosulfinates do not undergo oxygen migration like RS(O)SR′⇄RSS(O)R′.[15]

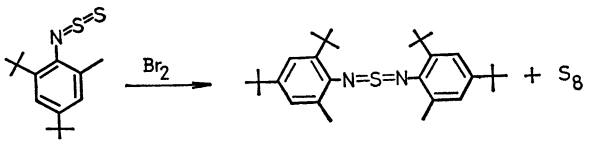
In view of this conclusion and the reversible cyclization between **11a** and **11b**,[3] the most attracting route to **13** and **14** is that involving cycloreversion of **12** to **12′** as shown in Scheme 2,[16] the driving force of which is aromatization. There still remain, however, other possibilities, because **12** is not a simple *S*-alkyl thiosulfinate for which the above conclusion by Block was obtained.[17] For example, isomerization of **12′** to **12‴** is also possible *via* **12″**, which proceeds through sulfur migration.[18] We have no experimental evidence to conclude which mechanism is actually operative. In any case, however, this reaction represents a new mode of isomerization in thiosulfinate type compounds.



Ar=2,4,6-tri-*t*-butylphenyl

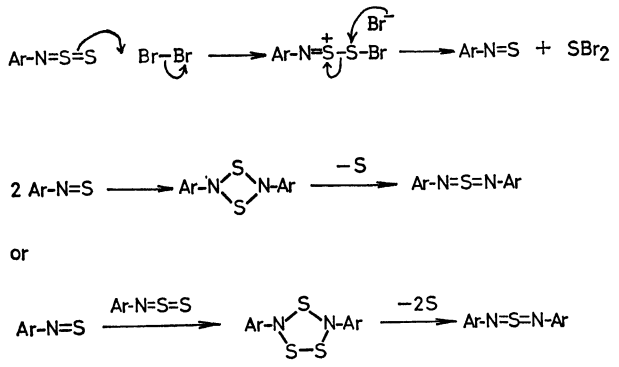
Scheme 2.

Reactions with Bromine and Other Electrophiles. Reaction of **1** with an equimolar amount of bromine afforded *N,N'*-bis(2,4-di-*t*-butyl-6-methylphenyl)sulfur diimide (**17**) in 64.4% yield and sulfur in 17.2% yield. Considering the formation of a sulfur diimide *via* a



1 **17**

thionitroso intermediate demonstrated in the reaction of *N*-thiosulfinylanilines with triphenylphosphine,[19] the reaction mechanism (Scheme 3) starting with electrophilic attack of bromine on the terminal sulfur atom seems probable.



Ar=2,4-di-*t*-bulyl-6-methylphenyl

Scheme 3.

In contrast to the above reactions, electrophilic reagents such as trimethylsilyl chloride or trimethyloxonium tetrafluoroborate did not react with **1** at room temperature.

Experimental

All melting points were uncorrected. The IR and UV spectra were recorded with Hitachi EPI-G2 and EPS-3 spectrophotometers, respectively. The NMR spectra were measured with a Hitachi R-20B (60 MHz) spectrometer using tetramethylsilane as an internal standard. The mass spectra were recorded with a Hitachi RMU-6L mass spectrometer (70 eV). Chromatographic separations were carried out using dry column chromatography (Woelm silica gel for dry column chromatography).

Reactions of N-*Thiosulfinylanilines with* m-*Chloroperbenzoic Acid (MCPBA).* In each of the following reactions, a slightly deficient amount of MCPBA was used assuming the purity of MCPBA as 80%.

*1) Reaction of 2,4-Di-*t*-butyl-6-methyl-*N*-thiosulfinylaniline (1):* To a dichloromethane solution (15 ml) of **1** (503 mg, 1.79 mmol),[3] was added dropwise at 0 °C a dichloromethane solution (8 ml) of MCPBA (395 mg) cooled to *ca.* 0 °C. After being stirred for 1.5 h at 0 °C and 1.5 h at room temperature, the reaction mixture was shaken with aq $NaHCO_3$, washed with water, and dried over $MgSO_4$. Removal of the solvent followed by dry column chromatography (DCC, silica gel, hexane) gave 75 mg (14.9%) of **1**, 146 mg (30.8%) of **2**, and 162 mg (41.3%) of **3**. These products were identified by comparison of the IR and NMR with those of authentic samples.

*2) Oxidation of 2,4,6-tri-*t*-butyl-7,8-dithia-9-azabicyclo[4.3.0]-nona-2,4,9-triene (11a):* Reaction at 22 °C was described below as a typical example and the reactions at other temperatures were carried out similarly. To a dichloromethane solution (20 ml) of **11a** (496 mg, 1.53 mmol)[3] was added MCPBA (280 mg) in the same solvent. The mixture was stirred for 30 min, shaken with aq $NaHCO_3$, washed with water, and dried over $MgSO_4$. After removal of the solvent, the residue was treated with hexane to give 166 mg of 4,6-di-*t*-butyl-3*H*-1,2,3-benzodithiazole 2-oxide (**13**) as colorless crystals, which showed IR and NMR spectra identical with those of an authentic sample obtained by thermolysis of **11a**.[14] The hexane-soluble part was subjected to DCC (silica gel, hexane) and three fractions (a brownish yellow fraction with the highest R_f value, an orange fraction and a yellow fraction) were obtained. From the brownish yellow fraction was recovered 44.8 mg (9.0%) of **11a**. The orange fraction gave 25 mg (5.8% based on consumed **11a**) of **14**, which was identified by comparing the IR and NMR spectra with those of an authentic sample. The most polar yellow part was again chromatographed on silica gel with hexane–CH_2Cl_2 (1:4) as eluent and divided into two fractions. A yellow fraction gave 172 mg (36.3% based on consumed **11a**) of 2,4,*r*-6-tri-*t*-butyl-7,8-dithia-9-azabicyclo[4.3.0]nona-2,4,9-triene *t*-7-oxide (**12**) as pale yellow crystals, which were recrystallized three times from aq methanol, mp 124.7—125.7 °C; IR (KBr): 1080 cm^{-1} (ν_{SO}); NMR (CCl_4): δ 1.05 (s, 9H), 1.18 (s, 9H), 1.37 (s, 9H), 6.01 (d, J=1.5 Hz, 1H), and 6.22 (d, J=1.5 Hz, 1H); λ_{max}^{hexane} (ε): 233 (9490) and 345 nm (2030), the latter band was very broad (293—450 nm); *m/e*: 339 (M^+, 0.7%), 307 (0.4), 291 (30.7), 266 (100), and 250 (24.6).

Found: C, 63.46; H, 8.85; N, 3.90; S, 18.82%. Calcd for $C_{18}H_{29}NOS_2$: C, 63.67; H, 8.61; N, 4.13; S, 18.88%.

Another fraction gave 8 mg of **13**. Thus total yield of **13** was 174 mg (44.0% based on consumed **11a**).

Thermolysis of 12. A benzene solution (10 ml) of **13** (163 mg, 0.480 mmol) was refluxed for 3.5 h under nitrogen. Removal of the solvent followed by preparative TLC (silica gel, hexane–CH_2Cl_2 (3:7)) afforded four fractions. An orange fraction with the highest R_f value gave 88.0 mg of orange crystalline material, which was purified by preparative TLC (silica gel–hexane, followed by silica gel–CCl_4) to give 36 mg (24.4%) of **14** and 21 mg of 2,4,6-tri-*t*-butylaniline (**18**). A pale yellow fraction gave 15 mg of **18**. Thus total yield of **18** was 36 mg (28.7%). From another pale yellow fraction was recovered 23 mg (14.1%) of **12**. A colorless fraction with the lowest R_f value gave 16 mg (11.6%) of **13**.

*Examination of Stability of 2,4,r-6-tri-*t*-butyl-7,8-dithia-9-azabicyclo[4.3.0]nona-2,4,9-triene* t*-7-Oxide (12).* A solution of **12** (126 mg, 0.37 mmol) and *m*-chlorobenzoic acid (66 mg, 0.42 mmol) in dichloromethane (6 ml) was allowed to stand for 3 h at room temperature. At this point, **13** was not detected on TLC (silica gel, CH_2Cl_2). Although the reaction mixture was subsequently refluxed for 3 min, no **13** was detected on TLC. The reaction mixture was washed with aq $NaHCO_3$ and dried over $MgSO_4$. Removal of the solvent followed by preparative TLC (silica gel, CH_2Cl_2) afforded 120 mg (96%) of **12**, which was identified by the IR and NMR spectra.

Examination of Stability of 11a. A solution of **11a** (145 mg, 0.45 mmol) and *m*-chlorobenzoic acid (79 mg, 0.50 mmol) in dichloromethane (6 ml) was stirred for 1 h at room temperature. However, neither **13** nor **12** was detected on TLC.

Reaction of 1 with Bromine. To a solution of **1** (204

mg, 0.725 mmol) in carbon tetrachloride (10 ml) was added 0.8 ml of carbon tetrachloride solution of bromine (0.909 M). The mixture was stirred for 1.5 h at 0 °C. Removal of the solvent followed by treatment with preparative TLC (silica gel, CCl_4) afforded three fractions. The first fraction gave 8 mg of sulfur. The next orange fraction gave 109 mg (64.4 %) of **17**. The third fraction gave 214 mg of partly crystalline brown tar. Its crystallization from ethyl acetate afforded 23 mg of white crystals, which could not be identified.

References

1) For Part III, see Y. Inagaki, R. Okazaki, N. Inamoto, K. Yamada, and H. Kawazura, *Bull. Chem. Soc. Jpn.*, **52**, 2008 (1979).

2) D. H. R. Barton and M. J. Robson, *J. Chem. Soc., Perkin Trans. 1*, **1974**, 1245.

3) Y. Inagaki, R. Okazaki, and N. Inamoto, *Tetrahedron Lett.*, **1975**, 4575; *Bull. Chem. Soc. Jpn.*, **52**, 1998 (1979).

4) Part of this work was reported in a preliminary form. Y. Inagaki, R. Okazaki, and N. Inamoto, *Chem. Lett.*, **1978**, 1095.

5) R. Okazaki, T. Hosogai, E. Iwadare, M. Hashimoto, and N. Inamoto, *Bull. Chem. Soc. Jpn.*, **42**, 3611 (1969).

6) B. Zwanenburg and J. Strating, *Quart. Repts. Sulfur Chem.*, **5**, 79 (1971) and references cited therein.

7) D. H. R. Barton, S. V. Ley, and P. D. Magnus, *J. Chem. Soc., Chem. Commun.*, **1975**, 855.

8) R. Okazaki and O. Simamura, *Bull. Chem. Soc. Jpn.*, **47**, 1981 (1974).

9) A compound of type $R_2S{=}S$ is known to be very unstable to decompose into R_2S with extrusion of sulfur. G. Hofle and J. E. Baldwin, *J. Am. Chem. Soc.*, **93**, 6307 (1971). R. D. Baechler and S. K. Daley, *Tetrahedron Lett.*, **1978**, 101; R. D. Baechler and S. K. Daley, B. Daley, and K. McGlynn, *ibid.*, **1978**, 105.

10) A private communication from Prof. F. Iwasaki, the University of Electro-Communications. The details will be reported elsewhere.

11) A similar hydrolysis has been reported. W. K. Warburton, *Chem. Rev.*, **57**, 1101 (1957); *cf.* also L. D. Huestis, M. L. Walsh, and N. Hahn, *J. Org. Chem.*, **30**, 2763 (1965).

12) Of possible two diastereomers only one seems to be formed as judged from NMR spectroscopy. The orientation of S–O bond is tentatively assumed, on steric ground, to be *anti* with respect to the *t*-butyl group attached to carbon adjacent to S^1.

13) The dithiazole **11** is thermally more stable than **12**; its complete decomposition requires refluxing in benzene for about 10 h.[14]

14) Y. Inagaki, R. Okazaki, and N. Inamoto, *Bull. Chem. Soc. Jpn.*, **52**, 2002 (1979).

15) E. Block and J. O'Connor, *J. Am. Chem. Soc.*, **96**, 3921, 3929 (1974) and references cited therein.

16) For examples of sulfur extrusion in S(IV)-thiocumulenes and possible existence of such species as X=S(=O)=Y as 1, 3-dipole, see R. M. Kellogg, *Tetrahedron*, **32**, 2165 (1976); Y. Inagaki and R. Okazaki, *Yuki Gosei Kagaku Kyokai Shi*, **36**, 1 (1978).

17) The occurrence of oxygen migration has been suggested by a tracer study for *S*-aryl arenethiosulfinates. P. Koch, E. Ciuffarin, and A. Fava, *J. Am. Chem. Soc.*, **92**, 5971 (1970).

18) We thank a referee for his suggestion on the possibility of S-migration.

19) Y. Inagaki, R. Okazaki, T. Hosogai, and N. Inamoto, *Bull. Chem. Soc. Jpn.*, in press.