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Studies of *N*-Sulfinyl Compounds. VI.[1] The Preparation of *N*-Sulfinylbenzamide and Its Reaction with Styrene Oxide

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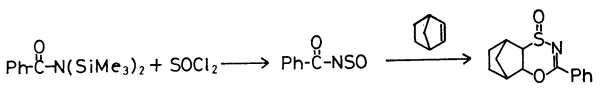
The reaction of benzamide with thionyl chloride in the presence of pyridine gave *N*-sulfinylbenzamide and *N,N'*-dibenzoylsulfurdiimide. It has been found that *N*-sulfinylbenzamide reacted with styrene oxide in the presence of tetraethylammonium bromide to give 4-oxo-5-benzoyl-2,6-diphenyl-1,4,3,5-oxathiadiazepine as the main product, accompanied by lesser quantities of two *N*-benzoyl-phenylaminoethanols, 2,5-diphenyloxazoline, benzonitrile, and benzamide. The pathways for the formation of the products are suggested.

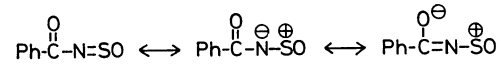
In previous papers in which the reactions of *N*-sulfinylanilines (Ar-NSO)[2] and of *N*-sulfinyl-*p*-toluenesulfonamide (Tos-NSO)[3] with styrene oxide in the presence of tetraethylammonium bromide (Et_4NBr) were investigated, the corresponding two tetraarylpiperazines were formed in the reactions of *N*-sulfinylanilines, while the reaction of *N*-sulfinyl-*p*-toluenesulfonamide gave the 1-oxo-1,2,5-thiadiazolidine compound, accompanied by two aminoalcohols.

Recently, it has been reported by Scherer and Schmitt[4] that *N*-sulfinylbenzamide (I) which had been prepared from the reaction of *N,N*-bis-trimethylsilylbenzamide with thionyl chloride, reacted with norbornene to give the (2+4) cycloadduct, 4-oxo-2-phenyl-4a,5,6,7,8,8a-hexahydro-5,8-methano-1,4,3-benzoxathiazine.



I

On the basis of the above fact, it may be inferred that I is not only more reactive than *N*-sulfinylanilines, but also behaves as the 1,4-dipole in the following resonance structures.



Accordingly, the reaction of I with styrene oxide can be expected to give products of a different type from those in the reactions of *N*-sulfinylanilines and of *N*-sulfinyl-*p*-toluenesulfonamide.

In the present paper we wish to report on the preparation of I by the reaction of benzamide with thionyl chloride, and on the formation of the 1,4,3,5-oxathiadiazepine compound as the main product in the reaction of I with styrene oxide.

Results and Discussion

The Reaction of Benzamide with Thionyl Chloride. It has been found by Olah[5] that benzamide reacted with thionyl chloride to give *N*-sulfinylbenzamide (I), but he failed to isolate I in a pure form.

After the reaction of benzamide with thionyl chloride was conducted in a mixed solvent of benzene and pyridine at temperatures below 10°C, the reaction mixture was rapidly filtered to remove the pyridine hydrochloride; then the filtrate was distilled under reduced pressure to give I, bp 76°C/0.16 mmHg (lit,[4] bp 70°C/0.1 mmHg), as an yellow oil in a 62% yield and dark brown crystals (II), together with a small amount of benzonitrile. It is very important that distillation is carried out at temperatures below 100°C, because an appreciable decomposition of I takes place above 100°C.

As I proved rather unstable and was decomposed by moisture in the air, the elemental analysis of I was not carried out. However, the IR spectrum of I was in agreement with that reported by Scherer and Schmitt.[4] Furthermore, I was easily hydrolyzed to give benzamide, and was violently decomposed at 130°C to yield benzonitrile.

1) Part V of this series: O. Tsuge and S. Mataka, *Nippon Kagaku Zasshi*, **92**, 543 (1971).

2) O. Tsuge and S. Mataka, This Bulletin, **44**, 1896 (1971).

3) O. Tsuge and S. Mataka, *Nippon Kagaku Zasshi*, **92**, 543 (1971).

4) O. J. Scherer and R. Schmitt, *Chem. Ber.*, **101**, 3302 (1968).

5) The authors wish to express their appreciation to Professor G.A. Olah of Case-Western Reserve University for his personal communication.

On the other hand, the compound II which was obtained as a residue on distillation, was also unstable and was easily hydrolyzed to give benzamide. Although II could not be isolated in a pure form, its

$$PhCONH_2 + SOCl_2 \longrightarrow PhCONSO + PhCON{=}S{=}NCOPh$$

I II

II → (EtOH) PhCONH(EtO)S=N-COPh (III)

II → (NaBH$_4$) PhCONH-S-NHCOPh + $PhCONH_2$ (IV)

structure was assumed to be *N,N'*-dibenzoylsulfurdiimide (II) on the basis of the following chemical transformations.

The treatment of II with excess amounts of ethanol gave *S*-benzamido-*S*-ethoxy-*N*-benzoylsulfilimine (III), mp 135—140°C (decomp.), which was then gradually decomposed on standing at room temperature to give benzamide in a low yield. The structure of III was confirmed by a study of its IR spectrum as well as by the elemental analysis. Furthermore, II was reduced with sodium borohydride, affording *N,N'*-thiodibenzamide (IV) and benzamide under the elimination of hydrogen sulfide.

It is known[6] that *N*-sulfinyl compounds react with a base to give the corresponding sulfurdiimides under the elimination of sulfur dioxide. Although Scherer and Schmitt[4] reported that attempts to prepare II by the reaction of I with a trace amount of a base were unsuccessful, it may be considered that II was obtained *via* the reaction with pyridine of I formed from benzamide and thionyl chloride.

The Reaction of N-*Sulfinylbenzamide with Styrene Oxide.* When a solution of *N*-sulfinylbenzamide (I) and styrene oxide (V) in benzene was refluxed with Et_4NBr for 1 hr, a colorless crystalline compound VII, mp 171—172°C (decomp.), was obtained as the main product, accompanied by lesser quantities of crystals, VI, mp 126—7°C, a pale green liquid, VIII, benzonitrile and benzamide.

Although VI was proved, by the elemental analysis as well as by a comparison of its IR and NMR spectra with those of authentic samples of *N*-benzoyl-*β*-phenyl-*β*-aminoethanol (VIa), mp 151°C (lit,[7] mp 154—154.5°C), and *N*-benzoyl-*α*-phenyl-*β*-aminoethanol (VIb), mp 147—148°C (lit,[8] mp 148.6—149.1°C), to be a mixture of nearly equal amounts of VIa and VIb, attempts to isolate VIa and VIb in pure forms were unsuccessful.

The results of the elemental analysis and the molecular weight (M^+ *m/e* 390) of VII were consistent with those of the compound derived from a 2:1 adduct of I and V under the elimination of sulfur dioxide. The IR spectrum of VII showed characteristic bands ascribed to the C=O and/or C=N bonds at 1660 and 1630 cm^{-1}, while the NMR spectrum in deuteriochloroform ($CDCl_3$) exhibited double doublets at δ 4.75 (H_A, 1H), 5.64 (H_B, 1H) and 6.25 ppm (H_X, 1H), with coupling constants of J_{AB}=8, J_{BX}=2, and J_{AX}=7 Hz, besides a signal of aromatic protons (15H).

On the basis of the above observations and inspections of reaction courses, the following compounds (VII-1—VII-7) can be said to be possible for the structure of VII (Chart 1); the compounds VII-1—VII-3 correspond to the apparent cycloadducts of I to 1-benzoyl-2-phenylaziridine,[9] while compounds VII-4—VII-7 correspond to the cycloadducts of I to the sulfurdiimide II.

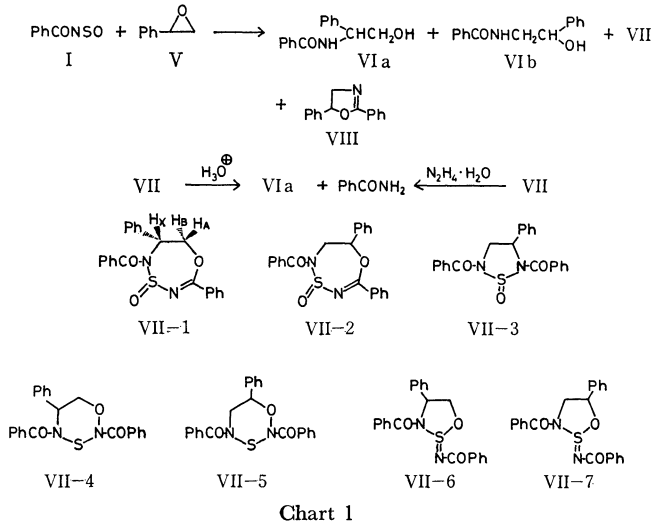


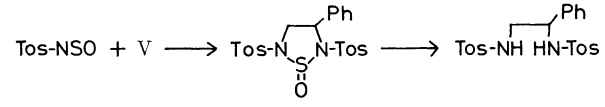
Chart 1

The hydrolysis of VII with hydrochloric acid in methanol gave the aminoethanol VIa and benzamide in 38 and 97% yields respectively. Also, VII reacted with hydrazine hydrate under the elimination of hydrogen sulfide, affording VIa and benzamide in good yields. The production of VIa from VII eliminated the possibility of VII-2, VII-5 and VII-7 for the structure of VII.

On the other hand, the mass spectrum of VII showed peaks at *m/e* 390 (M^+), 389 (M^+–H), 342 (M^+–SO), 238 (342$^+$–PhCH=CH_2), 223 (M^+–PhCONSO and/or 342$^+$–PhCON, base peak), 193 (223$^+$–CH_2O), and 105 ($PhCO^+$). The appearance of the peak at *m/e* 342 in the spectrum excluded the compounds VII-4 and VII-6 as the possible structure of VII.

Previously,[3] we reported that 1-oxo-2,5-di(*p*-toluenesulfonyl)-3-phenyl-1,2,5-thiadiazolidine, which had been obtained from the reaction of *N*-sulfinyl-*p*-toluenesulfonamide with V, was hydrolyzed with hydrochloric acid in methanol, thus affording *N,N'*-di(*p*-toluenesulfonyl)-1-phenylethylene-1,2-diamine in a good yield.

If VII is the 1,2,5-thiadiazolidine VII-3, the corresponding ethylenediamine compound should be given



6) G. Kresze and W. Wucherpfennig, *Angew. Chem.*, **79**, 109 (1967).

7) S. Gabriel and J. Colman, *Ber.*, **47**, 1871 (1914).

8) A. J. Castro, D. K. Brain, H. D. Fischer, and R. K. Fuller, *J. Org. Chem.*, **19**, 1444 (1954).

9) 1-Benzoyl-2-phenylaziridine corresponds to the compound derived from the 1:1 adduct of I and V under the elimination of sulfur dioxide.

by the hydrolysis of VII.

Consequently, it may be deduced that the most reasonable structure for VII is 4-oxo-5-benzoyl-2,6-diphenyl-1,4,3,5-oxathiadiazepine (VII-1).

On the other hand, VIII was proved to be 2,5-diphenyloxazoline by the spectral studies as well as by the identification of its picrate with the authentic sample prepared by the method of Wolfheim.[10]

The formation of 4-oxo-1,4,3,5-oxathiadiazepine VII is of interest in connection with the contribution of the 1,4-dipole of I.

Several pathways for the formation of VII and oxazoline VIII are possible.[11] On the basis of the previously reported results,[3,4,12-14] and of the formation of aminoalcohols VIa and VIb, however, we considered that compounds VII and VIII were derived from the 2-oxo-1,2,3-oxathiazolidine intermediates A and B which were formed by the (2+3)cycloaddition of I to 1,3-dipoles arising from the cleavage of the bond *a* or *b* in V, as shown in Chart 2.

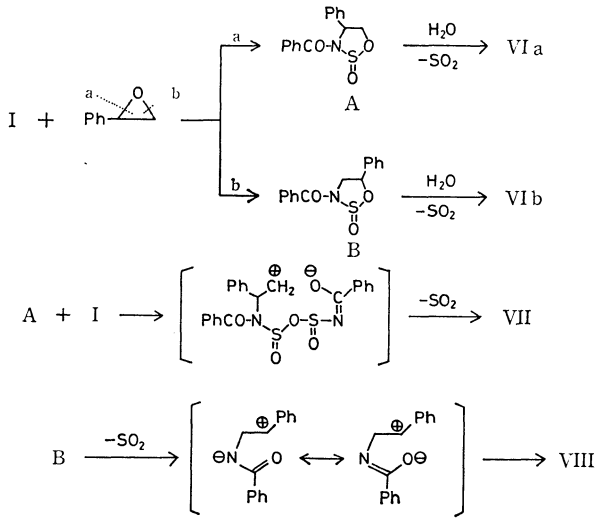


Chart 2

As has previously been reported,[3] reactive *N*-sulfinyl-*p*-toluenesulfonamide reacted with V under similar conditions, giving 1-oxo-1,2,5-thiadiazolidine whose structure corresponded to the compound derived from a 2:1 adduct of the *N*-sulfinyl compound and V under the elimination of sulfur dioxide.

Because I as well as *N*-sulfinyl-*p*-toluenesulfonamide is more reactive than *N*-sulfinylanilines, I will be able to further attack 2-oxo-1,2,3-oxathiazolidine intermediates; the attack of I on A will be preferable to that on B having 5-phenyl group.

As is shown in Chart 2, the reaction of I with A leads to the formation of VII under the elimination of sulfur dioxide. On the other hand, the elimination of sulfur dioxide from the intermediate B and subsequent ring closure results in the formation of VIII. The by-products, benzonitrile and benzamide, may be secondarily formed from I and VII.

Experimental

All the melting and boiling points are uncorrected. The NMR spectra were determined at 60 MHz with a Hitachi-20 NMR spectrometer, using TMS as the internal reference, while the mass spectra were obtained on a Hitachi RMS-4 mass spectrometer, using a direct inlet and an ionization energy of 70 eV.

Reaction of Benzamide with Thionyl Chloride. To a stirred solution of 48.2 g of benzamide and 64.0 g of pyridine in 400 m*l* of benzene, a solution of 47.6 g of thionyl chloride in 200 m*l* of benzene was added, drop by drop, at a temperature below 10°C over a period of 12 hr. After the reaction mixture was allowed to stand overnight at room temperature, the precipitated pyridine hydrochloride was rapidly removed by filtration. The filtrate was evaporated *in vacuo* to remove the solvents and benzonitrile, and then a residue was distilled under reduced pressure to give 41.3 g (62%) of *N*-sulfinylbenzamide (I), bp 76°C/0.16 mmHg (lit,[4] bp 70°C/0.1 mmHg), as an yellow oil, and to leave 10 g of crude *N,N'*-dibenzoylsulfurdiimide (II) as dark brown crystals.

The IR spectrum (neat) of I was in agreement with that reported by Scherer and Schmitt.[4] The main absorption bands are as follows: 3060, 1700, 1675, 1600, 1585, 1490, 1450, 1380, 1320, 1240, 1180, 1140, 1100, 1075, 1030, 1005, 950, 850, 810, 740, 710, 685, 655, 620, and 520 cm^{-1}.

The treatment of crude II, whose IR spectrum was similar to that of I, with an excess of ethanol gave colorless crystals. The crystals were rapidly collected by filtration and washed with ethanol to give *S*-benzamido-*S*-ethoxy-*N*-benzoylsulfilimine (III), mp 135—140°C (decomp.), which gradually decomposed on standing in air to give benzamide.

Found: C, 60.79; H, 4.76; N, 8.87%. Calcd for $C_{16}H_{16}O_3N_2S$: C, 60.75; H, 5.10; N, 8.86%. IR (KBr): 3040 (ν_{NH}), 1683 cm^{-1} (ν_{CO}).

Reduction of N,N'*-Dibenzoylsulfurdiimide (II) with Sodium Borohydride.* A suspension of 1.74 g of crude II in 20 m*l* of diethyl ether was stirred with 0.25 g of sodium borohydride at room temperature for 24 hr. The reaction mixture was poured into an ice-water mixture and was then extracted with chloroform. The chloroform-extract was washed with water, dried over sodium sulfate, and then evaporated *in vacuo* to give 0.82 g of crystals. Recrystallization from acetonitrile gave 0.28 g (16%) of *N,N'*-thiodibenzamide (IV), mp 191°C (decomp.) (lit,[15] mp 188°C), as colorless needles.

Found: C, 61.58; H, 4.29; N, 10.21%. Calcd. for $C_{14}H_{12}O_2N_2S$: C, 61.76; H, 4.44; N, 10.29%. IR (KBr): 3220 (ν_{NH}), 1655 cm^{-1} (ν_{CO}).

The mother liquor was concentrated *in vacuo* to leave a residue, which was then recrystallized from carbon tetrachloride to give 0.41 g (26%) of benzamide.

Reaction of N-*Sulfinylbenzamide (I) with Styrene Oxide (V).* After a solution of 1.01 g (0.006 mol) of I and 0.73 g (0.006 mol) of V in 10 m*l* of benzene had been refluxed with 0.06 g (0.0003 mol) of Et_4NBr for 1 hr, the reaction mixture was concentrated *in vacuo* to leave a residue. The residue was

10) F. Wolfheim, *Ber.*, **47**, 1440 (1914).

11) The sulfurdiimide II did not react with V in the presence of Et_4NBr. On the other hand, it has been found that the reaction of I with 1-*p*-toluenesulfonylaziridine did not give a compound of VII type, but 1-oxo-2-benzoyl-5-*p*-toluenesulfonyl-1,2,5-thiadiazolidine and 1,2,3,6-thiatriazine compounds: the results will be reported in detail elsewhere.

12) O. Tsuge, S. Mataka, M. Tashiro, and F. Mashiba, This Bulletin, **40**, 2709 (1967).

13) V. S. Etlis, A. P. Sineokov, and M. E. Sergeeva, *Khim. Geterotskil. Soedin.* **1966**, 682; *Chem. Abstr.*, **66**, 55150s (1967).

14) F. Yamada, T. Nishiyama, M. Kinugasa, and M. Nakatani, This Bulletin, **43**, 3611 (1970).

15) K. G. Naik, *J. Chem. Soc.*, **119**, 1168 (1921).

triturated with 5 m*l* of methanol to give colorless crystals, which on recrystallization from methanol, gave 0.47 g (41%) of 4-oxo-5-benzoyl-2,6-diphenyl-1,4,3,5-oxathiadiazepine (VII), mp 171—172°C (decomp.), as colorless prisms.

Found: C, 67.70; H, 4.39; N, 7.11%. Calcd. for $C_{22}H_{18}O_3N_2S$: C, 67.68; H, 4.65; N, 7.18%. IR (KBr): 1660 (ν_{CO}), 1630 cm^{-1} ($\nu_{C=N}$).

The filtrate was concentrated *in vacuo* to give a residue, which was then chromatographed on alumina using benzene and then methanol as eluents. A trace amount of benzonitrile and 0.23 g (17%) of 2,5-diphenyloxazoline (VIII) were obtained from the benzene-eluent. The methanol-eluent was evaporated *in vacuo* to leave a viscous substance, which was then extracted with hot carbon tetrachloride. The colorless solid obtained from the carbon tetrachloride-extract was treated with 10 m*l* of aqueous hydrochloric acid to dissolve the benzamide (0.1 g). The recrystallization of insoluble crystals from carbon tetrachloride gave 0.05 g (3.5%) of colorless crystals, mp 126—127°C, which were found to be a mixture of nearly equal amounts of *N*-benzoyl-*β*-phenyl-*β*-aminoethanol (VIa) and *N*-benzoyl-*α*-phenyl-*β*-aminoethanol (VIb) by NMR spectroscopy.

A similar reaction of V with two molar quantities of I gave VI, VII and VIII in yields of 12, 32, and 3% respectively, accompanied by trace amounts of benzonitrile and benzamide.

The IR spectrum of VI mp 126—127°, revealed all the distinctive bands of authentic samples of VIa and VIb, the results of elemental analysis agreed with the calculated values of VI.

Found: C, 74.99; H, 6.26; N, 5.36%. Calcd. for $C_{15}H_{15}O_2N$: C, 74.66; H, 6.27; N, 5.81%.

On the other hand, VIII (M^+ *m/e* 223), a pale green oil whose IR spectrum showed the characteristic band ascribed to $\nu_{C=N}$ at 1650 cm^{-1}, was derived to its picrate, mp 141—142°C. The picrate was identical with the picrate, mp 141—142°C (lit,[10] mp 141—142°C) of 2,5-diphenyloxazoline prepared by the method of Wolfheim.[10]

N-Benzoyl-α-phenyl-β-aminoethanol (VIb). To a suspension of 17 g of a mixture of *α*-phenyl- and *β*-phenyl-*β*-aminoethanol, bp 119—126°C/6 mmHg (lit.[16] bp 135—144°C/4—6 mmHg), which had been prepared from styrene oxide and ammonia according to the method of Castro *et al.*[8], in 50 m*l* of diethyl ether and 100 m*l* of 10% aqueous sodium hydroxide, 25 m*l* of benzoyl chloride was added, drop by drop, at 0°C. The precipitated solid was collected by filtration, washed with water, and dried. Several recrystallizations from benzene gave 6.3 g of VIb, mp 147—148°C (lit,[8] mp 148.6—149.1°C), as colorless plates.

Found: C, 74.21; H, 6.17; N, 5.73%. Calcd. for $C_{15}H_{15}O_2N$: C, 74.66; H, 6.27; N, 5.81%. IR(KBr): 3440 (ν_{OH}), 3320 (ν_{NH}), 1623 cm^{-1} (ν_{CO}). NMR (DMSO-d_6): δ 3.35—3.6 (multiplet, 2H, $-CH_2-$), 4.7—5.0 (multiplet, 1H, $>CH$), 5.55 (doublet, 1H,–OH, exchanged with D_2O), 7.2—8.0 (multiplet, 10H, aromatic protons), 8.55 ppm (triplet, 1H, –NH–, exchanged with D_2O).

Reaction of VII with Hydrazine Hydrate. When 2 m*l* of hydrazine hydrate was added to a solution of 0.5 g of VII in 20 m*l* of ethanol at room temperature, hydrogen sulfide evolved immediately. After the reaction mixture had been stirred at room temperature for 1 hr, it was concentrated *in vacuo* to leave crystals. The crystals were washed with benzene and then recrystallized from carbon tetrachloride, thus affording 0.22 g (68%) of *N*-benzoyl-*β*-phenyl-*β*-aminoethanol (VIa), mp 151°C (lit,[7] mp 154—154.5°C), as colorless needles.

Found: C, 74.34; H, 6.06; N, 5.69%. Calcd. for $C_{15}H_{15}O_2N$: C, 74.66; H, 6.27; N, 5.81%. IR (KBr): 3440 (ν_{OH}), 1630 cm^{-1} (ν_{CO}). NMR (DMSO-d_6): δ 3.71 (double doublet, 2H, $-CH_2-$), 4.8—5.4 (multiplet, 2H, $>CH$, and –OH), 7.2—8.2 (multiplet, 10H, aromatic protons), 8.75 ppm (doublet, 1H, –NH–).

The benzene washings were evaporated *in vacuo*, leaving 0.17 g (100%) of benzamide.

The hydrolysis of 0.3 g of VII with hydrochloric acid in methanol gave 70 mg (38%) of VIa and 90 mg (97%) of benzamide.

16) R. F. Nystrom and W. G. Brown, *J. Amer. Chem. Soc.*, **70** 3738 (1948).