The Preparation of 2*H*-1,2,3-Benzothiadiazine-1,1-dioxides, 11*H*-11,11a-Dihydrobenzimidazo[1,2-*b*] [1,2] benzisothiazole-5,5-dioxides, 6*H*-Dibenzo[*c*,*g*] [1,2,5] thiadiazocine-5,5-dioxides and 5*H*-Dibenzo[*c*,*g*] [1,2,6] thiadiazocine-6,6-dioxides

John B. Wright

Department of Chemistry, The Upjohn Company

o-Benzoylbenzenesulfonyl chlorides (I) were prepared conveniently from aminobenzophenones by diazotization followed by reaction with sulphur dioxide in the presence of Cu$^+$, according to the general method of Meerwein.

Reaction of the sulfonyl chlorides with hydrazine led to 4-phenyl-2*H*-1,2,3-benzothiadiazine-1,1-dioxides (II). The latter compounds could be methylated and acetylated readily in the 2-position. The 2-methyl derivative (III) could be prepared also by reaction of the sulfonyl chloride (Ia) with methylhydrazine. Catalytic hydrogenation of 6-chloro-4-phenyl-2*H*-1,2,3-benzothiadiazine-1,1-dioxide (IIa) gave the 3,4-dihydro derivative (V). Reaction of the sulfonyl chlorides (I) with *o*-phenylenediamine followed by cyclodehydration led to 11*H*-11,11a-dihydrobenzimidazo[1,2-*b*][1,2]benzisothiazole-5,5-dioxides (VII). One of the latter compounds (VIIa) in sodium hydroxide solution in the presence of methyl iodide or benzyl chloride was transformed into 6-methyl- and 6-benzyl-5*H*-dibenzo[*c*,*g*][1,2,6]thiadiazocine-5,5-dioxides (VIII), respectively.

5*H*-Dibenzo[*c*,*g*][1,2,6]thiadiazocine-6,6-dioxides (XIV) were prepared also by cyclodehydration of 2-amino-2′-benzoylbenzenesulfonanilides (XIII).

As a continuation (1) (2) of work underway in these laboratories on the preparation of new heterocyclic systems containing a sulfonamido group as part of the ring we were interested in synthesizing and investigating the chemistry of 2*H*-1,2,3-benzothiadiazine-1,1-dioxides (II), 6*H*-dibenzo[*c*,*g*][1,2,5]thiadiazocine-5,5-dioxides (VIII) and 5*H*-dibenzo[*c*,*g*][1,2,6]thiadiazocine-6,6-dioxides (XIV).

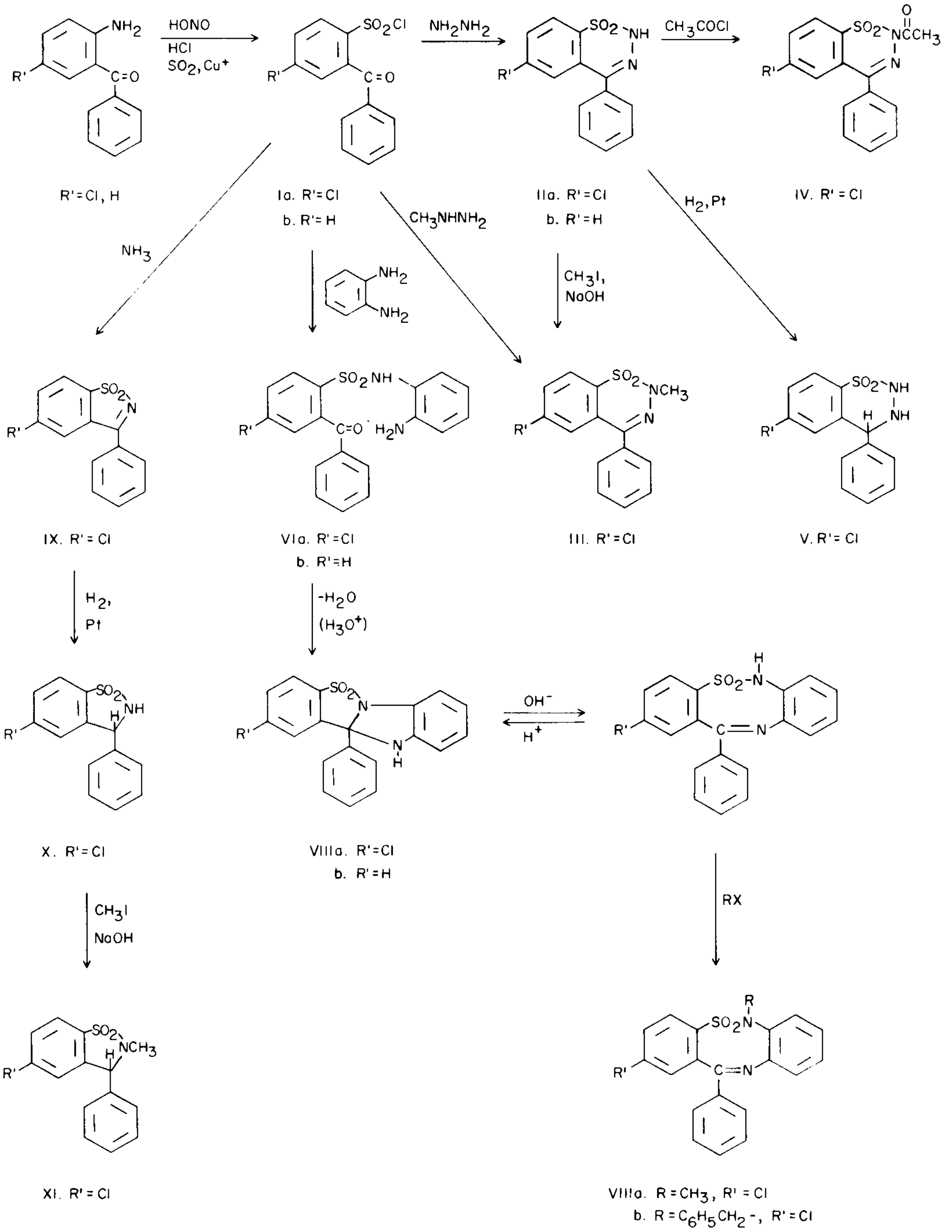
2*H*-1,2,3-Benzothiadiazine-1,1-dioxides have been studied very little, previously. 1,2,3-Benzothiadiazin-4(3*H*)-one-1,1-dioxide (3), 4-hydrazino-1,2,3-benzothiadiazine-1,1-dioxides (4) and 4-(3′,5′-dimethylpyrazole-1′)-1,2,3-benzothiadiazine-1,1-dioxides (4a), the latter compounds prepared from the 4-hydrazino derivatives by reaction with 2,4-pentane dione, appear to be the only recorded instances of this ring system in the literature.

It was found that 4-aryl-2*H*-1,2,3-benzothiadiazine-1,1-dioxides (II) could be prepared conveniently in very good yield by the reaction of hydrazine with *o*-benzoylbenzenesulfonyl chlorides (I) (Figure I). The latter compounds could be prepared from *o*-aminobenzophenones by diazotization followed by treatment with sulfur dioxide in the presence of cuprous ion, according to the general method of Meerwein (5).

6-Chloro-4-phenyl-2*H*-1,2,3-benzothiadiazine-1,1-dioxide (IIa) showed infrared absorption bands attributable to NH (3090 cm^{-1}). Its NMR spectrum showed only one proton at low field strength (*ca.* 11.9 δ), attributable to the proton in the 2 position, in addition to aromatic protons. Its mass spectrogram showed a parent m/e of 292.

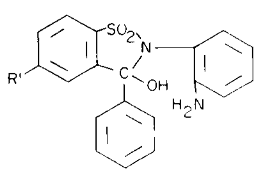
The 4-phenyl-2*H*-1,2,3-benzothiadiazine-1,1-dioxides prepared (IIa and IIb) were readily soluble in dilute sodium hydroxide. Treatment of 6-chloro-4-phenyl-2*H*-1,2,3-benzothiadiazine-1,1-dioxide (IIa) with methyl iodide in the presence of sodium hydroxide gave the 2-methyl derivative (III). 6-Chloro-2-methyl-4-phenyl-1,2,3-benzothiadiazine-2,2-dioxide (III) could be prepared also by treatment of 2-benzoyl-4-chlorobenzenesulfonyl chloride (Ia) with methylhydrazine. The 6-chloro derivative (IIa) was acetylated with refluxing acetyl chloride to give 2-acetyl-6-chloro-1,2,3-benzothiadiazine-1,1-dioxide (IV) and could be hydrogenated in the presence of platinum (Adams catalyst) in acetic acid solution to give 6-chloro-3,4-dihydro-4-phenyl-2*H*-1,2,3-benzothiadiazine-1,1-dioxide

Figure I



(V). The NMR spectrum of the reduction product showed a singlet at 8.3 δ having an area of one proton and exchangeble with deuterium oxide (attributable to the proton in the 2 position) and a broad low band at 5.35-6.8 δ possessing an area of two protons which became a sharp singlet in deuterium oxide possessing an area of one proton at 5.45 δ (attributable to the tertiary hydrogen in the 4 position).

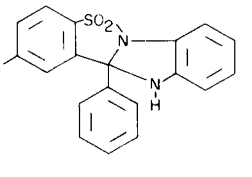
Reaction of *o*-benzoylbenzenesulfonyl chlorides (I) with an excess of *o*-phenylenediamine gave good yields of the corresponding 2′amino-2-benzoylbenzenesulfonanilides (VI). An alternate structure (XV) is possible for these



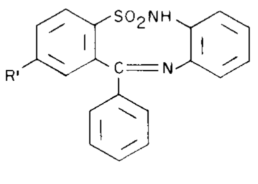
XV

compounds, especially in view of the reaction of *o*-aroylbenzoic acid with amines (6). However, the reaction products were soluble in dilute sodium hydroxide solution, which would be expected of structure VI but not of structure XV. Furthermore, the reaction products showed carbonyl absorption in the infrared spectra at 1650 cm^{-1} (for VIa) and 1665 cm^{-1} (for VIb). On the basis of these facts, structure VI is assigned to these reaction products.

The 2'-amino-2-benzoylbenzenesulfonanilides (VI) underwent cyclodehydration readily when refluxed in toluene solution in the presence of *p*-toluenesulfonic acid. The resulting products could have either structures VII or XVI.



VIIa. R' = Cl
b. R' = H



XVIa. R' = Cl
b. R' = H

The 2-chloro compound (VIIa or XVIa) in its mass spectrum showed a parent m/e of 368. Its NMR spectrum showed only one exchangeable proton at 4.66 δ in addition to aromatic protons. It was slightly soluble in dilute sodium hydroxide solution and was reprecipitated from alkaline solution upon the addition of acid. The ultraviolet absorption spectra showed λ max (EtOH), 253 mμ (sl. sh., ϵ = 5,450) and 298 mμ (ϵ = 4,050). In ethanolic potassium hydroxide solution, the spectra was very different, λ max 255 mμ (ϵ = 16,550) and 350 mμ (ϵ = 2,400). The spectra in ethanolic hydrogen chloride was essentially the same as that shown in neutral ethanolic solution. The spectra obtained in alkaline solution was similar to that obtained for the isomeric compound XIVa [λ max (EtOH), 259 mμ (ϵ = 17,500), 285 mμ (sh., ϵ = 9,500), 330 mμ (sh., ϵ = 2,100)] which can exist only in the tricyclic form.

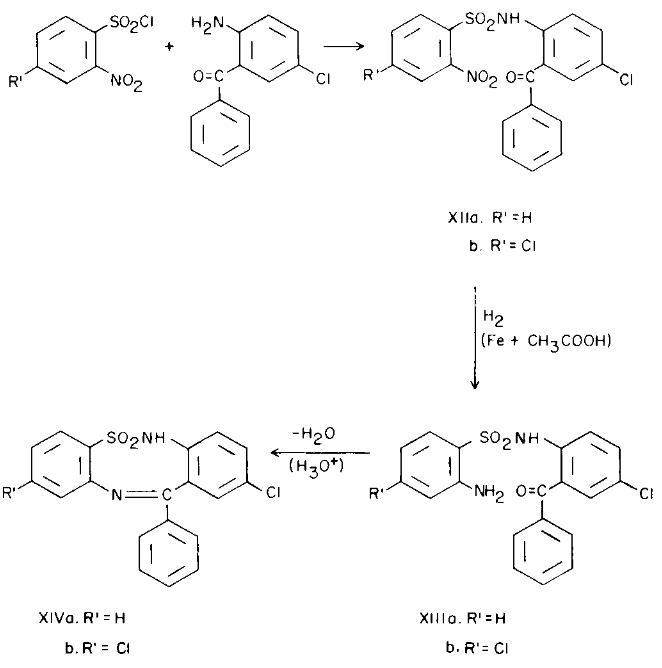
The compound obtained above was shown by x-ray crystallographic studies (7) to exist in the crystalline state as the tetracyclic structure (*i.e.* VIIa). In view of the ultraviolet spectral data, it would appear that in alkaline solution the compound exists in the tricyclic form (*i.e.* XVIa) and that a *p*H dependent equilibrium exists between the two possible structures.

Treatment of the 2-chloro compound (VIIa) with methyl iodide and benzyl chloride in the presence of sodium hydroxide gave good yields of 2-chloro-6-methyl-12-phenyl-6*H*-dibenzo[*c*,*g*]thiadiazocine-5,5-dioxide (VIIIa) and 2-chloro-6-benzyl-12-phenyl-6*H*-dibenzo[*c*,*g*][1,2,5]thiadiazocine-5,5-dioxide (VIIIb) respectively. The ultraviolet absorption spectra for the *N*-methyl derivative (VIIIa) was very similar [λ max (EtOH), 258 mμ (ϵ = 17,550), 329 mμ (ϵ = 2,550)] to that shown for the starting material in alkaline solution.

Treatment of 2-benzoyl-4-chlorobenzenesulfonyl chloride (Ia) with concentrated ammonium hydroxide at room temperature gave 5-chloro-3-phenyl-1,2-benzoisothiazole-1,1-dioxide (IX) (8). The product was reduced readily by hydrogenation in the presence of platinum catalyst to give 5-chloro-3-phenyl-1,2-benzisothiazoline-1,1-dioxide (X) (9). The latter compound was readily soluble in dilute sodium hydroxide solution and its infrared spectrum showed the presence of NH absorption (3240 cm^{-1}). Its nmr spectrum showed a singlet at 6.0 δ attributable to the tertiary hydrogen at position 3.

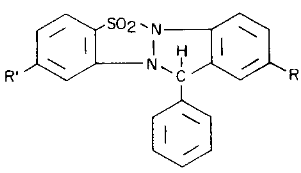
Methylation of 5-chloro-3-phenyl-1,2-benzisothiazoline-1,1-dioxide (X) to give the corresponding 2-methyl compound (XI) was carried out in excellent yield with methyl iodide in the presence of sodium hydroxide.

Figure II



12-Phenyl-5*H*-dibenzo[*c,g*][1,2,6]thiadiazocine-6,6-dioxides (XIV) were prepared as outlined in Figure II. Treatment of 2-aminobenzophenones with *o*-nitrobenzenesulfonyl chlorides in the presence of pyridine gave the corresponding 2′-benzoyl-2-nitrobenzenesulfonanilides (XII) in very good yields. Reduction of the latter compounds with iron and acetic acid gave 2′-benzoyl-2-aminobenzenesulfonanilides (XIII).

The 2-benzoyl-2-aminobenzenesulfonanilides (XIII) underwent cyclodehydration readily on refluxing in toluene solution in the presence of *p*-toluenesulfonic acid to give 12-phenyl-5*H*-dibenzo[*c,g*] [1,2,6]thiadiazocine-6,6-dioxides (XIV). An alternate structure (XVII) may be written for these latter compounds. However, the tetracyclic structure (XVII) is rejected in view of the ready solubility of the compounds in dilute sodium hydroxide solution.



XVII

2-Chloro-12-phenyl-5*H*-benzo[*c,g*][1,2,6]thiadiazocine-6,6-dioxide (XIVa) in its NMR spectrum showed only a broad band centered at about 1.03 δ, attributable to the sulfonamide hydrogen at position 5, in addition to aromatic protons. The mass spectra showed a parent m/e of 368.

EXPERIMENTAL

All melting points are corrected. The NMR spectra were recorded on a Varian A-60 or a Varian DP-60 spectrometer using tetramethylsilane as the internal reference standard.

2-Benzoyl-4-chlorobenzenesulfonyl Chloride (Ia).

To a stirred solution of 32.4 g. (0.14 mole) of 5-chloro-2-aminobenzophenone in 140 ml. of acetic acid and 48 ml. of concentrated hydrochloric acid was added at 0-5° a solution of 10.6 g. of sodium nitrite in 17 ml. of water. The mixture was stirred at the same temperature for 0.5 hour before adding a solution of 33.6 g. of sulfur dioxide in 100 ml. of acetic acid to which had been previously added a solution of 5.6 g. of cupric chloride in 10 ml. of water. The mixture was allowed to warm to room temperature with stirring over the course of 1 hour and then poured into ice water. The pale yellow solid was removed by filtration, 41.60 g. (96%), m.p. 126-130°. Recrystallization from cyclohexane raised the melting point to 129-131°. The infrared spectrum showed carbonyl absorption at 1665 cm^{-1}.

Anal. Calcd. for $C_{13}H_8Cl_2O_3S$: C, 49.54; H, 2.56; Cl, 22.50; S, 10.17. Found: C, 49.86; H, 2.73; Cl, 22.35; S, 9.87.

6-Chloro-4-phenyl-2*H*-1,2,3-benzothiadiazine-1,1-dioxide (IIa).

A stirred mixture of 18.9 g. (0.06 mole) of 2-benzoyl-4-chlorobenzenesulfonyl chloride, 3.0 g. (0.06 mole) of hydrazine hydrate, 9.85 g. (0.12 mole) of sodium acetate and 200 ml. of ethanol was heated under reflux for 3 hours. The ethanol was removed by distillation and the residue diluted with water. The solid was removed by filtration and recrystallized from ethanol. There was obtained 12.25 g. (70%) of yellow prisms melting at 184°, dec. Additional recrystallization from ethyl acetate raised the melting point to 187°; dec., λ max (ethanol), 211 mμ (ε = 35,800), sh 243 mμ (ε = 15,500), 313.5 mμ (ε = 5,350), sh 354 mμ (ε = 527).

Anal. Calcd. for $C_{13}H_9ClN_2O_2S$: C, 53.34; H, 3.10; Cl, 12.11; N, 9.57; S, 10.95. Found: C, 53.65; H, 3.26; Cl, 11.96; N, 9.56; S, 10.98.

6-Chloro-2-methyl-4-phenyl-1,2,3-benzothiadiazine-1,1-dioxide (III).

To a solution of 2.93 g. (0.01 mole) of 6-chloro-4-phenyl-2*H*-1,2,3-benzothiadiazine-1,1-dioxide in 20 ml. of a 2.5% sodium hydroxide solution was added 30 ml. of ethanol and 2 ml. of methyl iodide. The mixture was stirred at room temperature for 4 hours using a reflux condenser to prevent the loss of methyl iodide. An additional 2 ml. of methyl iodide was added and stirring continued for 18 hours.

The mixture was diluted with an equal volume of water. The solid was removed by filtration, dissolved in benzene and the benzene solution washed once with a 1% sodium hydroxide solution and once with water. The benzene layer was separated, the benzene removed and the residue recrystallized from ethanol. There was obtained 1.90 g. (62%) of colorless needles melting at 121-125°. Additional recrystallization raised the melting point to 124-125°; λ max (ethanol), 213 mμ (ε = 37,000), sh 245 mμ (ε = 13,800), 321 mμ (ε = 6,250).

Anal. Calcd. for $C_{14}H_{11}ClN_2O_2S$: C, 54.81; H, 3.62; Cl, 11.56; N, 9.13; S, 10.45. Found: C, 54.50; H, 3.48; Cl, 11.68; N, 9.10; S, 10.29.

6-Chloro-2-methyl-4-phenyl-1,2,3-benzothiadiazine-1,1-dioxide (III).

To a stirred solution of 9.45 g. (0.03 mole) of 2-benzoyl-4-chlorobenzenesulfonyl chloride in 25 ml. of pyridine was added a solution of 1.38 g. (0.03 mole) of methylhydrazine in 10 ml. of pyridine. During this addition, the reaction temperature was kept below 40° by means of an ice bath. The mixture was heated on the steam bath for 90 minutes and then concentrated under vacuum using a water bath at 60°.

To the residue was added 100 ml. of toluene and 20 mg. of *p*-toluenesulfonic acid and the mixture refluxed for 16 hours using a Dean-Stark water separator. The toluene solution was allowed to cool and was separated from a small amount of tar by decantation and washed with a 1% sodium hydroxide solution. The toluene layer was separated, the toluene removed by distillation under vacuum and the residue recrystallized from cyclohexane. There was obtained 2.12 g. of material melting at 122-125°. The infrared spectrum of this material was identical to that obtained above by methylation of 6-chloro-4-phenyl-2*H*-1,2,3-benzothiadiazine-1,1-dioxide. A mixed melting point of the two samples also showed no depression.

Anal. Calcd. for $C_{14}H_{11}ClN_2O_2S$: C, 54.81; H, 3.62; Cl, 11.56; N, 9.13; S, 10.45. Found: C, 55.04; H, 3.83; Cl, 11.95; N, 8.87; S, 10.18.

2-Acetyl-6-chloro-4-phenyl-1,2,3-benzothiadiazine-1,1-dioxide (IV).

A solution of 3.90 g. (0.013 mole) of 6-chloro-4-phenyl-2*H*-1,2,3-benzothiadiazine-1,1-dioxide and 10 ml. of acetyl chloride in 50 ml. of chloroform was heated under reflux for 1 hour. The chloroform and excess acetyl chloride were removed by distillation and the residue triturated with ether and the solid removed by filtration. Weight, 3.85 g. (87%), m.p. 139-140.5°. Recrystallization from ether raised the melting point to 140-142°.

Anal. Calcd. for $C_{15}H_{11}ClN_2O_3S$: C, 53.82; H, 3.31; C, 10.59; N, 8.37; S, 9.58. Found: C, 53.92; H, 2.93; Cl, 10.84; N, 8.88; S, 9.66.

6-Chloro-3,4-dihydro-6-chloro-2*H*-1,2,3-benzothiadiazine-1,1-dioxide (V).

A suspension of 5.84 g. (0.02 mole) of 6-chloro-4-phenyl-2*H*-1,2,3-benzothiadiazine-1,1-dioxide in 150 ml. of acetic acid was warmed until a homogeneous solution was obtained. The warm solution was hydrogenated at 3 atmospheres of hydrogen using 200 mg. of platinum oxide as catalyst. When the theoretical amount of hydrogen had been absorbed (40 minutes) the hydrogenation was stopped, the catalyst removed by filtration and the filtrate concentrated under aspirator vacuum. The residue was stirred with water, filtered, and the solid recrystallized from 2-propanol. There was obtained 3.60 g. (61%) of colorless prisms melting at 142°, dec; λ max (ethanol), sl. sh. 230 mμ (ε = 14,300), sh. 251 mμ (ε = 2,650), sh. 264 mμ (ε = 1,800), sh. 272 mμ (ε = 1,600), 281 mμ (ε = 1,350), 305 mμ (ε = 846), 358 mμ (ε = 687).

Anal. Calcd. for $C_{13}H_{11}ClN_2O_2S$: C, 52.97; H, 3.76; Cl, 12.03; N, 9.51; S, 10.88. Found: C, 52.96; H, 3.59; Cl, 11.72; N, 9.77; S, 10.78.

2-Benzoylbenzenesulfonyl Chloride (Ib).

The procedure described above for 2-benzoyl-4-chlorobenzenesulfonyl chloride was employed using an equivalent amount (27.58 g.) of 2-aminobenzophenone, yield, 23.2 g. (59%), m.p. 88-91°. Recrystallization from cyclohexane-benzene (5:1) gave colorless prisms melting at 95.5-96.5° (10). The infrared spectrum showed carbonyl absorption at 1670 cm^{-1}.

Anal. Calcd. for $C_{13}H_9ClO_3S$: C, 55.62; H, 3.23; Cl, 12.63; S, 11.42. Found. C, 55.66; H, 3.13; Cl, 12.30; S, 10.99.

4-Phenyl-2*H*-1,2,3-benzothiadiazine-1,1-dioxide (IIb).

A stirred mixture of 13.3 g. (0.048 mole) of 2-benzoylbenzenesulfonyl chloride, 100 ml. of ethanol, 2.38 g. (0.048 mole) of hydrazine hydrate and 7.8 g. (0.095 mole), of sodium acetate was heated under reflux for 3 hours. The ethanol was removed by distillation and the residue stirred with ice water and filtered. After recrystallization from ethanol there was obtained 4.80 g. (39%) of material melting at 178°, dec. Additional recrystallization gave colorless prisms melting at 192° dec.

Anal. Calcd. for $C_{13}H_{10}N_2O_2S$: C, 60.45; H, 3.90; N, 10.85; S, 12.41. Found: C. 60.45; H, 4.06; N, 11.05; S, 12.34.

2′-Amino-2-benzoyl-4-chlorobenzenesulfonanilide (VIa).

A mixture of 15.75 g. (0.05 mole) of 2-benzoyl-4-chloro benzenesulfonyl chloride, 27.0 g. (0.25 mole) of *o*-phenylenediamine and 300 ml. of benzene was stirred and heated under reflux for 2 hours. After cooling, the mixture was filtered and the filtrate was extracted with a 1% sodium hydroxide solution. The basic extracts were acidified with acetic acid and the precipitate removed by filtration and washed with water. Weight, 19.0 g. (98%), m.p. 168-171°. Recrystallization from ethanol gave prisms melting at 171.5-173.5°. The infrared spectrum (mull) showed carbonyl absorption at 1650 cm^{-1}.

Anal. Calcd. for $C_{19}H_{15}ClN_2O_3S$: C, 58.99; H, 3.91; Cl, 9.16; N, 7.24; S, 8.29. Found: C, 59.26; H, 3.93; Cl, 9.21; N, 7.45; S, 8.50.

2-Chloro-11,11a,dihydro-11a-phenylbenzimidazo[1,2-*b*][1,2]-benzisothiazole-5,5-dioxide (VIIa).

A mixture of 19.35 g. (0.05 mole) of 2′-amino-2-benzoyl-4-chlorobenzenesulfonanilide, 2.0 g. of *p*-toluenesulfonic acid and 150 ml. of toluene was heated under reflux using a Dean-Stark water trap until the theoretical amount of water was separated (20 hours). The solution was extracted with a 1% ammonium hydroxide solution and once with water. The toluene layer was separated and concentrated by distillation under reduced pressure. The residue was dissolved in anhydrous ether and an excess of an ethereal hydrogen chloride solution added (to remove remaining starting material). The solid was removed by filtration and the ethereal filtrate concentrated. The weight of the residue was 13.8 g. (75%), m.p. 173.5-177.5°. Recrystallization from ethanol gave tan prisms melting at 180-181°. The NMR spectrum (deuteriochloroform) showed only one exchangeable proton at 4.66 δ in addition to aromatic protons.

Anal. Calcd. for $C_{19}H_{13}ClN_2O_2S$: C, 61.87; H, 3.55; Cl, 9.61; N, 7.60; S, 8.69. Found: C, 61.55; H, 3.89; C, 9.73; N, 7.34; S, 8.73.

2-Chloro-6-methyl-12-phenyl-6*H*-dibenzo[*c*,*g*][1,2,5]thiadiazocine-5,5-dioxide (VIIIa).

To a solution of 3.68 g. (0.01 mole) of 2-chloro-11,11a, dihydro-11a-phenylbenzimidazo[1,2-b][1,2]-benzisothiazole-5,5-dioxide in 30 ml. of 1.67% sodium hydroxide solution was added 30 ml. of ethanol and 2 ml. of methyl iodide. The mixture was stirred at room temperature for 5 hours, using a reflux condenser to prevent loss of methyl iodide. An additional 2 ml. of methyl iodide was added and stirring was continued for an additional 48 hours.

The mixture was diluted with an equal volume of water and the solid removed by filtration. Weight, 3.61 g., m.p. 192-195°. Recrystallization from benzene raised the melting point to 195-197°.

Anal. Calcd. for $C_{20}H_{15}ClN_2O_2S$: C, 62.74; H, 3.95; Cl, 9.26; N, 7.32; S, 8.37. Found: C, 62.47; H, 4.09; Cl, 9.22; N, 7.20; S, 7.98.

6-Benzyl-2-chloro-12-phenyl-6*H*-dibenzo[*c*,*g*][1,2,5]-thiadiazocine-5,5-dioxide (VIIIb).

To a stirred solution of 3.68 g. (0.01 mole) of 2-chloro-11, 11a, dihydro-11a-phenyl benzimidazo[1,2-b][1,2]-benzisothiazole-5,5-dioxide in 30 ml. of 1.67% of sodium hydroxide solution was added 30 ml. of ethanol and 1.27 g. (0.01 mole) of benzyl chloride. The mixture was stirred for 18 hours, diluted with an equal volume of water and the precipitate removed by filtration. Weight, 2.95 g. (64%), m.p. 192-196°. Recrystallization from ethanol gave yellow prisms melting at 198-199°.

Anal. Calcd. for $C_{26}H_{19}ClN_2O_2S$: C, 68.04; H, 4.17; Cl, 7.72; N, 6.11; S, 6.99. Found: C, 68.20; H, 4.36; Cl, 7.85; N, 5.90; S, 6.95.

2′-Amino-2-benzoylbenzenesulfonanilide (VIb).

A mixture of 14.0 g. (0.05 mole) of 2-benzoylbenzenesulfonyl chloride, 27.0 g. (0.25 mole) of *o*-phenylenediamine and 300 ml. of benzene was stirred and heated under reflux for 2 hours. The reaction mixture was allowed to cool to room temperature and the solid was removed by filtration. The solid was added to benzene and the mixture extracted with a 1% sodium hydroxide solution. The alkaline extract was then used to extract the original reaction mixture filtrate. The combined basic extracts were acidified with acetic acid and the precipitate was removed by filtration. After recrystallization from ethyl acetate there was obtained 11.84 g. (67%) of yellow prisms melting at 188-189°. The infrared spectrum (mull) showed carbonyl absorption at 1665 cm^{-1}.

Anal. Calcd. for $C_{19}H_{16}N_2O_3S$: C, 64.76; H, 4.58; N, 7.95; S, 9.10. Found: C, 64.86; H, 4.31; N, 7.80; S, 9.34.

11,11a-Dihydro-11a-phenylbenzimidazo[1,2-*b*][1,2]benzisothiazole-5,5-dioxide (VIIb).

A mixture of 8.8 g. (0.025 mole) of 2′-amino-2-benzoylbenzenesulfonanilide, 0.25 g. of *p*-toluenesulfonic acid and 100 ml. of toluene was heated under reflux using a Dean-Stark water trap until the theoretical amount of water had separated (8 hours). The mixture was filtered, the filtrate washed with a 1% ammonium hydroxide solution and the toluene removed by distillation under reduced pressure. The residue was recrystallized from ethanol to give 7.05 g. (84%) of yellow prisms melting at 165.5-170°. Additional recrystallization raised the melting point to 169-170.5°.

Anal. Calcd. for $C_{19}H_{14}N_2O_2S$: C, 68.24; H, 4.22; N, 8.38; S, 9.59. Found: C, 68.07; H, 4.39; N, 8.21; S, 9.44.

5-Chloro-3-phenyl-1,2-benzisothiazole-1,1-dioxide (IX).

A mixture of 31.52 g. (0.1 mole) of 2-benzoyl-4-chlorobenzenesulfonyl chloride and 100 ml. of concentrated ammonium hydroxide was stirred at room temperature for 4 hours, filtered, and the precipitate washed well with water. Recrystallization from ethanol gave 24.30 g. (88%) of colorless prisms melting at 162.5-163.5°; λ max (ethanol), 231 mμ (ϵ = 22,350), 283 mμ (ϵ = 10,600). The NMR spectrum (DMF-d_6) showed only aromatic protons.

Anal. Calcd. for $C_{13}H_8ClNO_2S$: C, 56.22; H, 2.90; Cl, 12.77; N, 5.04; S, 11.54. Found: C, 56.45; H, 2.93; Cl, 12.31; N, 4.99; S, 11.22.

5-Chloro-3-phenyl-1,2-benzisothiazoline-1,1-dioxide (X).

A mixture of 11.11 g. (0.04 mole) of 5-chloro-3-phenyl-1,2-benzisothiazole-1,1-dioxide and 200 ml. of acetic acid was warmed until a homogeneous solution was obtained. One-half gram of platinum oxide catalyst was added and the mixture was hydrogenated at an initial pressure of 3 atmospheres. The theoretical amount of hydrogen was absorbed in 15 minutes. The catalyst was removed by filtration and the filtrate concentrated under reduced pressure. The residue was dissolved in a benzene-methylene dichloride (1:1) mixture and the resulting solution extracted with a 5% sodium hydroxide solution. The alkaline extracts were acidified with acetic acid and the precipitate removed by filtration. The crude product was recrystallized from benzene. There was obtained 4.71 g. (42%) of colorless prisms melting at 166.5-169.5°; λ max (ethanol), sl. sh. 225 mμ (ϵ = 16,450), sh. 252 mμ (ϵ = 586), 258 mμ (ϵ = 637), 264 mμ (ϵ = 710), 271 mμ (ϵ = 795), 279 mμ (ϵ = 710).

Anal. Calcd. for $C_{13}H_{10}ClNO_2S$: C, 55.81; H, 3.60; Cl, 12.68; N, 5.01; S, 11.46. Found: C, 55.86; H, 3.83; Cl, 12.86; N, 4.95; S, 11.18.

5-Chloro-2-methyl-3-phenyl-1,2-benzisothiazoline-1,1-dioxide (XI).

To a solution of 8.38 g. (0.03 mole) of 5-chloro-3-phenyl-1,2-benzisothiazoline-1,1-dioxide in 60 ml. of 2.5% sodium hydroxide solution was added 90 ml. of ethanol and 6 ml. of methyl iodide. The mixture was stirred at room temperature for 4 hours, using a reflux condenser to prevent loss of the methyl iodide. An additional 6 ml. of methyl iodide was added and stirring was continued for an additional 20 hours. The mixture was diluted with 200 ml. of water and the precipitate removed by filtration and recrystallized from ethanol. There was obtained 7.32 g. (83%) of colorless prisms melting at 166.5-168.5°.

Anal. Calcd. for $C_{14}H_{12}ClNO_2S$: C, 57.24; H, 4.12; Cl, 12.07; N, 4.77; S, 10.91. Found: C, 57.49; H, 3.84; Cl, 11.80; N, 4.59; S, 11.01.

2′-Benzoyl-4-chloro-2-nitrobenzenesulfonanilide (XIIa).

A solution of 25.0 g. (0.108 mole) of 2-amino-5-chlorobenzophenone, 23.9 g. (0.108 mole) of *o*-nitrobenzenesulfonyl chloride and 50 ml. of pyridine was heated under reflux for 1 hour and then concentrated under reduced pressure. The residue was washed with water and recrystallized from ethanol. There was obtained 35.20 g. (78.5%) of tan prisms melting at 118-120°.

Anal. Calcd. for $C_{19}H_{13}ClN_2O_5S$: C, 54.74; H, 3.14; Cl, 8.51; N, 6.72; S, 7.69. Found: C, 54.81; H, 2.89; Cl, 8.59; N, 6.90; S, 7.86.

2-Amino-2′-benzoyl-4′-chlorobenzenesulfonanilide (XIIIa).

To a stirred solution of 13.7 g. (0.033 mole) of 2′-benzoyl-4′-chloro-2-nitrobenzenesulfonanilide in 200 ml. of acetic acid at 90-95° was added over a period of 75 minutes 10 g. of iron powder. The mixture was stirred and heated at the same temperature for 45 minutes additional and then 15 ml. of water was added. Stirring at 90-95° was continued for 2 hours. The mixture was allowed to cool, was diluted with 400 ml. of ice water and extracted with methylene chloride. The solvent was removed and the residue recrystallized from ethanol. There was obtained 10.80 g. (85%) of tan prisms melting at 96.5-97.5°. The infrared spectrum showed carbonyl absorption at 1645 cm^{-1}.

Anal. Calcd. for $C_{19}H_{15}ClN_2O_3S$: C, 58.99; H, 3.91; Cl, 9.16; H, 7.24; S, 8.29. Found: C, 58.92; H, 3.99; Cl, 9.27; N, 6.90; S, 8.26.

2-Chloro-12-phenyl-5*H*-dibenzo[*c,g*][1,2,6]thiadiazocine-6,6-dioxide (XIVa).

A mixture of 5.0 g. (0.013 mole) of 2-amino-2′-benzoyl-4′-chlorobenzenesulfonanilide, 200 mg. of *p*-toluenesulfonic acid and 50 ml. of toluene was heated under reflux using a Dean-Stark water trap until the theoretical amount of water was collected (16 hours). The solution was allowed to cool and was washed with a 1% ammonium hydroxide solution then with water. The aqueous extracts were extracted with methylene chloride and this extract added to the original toluene extract. The combined toluene-methylene chloride extract was then extracted with a 1% sodium hydroxide solution. The alkaline extract was acidified with acetic acid and the precipitate removed by filtration and recrystallized from ethanol. There was obtained 2.12 g. (44%) of yellow prisms melting at 188-189°.

Anal. Calcd. for $C_{19}H_{13}ClN_2O_2S$: C, 61.87; H, 3.55; C, 9.61; N, 7.60; S, 8.69. Found: C, 61.89; H, 3.36; Cl, 9.71; N, 7.61; S, 8.62.

2′-Benzoyl-4,4′-dichloro-2-nitrobenzenesulfonanilide (XIIb).

A solution of 25.0 g. (0.108 mole) of 2-amino-5-chlorobenzophenone, 27.63 g. (0.108 mole) of 4-chloro-2-nitrobenzenesulfonyl chloride and 50 ml. of pyridine was heated under reflux for 1 hour. The pyridine was removed by distillation under reduced pressure and the residue triturated with water and then with boiling alcohol. There was obtained 37.8 g. (78%) of material melting at 161-167.5°. Recrystallization from ethyl acetate raised the melting point to 168-170°.

Anal. Calcd. for $C_{19}H_{12}Cl_2N_2O_5S$: C, 50.56; H, 2.68; Cl, 15.71; N, 6.21; S, 7.11. Found: C, 50.79; H, 2.31; Cl, 15.82; H, 6.17; S, 7.15.

2-Amino-2′-benzoyl-4,4′-dichlorobenzenesulfonanilide (XIIIb).

The procedure described above for 2-amino-2′-benzoyl-4′-chlorobenzenesulfonanilide was employed using an equivalent amount of 2′-benzoyl-4,4′-dichloro-2-nitrobenzenesulfonanilide (14.9 g., 0.033 mole). After recrystallization from ethanol there was obtained 11.41 g. (82%) of tan prisms melting at 108-109°. The infrared spectrum showed carbonyl absorption at 1630 cm^{-1}.

Anal. Calcd. for $C_{19}H_{14}Cl_2N_2O_3S$: C, 54.17; H, 3.35; Cl, 16.83; N, 6.65; S, 7.61. Found: C, 53.90; H, 3.04; Cl, 16.66; N, 6.53; S, 7.65.

2,9-Dichloro-12-phenyl-5*H*-dibenzo[*c,g*][1,2,6]thiadiazocine-6,6-dioxide (XIVb).

The procedure described above for 2-chloro-12-phenyl-5*H*-dibenzo[*c,g*][1,2,6]thiadiazocine-6,6-dioxide was employed using an equivalent amount of 2-amino-2′-benzoyl-4,4′-dichlorobenzenesulfonanilide (5.47 g., 0.013 mole), yield, 1.80 g. (34%), m.p. 242-243°.

Anal. Calcd. for $C_{19}H_{12}Cl_2N_2O_2S$: C, 56.59; H, 3.00; Cl, 17.58; N, 6.95; S, 7.95. Found: C, 56.72; H, 3.37; Cl, 17.65; N, 6.80; S, 8.08.

Acknowledgment.

The author is indebted to Mr. Norman Knight and his co-workers of these laboratories for the microanalytical data, to Miss Lorraine Pschigoda and Mr. Paul Meulman for the infrared spectral data, to Miss Betty Zimmer and Dr. William Kreuger for the ultraviolet spectral data, to Dr. George Slomp, Mr. Forrest MacKellar and Mr. John Zieserl, Jr., for the NMR spectral data and to Dr. Marvin Grostic and Mr. Richard Wnuk for the mass spectral data. He is especially indebted to Dr. David Duchamp for carrying out x-ray crystallographic studies on compound VIIa and to Mr. Albert Lallinger for excellent technical assistance.

REFERENCES

(1) J. B. Wright, *J. Org. Chem.*, 29, 1905 (1964).

(2) J. B. Wright, *ibid.*, 30, 3960 (1965).

(3) B. Loev and M. Kormendy, *ibid.*, 27, 1703 (1962).

(4a) P. Schmidt, K. Eichenberger and M. Wilhelm, *Helv. Chim. Acta*, 45, 996 (1962). (b) Ciba Ltd., Belgian Patent, 608,898; Belgian Patent, 615,374. (c) E. Schrader, *J. Prakt. Chem.*, [2], 96, 183 (1917). (d) J. E. Robertson and J. H. Biel, U. S. Patent, 3,153,164; *Chem. Abstr.*, 62, 1675^b (1965). (e) M. Goddal, P. Vernadeau and J. Vernadeau, French Patent, M 2,166; *Chem. Abstr.*, 60, 8048^e (1964).

(5) H. Meerwein, E. Buchner and K, van Emster, *J. Prakt. Chem.*, [2], 152, 251 (1939); H. Meerwein, G. Dittmar, R. Gollner, K. Hafner, F. Mensch and O. Steinfort, *Chem. Ber.*, 90, 841 (1957).

(6a) T. S. Sulkowski, M. A. Wille, A. Mascitti and J. L. Diebald, *J. Org. Chem.*, 32, 2180 (1967). (b) W. Metlesics, T. Anton and L. H. Sternbach, *J. Org. Chem.*, 32, 2185 (1967). (c) W. Graf, E. Girod, E. Schmidt and W. G. Stoll, *Helv. Chem. Acta*, 42, 1085 (1959).

(7) These x-ray crystallographic studies were carried out by Dr. David Duchamp of these laboratories. These results will be reported elsewhere by Dr. Duchamp.

(8a) I. Remsen and A. P. Saunders, *Amer. Chem. J.*, 17, 358 (1895). (b) S. Horii, Japanese Patent, 8,832 (1964). (c) L. L. Bambas in "The Chemistry of Heterocyclic Compounds," Vol. 4, A. Weissberger, Ed., Interscience Publishers, Inc., London and New York, 1952, p. 278.

(9a) S. J. Childress and T. Baum, U. S. Patent, 3,164,602. (b) Y. Nitta, M. Shindo, T. Takasu and C. Isono, *Yakugaku Zasshi*, 84, 493 (1964).

(10) I. Remsen and A. P. Saunders [*Amer. Chem. J.*, 17, 354 (1895)], who prepared this compound in a different manner, report a melting point of 96-97°.

Received May 22, 1968 Kalamazoo, Mich. 49001