[CONTRIBUTION FROM THE ORGANIC CHEMICAL RESEARCH SECTION, LEDERLE LABORATORIES DIVISION, AMERICAN CYANAMID CO., PEARL RIVER, N. Y.]

Sulfamoyl Chloride, Sulfamides and Sulfimide

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The use of sulfamoyl chloride to prepare a new heterocyclic ring system, 1H-2,1,3-benzothiadiazin-4(3H)-one 2,2-dioxide, has been illustrated with various anthranilic acid derivatives. The cleavage of *o*-nitrophenylsulfamide has been investigated in detail. Mechanistic considerations and kinetic studies are included in the discussion concerning the solvolytic and transfer reactions of this sulfamide.

The discovery of the heretofore unobtainable sulfamoyl chloride, NH_2SO_2Cl, by Graf,[1] prompted us to investigate the applications of this novel sulfamoylating agent. The first part of this paper details the reactions of sulfamoyl chloride with aromatic amines, leading in one series to a novel heterocyclic system. The second portion is concerned with the mechanism and kinetic study of an unusual cleavage of a sulfamide. This aspect has been utilized in the trapping of sulfimide, $NHSO_2$, by aromatic amines.

Sulfamoyl chloride (*1*) was prepared as[1c]

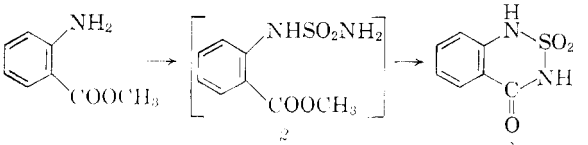
$$SO_3 + CNCl \longrightarrow O{=}C{=}NSO_2Cl \xrightarrow{H_2O} \underset{1}{H_2NSO_2Cl}$$

Appel and Senkpiel[2] have used *1* to form sulfamic esters by the reaction

$$H_2NSO_2Cl + NaOR \longrightarrow H_2NSO_3R + NaCl$$
$$R = \text{lower alkyl}$$

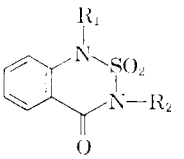
The same authors have also reported[3] the preparation of sulfamoyl fluoride, H_2NSO_2F. Most of the reactions of sulfamoyl chloride with amines have been reported by Graf,[1c] who prepared a series of *p*-substituted sulfamides.

Our initial efforts utilized methyl anthranilate with sulfamoyl chloride to give the intermediate ester *2*. This ester was difficult to purify and in subsequent experiments the crude material was dissolved in base and acidified to yield 1H-2,1,3-benzothiadiazin-4(3H)-one 2,2-dioxide (*3*).



2 *3*

This new heterocycle is highly acidic (dissolves readily in sodium bicarbonate solution) and can be monoalkylated with methyl sulfate at room temperature to form *4*, or dialkylated with excess methyl sulfate to yield *5*.



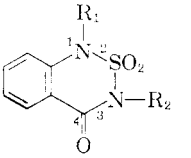
4, $R_1 = H$, $R_2 = CH_3$
5, $R_1 = R_2 = CH_3$
6, $R_1 = CH_3$, $R_2 = H$

(1) (a) German Patent 937,645, Farbwerke Hoechst A. G. (1956); (b) German Patent 947,554; *C. A.*, **51**, 4426 (1957); (c) R. Graf, *Ber.*, **92**, 509 (1959).
(2) R. Appel and W. Senkpiel, *Angew. Chem.*, **70**, 504 (1958).
(3) Reference 2, p. 572.

The N^1-methyl compound *6* was prepared by the reaction of methyl N-methylanthranilate with sulfamoyl chloride, followed by cyclization with base; *5* can also be prepared from *4* or *6* by alkylation with methyl sulfate.

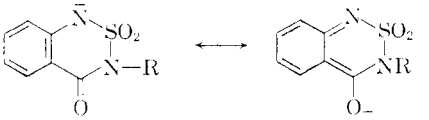
Confirmation of the assigned structures was obtained by a study of the ultraviolet spectra of the compounds in basic and neutral (ethanol) media.

SUBSTITUTED 2,1,3-BENZOTHIADIAZIN-4(3H)-ONE-2,2-DIOXIDES



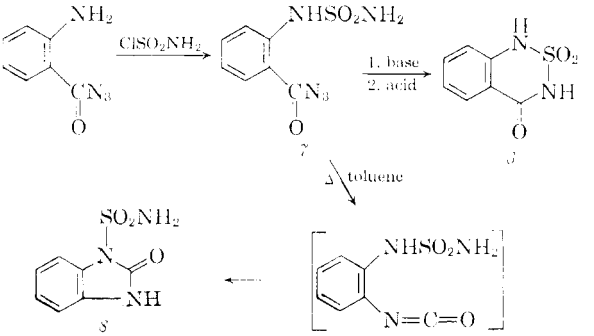
R_1	R_2	λ_{max}, mμ (ε) ethanol	λ_{max}, mμ (ε) base	μ
H	H	312 (2400)	345 (3560)	2.9, 3.6
CH_3	CH_3	305 (1810)	305 (1810)	...
CH_3	H	320 (2200)	315 (2960)	3.6
H	CH_3	315 (2040)	340 (3220)	3.0

There is a decided bathochromic shift observed in base with the compounds bearing a hydrogen on N^1, presumably due to an extension of conjugation through the ring



The last column shows the observed bands in the N–H stretching region of the infrared. The 3.6 μ band is unusually high but in this series, at least, it served as an empirical method of assigning structure.

Another synthesis of *3* was accomplished by treating anthranilazide with sulfamoyl chloride in benzene, followed by base and acid treatment. However, if the intermediate sulfamide azide *7* was isolated before base treatment and refluxed in

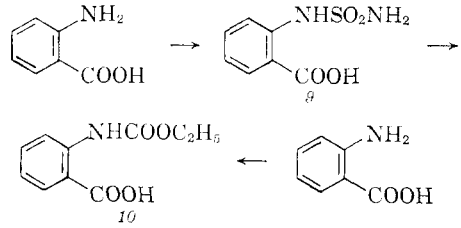


7 *3* *8*

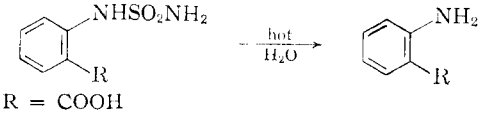
toluene, a Curtius rearrangement occurred, followed by cyclization of the isocyanate to yield N-sulfamoylbenzimidazolone (8).

Compound *8* hydrolyzes readily in hot water to form benzimidazolone. This type of cleavage occurred readily with a variety of sulfamide compounds.

When anthranilic acid was treated with sulfamoyl chloride, a good yield of N-sulfamoylanthranilic acid (*9*) was obtained. In an attempt to amidate *9* by the mixed carbonic-carboxylic acid anhydride procedure, an unexpected product formed which contained *no* sulfur. From the analysis ($C_{10}H_{11}NO_4$), melting point and infrared spectrum a reasonable possibility was N-carbethoxyanthranilic acid (*10*). This, indeed, was verified by a comparison of the infrared curve of *10* with that of the authentic compound prepared by an alternative literature method.[4]



N-Sulfamoylanthranilic acid (*9*) in contrast to phenylsulfamide (*11*) is unstable to boiling water and cleaves readily to form anthranilic acid. The same facile splitting was noticed when *o*-nitrophenylsulfamide (*12*) prepared from *o*-nitroaniline



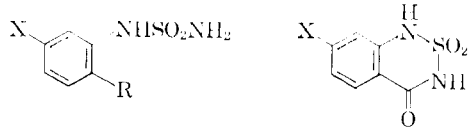
9, R = COOH
11, R = H
12, R = NO_2
13, R = NH_2

R = COOH or NO_2

and sulfamoyl chloride, was treated with hot water.[5] This "cleavage" reaction will be discussed in detail shortly.

o-Aminophenylsulfamide (*13*) was formed by catalytic reduction of the nitro compound *12*.

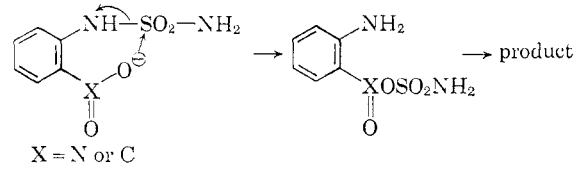
To extend the study of reactions of sulfamoyl chloride with anthranilic acid derivatives, methyl 4-chloroanthranilate and anthranilamide were used



14, X = Cl, R = $COOCH_3$ *16*, X = Cl
15, X = H, R = $CONH_2$ *3*, X = H

to prepare their respective sulfamides *14* and *15*. Basic cyclization of *14* yielded *16*, and similarly *15* afforded *3*.

In order to elucidate the mechanism of the previously mentioned "cleavage" reaction, experiments were run to determine the effect of *p*-substituents on the phenylsulfamides. This could confirm or deny the role of any direct participation of the *ortho* functional groups, as



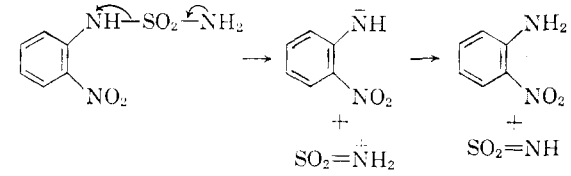
X = N or C

We were unable to prepare the *p*-carboxyphenylsulfamide, but *p*-nitrophenylsulfamide (*17*) was obtained by the usual procedures. This, indeed, did cleave to form *p*-nitroaniline, but at a slower rate than the *o*-isomer. Therefore, it is probably a question of the inductive effect of the nitro groups rather than an internal displacement.[6]

The instability and high reactivity of N-carbamoyl or N-acetyl heterocycles is well documented, but very little is known of the N-sulfamoyl compounds.[7]

It does not seem reasonable that any of the "cleavage" reactions occurs by direct nucleophilic displacement (SN2) on sulfur, since the analogous ureas are stable.[5a,8]

Another possible mode of cleavage is:



This is similar to the observation by Staab[7b] that 1-benzimidazolecarboxanilide (a) dissociates into benzimidazole and phenyl isocyanate at room temperature in chloroform.

(4) V. Niementowski and A. Rozanski, *Ber.*, **22**, 1674 (1889).

(5) (a) This behavior of sulfamide groups is quite different from the corresponding substituted ureas. One can recrystallize *o*-nitrophenylurea from hot water; under the same conditions N-carbamylanthranilic acid cyclizes to benzoylene urea [M. T. Bogert and G. Scatchard, *J. Am. Chem. Soc.*, **41**, 2052 (1919)]. (b) There is a statement in a review article by L. F. Audrieth, *et al.* [*Chem. Revs.*, **26**, 69 (1940)] that when arylsulfamides have nitro groups attached to the ring "the resulting sulfamide is easily split by hydrolysis." There is no reference given to the preparation of these compounds nor did a search of the literature reveal any such compounds. It is not clear from the article which substituents, if any, are on the sulfamide side chain. As will be shown, substitution does affect the rate of hydrolysis.

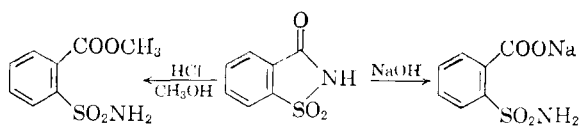
(6) The reason that *17* cleaves slower than *12* may be related to the base strengths of the amines. o-Nitroaniline is a much weaker base than the *p*-isomer [M. A. Paul, *J. Am. Chem. Soc.*, **76**, 3236 (1954)]: pK_a (*ortho*) −0.25; pK_a (*para*) +1.0. Since the resonance structures are the same for both compounds, the inductive effect appears to be the decisive factor.

(7) (a) In "Heterocyclic Compounds," John Wiley & Sons, Inc., New York, N. Y.,Vol. V, ed. R. C. Elderfield, 1957, p. 97, 183, 433, examples are cited of the instability of acyl derivatives of pyrazole, indazoles and benzoxazolones; (b) W. Otting and H. A. Staab, *Ann.*, **622**, 23 (1959), and references cited therein.

(8) (a) J. H. Brewster and C. J. Ciotti, *J. Am. Chem. Soc.*, **77**, 6214 (1955). Carbonyls in general are more electrophilic than sulfonyls as illustrated by the fact that the reaction of benzoic acid and benzenesulfonyl chloride in pyridine, followed by aniline, afforded benzanilide in 97% yield.

$C_6H_5COOH \longrightarrow C_6H_5COOSO_2C_6H_5 \longrightarrow C_6H_5CONHC_6H_5$

(b) "The Organic Chemistry of Sulfur," ed. C. M. Suter, John Wiley and Sons, Inc., New York, N. Y., 1944, p. 623, shows another example with saccharin.



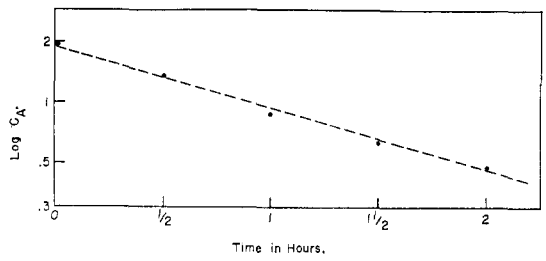
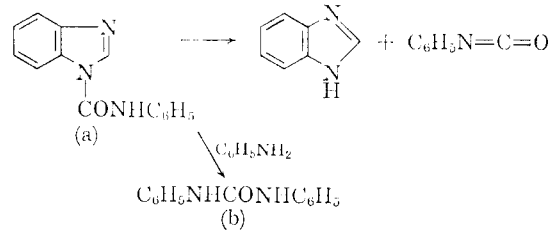


Fig. 1.—Rate of decomposition of *o*-nitrophenylsulfamide, A, in 1% aqueous ethanol at 50°; $k = 1.71 \times 10^{-4}$ sec.$^{-1}$.

In addition, (a) was treated with aniline to form diphenylurea (b).[9]



In order to distinguish between an initial proton removal, followed by elimination of $NH{=}SO_2$, and the mechanism suggested above (loss of $\overset{+}{N}H_2{=}$

TABLE I

RATE OF DECOMPOSITION OF *o*-NITROPHENYLSULFAMIDE IN VARIOUS SOLVENTS

Solvent	Temp., °C.	Dielectric constant (temp., °C.)	Rate, $k \times 10^4$ sec.$^{-1}$
Abs. ethanol	50	20.87 (50)	1.04
1% aq. ethanol	50	~21 (50)	1.70
5% aq. ethanol	50	~22.5 (50)	2.71
10% aq. ethanol	50	24.1 (50)	5.43
1% aq. ethanol	34	24.3 (25)	0.37
1% aq. ethanol	68		9.31
1% aq. *t*-BuOH	50	~11 (30)	1.38
1% aq. dioxane	50	~ 3 (25)	No reacn.
5% aq. dioxane	50		1.27
Benzene	50	2.28 (20)	No reacn.
Nitrobenzene	60	35.7 (20)	No reacn.
Nitromethane	80	37.5 (20)	No reacn.
Dimethylformamide	60	37.6 (20)	No reacn.
2% aq. D.M.F.	60		Slow
1% 1 *N* NaOH in EtOH	50		No reacn.
100% 1 *N* NaOH	25		No reacn.
1% 3 *N* HCl in EtOH	50		3.34
1% 12 *N* HCl in EtOH	50		3.54
0.01 *M* α-pyridone in MeOH	50		1.42
1% pyridine in EtOH	50		1.04
Gl. acetic acid	25	6.15 (20)	No reacn.
1 g. NaAc in 99 ml. of EtOH	50		0.35
1 g. phenol in 99 ml. EtOH	50		0.65
100% formamide	50	109 (20)	1.63
1 ml. formamide in 99 ml. EtOH	50		0.50
100% N-methylformamide	50	190.5 (20)	3.98

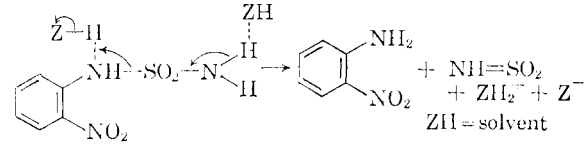
(9) Recently, F. L. Scott, C. E. Schaumann and J. P. King, *J. Org. Chem.*, **26**, 985 (1961), described the thermal rearrangement of diphenylsulfamide, $C_6H_5NHSO_2NHC_6H_5$, to *p*-$NH_2C_6H_4SO_2NHC_6H_5$. The authors presented evidence for the involvement of "sulfamylonium" ions $(RNHSO_2)^+$.

SO_2), the following experiment was run. N,N-Diethyl-*o*-nitrophenylsulfamide (*18*) was prepared and subjected to the same hydrolytic conditions. No cleavage occurred, and therefore it can be assumed that at least one hydrogen on the terminal nitrogen is necessary for the reaction.

To learn more about this system, it was decided to study the kinetics of the decomposition of *o*-nitrophenylsulfamide (*12*). The equations that were used and the methods for following the reaction are outlined in the Experimental section. Briefly, the change in the concentration of the starting material was determined by following the formation of *o*-nitroaniline in the visible spectrum (400 mμ) at fixed time intervals. The results, using various solvents, are listed in Table I.

From this table the important features observed are: (1) first-order or pseudo-first order kinetics (see Fig. 1); (2) the unreactivity of *12* in non-aqueous or non-alcoholic solvents of high dielectric constant (*e.g.*, nitrobenzene, nitromethane and dimethyl formamide); (3) the absence of catalysis with mineral acid; (4) the complete inhibition of reaction in aqueous base; (5) the increase in the rate with higher percentages of water in the ethanol.

At this point, it appeared that it was necessary to have a basic atom (oxygen or nitrogen) removing a proton from the terminal nitrogen, while the anilino nitrogen was being solvated. This type of solvolytic reaction might be illustrated as



The evidence in favor of this was: (1) The necessity of having a hydrogen atom on the terminal nitrogen (the N,N-diethyl compound is stable). (2) The *o*-nitro group weakens the $-NH-SO_2-$ bond, but the reaction does go with a *p*-nitro group ($k = 0.84 \times 10^{-4}$ sec.$^{-1}$ at 60° in 50% ethanol). (3) Dimethylformamide cannot solvate the anilino nitrogen; therefore, there is no reaction (N-methylformamide, however, is effective); (4) Strong aqueous base can completely ionize the more acidic hydrogen on the anilino nitrogen, thereby, preventing the cleavage of the $>N-SO_2-$ bond ($>\bar{N}-SO_2-NH_2$). (5) In acid media, the reaction should be enhanced and this is observed (Table I). When more acid is added, there is no further rate increase, and, therefore, the effect of acidity on the kinetics is negligible.

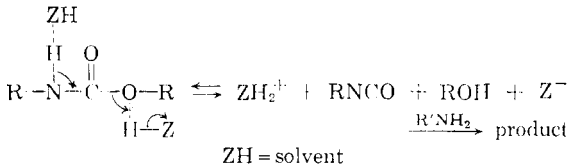
Hammett has observed a pseudo-first-order reaction in the alcoholysis of benzhydryl chloride which shows a steady increase in rate as water is added to alcohol. This was shown to be independent of the dielectric constant and was pictured as a polymolecular solvolytic reaction.[10]

Mukaiyama and Iwanami observed a similar phenomenon in the thermal dissociation of urethanes in amine solvents, and wrote the equations[11]

(10) N. T. Farinacci and L. P. Hammett, *J. Am. Chem. Soc.*, **59**, 2542 (1937).

(11) T. Mukaiyama and M. Iwanami, *ibid.*, **79**, 73 (1957).

$$RNHCOOR \longrightarrow [RN{=}C{=}O] \xrightarrow{R'NH_2} RNHCONHR'$$



These authors measured the energy of activation (E) and entropy of activation ($\Delta S^{\ddagger}$) in a series of compounds. The $\Delta S^{\ddagger}$ values ranged from -20 to -37 e.u. These high negative entropy values are indicative of strain or rigidity in the transition state caused by solvent interactions.

In our case, we were able to obtain an E value of 20,100 cal. by plotting the rate values in 99% ethanol at various temperatures (Table I) against the reciprocal of the absolute temperature (see Fig. 2). The gradient of this plot determines the activation energy.

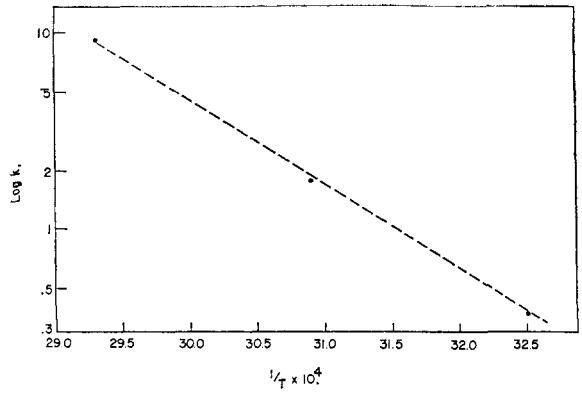
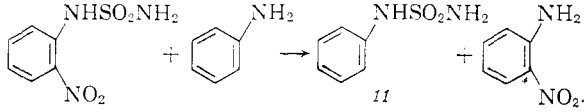


Fig. 2.—Rate of decomposition of *o*-nitrophenylsulfamide in ethanol as a function of temperature; activation energy determined from the slope.

From the theory of absolute reaction rate, the $\Delta S^{\ddagger}$ was obtained by substituting the proper terms in the Boltzmann equation.[12] The value found for $\Delta S^{\ddagger}$ was -13.6 e.u. This large negative value is consistent with the mechanism proposed.

The interpretation of the kinetics became more complicated when the reaction was run in an unreactive solvent (benzene or dimethylformamide) using aniline or dimethylaniline as the base. In the case of aniline, the products isolated in high yield from the reaction were phenylsulfamide (*11*) and *o*-nitroaniline.



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Using dimethylaniline, *o*-nitroaniline and an inorganic material were the products. (The nature of the inorganic material will be discussed later.)

The results of these kinetic runs are listed in Table II.[13]

An inspection of runs 1 and 3 (Table II) shows immediately that a simple first-order reaction is

(12) "Textbook of Physical Chemistry," S. Glasstone, D. Van Nostrand Co., Inc., New York, N. Y., 1940, p. 1082.

(13) Additional examples of the trapping of sulfimide, $NHSO_2$, are presented at the end of this section.

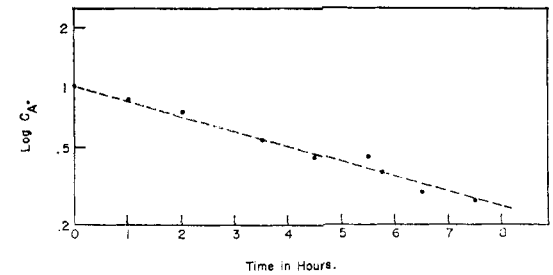


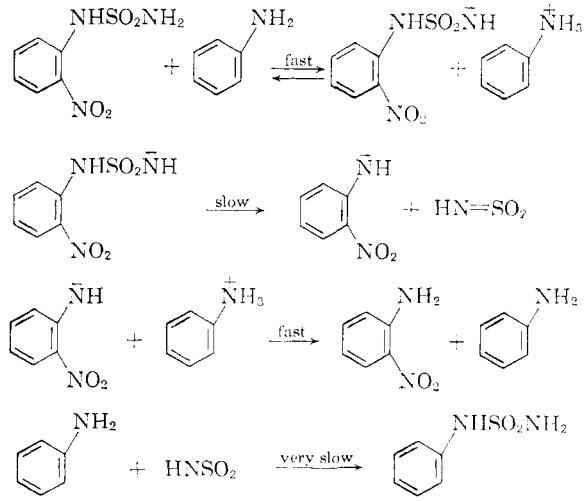
Fig. 3.—Rate of decomposition of *o*-nitrophenylsulfamide, A, in the presence of an equivalent amount of aniline, B; $k = 5.12 \times 10^{-5}$.

not present. (The rate should be independent of the concentration of the starting material.) However, a straight line was always obtained when log A was plotted *versus* the time (see Fig. 3). A comparison of runs 1 through 4 appears to indicate a second-order reaction. (Half the concentration of A or B decreased the rate by approximately one-half.) However, the data did not fit a second or higher order rate expression.

How then could the aniline be consumed to form the product (phenylsulfamide) while its concentration factor does not appear in the rate expression? One possibility is an autocatalytic reaction whereby the products effect the decomposition of the starting material. This solution was eliminated by the observation that the reaction stopped at 50% of completion when one-half an equivalent of aniline was used (run 2).

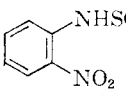
A second possibility, though remote, was that *o*-nitroaniline or phenylsulfamide could compete favorably with aniline as a nucleophile to continue the first-order reaction as the aniline was being used up. Since no reaction occurred when either product was added to the starting material in the absence of aniline, this explanation could not be correct.

A third possibility can be illustrated as



For these equations to fit first-order kinetics, one would have to assume that the reaction of aniline with sulfimide was the slowest step, but the concentration of aniline did not enter into the kinetics because the reaction is followed only until the formation of *o*-nitroaniline. The net effect

TABLE II

RATE OF REACTION OF  WITH VARIOUS BASES AT 67°

A

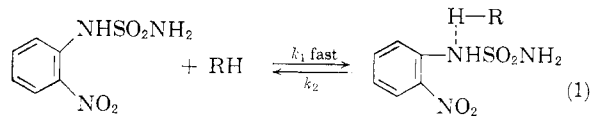
Run	Concn. of A, mole/liter	Base B	Concn. of B, mole/liter	Solvent	Rate, $k \times 10^5$ sec.$^{-1}$	Half-life ($t_{1/2}$), sec.
1	0.0184	Aniline	0.0184	Benzene	5.12	14,220
2	.0184	Aniline	.0092	Benzene	2.41[a]	27,900
3	.0092	Aniline	.0184	Benzene	2.18	31,500
4	.0092	Aniline	.0092	Benzene	1.30	55,800[d]
5	.0184	Aniline	.107	Benzene	16.7	4,080
6	.0184	Aniline and *o*-nitroaniline	.0184 .0184	Benzene	2.26	
7	.0184	Aniline and phenylsulfamide	.0184 .0184	Benzene	6.25	
8	.0092	Aniline and *o*-nitroaniline and phenylsulfamide	.0092 .0092 .0092	Benzene	2.58 (2.47)[e]	
9	.0184	Aniline	.0184	Dimethylformamide	2.68	
10	.0092	Aniline	.0184	Dimethylformamide	4.74	
11	.0184	Aniline	.107	Dimethylformamide	7.31	
12	.0184	N,N-Dimethylaniline	.0184	Benzene	6.42[b]	
13	.0184	N,N-Dimethylaniline	.184	Benzene	Erratic[c]	1,020

[a] The reaction stopped at 50% of completion. [b] The reaction was very slow after 50% of completion. [c] The data did not fit a simple first- or second-order plot. [d] An extrapolated value from the straight line. [e] This is a duplicate run using the same concentrations of all the substituents.

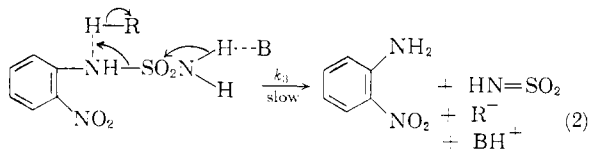
would be that the concentration of aniline remains constant throughout any one run. (Aniline functions as a catalyst.)

This interpretation does not explain the precipitation of phenylsulfamide that occurred when the reaction mixture from one run was cooled after completion. It is unreasonable to expect aniline and sulfimide to remain unreacted for several hours and then suddenly condense. Therefore, the above argument is untenable.

A variation of this explanation that assumes the *base* concentration to remain constant during any one run was postulated by Albright and Snyder in their study on the reactions of indole Mannich bases.[14] In our case, the reactions would be



(1)



(2)

$$C_6H_5NH_2 + HN{=}SO_2 \xrightarrow{\text{fast}} C_6H_5NHSO_2NH_2 \qquad (3)$$

$$\text{rate} = k_3 K_{eq} [A] [B] [RH]$$

where $K_{eq} = k_1/k_2$, A = *o*-nitrophenylsulfamide, B = aniline or the anion of the starting material (R^-) or the anion of the product ($C_6H_5NHSO_2\bar{N}H$) and RH = another molecule of the starting material or the product itself.

To obtain a first-order plot, the following assumptions are necessary: (1) RH would remain constant since a mole of product is formed for each mole of starting material consumed. (2) By assigning several possible compounds to act as the base, it is conceivable that there is no net change in the effective concentration of the base. As the aniline is being removed, phenylsulfamide (RH) is being formed and it can form a hydrogen bond with the starting material. In step 2, each decomposition of A forms the anion R^-, and the process continues.

Using these definitions, pseudo-first-order kinetics would be obtained. The rate would be faster for any run if the concentration of A or B were increased. This is borne out in the data. Hydrogen bonding in benzene solution is a reasonable assumption, and, in fact, might explain the reaction being faster in benzene than in dimethylformamide (compare runs 1 and 9).

The addition of phenylsulfamide (RH) to the starting material (run 7) does show an increase in rate compared to run 1. It is even more pronounced in the less concentrated reaction (compare runs 4 and 8).

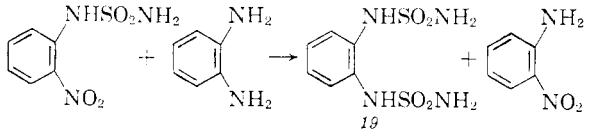
The inhibition of the reaction with added *o*-nitroaniline (run 6) is difficult to explain. The effect may be due to a complex formation of *o*-nitroaniline with aniline or to the dissipation of the charge on $C_6H_5NHSO_2\bar{N}H$ by proton transfer from *o*-nitroaniline before it can react further. At lower concentration (run 8) this effect disappeared.

The anomaly of run 8 having a rate constant of approximately one-half of run 1 is still perplexing. Obviously, at the half-life of run 1, the conditions of run 8 should apply. Perhaps, the rate "constants" are indeed multiples of the true constant and the concentration. For any one run, the observed constant would be a function of the initial concentration of the reactants, and a pseudo-

(14) J. D. Albright and H. R. Snyder, *J. Am. Chem. Soc.*, **81**, 2239 (1959).

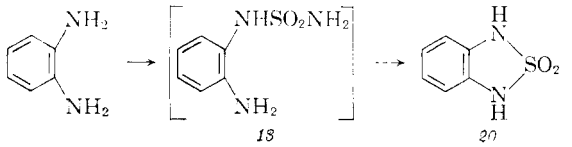
first-order reaction is obtained. *In any case, it seems eminently reasonable that one must postulate a transitory existence of sulfimide to explain these results.*

An extension of the transfer reaction by the trapping of sulfimide was accomplished with *o*-phenylenediamine to form the bis-sulfamoyl compound *19*.



19

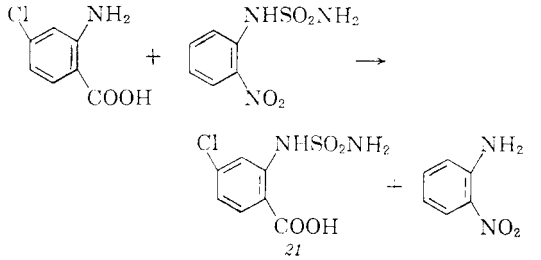
The yield of *19* was not very high (36%) and the evolution of ammonia was noticed during the reaction. It was suspected that the low yield of bis compound was due to a cyclization to 2,1,3-benzothiadiazole-2,2-dioxide (*20*) but no other crystalline product could be isolated.



13 *20*

Attempted cyclization of authentic *13*, prepared previously, under a variety of conditions proved unsuccessful. In most cases, ammonia was evolved, but no evidence of the desired product was obtained.[15]

Also, after several attempts to treat 4-chloroanthranilic acid with sulfamoyl chloride proved unsuccessful, the desired compound 4-chloro-N-sulfamoylanthranilic acid (*21*) was finally obtained, by an exchange reaction with the acid and o-nitrophenylsulfamide. By analogy with the preceding reactions, this is believed to proceed *via* sulfimide.



21

An interesting reaction occurred when *o*-nitrophenylsulfamide (*12*) was refluxed in benzene with an equivalent amount of benzoic acid; 12 decomposed to form *o*-nitroaniline and an inorganic material. Sulfimide and benzoic acid did not react as expected to form benzenesulfonamide.[16]

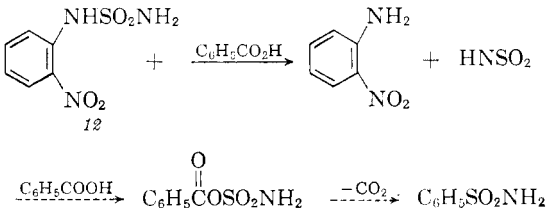
(15) Structurally, the ring system appears capable of existence but *20* has never been prepared previously. The closest analogy in the

i

literature is the deoxy compound, piazthiole (i) reported by O. Hinsberg, *Ber.*, **22**, 2899 (1889), and subsequent investigators.

(16) A similar reaction has been reported [*Chem. Zentr.*, **128**, 6265 (1957); German Patent 946,710].

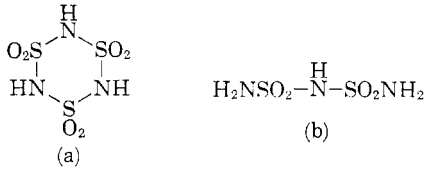
$$R_2NCOCl + ClSO_3H \longrightarrow R_2NCOOSO_2Cl \longrightarrow R_2NSO_2Cl$$



12

The other reaction product was a water-soluble inorganic solid, m.p. 315°. It was strongly acidic and gave a positive barium sulfate test as well as a precipitate with ethanolic silver nitrate. The high melting solid did not give a satisfactory analysis but contained mainly sulfur, nitrogen, oxygen and hydrogen (only 1% carbon was found).

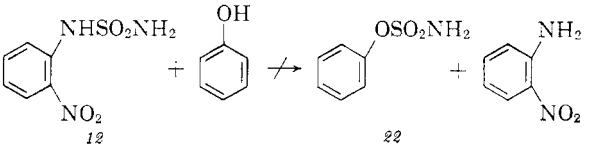
Several inorganic nitrogen–sulfur compounds have been prepared previously by other workers, but in most cases the materials were difficult to purify and consequently to analyze. The most likely possibilities for the above product, trisulfimide (a) and imidosulfamide (b) are reported to melt at 161° and 167°, respectively.[17]



(a) (b)

Another inorganic solid (m.p. 243–245°), whose structure has not been determined, was formed by the previously mentioned reaction of N,N-dimethylaniline and *12*. This substance was also water soluble, acidic and gave a positive test with barium sulfate. The infrared spectrum of the material was not very informative, but differed from that of the solid, m.p. 315°.

No reaction occurred when *12* was refluxed in benzene with an equivalent of phenol. The desired sulfamic ester *22* is not known, but the chlorosulfonylphenyl ester $ClSO_2OC_6H_5$ has been prepared.[18]



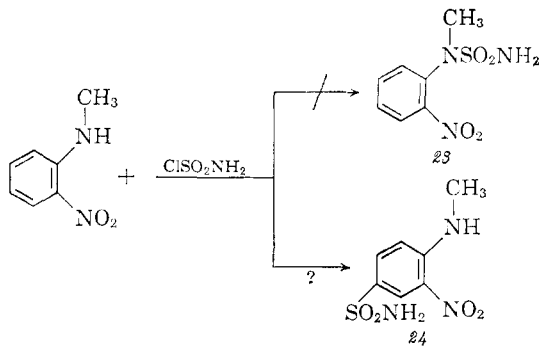
12 *22*

In an attempt to prepare N′-methyl-*o*-nitrophenylsulfamide (*23*) by treating N-methyl-*o*-nitroaniline with sulfamoyl chloride, an orange solid was isolated. This compound analyzed correctly for $C_7H_9N_3SO_4$, but from an examination of its infrared and ultraviolet spectra it is believed to be an isomer of the desired product. The spectral data are very similar to 3-nitrosulfanilamide and hence structure *24* has been tentatively assigned.

(17) (a) A. Hantzsch and A. Holl, *Ber.*, **34**, 3430 (1901); (b) A. V. Kerzanov and Yu. M. Zolotov, *C. A.*, **45**, 1451[b] (1951); (c) R. Appel and M. Goehring, *Z. anorg. allgem. Chem.*, **271**, 171 (1953), prepared $(AgNSO_2)_3$.

(18) "Stickstoff-Verbindungen II/III," Houben-Weyl, Vol. 11, Part 2, 1960, p. 695. When chlorosulfonylphenyl ester is treated with an amine, phenol is liberated and a sulfamide is formed, not the sulfamic ester.

$$R_2NH + ClSO_3C_6H_5 \longrightarrow R_2NSO_2NR_2 + C_6H_5OH$$



Acknowledgment.—We wish to thank Drs. E. F. Ullman and A. S. Kende for their valuable suggestions and helpful discussions during the course of this work. We also wish to express our appreciation to Mr. L. Brancone and his staff for the microanalytical results and to Dr. H. G. Arlt, Jr., and his group for the preparation of large quantities of sulfamoyl chloride, and to Mr. C. Pidacks and his group for the purification of compound *21*.

Experimental[19]

1H-2,1,3-Benzothiadiazin-4(3H)-one 2,2-Dioxide (3).—A 4.0-g. (0.026 mole) sample of methyl anthranilate was dissolved in 10 ml. of benzene and added rapidly to a stirred solution of 1.5 g. (0.013 mole) of sulfamoyl chloride in 10 ml. of benzene at 10°. A gum formed immediately, and after 2 minutes, 20 ml. of 6 *N* sodium hydroxide was added. The aqueous layer that formed was separated and acidified with concentrated hydrochloric acid. Upon cooling the mixture, a white crystalline solid precipitated and was filtered off. The crude yield was 2.0 g. (66%). The product is completely soluble in sodium bicarbonate.

A small amount of the product was purified by dissolving in base and reprecipitating with acid; m.p. 228–230°. In the infrared, bands at 5.9 (carbonyl), 7.5 and 8.6 μ (sulfonamide) were observed.

Anal. Calcd. for $C_7H_6N_2SO_3$: C, 42.5; H, 3.02; N, 14.1; S, 16.2. Found: C, 42.6; H, 3.32; N, 14.0; S, 16.5.

An alternative synthesis of *3* was accomplished by using anthranilazide in place of the ester under the same reaction conditions.

Or thirdly, a sample of 0.20 g. (0.00093 mole) of N-sulfamoylanthranilamide (*15*) was dissolved in 5 ml. of 1 *N* sodium hydroxide and heated on the steam-bath for 4.5 hours. Ammonia was evolved during this period. After cooling the solution and acidifying it, 0.10 g. (55%) of off-white fibers precipitated, m.p. 218°. The infrared spectrum of the product was identical with that of an authentic sample of 1H-2,1,3-benzothiadiazin-4(3H)-one-2,2-dioxide.

The same product was obtained when the acidic mother liquors from the original preparation of (*15*) were concentrated *in vacuo*

1H-2,1,3-Benzothiadiazin-4(3H)-one-3-methyl 2,2-Dioxide (4).—A mixture of 2.0 g. (0.010 mole) of *3* in 40 ml. of sodium bicarbonate and 1.5 g. (0.010 mole) of methyl sulfate was stirred for 3 hours at room temperature. A small amount of solid (0.080 g.) was filtered off; m.p. 95–99°. This proved to be the dimethyl compound.

The filtrate was acidified to form 1.3 g. (62%) of an off-white solid, m.p. 155–160°. This material was recrystallized from ethanol–water and then from base and acid. The purified product, m.p. 201–203°, still retained a trace of color.

Anal. Calcd. for $C_8H_8N_2SO_3$: C, 45.2; H, 3.77; N, 13.2; S, 15.1. Found: C, 45.1; H, 3.91; N, 12.8; S, 15.0, 14.9.

(19) All melting points are uncorrected. Infrared spectra were taken as mineral oil mulls with a Perkin-Elmer Infracord. Ultraviolet spectra were taken with a Cary recording spectrophotometer, No. 11.

1-H-2,1,3-Benzothiadiazin-4(3H)-one-1,3-dimethyl 2,2-Dioxide (5). (a).—A 0.50-g. (0.0025 mole) sample of *3* was dissolved in 10 ml. of sodium bicarbonate and stirred at room temperature with 1.0 ml. (0.010 mole) of methyl sulfate. While the reaction was progressing a solid began precipitating. After 3 hours, the crude solid was filtered off; 0.35 g. (62%) was obtained, m.p. 85–95°.

A small amount of the solid was recrystallized from ethanol–water; m.p. 98–100°.

Anal. Calcd. for $C_9H_{10}N_2SO_3$: C, 47.8; H, 4.43; N, 12.4; S, 14.2. Found: C, 47.5; H, 4.89; N, 12.1; S, 14.4.

(b).—The monomethyl compound *4* (2.1 g., 0.010 mole) was dissolved in 40 ml. of 10% sodium bicarbonate and treated with 4.6 g. (0.0030 mole) of methyl sulfate. After stirring the mixture for 3 hours at room temperature, 1.3 g. (56%) of an off-white solid was filtered off, m.p. 96–98° (eff.). Acidification of the filtrate yielded 0.60 g. of the starting material. An infrared spectrum of the base-insoluble material was identical with that of the product from method a.

1H-2,1,3-Benzothiadiazin-4(3H)-one-1-methyl 2,2-Dioxide (6).—A solution of 0.58 g. (0.0050 mole) of sulfamoyl chloride in 10 ml. of benzene was stirred at 10° during the addition of 1.7 g. (0.010 mole) of methyl N-methylanthranilate in 5 ml. of benzene. An opaque liquid and an oil formed. After stirring the mixture at 10° for 10 minutes and 20° for 20 minutes, 20 ml. of 5 *N* sodium hydroxide was added. Two layers formed and were separated. The benzene layer was extracted with two 5-ml. portions of 1 *N* sodium hydroxide which were then combined with the aqueous layer. Upon acidification of the solution, 0.65 g. (59%) of white solid precipitated, m.p. 204–207°.

A 0.40-g. sample was purified by dissolving in sodium bicarbonate and reprecipitating with acid. A fine white powder formed; 0.30 g., m.p. 205–208°.

Anal. Calcd. for $C_8H_8N_2SO_3$: C, 45.2; H, 3.77; N, 13.2; S, 15.1. Found: C, 45.2; H, 3.92; N, 13.0; S, 15.2.

N-Sulfamoylbenzimidazolone (8).—A mixture of 6.4 g. (0.055 mole) of sulfamoyl chloride in 125 ml. of benzene and 8.0 g. (0.055 mole) of anthranilazide in 75 ml. of benzene was stirred at 10–15° for 1 hour. The flask was then warmed on the steam-bath and scratched to yield a yellow solid. After filtering off the product, it was washed with water to remove salts, filtered, and triturated with a small amount of cold ethanol. An off-white solid, 4.3 g. (32%), resulted. The azide explodes on heating at 130°.

The intermediate azide (4 g.) was refluxed with 100 ml. of toluene for 2 hours. After cooling the mixture, a light tan solid was filtered off. This material, 3.7 g., was a mixture of product and starting material. By taking advantage of the acidity of the sulfonamide group, it was possible to extract the product from the mixture with an ice-cold 10% sodium carbonate solution. A rapid acidification of the solution afforded 2.2 g. (62%) of white needles, m.p. 182–183°. If the carbonate solution was not acidified after 5 minutes, extensive cleavage occurred.

Anal. Calcd. for $C_7H_7N_3SO_3$: C, 39.5; H, 3.29; N, 19.7; S, 15.0. Found: C, 39.2, 39.9; H, 3.63, 3.57; N, 19.6, 19.3; S, 14.3, 14.6.

N-Sulfamoylanthranilic Acid (9).—A sample of 6.9 g. (0.050 mole) of anthranilic acid was dissolved in 150 ml. of dry ether and stirred at ice temperature while 5.8 g. (0.050 mole) of sulfamoyl chloride in 100 ml. of dry benzene was added rapidly. After 45 minutes, during which time a white solid precipitated, the reaction mixture was treated with 10 ml. of 3 *N* sodium hydroxide. Two layers formed and were separated. The benzene layer was washed with dilute base and all of the aqueous fractions were combined and acidified. A white precipitate formed; 6.1 g. of crude product.

All of this solid was dissolved in sodium bicarbonate and reprecipitated with dilute hydrochloric acid. The yield of pure product was 5.1 g. (47%). A small sample was purified by the same procedure and sent for analysis; m.p. 167°.

Anal. Calcd. for $C_7H_8N_2SO_4$: C, 38.9; H, 3.71; N, 12.9; S, 14.8. Found: C, 38.9; H, 4.03; N, 13.0; S, 14.8.

N-Carbethoxyanthranilic Acid (10).—A 1.0-g. (0.0046 mole) sample of N-sulfamoylanthranilic acid was dissolved

in 10 ml. of dry dimethylformamide and stirred at −5° with 0.80 g. (1.1 ml., 0.0046 mole) of tri-*n*-butylamine. To this mixture was added 0.50 g., 0.45 ml. (0.0046 mole) of ethyl chlorocarbonate. After stirring the reactants for 5 minutes, 5 ml. of ice-cold concentrated ammonium hydroxide was introduced fairly rapidly. (Subsequent experiments yielded the same results with the addition of water instead of ammonia.) The mixture was stirred for 20 minutes at ice temperature and 60 minutes at room temperature and then it was evaporated to dryness. The gummy residue was dissolved in dilute sodium hydroxide, extracted with ether, and then the aqueous layer was acidified to yield 0.60 g. (62.5%) of light yellow crystals.

The solid was purified by dissolving in sodium bicarbonate and reprecipitating with dilute acid; m.p. 123–125°. A recrystallization from hot water did not raise the melting point.

Anal. Calcd. for $C_{10}H_{11}NO_4$: C, 57.4; H, 5.26; N, 6.70. Found: C, 57.1; H, 5.30; N, 6.86.

An alternate literature preparation[4] of the product, N-carbethoxyanthranilic acid, afforded a solid, m.p. 121–123°, which did not depress the melting point of the material described above. In the infrared, bands at 5.86 (–N–COOR) and 5.95 μ (COOH) were observed.

Phenylsulfamide (11). (a) **By Reaction with Sulfamoyl Chloride.**—To a solution of 3.5 g. (0.030 mole) of sulfamoyl chloride in 50 ml. of dry benzene stirred at ice temperature was added dropwise 5.7 g. (0.060 mole) of aniline. After 10 minutes, 10 ml. of 6 *N* sodium hydroxide was poured into the mixture to dissolve the gum that had formed. The aqueous layer was separated, combined with a basic wash of the benzene layer, and acidified to form the product. A white solid was filtered off; 2.4 g. (46.5%), m.p. 105–106°, reported[10] m.p. 102–103°.

(b) **By an Exchange Reaction of Aniline and *o*-Nitrophenylsulfamide.**—A mixture of 0.35 g. (0.0016 mole) of *o*-nitrophenylsulfamide and 0.20 g. (0.0016 mole) of aniline in 40 ml. of benzene was refluxed for 6 hours. After cooling the solution, 0.20 g. (72%) of yellow plates precipitated; m.p. 113–115°. Recrystallization of the solid from benzene formed white plates, m.p. 102–103°. This material had an identical infrared spectrum with that of authentic material prepared above.

During the reaction, an aliquot was removed and its visible spectrum revealed a strong absorption at 405 mμ. This is indicative of *o*-nitroaniline. In subsequent experiments, an almost quantitative yield of *o*-nitroaniline was isolated.

***o*-Aminophenylsulfamide (13).**—A 2.2-g. (0.010 mole) sample of *o*-nitrophenylsulfamide was dissolved in 90 ml. of ethanol and reduced in a Parr shaker with 0.050 g. of platinum oxide. After 7 minutes, the calculated hydrogen uptake was complete. The catalyst was filtered off and the solution was concentrated to an oil. Upon cooling the oil, 1.6 g. (84%) of a buff solid formed; m.p. 105–106°. Recrystallization of the solid twice with ether raised the melting point to 106–108° and formed fine white needles.

Anal. Calcd. for $C_6H_9N_3SO_2$: C, 38.5; H, 4.81; N, 22.4; S, 17.2. Found: C, 38.5; H, 5.08; N, 22.6; S, 17.0.

***o*-Nitrophenylsulfamide (12).**—A mixture of 2.0 g. (0.015 mole) of recrystallized *o*-nitroaniline in 15 ml. of ether and 0.84 g. (0.0073 mole) of sulfamoyl chloride in 15 ml. of benzene was stirred at ice temperature for 1 hour. The clear yellow solution was concentrated almost to dryness on the steam-bath while a yellow solid was precipitating. This material, 1.9 g., was filtered off and recrystallized from benzene to yield 1.0 g. (63%), m.p. 135–137°. The product is soluble in carbonate and insoluble in bicarbonate.

Anal. Calcd. for $C_6H_7N_3SO_4$: C, 33.2; H, 3.22; N, 19.4; S, 14.7. Found: C, 32.8; H, 3.48; N, 19.6; S, 14.8.

Methyl 4-Chloro-N-sulfamoylanthranilate (14).—A solution of 18.6 g. (0.100 mole) of methyl 4-chloroanthranilate in 180 ml. of benzene was stirred at 10° while 5.8 g. (0.050 mole) of sulfamoyl chloride in 300 ml. of benzene was added rapidly. After 20 minutes, the solution was decanted from a brown gum that had formed in the flask and the liquid was stirred for an additional hour. During this time, a solid had formed and it was filtered; 8.6 g., m.p. 179–181°.

Upon concentration of the filtrate, several batches were formed; 2.5 g., m.p. 188–193°; 0.90 g., m.p. 158–180°; 2.9 g., m.p. 65–68°. From the brown gum, trituration with acetone afforded 0.60 g., m.p. 165–182°.

All of the high melting solids were recrystallized from acetone, after being clarified with Norit. The total yield was 7.3 g. (55%), m.p. 189–200°. This material was very difficult to purify further and was generally used in this form for the next reaction.

From one of the previous runs, a pure sample was obtained from acetone; m.p. 193–197°. This material had the same infrared spectrum as the solids cited above.

Anal. Calcd. for $C_8H_9N_2SClO_4$: C, 36.3; H, 3.40; N, 10.6; S, 12.1; Cl, 13.4. Found: C, 36.4; H, 3.58; N, 10.9; S, 12.0; Cl, 13.5.

7-Chloro-1H-2,1,3-benzothiadiazin-4(3H)-one 2,2-Dioxide (16).—A 7.9-g. (0.030 mole) sample of *14* was heated with 60 ml. of 1 *N* sodium hydroxide for 30 minutes on the steam-bath. The solution was cooled and acidified to yield an off-white solid. This crude cake was recrystallized from 200 ml. of hot water and then from ethanol–water. Three crops were obtained; 0.90 g., m.p. 192°; 1.4 g., m.p. 208–210°; and 0.25 g., m.p. 225°.

The lowest melting material was recrystallized from ethanol–water and its melting point was raised to 208°.

A small sample of the material melting at 208–210° was recrystallized from ethanol–water for analysis; m.p. 219–221°.

Anal. Calcd. for $C_7H_5N_2SClO_3$: C, 36.1; H, 2.15; N, 12.0; S, 13.8; Cl, 15.3. Found: C, 36.3; H, 2.34; N, 12.0; S, 13.4; Cl, 15.2.

N-Sulfamoylanthranilamide (15).—To a stirred solution of 1.4 g. (0.010 mole) of anthranilamide in 100 ml. of ether was added 0.58 g. (0.0050 mole) of sulfamoyl chloride in 10 ml. of benzene at a bath temperature of 10°. Immediately, a milky white layer formed and the mixture was stirred for 1 hour. To the mixture was added 20 ml. of 1 *N* sodium hydroxide and the resulting two layer system was separated. The aqueous layer was acidified to yield 0.60 g. (56%) of product, m.p. 160–161°.

A small portion was dissolved in base and reprecipitated with acid to afford a sample for analysis; m.p. 162°.

Anal. Calcd. for $C_7H_9N_3SO_3$: C, 39.1; H, 4.18; N, 19.5; S, 14.9. Found: C, 38.8; H, 4.18; N, 19.2; S, 14.7, 15.0.

***p*-Nitrophenylsulfamide (17).**—A slurry of 1.0 g. (0.0072 mole) of *p*-nitroaniline in 40 ml. of ether was poured into 10 ml. of benzene containing 0.42 g. (0.0036 mole) of sulfamoyl chloride, and stirred at ice temperature for 1 hour. The yellow solution was concentrated to a small volume while crystals precipitated. The filtered yellow solid was washed with water to remove salts, and then recrystallized from hot benzene to afford 0.15 g. (19.3%) of product, m.p. 170–173°.

Anal. Calcd. for $C_6H_7N_3SO_4$: C, 33.2; H, 3.22; N, 19.4; S, 14.7. Found: C, 33.0, 33.5, 33.2; H, 3.77, 3.48, 3.57; N, 19.3; S, 14.7.

N,N-Diethyl-*o*-nitrophenylsulfamide (18).—A mixture of 1.24 g. (0.00730 mole) of freshly distilled diethylsulfamoyl chloride and 2.00 g. (0.0146 mole) of *o*-nitroaniline was heated for 6 hours on the steam-bath. During the reaction, the mixture slowly solidified. The residue was dissolved in 1 *N* sodium hydroxide, clarified with Norit and acidified with hydrochloric acid. A yellow oil formed which crystallized in the refrigerator after 2 days. The yield of yellow crystals was 0.500 g. (25%), m.p. 43–45°. The melting point was unchanged after recrystallization from cyclohexane.

Anal. Calcd. for $C_{10}H_{15}N_3SO_4$: C, 44.0; H, 5.50; N, 15.4; S, 11.7. Found: C, 43.6; H, 5.70; N, 15.5; S, 11.4.

1,1′-(*o*-Phenylene)-disulfamide (19).—A solution of 1.0 g. (0.0046 mole) of *o*-nitrophenylsulfamide and 0.50 g. (0.0046 mole) of *o*-phenylenediamine in 250 ml. of benzene was refluxed for 19 hours. The benzene was decanted and the remaining yellow solid was triturated with ether and filtered; 0.22 g. (36%), m.p. 167–168°.

The product was recrystallized from benzene–ethyl acetate to form an off-white solid, m.p. 169–171°. This material [λ_{max} 222 mμ (ϵ 10,100), λ_{max} 270 mμ (ϵ 1060) in ethanol and λ_{max} 240 mμ (ϵ 10,200), λ_{max} 285 mμ (ϵ 2560) in base] was very similar in its ultraviolet spectral absorption to that of phenylsulfamide.

Anal. Calcd. for $C_6H_{10}N_4S_2O_4$: C, 27.1; H, 3.76; N, 21.1; S, 24.0. Found: C, 27.4; H, 3.76; N, 20.9; S, 23.0.

4-Chloro-N-sulfamoylanthranilic Acid (21).—A sample of 5.1 g. (0.030 mole) of 4-chloroanthranilic acid was dissolved in 300 ml. of refluxing ether. To the solution was added 240 ml. of benzene and the mixture was concentrated until the reflux temperature reached 50°. A hot solution of 6.5 g. (0.030 mole) of *o*-nitrophenylsulfamide in 600 ml. of benzene was added and the combined solutions were refluxed for 17 hours. After concentrating the reaction mixture to 350 ml., it was cooled and 5.0 g. of a dark yellow solid precipitated, m.p. 188–220°.

Most of this solid was dissolved in 150 ml. of 10% sodium bicarbonate, decolorized with Norit, and reprecipitated with acid to form 1.6 g. of a yellow solid, m.p. softens 180°, dec. > 260°.

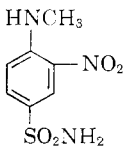
Purification was achieved by partition chromatography with *n*-heptane, ethyl acetate, methanol and water (60:40:17:4). An off-white solid was obtained which was dissolved in base and reprecipitated with acid to yield a white solid, m.p. softens 175°, dec. 261°.

Anal. Calcd. for $C_7H_7N_2SClO_4$: C, 33.5; H, 2.79; N, 11.2; S, 12.8; Cl, 14.2. Found: C, 33.9; H, 3.07; N, 11.0; S, 12.6; Cl, 14.4.

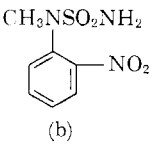
3-Nitro-N⁴-methylsulfanilamide (24).—A solution of 3.0 g. (0.020 mole) of N-methyl-*o*-nitroaniline in 15 ml. of ether was added rapidly to a stirred solution of 1.2 g. (0.010 mole) of sulfamoyl chloride in 20 ml. of benzene. After 1 hour at room temperature, the dark orange solution was concentrated to dryness on the steam-bath. After extracting the dark residue with ether and concentrating, a small amount of material was obtained. This was recrystallized from hot water to yield an orange solid, m.p. 255° dec. This material had a substantial absorption in the visible spectrum at 400 mμ which is incompatible with an N-sulfamoyl compound. In addition, its infrared spectrum as well as the ultraviolet and visible spectra strongly resembled 3-nitrosulfanilamide.

Anal. Calcd. for $C_7H_9N_3SO_4$: C, 36 3; H, 3.90; S, 13.9. Found: C, 36.4; H, 4.00; S, 13.9.

The mostly likely product is therefore 3-nitro-N⁴-methylsulfanilamide (a),



(a)



(b)

which is an isomer of the desired material (b).

The Reaction of *o*-Nitrophenylsulfamide with Benzoic Acid.—Equimolar amounts of *o*-nitrophenylsulfamide and benzoic acid were refluxed in benzene for 6 hours. An aliquot removed after 4 hours showed an appreciable amount of *o*-nitroaniline in the visible spectrum. After cooling the solution, a small amount of yellow solid was filtered off; m.p. 280–285°. The solid was water soluble and acidic to litmus. The material was transparent in the carbonyl region of the infrared, and its spectrum in a KBr disk showed no C–H absorption. (This eliminates the expected product, $C_6H_5COOSO_2NH_2$.)

The solid was "purified" by refluxing in ethyl acetate. The color went into solution, and a white solid remained, m.p. ~315°. The solid gave a positive test with barium hydroxide and formed a precipitate with ethanolic silver nitrate, but not with aqueous silver nitrate. (Trisulfimide is reported to form a silver salt only in basic or neutral media.[17a])

Anal. Calcd. for $(HNSO_2)_x$: H, 1.27; N, 17.7; S, 40.5. Found: H, 3.88; N, 12.1; S, 19.6; C, 1.50.

There is still a small amount of organic material in this sample. The nitrogen–sulfur ratio is closer to 3/2 than 1/1 which is required for the expected dimer or trimer of sulfimide.[20]

Kinetics.—The solvents used in Table I were all reagent grade. Trace amounts of water had no effect on the rate, and, therefore, no elaborate purification or drying was necessary.

For Table I, the concentration of *o*-nitrophenylsulfamide was approximately 25 or 50 γ per ml. Either concentration gave the same rate. The solutions, in a stoppered volumetric flask, were placed in a thermostated water bath. Aliquots were taken at fixed time intervals and most of the reactions were taken to at least 70% of completion.

The reaction was followed by observing the change in the visible spectrum at 400 mμ where the product, *o*-nitroaniline, absorbs; ϵ for *o*-nitroaniline in ethanol at this wave length was 5.52×10^3; ϵ_{400} for *o*-nitrophenylsulfamide was 1.39×10^3. At zero time the exact initial concentration was calculated for each run from the optical density. Appropriate changes in ϵ-values were made for each solvent.

The equations used to calculate the concentration of *o*-nitrophenylsulfamide (12) at time (t) were derived as

A = *o*-nitrophenylsulfamide, B = *o*-nitroaniline, Y = $NHSO_2$ or its equiv.
C_A = molar concn. of A, C_{A_0} = [A] at zero time
C_B = molar concn. of B
ϵ_A = molar extinction coefficient of A
ϵ_B = molar extinction of B
d = optical density
d_{obsd} = opt. dens. at 400 mμ for the mixt. at fixed time intervals

Since A→B + Y

$$C_B = C_{A_0} - C_A$$
$$d = \epsilon C$$
$$d_A = \epsilon_A C_A$$
$$d_B = \epsilon_B C_B = \epsilon_B (C_{A_0} - C_A)$$
$$d_{obsd} = d_A + d_B = \epsilon_A C_A + \epsilon_B (C_{A_0} - C_A)$$
$$= C_A(\epsilon_A - \epsilon_B) + C_{A_0}\epsilon_B$$
$$\frac{d_{obsd} - C_{A_0}\epsilon_B}{(\epsilon_A - \epsilon_B)} = C_A$$

When log C_A was plotted *versus* time (Fig. 1), a straight line was obtained. The rate constant k was evaluated from the slope of the line in the usual manner. In some cases, a check on the values was made by calculating k from the first-order equation

$$k = \frac{2.303}{t} \log \frac{D_\infty - D_0}{D_\infty - D_t}$$

where

D_∞ = opt. dens. of *o*-nitroaniline
D_t = opt. dens. at time, t
D_0 = opt. dens. at zero time

In Table II are listed the concentrations of aniline or dimethylaniline used with *o*-nitrophenylsulfamide. In these cases, an aliquot of the benzene or dimethylformamide solution was diluted 50- or 100-fold in ethanol and the spectrum was run immediately. In all cases a good first-order plot was obtained (Fig. 3). Attempts to fit the data to second or higher order reactions were in vain. To check on the accuracy of the spectral method for determining the extent of the reaction, an authentic mixture of the four components (*i.e.*, *o*-nitrophenylsulfamide, aniline, *o*-nitroaniline and phenylsulfamide) was prepared (run 8). The ultraviolet absorption at 400 mμ at zero time was identical to that of aniline and *o*-nitrophenylsulfamide (run 1) at one-half time.

In addition, after one run had been taken to 76% of completion, 52% of phenylsulfamide was isolated. (Some of the losses can be attributed to the withdrawn aliquots that were discarded.) No other organic material besides *o*-nitroaniline was ever isolated.

(20) Other inorganic sulfur–nitrogen–oxygen compounds are reported by H. A. Lehmann and G. Kempe, *Z. anorg. u. allgem. Chem.*, **307**, 70, 79 (1961); M. Goehring, *et al.*, *ibid.*, **273**, 200 (1953); and M. Goehring, *Quart. Revs.*, **10**, 437 (1956).