220° with effervescence. It gave strong tests for sulfur and chlorine and was identified as 2-thio-4-methyl-5-(β-chloropropyl)-6-oxypyrimidine. A mixture of the hydrolytic product and this 2-thiopyrimidine melted at exactly the same temperature. The mechanism of the reaction may be represented by the preceding formulas. We obtained no evidence of the formation of 2,6-dioxy-4-methyl-5-(β-mercaptopropyl)pyrimidine.

The Conversion of 2-Ethylmercapto-6-oxypyrimidine into Uracil by Digestion with Chloroacetic Acid,

Five grams of the 2-mercaptopyrimidine (m. 152°) and two molecular proportions of chloroacetic acid (5 grams) were dissolved in water and the mixture boiled for one hour. Ethylmercaptan was evolved. After concentration and cooling of the solution 3.0 grams of pure uracil separated while a theoretical yield would have been 3.6 grams. The uracil was absolutely free from sulfur and crystallized in characteristic corpuscular crystals which showed no signs of melting below 300°.

NEW HAVEN, CONN.

[CONTRIBUTIONS FROM THE SHEFFIELD CHEMICAL LABORATORY OF YALE UNIVERSITY.]

RESEARCHES ON AMINES. IV.[1] THE ALKYLATION AND HYDROLYSIS OF ALIPHATIC SULFONAMIDES. A NEW SYNTHESIS OF SARCOSINE.[2]

BY TREAT B. JOHNSON AND JOSEPH A. AMBLER.

Received December 20, 1913.

CONTENTS: 1. Hinsberg's Method of Alkylation and its Practical Application. 2. The Application of Hinsberg's Reaction with Aliphatic Sulfonamides. 3. Experimental Work.

1. Hinsberg's Method of Alkylation and its Practical Application.

That sulfonamides possess acidic properties was apparently first observed by Gerhardt and his co-worker Chiozza. The announcement of this characteristic property was made in their paper entitled, "Untersuchungen über die Amide," which was published in 1853.[3] These investigators showed that acid amides are formed by the interaction of amines and acid chlorides. They not only applied this reaction successfully with chlorides of carboxylic acids, but also effected an analogous

[1] Johnson and Guest, *Am. Chem. J.*, 42, 340; 43, 310; THIS JOURNAL, 32, 761

[2] The Chairman's address, Organic Chemistry Section, 48th meeting A. C. S., Rochester, September 8–12, 1913, comprised the historical and theoretical parts of this paper.

[3] *Ann.*, 87, 299.

change with benzene sulfone chloride. They prepared in this manner, by the action of ammonia, benzenesulfone amide, $C_6H_5SO_2NH_2$, and made the important observation that this substance is a strong acid dissolving immediately in alkaline solutions and forming stable salts with the alkali metals and silver. The solubility in alkali of secondary sulfonamides was later observed by Romburgh[1] and Behrend.[2] It is now a well known fact that the solubility of such compounds in alkali is due to the presence in their molecules of the acidic grouping —SO_2.NH— In fact, it is a characteristic property which distinguishes this type of acid amides from the amide derivatives of carboxylic acids. It is of especial interest, however, to note here that acid amides containing the grouping SO_2.NH have been described, which are insoluble in alkali.[3]

Following Gerhardt's investigations numerous sulfonamides of all types were synthesized and investigated but apparently, not until about 38 years after the publication of Gerhardt's and Chiozza's paper was the real significance of this property of dissolving in alkali recognized from a synthetical standpoint. In 1891, Hinsberg[4] utilized these compounds for synthetical purposes and published his method of synthesizing secondary amines from primary amines. This is based, as is well known, on two facts, namely, that the alkali salts of sulfonamides easily interact with alkylhalides, in alcoholic solution, giving nitrogen substituted compounds, and secondly, that the latter, when subjected to hydrolysis with acids, are cleaved with formation of amines and a sulfonic acid. His method of alkylation involves no difficult manipulation; the yields of amines are generally very good, and consequently it has met with a wide application.

In the practical application of Hinsberg's method for the synthesis of primary and secondary amines the final operation is to subject the alkylated sulfonamide to hydrolysis with acids in order to cleave the amine from the sulfonyl group. No serious difficulty is generally encountered in effecting this change. It is accomplished generally by heating the amide with concentrated hydrochloric acid under pressure, when the amine is obtained in the form of its hydrochloride, mixed with the sulfonic acid. In order to obtain the free base, the general custom is to make the solution strongly alkaline and then separate the amine by steam distillation or extraction with ether.

The necessity of hydrolyzing the sulfonamides under pressure, however, is disadvantageous for several important reasons. Several attempts have been made by different investigators to hydrolyze with other reagents.

[1] *Rec. trav. chim.*, 3, 7 (1884).

[2] *Ann.*, **222**, 116 (1884).

[3] Solonina, *J. Russ. Phys. Chem. Soc.*, **29**, 410; *Ibid.*, **31**, 640; *Chem. Centr.*, **2**, 848 (1897); *Ibid.*, **2**, 867 (1899).

[4] *Ann.*, **265**, 178; Hinsberg and Steupler, *Ibid.*, **287**, 220.

Some have been impractical while others perhaps have possessed some advantages over Hinsberg's original method. Marckwald and Huelshoff[1] introduced chlorosulfonic acid (I) as the hydrolytic agent. This chloride reacts with the sulfonamide, on heating, with regeneration of the original sulfonchloride and formation of amidosulfonic acids (II). The free amines are then obtained by digestion of their sulfonic acids with strong alkali when they undergo hydrolysis and the amine is obtained in a pure condition by distillation with steam. The changes involved may be represented by the following equations:

$$C_6H_5SO_2NRR' + HO.SO_2Cl = C_6H_5SO_2Cl + HOSO_2.NRR'$$
I.

$$HOSO_2.NRR' + 2NaOH = Na_2SO_4 + H_2O + HNRR'$$
II.

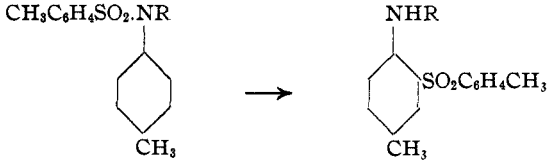
This modification of Hinsberg's method has never received, however, a wide application.

All attempts to hydrolyze the sulfonamides, by heating with alkali, have been unsuccessful. Ullman[2] employed for hydrolysis a mixture of concentrated sulfuric acid and glacial acetic acid. With these reagents he found that a cleavage of the sulfonyl group could easily be accomplished, in those cases investigated by him, by heating the amides with the mixture of acids at 120°. Schroeter and Eisleb[3] later used raw, concentrated sulfuric acid at ordinary temperature, but they found that this acid could not be employed when working with certain aromatic compounds because of the susceptibility of such substances to sulfonation. Their method of hydrolysis, therefore, proved to be of no practical utility, unless sulfanilic acid derivatives were desired as products of the reaction.

The most recent modification of Hinsberg's method of alkylation is that recommended by Witt and Uermenyi.[4] These investigators used strong sulfuric acid as the hydrolytic agent, but employed a different sulfonic acid than that used by Hinsberg. Observing that toluene sulfonic acid is insoluble in strong sulfuric acid at ordinary temperature, they heat the corresponding sulfonamide derivatives with 80% sulfuric acid at 130–150°; when a cleavage of the amide is easily effected. On cooling, the sulfuric acid solution, the toluene sulfonic acid then crystallizes out and can be separated by filtration. The free amine is then obtained by distillation with steam from an alkaline solution. Their modification is, therefore, no improvement whatever over Hinsberg's original method, and involves the same number of operations. On the other hand, there is a very serious objection to using it in the case of aromatic compounds

[1] *Ber.*, **31**, 3261.
[2] *Ann.*, **327**, 104.
[3] *Ibid.*, **367**, 101.
[4] *Ibid.*, **46**, 296.

because of the tendency of the sulfonamides to undergo molecular rearrangements when heated with sulfuric acid. They are transformed under these conditions into sulfones (III). The extent of these rearrangements varies with the different aromatic amines used.



III.

In all the modifications, therefore, which have been recommended as improvements over Hinsberg's original method, resort is always finally made to steam distillation. In fact, it is the only practical method available for separating the amines from the sulfonic acid solution without introduction of other operations and consequently with great loss of the base. There is no apparent advantage in using sulfuric acid as the hydrolytic agent instead of hydrochloric. While steam distillation can generally be applied successfully for the separation of the amines after hydrolysis, on the other hand, there are cases where such an operation would be useless. In the application of Hinsberg's method for the alkylation of amino acids, for example, amphoteric compounds are obtained on hydrolysis which are not volatile with steam. In such cases, the only practical method of separation at present feasible, when benzene sulfone derivatives are used, is precipitation of the amino acids with an alkaloidal reagent. This, however, introduces another operation and furthermore the precipitations are generally not quantitative.

Schotten and Schlömann[1] encountered the difficulty of separating an amino acid from benzene sulfonic acid when working with the corresponding sulfone derivative of amino valerianic acid, $C_6H_5SO_2NH(CH_2)_4COOH$. After hydrolysis with hydrochloric acid, they obtained a stable sulfonic acid salt of the amino acid, $C_6H_5SO_3H.NH_2(CH_2)_4COOH$, which they finally succeeded in decomposing by heating with concentrated hydrochloric acid at 250° in the presence of barium chloride. The sulfonic acid was completely destroyed by this treatment with formation of barium sulfate and benzene. After removal of the excess of barium the amino acid was finally obtained in the form of its hydrochloride by evaporating the solution. This procedure, however, is not of general application because of the danger of decomposing the amino acids by heating with strong acids at such a high temperature.

Johnson and McCollum[2] encountered the same difficulty when an attempt was made to obtain sarcosine from the benzene sulfone deriva-

[1] *Ber.*, **24**, 3687.

[2] *Am. Chem. J.*, **35**, 54.

tive of this amino acid, $C_6H_5SO_2N(CH_3)CH_2COOH$. When this compound was hydrolyzed a stable, crystalline sulfonic acid salt was obtained, $C_6H_5SO_3H.CH_3NHCH_2COOH$. In such cases as these, Witt and Uermenyi's[1] modification is apparently applicable and has recently been used successfully by Fischer and Bergmann[2] in the preparation of sarcosine. They have successfully applied Hinsberg's method of alkylation with sulfone derivatives of α-amino acids and find, for example, that the *p*-toluene sulfone derivative of glycocoll, $CH_3C_6H_4SO_2.NH.CH_2COOH$, can easily be converted into the corresponding sarcosine derivative, $CH_3C_6H_4SO_2N(CH_3)CH_2COOH$. When this compound was hydrolyzed with hydrochloric acid the insoluble toluene sulfonic acid was easily separated by filtration and the hydrochloride of sarcosine obtained in good yield by concentration of the acid solution. On the other hand, when the benzene sulfone derivatives were subjected to hydrolysis they were obliged to precipitate the amino acids with phosphotungstic acid in order to separate them from the benzene sulfonic acid. They applied Hinsberg's reaction with the benzene sulfone derivatives of ornithine (IV), and *d*-aminovalerianic acid (VI), and synthesized the corresponding methyl derivatives represented by formulas V and VII.

$$C_6H_5SO_2NHCH_2CH_2CH_2CH(NHSO_2C_6H_5)COOH$$

$$\downarrow \text{IV.}$$

$$CH_3NH.CH_2CH_2CH_2CH(NHCH_3)COOH$$

V.

$$C_6H_5SO_2NHCH_2CH_2CH_2CH_2COOH$$

$$\downarrow \text{VI.}$$

$$CH_3NH.CH_2CH_2CH_2CH_2COOH$$

VII.

It is apparent from what has already been presented that the practical utility of Hinsberg's reaction, for amino acid syntheses, would be greatly increased if some method was developed for separating easily the amino acid from the sulfonic acid. If toluene sulfone derivatives are used for experimental purposes this can be accomplished, as is illustrated by Fischer's and Bergmann's synthesis of sarcosine. Toluene sulfone chloride, however, is not always accessible in quantity. The simplest method would be to use a sulfonic acid, which would be easily decomposed by heating with hydrochloric acid. Schotten and Schlömann[1] attempted to meet this condition by heating the benzene sulphone derivative with hydrochloric acid in the presence of barium chloride. Such an energetic treatment, however, is not always permissible. An ideal condition would be

[1] *Loc. cit.*

[2] *Ann.*, 398, 96.

that where the hydrolysis could be effected at a temperature below 150° and the complete destruction of the sulfonic acid be accomplished at the same temperature. Furthermore, if the sulfonic acid underwent decomposition giving products, which were volatile with steam, then the hydrochloric acid solution could simply be evaporated to dryness and the hydrochloride of the amine would be the only product left behind. The free base or amino acid could then be separated easily if necessary. Hydrochloric acid could be used as the hydrolytic agent and the whole synthesis of an alkylated amine or amino acid could be accomplished in two operations, namely, *alkylation* and *hydrolysis*. In the following chapter we shall describe a modification of Hinsberg's method of alkylation, which meets all these conditions.

2. The Application of Hinsberg's Reaction with Aliphatic Sulfonamides.

The aromatic sulfonic acids, which contain the sulfonic rest in the benzene nucleus, are characterized by their great stability in the presence of hydrochloric acid. They can be decomposed by this reagent, however, if heated at a high temperature, and break down, giving sulfuric acid and a hydrocarbon, as expressed by the following equation:

$$C_6H_5.SO_2OH + H_2O = C_6H_6 + H_2SO_4$$

On the other hand, the isomeric sulfonic acids, in which the acid radical is substituted in the aliphatic side chain, are far less stable. These compounds are very unstable at high temperatures and their derivatives, so far as examined, are easily decomposed under conditions where the corresponding aromatic compounds exhibit great stability. For example, Pechmann[1] observed that benzylsulfonyl chloride (VIII) dissociates, on heating, giving sulfur dioxide and benzyl chloride. In fact, the transformation is practically quantitative. Mohr[2] observed that *p*-nitro-

$$C_6H_5CH_2SO_2Cl = SO_2 + C_6H_5CH_2Cl.$$

VIII.

benzylsulfonyl chloride, $NO_2C_6H_4CH_2SO_2Cl$, and *p*-brombenzylsulfonylchloride, $Br.C_6H_4CH_2SO_2Cl$, also dissociate in a perfectly analogous manner, forming nitrobenzyl- and bromobenzyl chlorides, respectively, with evolution of sulfur dioxide. Mohr states, in his paper, that the acid chlorides of all benzylsulfonic acids examined, decompose in this manner, and consequently it is difficult, on this account, to obtain them in a pure condition.

The amides of a limited number of benzylsulfonic acids only have been prepared and, so far as the writers are aware, their behavior on hydrolysis has not been investigated. Pechmann[3] synthesized benzylsulfonylamide, $C_6H_5CH_2SO_2NH_2$, by the action of ammonia on the acid chloride

[1] *Ber.*, 6, 534.
[2] *Ann.*, 221, 215.
[3] *Loc. cit.*

of benzylsulfonic acid, but he gave no description whatever of the chemical behavior of the compound.[1] Mohr prepared the corresponding amide of *p*-nitrobenzylsulfonic acid, but did nothing apparently with the compound. Marckwald and Frahne[2] made the amide of nitro-*o*-hydroxybenzylsulfonic by the action of ammonia on the corresponding sultone and described several of its salts and its methyl ester. Fromme and Palma[3] also studied this type of sulfonamides and prepared Pechmann's benzylsulfonamide by interaction of ammonium carbonate and benzylsulfonyl chloride. They also described the anilide, *p*-toluidide and phenetidide of this acid.

As the behavior of this type of acid amides on hydrolysis had not been investigated, it was therefore of special interest to us to determine their chemical behavior when heated with strong hydrochloric acid. We found, to our surprise, that these amides decompose in an unique manner when heated with this reagent. In the first place, they undergo hydrolysis normally, as expected, with formation of the hydrochloric acid salt of an amine. The aliphatic sulfonic (VIII) acid, however, is not obtained

$$C_6H_5CH_2SO_2NHR + H_2O + HCl = C_6H_5CH_2SO_3H + HCl.H_2N.R$$
VIII.

since it undergoes complete destruction at the temperature of hydrolysis (130–150°). It is not converted under these conditions, however, into a hydrocarbon and sulfuric acid as shown in the case of aromatic sulfonic acids,[4] but is transformed quantitatively into sulfur dioxide and benzyl chloride. Whether this unique change first involves a dissociation of the sulfonic acid into sulfur dioxide and benzyl alcohol, or primarily a formation of the acid chloride and finally a dissociation of the latter is not known. The complete hydrolysis of benzylsulfonamide (IX), with hydrochloric acid, therefore, may provisionally be represented in the following manner:

$$C_6H_5CH_2SO_2NH_2 + H_2O = C_6H_5CH_2SO_2OH + NH_3.$$
$$NH_3 + HCl = NH_4Cl.$$
$$C_6H_5CH_2SO_2OH = SO_2 + C_6H_5CH_2OH$$
$$C_6H_5CH_2OH + HCl = H_2O + C_6H_5CH_2Cl$$

The products of the reaction are ammonium chloride, and benzyl chloride and sulfur dioxide which are volatile with aqueous vapor. This is apparently a normal reaction, and the yields of amine hydrochlorides are nearly quantitative.

Having established the fact that benzylsulfonamide is decomposed smoothly, by hydrolysis, giving benzyl chloride, sulfur dioxide and am-

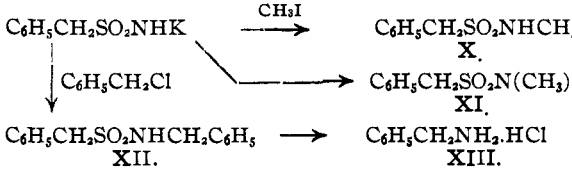
[1] *Loc. cit.*

[2] *Ber.*, **31**, 1854.

[3] *Ibid.*, **39**, 3308.

[4] Schotten and Schlömann, *loc. cit.*

monium chloride, we next turned our attention to the application of Hinsberg's reactions with this amide. We find that it forms well defined mono-potassium and sodium salts, which react smoothly with alkyl halides, forming the corresponding alkylsulfonamides. In this paper we describe the behavior of these salts towards methyl iodide, benzyl chloride, ethyl brom- and chloroacetates and chloroacetamide.[1] By alkylation of benzylsulfonamide with methyl iodide a mixture of the monomethyl (X), and dimethyl derivatives (XI), is obtained. Attempts were made to decrease the amount of the dimethyl derivative in various ways, but we found that it was always formed in practically constant proportion. Benzyl chloride, however, reacted more smoothly with the monopotassium salt, giving a monobenzyl derivative (XII). When this was subjected to hydrolysis with concentrated hydrochloric acid it was converted smoothly into the hydrochloride of benzylamine (XIII), benzyl chloride and sulfur dioxide.



Schotten and Baumann's reaction can be applied successfully with benzylsulfonylchloride and amines. An attempt was made to prepare benzylsulfonglycocoll in this manner, but the amount formed was so small that it was not a practical method of preparation. We also investigated the action of the ethyl esters of chloro- and bromoacetic acids on the potassium salt of the sulfonamide, but here also the reactions were not smooth and a large proportion of the amide was recovered unaltered. We next investigated the action of chloroacetamide on the alkali salts of the sulfonamide and made the interesting observation that they interact smoothly forming benzylsulfonacetamide (XIV). This amide, on digestion with alkalis, was converted quantitatively into the benzylsulfone derivative of glycocoll (XV):

$$C_6H_5CH_2SO_2NHK + ClCH_2CONH_2 = \underset{\text{XIV.}}{C_6H_5CH_2SO_2NHCH_2CONH_2} + KCl$$

$$C_6H_5CH_2SO_2NHCH_2CONH_2 + H_2O = \underset{\text{XV.}}{C_6H_5CH_2SO_2NHCH_2COOH} + NH_3$$

Benzylsulfonaminoacetamide dissolves immediately in alkali and un-

[1] We are continuing this investigation and shall investigate not only the alkylation products of benzylsulfonamide, but also incorporate in our work an investigation of other aliphatic sulfonamides. This type of compounds should be especially valuable for further interesting syntheses. It is not improbable that the potassium salt of benzylsulfonamide may prove as useful for synthetical purposes as the potassium salt of phthalimide (T. B. J.).

dergoes alkylation smoothly with methyl iodide, forming the amide of benzylsulfonsarcosine (XVI). This same amide is also formed by action of chloroacetamide on the sodium salt of methylbenzylsulfonamide (X). In fact, it was found by experience that the best method of preparation of the amide was to first alkylate benzylsulfonamide with methyl iodide, and then, without isolation of the methyl substitution product, to alkylate finally with chloroacetamide in presence of the required amount of alkali. In this way the desired amide was easily obtained pure in yields of 25–30% of the theoretical. When the amide of benzylsulfonsarcosine (XVI)

$$\underset{\text{XIV.}}{C_6H_5CH_2SO_2NHCH_2CONH_2} \xrightarrow{CH_3I} C_6H_5CH_2SO_2N(CH_3)CH_2CONH_2$$

$$\underset{\text{X.}}{C_6H_5CH_2SO_2NHCH_3} \xrightarrow{ClCH_2CONH_2} C_6H_5CH_2SO_2N(CH_3)CH_2CONH_2$$

XVI.

was digested with barium hydroxide solution it was converted quantitatively into the corresponding acid (XVII). This acid, on hydrolysis with hydrochloric acid, breaks down in a manner perfectly analogous to that in the case of the sulfone derivatives of amines. Sulfur dioxide and benzyl chloride are formed and pure sarcosine hydrochloride (XVIII) is obtained by evaporating the hydrochloric acid solution to dryness. Starting with the amide (XVI), the new synthesis of sarcosine therefore involves three operations and the yields are nearly quantitative at each stage. These changes are represented by the following formulas:

$$\underset{\text{XVI.}}{C_6H_5CH_2SO_2N(CH_3).CH_2CONH_2} \xrightarrow{\text{alkali}}$$

$$\underset{\text{XVII}}{C_6H_5CH_2SO_2N(CH_3)CH_2COOH} \xrightarrow{HCl}$$

$$\underset{\text{XVIII.}}{CH_3NH.CH_2COOH.HCl} + SO_2 + C_6H_5CH_2Cl$$

The characteristic feature of our modification of Hinsberg's method of alkylation is the fact that the sulfonic acid employed is completely decomposed by heating with hydrochloric acid and consequently renders it possible to obtain the hydrochlorides of the amines or amino acids absolutely free from the sulfonic acid without precipitation with an alkaloidal reagent. Benzylsulfonamide can easily be obtained in any quantity desired. The only unsatisfactory step in the synthesis is that involving alkylation in order to obtain the amide (XVI). Here the yield of purified product is generally at best only 25–30% of theory. Efforts are being made, however, to determine the best conditions for obtaining a maximum yield. New investigations are now in progress, and we shall ap-

ply the method for the preparation of other compounds of biochemical interest.[1]

Experimental Part.

Sodium Salt of Benzylsulfonic Acid, $C_6H_5CH_2SO_3Na$.—This salt was prepared according to the method of Fromm and Palma.[2] Two hundred and fifty grams of crystallized sodium sulfite, or 125 g. of the anhydrous salt, in about 200–250 cc. of 10% sodium hydroxide solution were boiled under a reflux condenser with 125 g. of benzyl chloride. After 3–4 hours' boiling the benzyl chloride had practically all disappeared and the hot solution, after diluting with water, was filtered through wet filter papers to remove unaltered benzyl chloride, and also the small amount of benzyl alcohol which is formed in the reaction. On cooling the aqueous solution the sodium salt separated in the form of glistening plates. More of the same salt separated after concentrating the solution. The salt was dried at 100° and used, without further purification, for the following experiments. The yield was about 80% of the theoretical:

Benzylsulfonchloride, $C_6H_5CH_2SO_2Cl$.—This chloride, which has been described by Pechmann, was prepared as follows: 50 g. of powdered, anhydrous sodium benzylsulfonate were mixed in a flask with 54 g. of pulverized phosphorus pentachloride and the mixture then moistened with phosphorus oxychloride. After a few minutes there was an energetic reaction and the flask was immersed in cold water to prevent decomposition of the sulfonchloride. After the violent reaction was over, the mixture was then heated at 70–89° for 4–5 hours. If heated at a higher temperature the sulfonchloride is gradually decomposed, forming sulfur dioxide and benzyl chloride. The semi-solid mass was finally poured into ice-water to decompose the phosphorus halides, when the sulfonchloride separated as a heavy oil, which finally solidified. After filtering and washing with water it was dried on a porous plate to remove traces of benzyl chloride, and finally converted into the acid amide.

Benzylsulfonamide, $C_6H_4CH_2SO_2NH_2$.[3]—The amide is easily prepared by mixing the acid chloride with a large excess of concentrated, aqueous ammonia. The chloride dissolved immediately. After concentration of the solution and cooling, the amide separated in the form of colorless needles. It was purified by crystallization from hot water and melted at 104–105°.

Sodium Salt of Benzylsulfonamide, $C_6H_5CH_2SO_2NHNa$.—This salt separated in a crystalline condition when the solutions of molecular amounts of sodium ethylate and benzylsulfonamide, in absolute alcohol,

[1] Owing to the departure of Dr. Ambler from this laboratory these researches will be continued by other investigators in our department (T. B. J.).

[2] *Loc. cit.*

[3] Peckmann, *loc. cit.*

were united. It is insoluble in ether, very soluble in cold water, and insoluble in cold alcohol. It was dried for analysis at 100°.

Calc. for $C_7H_8O_2NSNa$: N, 7.27%; found, N, 7.06%.

Potassium Salt of Benzylsulfonamide, $C_6H_5CH_2SO_2NHK$.—This was prepared by the action of potassium hydroxide on benzylsulfonamide in absolute alcohol. It separated as glistening, micaceous flakes. After filtering and washing with ether it was dried at 100°.

Calc. for $C_7H_8O_2NSK$: N, 6.71%; found, N, 6.52%.

Methyl Benzylsulfonamide, $C_6H_5CH_2SO_2NHCH_3$.—The potassium or sodium salts of benzylsulfonamide were suspended in absolute alcohol, an excess of methyl iodide added, and the mixture then warmed on the steam bath until the solution gave no alkaline reaction. The alcohol was then evaporated and the residue dissolved in the least possible amount of hot water. On cooling, a colorless solid separated, which was identified as a mixture of the mono- and dimethyl amides. These were separated by means of potassium hydroxide solution, in which the monomethyl amide is soluble. The insoluble dimethyl amide was removed by filtration and the filtrate acidified with hydrochloric acid, when the monomethyl compound separated as colorless needles. The amide is soluble in ether, alcohol and hot water and melts at 109–110° to a clear oil.

Calc. for $C_8H_{11}O_2NS$: N, 7.59%; found, N, 7.63%.

Dimethyl Benzylsulfonamide, $C_6H_5CH_2SO_2N(CH_3)_2$.—The crude dimethyl amide obtained above was washed with potassium hydroxide solution and then purified by recrystallization from hot water and absolute alcohol. It separated in thin plates, which melted at 102–103° to an oil. It was dried for analysis over sulfuric acid:

Calc. for $C_9H_{13}O_2NS$: N, 7.05%; found, N, 7.01, 7.26%.

Attempts were made to increase the yield of the monomethylamide by alkylation under different conditions. The reaction was applied with molecular amounts of the methyl iodide and the sodium or potassium salt of the amide in absolute and 95% alcohol, and also with two molecular proportions of the salts to one of methyl iodide in the same solvent, but in both cases the dimethyl amide was always formed. It was extremely difficult to separate the unaltered amide from the monomethyl derivative.

Molecular quantities of the sulfonamide, methyl iodide and potassium carbonate required for the equation,

$$C_6H_5CH_2SO_2NH_2 + CH_3I + K_2CO_3 = C_6H_5CH_2SO_2NHCH_3 + KI + KHCO_3,$$

were warmed in a mixture of two volumes of water to one of 95% alcohol until the methyl iodide had all disappeared, but here, also, the dimethyl as well as the monomethyl amide was formed. The best yield of pure monomethyl amide obtained in any experiment was 35% of the theoretical.

Ethyl Benzylsulfonaminoacetate, $C_6H_5CH_2SO_2NH.CH_2COOC_2H_5$.—This was prepared by digesting the potassium salt of benzylsulfonamide in alcohol with ethyl bromoacetate. After the reaction was complete the alcohol was then evaporated and the ester dissolved in ether and dried over calcium chloride. The ester was obtained as a viscous oil. Its potassium salt was obtained by digesting the ester in alcohol with the required proportion of potassium hydroxide. It separated as a colorless powder and was dried for analysis at 100°.

Calc. for $C_{11}H_{14}O_4NSK$: N, 4.76%; found, N, 4.51, 4.66, 4.46%.

The amount of ester obtained was very small. Attempts to improve the yield were made by boiling molecular proportions of ethyl bromo- and chloroacetate with the potassium salt of the amide in ether and benzene, but after two weeks' digestion a large proportion of the potassium salt was still unchanged. No better results were obtained by employing the silver salt of the amide. An attempt to prepare the ester in quantity by application of Schotten and Baumann's reaction was unsuccessful.

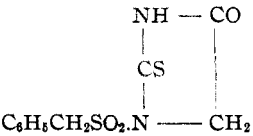
Benzylsulfonaminoacetamide, $C_6H_5CH_2SO_2NHCH_2CONH_2$.—The chloroacetamide used in this experiment was prepared according to the directions of Scholl.[1] Molecular proportions of chloroacetamide and the potassium salt of benzylsulfonamide were digested in absolute alcohol for about one hour, when the reaction was practically complete. Ammonia was always evolved during the digestion, indicating a partial hydrolysis of the amide. The alcohol was evaporated, when a dark colored residue was obtained, which dissolved in hot water. On cooling, the sulfonaminoacetamide separated in small, granular crystals. The compound was purified by crystallization from water or boiling 95% alcohol and melted at 157°. The amide is insoluble in absolute alcohol. It was dried for analysis over concentrated sulfuric acid.

Calc. for $C_9H_{12}O_3N_2S$: N, 12.30%; found, N, 12.08%.

Benzylsulfonaminoacetic Acid, $C_6H_5CH_2SO_2NHCH_2COOH$.—A quantitative yield of the sodium salt of this acid is obtained by digesting the above amide in sodium hydroxide solution until no more ammonia is evolved. After cooling the solution and acidifying with hydrochloric acid the sulfonglycocoll separates immediately on the form of plates. It crystallizes from boiling water or 95% alcohol in plates which melt at 149–150° to an oil. Schotten and Baumann's reaction was also applied with benzylsulfonchloride and glycocoll, but the yield of the acid was small and the greater portion of the acid chloride was converted into the potassium salt of the sulfonic acid.

Calc. for $C_9H_{11}O_4NS$: N, 6.13%; found, N, 6.01%.

[1] *Ber.*, **29**, 2415.

2-Thio-3-benzylsulfonhydantoin  .—Two grams of benzylsulfonglycocoll and 1 g. of dry ammonium thiocyanate were heated on the steam bath with 9 cc. of acetic anhydride and 1 cc. of glacial acetic acid. After digesting for 20 minutes, the orange-colored solution was then poured into cold water, when the thiohydantoin separated as an oil, which finally solidified. This was purified by crystallization from boiling absolute alcohol and separated in yellow prisms, which decomposed at 204° with effervescence.

Calc. for $C_{10}H_{10}O_3N_2S_2$; N, 10.39%; found, N, 10.59%.

Benzylsulfonmethylaminoacetamide, $C_6H_5CH_2SO_2N(CH_3)CH_2CONH_2$. (1) *By alkylation of benzylsulfonaminoacetamide with methyl iodide.*—The potassium salt of benzylsulfonamide and the required amount of chloroacetamide were warmed in alcohol, as described above, in order to obtain the corresponding sulfonaminoacetamide. Without attempting to isolate the latter compound a molecular proportion of potassium hydroxide in absolute alcohol was added to the solution and finally an excess of methyl iodide. The mixture was then digested until neutral and the alcohol finally evaporated. We obtained a colored residue containing the above amide, which was dissolved in hot water. On cooling, the amide deposited in clusters of colorless crystals which melted at 206° to a clear oil. The amide is soluble in boiling alcohol and insoluble in cold water. It was dried for analysis at 100°.

Calc. for $C_{10}H_{14}O_3N_2S$: N, 11.59%; found, N, 11.46, 11.88, 11.80%.

(2) *By alkylation of methylbenzylsulfonamide with chloroacetamide.*—Benzylsulfonamide was first converted into its sodium or potassium salt and the latter then digested in alcohol with methyl iodide in order to obtain the correspondlng methylamide. When the reaction was complete, one molecular proportion of sodium ethylate in alcohol solution was added and finally the required proportion of chloroacetamide. There was an immediate reaction on warming and the solution was neutral to litmus and turmeric within 15–20 minutes. The alcohol was then evaporated under diminished pressure and the residue treated as in the first method. We obtained the amide melting at 206° to a clear oil. The yield was 25–30% of the theoretical, calculating from the amount of benzylsulfonamide used.

Benzylsulfonsarcosine, $C_6H_5CH_2SO_2N(CH_3)CH_2COOH$.—A quantitative yield of this acid was obtained by hydrolysis of the above amide with barium hydroxide. An aqueous solution of the amide and an excess of

barium hydroxide was boiled until ammonia was no longer evolved. The barium was then quantitatively precipitated with sulfuric acid and the solution then concentrated by evaporation on the steam bath. On cooling, the acid separated in colorless prisms, which melted at 136° to an oil. The acid is soluble in hot water and alcohol.

Calc. for $C_{10}H_{13}O_4NS$: N, 5.78%; found, N, 5.65%.

Hydrolysis of Benzylsulfonsarcosine with Hydrochloric Acid. The Formation of Sarcosine, $CH_3NH.CH_2COOH$.—This amide is slowly decomposed by boiling with concentrated hydrochloric acid. Sulfur dioxide is evolved and benzyl chloride distils with the aqueous vapor. The hydrolysis is effected easily by heating with hydrochloric acid at 120–130° in a pressure bottle. After heating for 2–4 hours the reaction was complete and benzyl chloride was suspended in the solution. The mixture was transferred to an evaporating dish and heated on the steam bath, when benzyl chloride volatilized with steam, leaving behind the hydrochloric acid salt of sarcosine. This was absolutely free from sulfur and dissolved easily in water. After decolorization with bone coal and concentrating the solution, sarcosine hydrochloride separated in colorless crystals. It was purified for analysis by recystallization from absolute alcohol and separated in colorless needles. The salt was dried for analysis by heating at 100°.

Calc. for $C_3H_8O_2NCl$: N, 11.18%; found, N, 11.3%.

Benzyl-benzylsulfonamide, $C_6H_5CH_2SO_2NHCH_2C_6H_5$.—This amide was prepared by digesting, in alcohol, benzyl chloride with the potassium salt of benzylsulfonamide. It was purified for analysis by recrystallization from 95% alcohol and separated in colorless needles, on cooling, which melted at 145–146°. The amide is insoluble in hot and cold water and only slightly soluble in aqueous sodium hydroxide solution. The yield of the purified monobenzyl compound was 62% of the theoretical.

Calc. for $C_{14}H_{15}O_2NS$: N. 5.37%; found, N, 5.01, 5.25%.

The Conversion of Benzyl-benzylsulfonamide into Benzylamine by Hydrolysis with Hydrochloric Acid, $C_6H_5CH_2NH_2$.—This amide was not changed by boiling with hydrochloric acid. On the other hand, when heated to 130° for 2.5–3 hours with hydrochloric acid, sulfur dioxide and benzyl chloride were formed, but only about one-fifth of the amide had been decomposed. Complete hydrolysis was effected by heating at 150° for 2–3 hours. After concentration of the solution the benzylamine hydrochloride was then identified by means of its double platinum salt. This was purified by crystallization from water and was dried for analysis at 100°.

Calc. for $C_{14}H_{20}N_2PtCl_6$; Pt, 30.65%; found, Pt, 31.0%.

NEW HAVEN, CONN.