

anhydride was determined in camphor by Rast's method. Molecular weight calcd. for $C_{23}H_{35}O_6N_4$: 524.3. Found: mol. wt., 544.0.

Lysine Anhydride Dihydriodide.—One gram of ϵ, ϵ' -dicarbobenzoyllysine anhydride was dissolved in 50 ml. of glacial acetic acid and the solution kept at 50° while a stream of dry hydrogen was passed through it; about 3–4 g. of phosphonium iodide was added in portions of about 1 g. during one and one-half to two hours. The end of the reduction was indicated by the ceasing of carbon dioxide evolution. A voluminous precipitate accumulated at the bottom of the reaction flask as the phosphonium iodide disappeared. At the end of the reduction the clear liquid was decanted and the precipitate washed several times with dry ether, and dissolved in the minimum quantity of water to decompose the excess phosphonium iodide. (When large amounts of water were used, the subsequent addition of alcohol and ether caused the lysine anhydride dihydriodide to separate out as an oily mass.) The aqueous solution was mixed with a few ml. of absolute alcohol, and the anhydride dihydriodide precipitated by the addition of 50 ml. of ether. After standing overnight in the ice box, the solvent was decanted from the crystalline precipitate and the latter dissolved in the minimum quantity of water. The aqueous solution was filtered and evaporated to dryness in a vacuum desiccator over sulfuric acid and sodium hydroxide. The solid residue was washed thoroughly with dry ether and dried *in vacuo*.

On analysis it proved to be pure lysine anhydride dihydriodide and was obtained in almost quantitative yield.

Anal. Calcd. for $C_{12}H_{26}O_2N_4I_2$: C, 28.1; H, 5.1; N, 10.9; amino N, 5.5; I, 49.6. Found: C, 28.1; H, 5.0; N, 10.8; amino N, 5.3; I, 50.0.

The highly hygroscopic lysine anhydride dihydriodide is very soluble in water but insoluble in organic solvents. On heating its aqueous solution with an alkaline solution of picric acid a deep red coloration was obtained indicating the presence of a diketopiperazine structure. The ninhydrin reaction was negative.

Lysine Anhydride Picrolonate.—Two hundred mg. of lysine anhydride dihydriodide was dissolved in 3 ml. of water and poured into a hot saturated aqueous solution containing about 400 mg. of picrolonic acid. A voluminous yellow precipitate separated out on cooling. After standing overnight in the ice box, the precipitate of lysine anhydride picrolonate was filtered and purified by dissolving in alcohol and precipitating by ether; yield 240 mg., 78% of the theoretical.

Anal. Calcd. for $C_{32}H_{40}O_{12}N_{12}$: C, 48.9; H, 5.1; N, 21.4. Found: C, 49.0; H, 5.3; N, 21.4.

On rapid heating, the picrolonate softens at 230° and decomposes at 235 – 237° .

It dissolves only sparingly in cold water but fairly readily in hot water. It is soluble in alcohol but insoluble in benzene and ethyl acetate.

Lysine Anhydride Picrate.—Five hundred mg. of lysine anhydride dihydriodide was dissolved in 10 ml. of water and 1 g. of solid picric acid was added. The mixture was heated until a clear solution was obtained and then allowed to cool down to room temperature. After standing overnight in the ice box, the yellow picrate was filtered off and washed several times with ether; yield 680 mg., 97% of the theoretical. For analysis the picrate was recrystallized from water.

Anal. Calcd. for $C_{24}H_{30}O_{16}N_{10}$: C, 40.3; H, 4.2; N, 19.6. Found: C, 40.3; H, 4.3; N, 19.6.

On rapid heating the substance liquefies at about 240° and explodes at 243 – 245° . It is soluble in hot water and in methyl and ethyl alcohol, but insoluble in ether and benzene.

Lysine Anhydride Dihydrochloride.—1.25 ml. of 1 *N* hydrochloric acid was added to 300 mg. of lysine anhydride picrate suspended in 5 ml. of water. The mixture was shaken several times with ether to remove the picric acid liberated. An equal volume of alcohol was then added to the aqueous solution and the mixture dried at room temperature in a vacuum desiccator over sulfuric acid and sodium hydroxide. The remaining hydrochloride was washed several times with dry ether and dried *in vacuo*. The yield was quantitative.

Anal. Calcd. for $C_{12}H_{26}N_4Cl_2$: Cl, 21.6. Found: Cl, 21.8.

The dihydrochloride is very soluble in water and gives a strong red coloration when heated with an alkaline solution of picric acid. The ninhydrin reaction is negative. The dihydrochloride is insoluble in organic solvents.

Summary

ϵ, ϵ' -Dicarbobenzoyllysine anhydride (II) was prepared by heating ϵ -carbobenzoyl-*L*-lysine methyl ester.

The two carbobenzoxy groups of (II) were removed by reduction with phosphonium iodide and lysine anhydride dihydriodide (III) was obtained.

From (III) the corresponding picrolonate, picrate and dihydrochloride were prepared.

JERUSALEM, PALESTINE

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

The Action of Sulfuric Acid on Tertiary Carboxylic Acids¹

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Bistrzycki⁴ investigated the cleavage of carbon monoxide from tertiary carboxylic acids in concentrated sulfuric acid. The product, yield, and conditions of his experiments are summarized in Table I.

Böeseken⁵ obtained a product similar to that

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(4) Bistrzycki and Mauron, *Ber.*, **40**, 4370 (1907).

(5) Böeseken, *Rec. trav. chim.*, **29**, 85 (1910).

TABLE I

	Starting material	Product	Yield, %	Temp., °C.
1	$(C_6H_5)_3CCOOH$	$(C_6H_5)_3COH$	90	25
2	$(C_6H_5)_2(CH_3)CCOOH$	$(C_6H_5)_2C=CH$	85	25
3	$C_6H_5(CH_2)_2CCOOH$	$C_6H_5SO_3H^a$	51	70
4	$(CH_3)_3CCOOH$	$C_4H_8S_2O_6H_2^a$	35	110

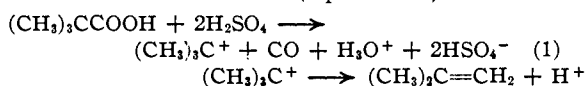
^a These products were analyzed, but the structures were not determined.

isolated by Bistrzycki by heating trimethylacetyl chloride to 100° in concentrated sulfuric acid. By stopping the reaction at 50° he was able to detect a small amount of isobutylene polymer.

In the present investigation the sulfonic acids isolated by Bistrzycki have been identified. The barium salt of the sulfonic acid from dimethylphenylacetic acid was prepared by duplicating Bistrzycki's experiment. Upon oxidation with alkaline permanganate this gave *o*-sulfobenzoic acid. No benzoic acid was isolated, which showed conclusively that sulfonation had taken place in the ring, and that the original product, $C_9H_9SO_3H$, was chiefly *o*-sulfo- α -methylstyrene and its polymers.

The sodium salt of the disulfonic acid from trimethylacetic acid was prepared and converted into the benzylthiuronium salt, the disulfonyl chloride, and the disulfonanilide. These three compounds were shown to be identical with the derivatives prepared from the dioxane salt of 2-methylpropene-1,3-disulfonic acid.⁶

The conversion of trimethylacetic acid into an isobutylene derivative by sulfuric acid at first suggests the formation of isobutylene as an intermediate in the reaction (equation 1). However,



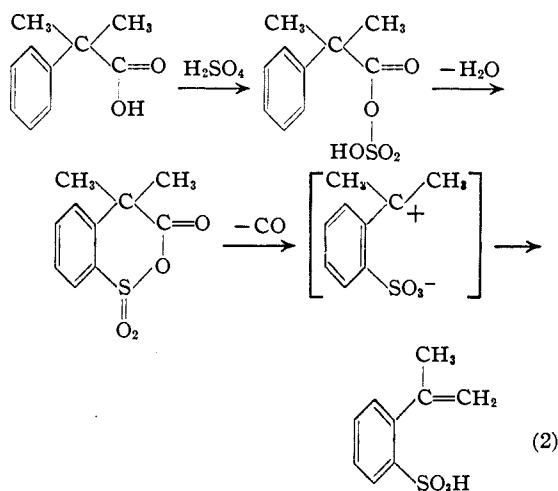
it is well known that both isobutylene⁷ and *t*-butyl alcohol are rapidly polymerized under these conditions. In an effort to find a reasonable mechanism for this conversion, several reactions have been investigated.

It was first thought that sulfonation rather than polymerization might take place in a dilute solution of trimethylcarbonium ions in concentrated sulfuric acid. To provide for the slow formation of this ion in solution, *t*-butyl chloride was stirred with concentrated sulfuric acid at 20°, and also at 100° for several hours. In each case hydrogen chloride was given off slowly and isobutylene polymers were isolated in high yield, but in neither experiment was any sulfonic acid found.

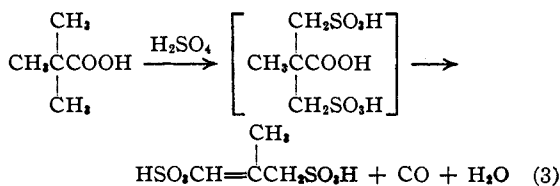
An effort was then made to determine the nature of the intermediate by allowing trimethylacetic acid to react with concentrated sulfuric acid in the presence of toluene, which could act as an ion acceptor to give *t*-butyltoluene. However, the toluene was sulfonated more readily than the trimethylacetic acid, causing dilution of the medium. No carbon monoxide was evolved, and the trimethylacetic acid was recovered unchanged. When chlorobenzene was substituted for toluene in this reaction, carbon monoxide was evolved, but no evidence of any substitution of the trimethylacetyl or *t*-butyl radical into the aromatic ring was found.

Since it does not seem reasonable to assume that the 2-methylpropene-1,3-disulfonic acid is formed by the sulfonation of isobutylene, as was first suggested by Böeseken,⁴ another mechanism is needed to explain the diversified products obtained by Bistrzycki. Triphenylacetic acid and

diphenylmethylacetic acid are sufficiently unstable in concentrated sulfuric acid to decompose at room temperature without sulfonation. The formation of a ring-sulfonated α -methylstyrene from dimethylphenylacetic acid is explained by the fact that this acid must be heated to 70° in concentrated sulfuric acid before decomposition is complete. At this temperature, toluene and its homologs are readily sulfonated in concentrated sulfuric acid. α -Methylstyrene gives a mixture of *m*- and *p*-sulfo- α -methylstyrenes when stirred at room temperature for two hours. Therefore, sulfonation of dimethylphenylacetic acid does not occur after the loss of carbon monoxide. But sulfonation of toluene and homologs of toluene occurs principally in the para position at elevated temperatures, and the volume effect of the dimethylacetic acid group would tend to hinder ortho-substitution; therefore, the normal product of sulfonation of dimethylphenylacetic acid should be *p*-sulfo-dimethylphenylacetic acid or *p*-sulfo- α -methylstyrene. Since the ortho-sulfonated product is formed, sulfonation must be influenced by the loss of carbon monoxide in some way. As most carboxylic acids form sulfuric anhydrides in sulfuric acid, a mechanism involving this intermediate would appear to be reasonable. Cyclo-dehydration of the sulfuric anhydride of dimethylphenylacetic acid would yield the *o*-sulfo-dimethylphenylacetic anhydride which could then lose carbon monoxide to give *o*-sulfo- α -methylstyrene (equation 2). The formation of 2-methyl-



propene-1,3-disulfonic acid from trimethylacetic acid is probably due to the formation of an unstable sulfonated, carboxylic acid as the intermediate (equation 3). The formation of such an



(6) Suter and Malkemus, *THIS JOURNAL*, **63**, 978 (1941).

(7) Ipatieff and Pines, *J. Org. Chem.*, **1**, 464 (1936); others.

intermediate is not without precedent, since β -sulfonation of aliphatic acids has previously been reported⁸ and β -substituted sulfonic acids are unstable.⁹ The isolation of some isobutylene in this reaction, as reported by Böeseke,⁵ would be expected since equation 1 would not be completely inhibited.

Experimental

Reaction of Trimethylacetic Acid.—Six grams (0.059 mole) of trimethylacetic acid was dissolved in 30 cc. of concentrated sulfuric acid, and heated to 105–110° in an oil-bath. At this temperature carbon monoxide was slowly evolved, and some charring took place. There was a noticeable odor of isobutylene polymer present. After four hours the reaction mixture was poured into 500 cc. of cold water, treated with barium carbonate to remove sulfate then with sodium carbonate to remove barium, and evaporated until crystals began to form. On cooling, flat plates were deposited. The yield was 7.7 g. or 50% of theoretical. This salt reduced potassium permanganate, and the oxidized solution precipitated barium sulfate when barium chloride was added, indicating an unsaturated linkage adjacent to sulfonic group.¹⁰

Benzylthiuronium Salt.—This derivative was prepared in the usual manner,¹¹ recrystallized twice from 50% ethyl alcohol, and dried for several hours in an Abderhalden drying pistol. After drying, it melted at 139–140°. The benzylthiuronium salt prepared from the dioxane salt of 2-methylpropene-1,3-disulfonic acid melts at 140–141°. A mixture shows no lowering of the melting point.

Anal. Calcd. for $C_{20}H_{28}O_6N_4S_4$: N, 10.22. Found: N, 10.49, 10.37.

2-Methylpropene-1,3-disulfonyl Chloride.—This derivative was prepared by the action of phosphorus oxychloride on the sodium salt. The product was extracted with chloroform, and recrystallized in long needles from carbon tetrachloride. It melts at 77–79°. A mixed melting point with an authentic sample was 77.8–78.4° (cor.).

2-Methylpropene-1,3-disulfonanilide.—This was prepared by refluxing aniline and the disulfonyl chloride in a dry solvent, and recrystallizing the derivative from chloroform. It melts at 171.6–172.4° (cor.). Mixed with an authentic sample, the melting point is identical.

Reaction of Dimethylphenylacetic Acid.—Ten grams (0.061 mole) of dimethylphenylacetic acid was dissolved in concentrated sulfuric acid, and let stand at room temperature for thirty-three hours, then heated to 72° for one hour. The mixture was poured over ice, and diluted until the final volume was approximately 500 cc. No unreacted dimethylphenylacetic acid was precipitated. Barium carbonate was added until the solution was neutral, and the barium sulfate filtered off. The clear solution was evaporated to dryness, leaving a glassy residue. This was ground to powder, and weighed 11 g., which is equivalent to a 67% yield of the barium salt of $(C_6H_5SO_3H)_2$.

Oxidation.—Three and one-half grams of the barium salt was dissolved in 100 cc. of water, and 8 g. of potassium permanganate and 1 cc. of 50% sodium hydroxide added. The mixture was refluxed several hours. The precipitated manganese dioxide was filtered off, and the clear solution acidified with hydrochloric acid. Several grams of solid barium chloride was added, and the solution evaporated until it became cloudy. On cooling, a salt separated, and was collected. The benzylthiuronium salt of this compound was prepared and recrystallized once. It forms beautiful flat plates, melting point 205–206°. Mixing with the dibenzylthiuronium salt of *o*-sulfobenzoic acid¹² showed no lowering of the melting point.

Anal. Calcd. for $C_{23}H_{26}O_6N_4S_4$: N, 10.25. Found: N, 10.35.

Sulfonation of α -Methylstyrene.—Approximately 20 g. (0.17 mole) of α -methylstyrene (b. p. 161–163°) was stirred into 177 g. (1.81 moles) of cold concentrated (96%) sulfuric acid. An orange opaque polymer was immediately formed with the evolution of heat. After stirring for one hour, the mixture was heated to 75° and stirred for two hours longer, so that the polymer first formed finally went into solution. After cooling, the amber solution was poured over ice and diluted to about 500-ml. volume. This acid solution was decolorized with Norite, and partially neutralized with 500 g. (1.6 moles) of barium hydroxide octahydrate, and then excess barium carbonate (70 g., 0.35 mole) was added with stirring. The neutral solution was filtered to remove the barium salts, and the clear filtrate evaporated to dryness. By this means, 31.4 g. of a golden yellow glassy barium salt of the sulfonated α -methylstyrene polymer was obtained.

A mixture of 15.7 g. of this polymer with 20 ml. of 25% sodium hydroxide solution and 72 g. (0.6 mole) of potassium permanganate was stirred and refluxed in 400 ml. of water for twenty-four hours. The precipitated manganese dioxide was removed by filtration, and the clear solution acidified with hydrochloric acid. No precipitate of benzoic acid appeared at this point, indicating that sulfonation of the aromatic ring had been complete. The solution was evaporated to dryness; final drying in an oven at 110°. A portion of the salt mixture obtained in this way was tested with S-benzylthiuronium chloride solution¹² and an oil was obtained. This indicates that the product of the oxidation is either *m*-sulfobenzoic acid or a mixture of the meta and para isomers. Little or no *o*-sulfobenzoic acid was present, since the S-benzylthiuronium salt of this acid is immediately precipitated, even in hot solutions.

The S-benzylthiuronium test was confirmed by converting the sulfobenzoates to the chlorobenzoic acids with phosphorus pentachloride.¹³ About 5 g. of the sulfobenzoate salt (22 g. of the salt mixture) was mixed with 15 g. of phosphorus pentachloride, sealed in a Carius bomb tube and heated for twenty-four hours at 178°. When the tube was opened, sulfur dioxide was evolved, and the oily residue was poured over ice. After boiling to completely decompose the acid chloride, the solution was cooled and filtered. The residue, after washing with water, was taken up in alkaline solution (some insoluble oil remained), treated with decolorizing charcoal, and reprecipitated with hydrochloric acid. This mixture of *m*- and *p*-chlorobenzoic acids melted 212–224° after one recrystallization from hot water, and careful recrystallization yielded a small sample of *p*-chlorobenzoic acid, m. p. 238–241°, which when mixed with an authentic sample melted at 239–241°.

The above experiments show that sulfonation of α -methylstyrene in 96% sulfuric acid at 75° yields a mixture of *meta*- and *para*-sulfonated polymers, with *para*-sulfonation probably predominating.

Summary

1. Dimethylphenylacetic acid gives *o*-sulfo- α -methylstyrene polymers in concentrated sulfuric acid. Trimethylacetic acid gives 2-methylpropene-1,3-disulfonic acid under similar conditions.

2. α -Methylstyrene and isobutylene are not the intermediates in these reactions. Some possible intermediates are discussed, and a mechanism for the reaction suggested.

3. α -Methylstyrene yields a mixture of *meta*- and *para*-sulfonated polymers in 96% sulfuric acid at 75°.

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(8) Kharasch, Chao and Brown, *THIS JOURNAL*, **62**, 2393 (1940).

(9) Kohler, *Am. Chem. J.*, **19**, 728 (1897).

(10) Kohler, *Am. Chem. J.*, **20**, 680 (1898).

(11) Donleavy, *THIS JOURNAL*, **58**, 1004 (1936).

(12) Suter and Campaigne, *THIS JOURNAL*, **64**, 3040 (1942).

(13) "Beilstein," 4th ed. Vol. XI, p. 369.