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Arylsulfimide Polymers. II. The Syntheses of Selected Monomeric Saccharins and Derivatives

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Arylsulfimide Polymers. II. The Syntheses of Selected Monomeric Saccharins and Derivatives†

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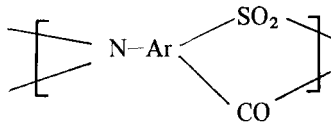
SUMMARY

Improved syntheses of 5- and 6-aminosaccharins are described. The preparation and characterization of 4-nitro-2-sulfobenzoic anhydride, ethyl 4-nitro- and 4-amino-2-sulfamidobenzoates, and triethylammonium 6-aminosaccharinate are also described. The direct ring nitration of saccharin and of two of its derivatives was attempted, and the results of these reactions and of the attempted preparation of aminosulfobenzoic anhydrides are detailed. A general procedure for the conversion of benzosulfonimide to the corresponding sulfobenzoic anhydride in high yield is also given.

INTRODUCTION

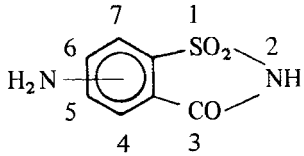
In the course of our investigation of thermally stable polymers, we became interested in polymers incorporating the benzosulfonimide group, including those possessing the following repeating unit (I):

†Taken in part from the Ph.D. dissertation of W. A. Fessler.

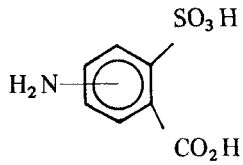


(I)

Monomers which would be suitable for generating this unit by polycondensations, such as transamidation or direct reactions, include the aminosaccharins (**II**), the aminosulfomenzoic acids (**III**), the aminosulfobenzoic anhydrides (**IV**), or appropriate derivatives of these compounds. Accordingly, this study was undertaken to develop useful synthetic routes to these compounds with a view to their subsequent use in polymerization reactions.



(II)



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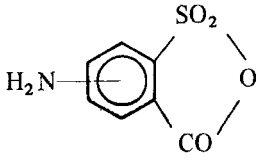


(IV)

Compounds in which the amino groups were located ortho to either of the acid functions were not investigated. It was felt that this arrangement of substituents would permit unwanted steric interactions or secondary intromolecular reactions to interfere with the desired polymerization reactions.

DISCUSSION

Warren and Hamor [1] reported the preparation of 5-amino-saccharin (**X**) starting with 2-methyl-4-nitroaniline (**V**) and using 2-methyl-4-nitrobenzenesulfonamide (**VIII**) as an intermediate. These authors did not give an overall yield for this synthesis. We repeated their work up to the preparation of 2-methyl-4-nitrobenzenesulfonamide with an overall yield of 1.6%. Since large amounts of the monomer were needed for prototype and polymerization studies, a more efficient synthesis of this critical intermediate was developed (Scheme I).

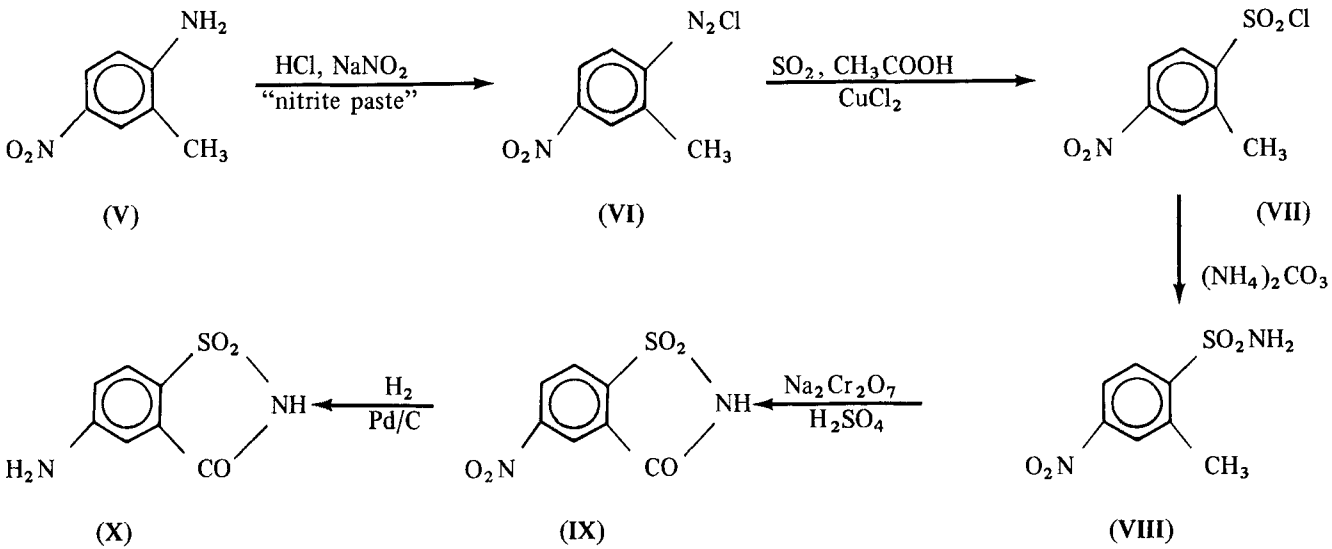
2-Methyl-4-nitroaniline was diazotized using an inverted method [2, 3] in which the amine and sodium nitrite were mixed with water to form a paste, which was then added in small portions to concentrated hydrochloric acid. Direct diazotization of the amine gave much lower yields, 20% overall from (**V**) → (**VII**) compared to 75% from (**V**) → (**VII**) for the inverted method.

Conversion of the diazonium salt (**VI**) to the sulfonyl chloride (**VII**) was accomplished by using a modification of the Sandmeyer reaction developed by Meerwein and co-workers [4]. The preparation of the sulfonamide (**VIII**) proceeded without complications, and the overall yield for this product starting from 2-methyl-4-nitroaniline (**V**) was 59%. This yield represents almost a 40-fold increase over that obtained by employing the procedures of Warren and Hamor [1].

All attempts to oxidize the methyl group of 2-methyl-4-nitrobenzenesulfonamide (**VIII**) using alkaline or neutral permanganate solution were unsuccessful, with only starting materials being isolated from the reaction mixtures. Warren and Hamor [1] reported using this reagent to convert compound (**XIII**) to (**IX**) in 30% yield; however, the conditions employed were not reported. Our attempts at permanganate oxidation were essentially those which Noyes [5] reported for the oxidation of 2-methyl-5-nitrobenzenesulfonamide.

Ultimately, 5-nitrosaccharin was prepared by oxidation of compound (**VIII**) with soidum dichromate in sulfuric acid according to the procedure

Scheme 1. Synthesis of 5-Aminosaccharin



of Chang [6]. This oxidation was very vigorous and some difficulty was experienced in keeping the reaction under control. Similar difficulties were encountered in the preparation of 6-nitrosaccharin and are discussed in greater detail in relation to that synthesis.

The final step in this synthetic sequence was the catalytic reduction of 5-nitrosaccharin (**IX**) to 5-aminosaccharin (**X**) [1]. The overall yield of this final product starting from 2-methyl-4-nitroaniline (**V**) was 16%, which is a substantial improvement over the 0.4% yield which could be expected by following published procedures.

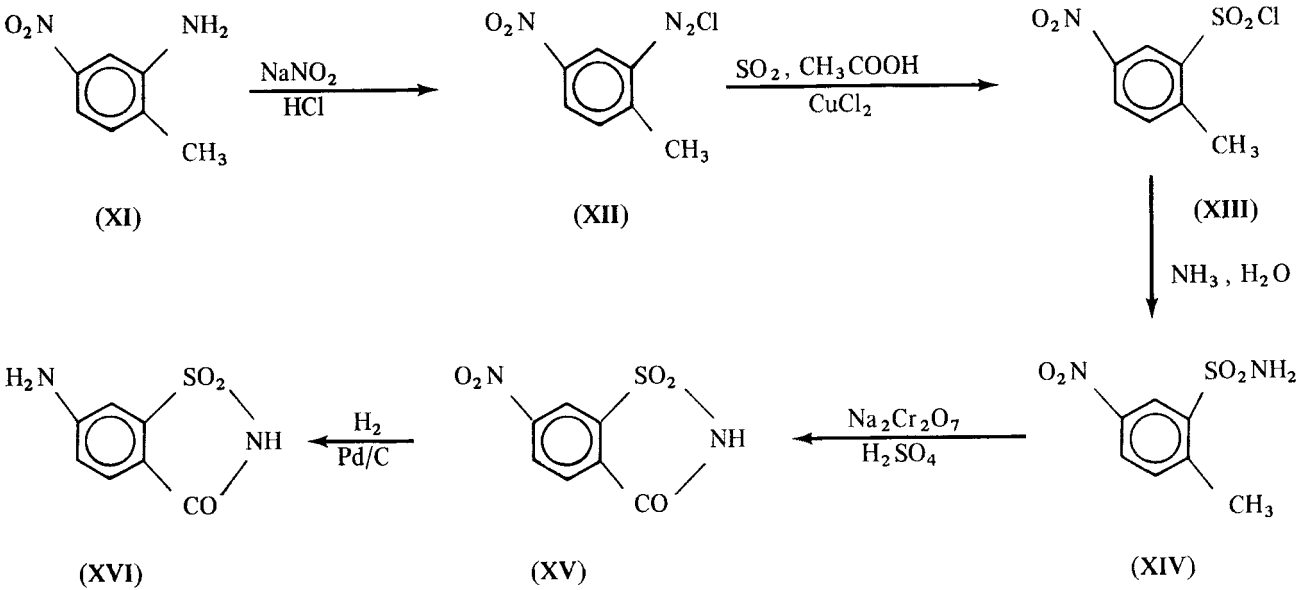
Synthesis of 6-aminosaccharin (**XVI**) had been previously reported by both Noyes [5] and Kastle [7], but no indication of overall yield was given by either of these authors. A modification [8] of the Noyes procedure, which started with p-nitrotoluene, was investigated, but the overall yield of 2-methyl-5-nitrobenzenesulfonamide (**XIV**) was only 25%, and this intermediate had to be carried through two more steps. Therefore, 6-aminosaccharin was prepared by a sequence of reactions (Scheme 2) analogous to that used in the synthesis of 5-aminosaccharin.

By this route, 2-methyl-5-nitrobenzenesulfonamide (**XIV**) was prepared from 2-methyl-5-nitroaniline (**XI**) in overall yields as high as 90%. Comparable yields were obtained from the inverted and direct methods of diazotization. The latter method was preferred for its relative speed and simplicity.

As was the case with the reaction relative to the preparation of 5-aminosaccharin, difficulties were encountered in the oxidation step of the 6-aminosaccharin synthesis. Several variations [5, 7, 9] of the permanganate oxidation of compound (**XIV**) were tried, but only starting materials were isolated from these reactions. Hamor [10] also reported difficulty in obtaining good yields from the permanganate oxidation of 2-methyl-5-nitrobenzenesulfonamide (**XIV**).

Of the several dichromate oxidation procedures [6, 11, 12] tested, the method of Chang proved most suitable. Initially, erratic results were given by this procedure, with some reactions proceeding smoothly while others were very violent and resulted in charring of the product. It was noted that the violent reactions were accompanied by the evolution of chlorine gas, and this feature was attributed to the presence of impurities such as 2-chloro-4-nitrotoluene in samples of the sulfonamide. The chloro compound is a minor by-product in the synthesis of 2-methyl-5-nitro-benzenesulfonyl chloride. Use of carefully recrystallized samples of the sulfonamide eliminated this problem. Control of the dichromate oxidations was achieved by limiting the scale of the reaction to a maximum of 17-20 g of sulfonamide

Scheme 2. The Synthesis of 6-Aminosaccharin



and by efficient dissipation of the heat of the reaction through vigorous stirring and the use of a cooling water bath.

The reduction of 6-nitrosaccharin (**XV**) to 6-aminosaccharin (**XVI**) was efficiently achieved by catalytic hydrogenation. The overall yield of 6-aminosaccharin from 2-methyl-5-nitroaniline was excellent, 67%, or four times higher than the yield of 5-aminosaccharin from the analogous reaction sequence.

Direct nitration of saccharin would seem to offer a more economical route to the aminosaccharins. However, our investigation of this reaction confirmed the work of Hamor [10], who reported obtaining a nitro derivative of o-sulfobenzoic anhydride from the attempted nitration of saccharin. We found that when saccharin was treated with a mixture of nitric and sulfuric acids at 95-100°C, a poor yield (13.9%) of nitro-o-sulfobenzoic anhydride was isolated. The melting point (212-218°C) of this anhydride corresponds closely to that reported by Stubbs [13] for 5-nitro-2-sulfobenzoic anhydride (mp 212°C). When the nitration reaction was carried out at room temperature, only saccharin itself was isolated from the reaction mixture.

Further attempts were made to nitrate directly the benzene ring of derivatives of saccharin, without success. The attempted direct ring nitration of N-acetylsaccharin yielded N-nitrosaccharin, and the attempted direct ring nitration of ethyl o-sulfamidobenzoate resulted in the elimination of ethanol and the formation of saccharin.

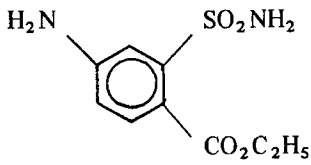
Both amino-2-sulfobenzoic anhydride and the corresponding free acid were of interest to us as possible monomers. As reported above, the 5-nitroanhydride could be obtained in poor yield from the attempted nitration of saccharin. The 5-nitroanhydride was also obtained in poor yield from the nitration of o-sulfobenzoic acid [13]. There have been a number of reports of the syntheses of various nitro- and amino-2-sulfobenzoic acids [13-17]. However, we prepared the 4-nitro acid and, via the acid, the 4-nitro anhydride by a reaction which involved both simpler work-up procedures and extremely good yields.

6-Nitrosaccharin was hydrolyzed in concentrated hydrochloric-90% nitric acids, and the almost pure product, 4-nitro-2-sulfobenzoic acid, was isolated in quantitative yield when the reaction mixture was evaporated to dryness. The product, as isolated, could then be converted to the anhydride in yields as high as 84% by treatment with acetic anhydride or thionyl chloride. This procedure for converting a benzosulfonimide to a sulfobenzoic anhydride was also adapted to the preparation of o-sulfobenzoic anhydride and the bianhydride of benzene-1,3-dicarboxyl-4,6-disulfonic acid [18].

4-Nitro-2-sulfobenzoic acid was converted to 4-amino-2-sulfobenzoic acid by catalytic hydrogenation in 92% crude yield. The neutralization equivalent and elemental analysis of the recrystallized product indicated that the acid, which did not melt up to 200°C, was not hydrated. While chemical reductions of this nitro group have been reported [14, 15, 17], no description of the catalytic procedure was located in the literature.

Reduction of the nitro group of 5-nitro-2-sulfobenzoic anhydride produced a yellow resin. 4-Nitro-2-sulfobenzoic anhydride was also subjected to catalytic hydrogenation. When an aliquot of the product mixture was quenched in ice, 4-amino-2-sulfobenzoic acid was isolated. A solid, isolated from the original product mixture, was characterized as a mixture of dimers and trimers of aminosulfobenzoic anhydride. It appears that, while the nitro groups of the anhydrides are readily reduced, the resulting products undergo spontaneous self-condensation. Similar behavior had been previously observed with 4-nitrophthalic anhydride [19]. Because of this tendency to polymerize, the amino anhydrides could not be isolated and characterized.

Ethyl 4-amino-2-sulfamidobenzoate (**XVII**) was synthesized from 6-nitrosaccharin. The imide was first solvolyzed by treatment with ethanol saturated with hydrogen chloride according to the procedure of Fahlberg and List [20]. The product was identified as ethyl 4-nitro-2-sulfamidobenzoate (**XVIII**) by its infrared spectrum and elemental analysis. When this compound was heated above its melting point (134-135°C), ethanol was eliminated and 6-nitrosaccharin was isolated from the melt.



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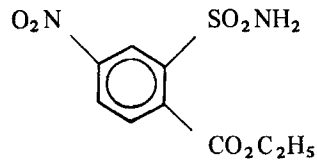
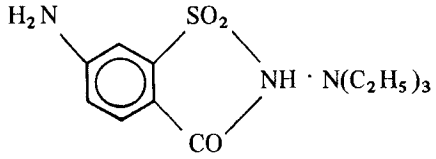


(XVIII)

Some difficulty was encountered in the catalytic hydrogenation of the nitro group of ethyl 4-nitro-2-sulfamidobenzoate. The optimum conditions for this reaction required a 2:1 ratio by weight of the nitro compound to palladium on charcoal catalyst. Under these conditions, a 75% yield of purified ethyl 4-amino-2-sulfamidobenzoate, mp 146-149°C, was obtained. The elemental analysis of this product was in agreement with the structural assignment. The differential thermogram of the product

showed a sharp inflection at 145°C corresponding to the melting point of the compound and an exotherm at 152°C. When a sample of the product was heated above its melting point, 6-aminosaccharin was isolated from the melt. Ethyl 4-amino-2-sulfamidobenzoate apparently eliminates a molecule of ethanol and cyclizes to the imide under these conditions.

Triethylammonium 6-aminosaccharinate (**XIX**), mp 177-180°C, was prepared in 87% yield by treating 6-aminosaccharin dissolved in benzene-ethanol with triethylamine. The structure assigned to the product of this reaction was confirmed by infrared spectroscopy and the elemental analysis.



(XIX)

EXPERIMENTAL

Preparation of 5-Aminosaccharin

Preparation of 2-Methyl-4-Nitrobenzenesulfonyl Chloride by the Method of Meerwein and Co-workers [4]. Sodium nitrite (18.75 g, 0.27 mole) was dissolved in water (17 ml). To this solution was added 2-methyl-4-nitroaniline (38.03 g, 0.25 mole) to make a paste. This paste was added in portions to hydrochloric acid (85 ml, 12 N) cooled in an ice bath. The temperature was maintained below 5°C. After the addition had been completed, the mixture was allowed to stand for 15 min at 5°C and was then filtered. A sulfur dioxide-acetic acid-copper (**II**) chloride was prepared by adding copper (**II**) chloride (9 g) dissolved in water (10 ml) to 200 ml of a 30% solution of sulfur dioxide in glacial acetic acid. The acetic acid solution was cooled to 5°C and the filtered diazonium chloride solution was added to it with vigorous stirring. The solution warmed to about 25°C and nitrogen was evolved. A yellow-orange solid precipitated and, after 30 min, was removed by filtration. There were obtained 42 g (75%) of 2-methyl-4-nitrobenzenesulfonyl chloride, mp 64-65°C.

Preparation of 2-Methyl-4-Nitrobenzenesulfonamide. Crude 2-methyl-4-nitrobenzenesulfonyl chloride (20.3 g, 0.08 mole) was heated on a steam

bath with ammonium carbonate (10 g) for 8 hr. The product was recrystallized from water. There were obtained 14 g (79%) of a pale-yellow solid, mp 155-157°C (lit. [21] 2-methyl-4-nitrobenzenesulfonamide, mp 157°C).

Chromic Acid Oxidation [6] of 2-Methyl-4-Nitrobenzenesulfonamide to 5-Nitrosaccharin. Water (52.5 g), sulfuric acid (143.5 g, specific gravity 1.84), and sodium dichromate (75 g, 0.25 mole, 1.51 equiv) were mixed in a 2-liter, three-necked, round-bottom flask equipped with a reflux condenser, a mechanical stirrer, and a dropping funnel. 2-Methyl-4-nitrobenzenesulfonamide (54 g, 0.25 mole, 1.50 equiv) was added to the dichromate mixture. Stirring was started and the mixture was heated to 57°C in a water bath. Sulfuric acid (161 g, specific gravity 1.84) was added cautiously from the dropping funnel. The first few drops caused a violent reaction in which the color of the mixture changed from bright red to green. After the reaction had subsided, the mixture was poured onto crushed ice. A white solid precipitated and was removed by filtration and dried in vacuo. There were obtained 21 g (39%) of a white solid, mp 150-200°C. After recrystallization from ethyl acetate, there was obtained a white solid, mp 210-213°C (lit. [1] 5-nitrosaccharin, mp 212-214°C).

Anal: Calculated for $C_7H_4N_2O_5S$: C, 36.81; H, 1.75; N, 12.29; S, 14.04. Found: C, 37.54; H, 1.90; N, 12.36; S, 14.21.

Preparation of 5-Aminosaccharin. 5-Nitrosaccharin (2 g, 0.009 mole) and 5% palladium-on-charcoal (0.7 g) were placed in a Parr bottle with absolute ethanol (50 ml). The bottle was placed on the Parr apparatus, flushed three times with hydrogen, and pressured with hydrogen (45 psi). The bottle and contents were shaken at room temperature for 12 hr. The catalyst was removed by filtration and the filtrate evaporated to a small volume at reduced pressure. A yellow solid precipitated and was removed by filtration. There were obtained 1.2 g (69%) of a solid, mp 291-293°C (lit. [1] 5-aminosaccharin, mp 291-293°C). 5-Aminosaccharin was observed to polymerize above its melting point.

Anal: Calculated for $C_7H_6N_2O_3S$: C, 42.40; H, 3.03; N, 14.15; S, 16.17. Found: C, 42.63; H, 3.23; N, 13.94; S, 16.08.

Preparation of 6-Aminosaccharin

Modified Preparation of 2-Methyl-5-Nitrobenzenesulfonamide. 2-Methyl-5-nitroaniline (152 g, 1.0 mole) and hydrochloric acid (340 ml, 12 N) were placed in a 2-liter beaker and cooled to less than 5°C. A solution

of sodium nitrite (75 g, 1.09 moles) in water (280 ml) was added, with vigorous stirring, at a rate such that the temperature of the reaction mixture remained below 5°C. After the addition had been completed, the mixture was stirred for 30 min and filtered; the acid residue was discarded. The filtrate was added to a stirred soltuion made by adding aqueous copper (II) chloride (40 g of copper (II) chloride in 36 ml of water) to acetic acid (400 ml) saturated with sulfur dioxide. A vigorous reaction occurred with the evolution of nitrogen and the formation of an oil layer. After stirring for 45 min, the oil was collected. The oil was added to a 500-ml beaker containing ammonium hydroxide (140 ml, 15 N) and water (140 ml). The mixture was heated on a steam bath for 30 min and acidified with dilute sulfuric acid. A white solid precipitated and was removed by filtration. The product was recrystallized from water and dried in vacuo. There were obtained 195 g (90%) of a white crystalline solid, mp 185-187°C (lit. [10] 2-methyl-5-nitrobenzenesulfonamide, mp 186-187°C).

Anal: Calculated for $C_7H_8N_2O_4S$: C, 38.90; H, 3.70; N, 13.00; S, 14.80. Found: C, 38.63; H, 3.42; N, 13.07; S, 14.95.

Oxidation of 2-Methyl-5-Nitrobenzenesulfonamide to 6-Nitrosaccharin. Water (21 g), sulfuric acid (57.6 g, specific gravity 1.84), and sodium dichromate (30 g, 0.1 mole, 0.6 eq) were placed in a 1-liter, three-necked, round-bottom flask equipped with a reflux condenser, a mechanical stirrer, and a dropping funnel. Twice-recrystallized 2-methyl-5-nitrobenzenesulfonamide (17.0 g, 0.086 mole, 0.48 equiv) was added, and the flask was placed in a water bath at 54°C. Stirring was started, and sulfuric acid (51 g, specific gravity 1.84) was added slowly from the dropping funnel. After the addition of the sulfuric acid had been completed, the green mixture was stirred for 45 min before pouring it onto crushed ice (500 g). A white solid precipitated and was removed by filtration.

This procedure was repeated using additional 2-methyl-5-nitrobenzenesulfonamide (17 g, 0.086 mole, 0.48 eq). The combined products were dissolved in aqueous sodium carbonate solution (150 ml, 0.3 M). The carbonate solution was filtered and the filtrate was acidified with dilute sulfuric acid. A cream-colored solid precipitated and was removed by filtration and dried. There were obtained 28.5 g (80%) of a cream-colored solid, mp 209-211°C (lit. [10] 6-nitrosaccharin, mp 206-209°C).

Anal: Calculated for $C_7H_4N_2O_5S$: C, 36.81; H, 1.75; N, 12.29; S, 14.04. Found: C, 36.58; H, 1.83; N, 12.43; S, 14.29.

Preparation of 6-Aminosaccharin. 6-Nitrosaccharin (10 g, 0.044 mole),

5% palladium-on-charcoal (1.0 g), and absolute ethanol (250 ml) were placed in a Parr bottle. The bottle was placed in the Parr apparatus, flushed three times with hydrogen, and filled with hydrogen (42 psi). The mixture was agitated at room temperature for 15-30 min, during which time the pressure dropped to approximately 32 psi. The bottle was again filled with hydrogen (42 psi), and the agitation was continued for an additional 30 min. The catalyst was removed by filtration and the filtrate was evaporated to dryness at reduced pressure. The solid residue was recrystallized from ethanol and dried. There were obtained 8.2 g (93%) of a yellow solid, mp 291-293°C (lit. [10] 6-aminosaccharin, mp 283-285°C). 6-Aminosaccharin was found to have an intrinisc viscosity $[\eta]$ = 0.002 dl/g in dimethylformamide at 20 ± 0.02°C and was observed to polymerize above its melting point.

Anal: Calculated for $C_7H_6N_2O_3S$: C, 42.40; H, 3.03; N, 14.15; S, 16.17. Found: C, 42.59; H, 2.85; N, 14.23; S, 16.28.

Amino Sulfobenzoic Acids and Anhydrides

5-Nitro-2-Sulfobenzoic Anhydride: From the Attempted Nitration of Saccharin. Nitric acid (11.25 ml, 90%) and sulfuric acid (35 ml, specific gravity 1.84) were mixed in a 100-ml, three-necked, round-bottom flask equipped with a reflux condenser, a mechanical stirrer, and an inlet for solid material. The mixed acid was heated to 70°C and saccharin (15.5 g, 0.085 mole) was added in four portions. After each portion had been added, the mixture was heated on a steam bath. The saccharin dissolved, and a vigorous reaction occurred. The temperature was maintained between 95 and 100°C by cooling, as required with an ice-water bath. When the reaction had subsided, the next portion of saccharin was added. When all the saccharin had been added, the mixture was heated on a steam bath for 45 min. It was then poured onto crushed ice (250 g). A white solid precipitated and was removed by filtration, washed with cold water, and dried. There were obtained 2.68 g (13.9%) of a white solid, mp 212-218°C. The mixture melting points were: (a) with saccharin, 185-210°C, and (b) with 6-nitrosaccharin, 180-210°C (lit. [10] nitro-2-sulfobenzoic anhydride, mp 213-220°C, lit. [13] 5-nitro-2-sulfobenzoic anhydride, mp 212°C).

Anal: Calculated for $C_7H_3NO_6S$ (nitro-2-sulfobenzoic anhydride): C, 36.60; H, 1.31; N, 6.12; S, 13.99. Found: C, 36.25; H, 1.48; N, 6.08; S, 14.08.

4-Nitro-2-Sulfobenzoic Acid. A mixture of 50.0 g (0.22 mole) of

6-nitrosaccharin and 270 ml of concentrated hydrochloric acid was heated to 60-65°C in a 2-liter, three-necked, round-bottom flask equipped with a condenser, a mechanical stirrer, and a dropping funnel; this temperature was maintained for 30 min with continuous stirring. Twenty-four ml of 90% nitric acid were added slowly to this mixture with stirring at 70°C. Some foaming occurred during the addition of nitric acid. The resulting clear yellow solution was then heated to 90°C, and this temperature was maintained for 3 hr. The solution was evaporated to dryness to give 55.0 g (99%) of the acid, a white solid with mp 138-142°C.

Four g of the crude diacid were recrystallized from water to give a glistening white solid, mp 138-140°C. The neutralization equivalent of the recrystallized compound was determined and indicated that the acid exists as a dihydrate (N.E. 142.2, calculated N.E. for dihydrate 141.5). For samples of the acid recrystallized from alcohol-water, a melting point of 76°C [16] has been reported. For the water-free acid, a melting point of 147°C has been recorded [16].

Anal: Calculated for $C_7H_5NO_7S \cdot 2H_2O$: C, 29.69; H, 3.18; N, 4.95; S, 11.30. Found: C, 29.82; H, 3.22; N, 5.10; S, 11.65.

4-Nitro-2-Sulfobenzoic Anhydride. *By the Action of Acetic Anhydride.* 4-Nitro-2-sulfobenzoic acid (2.0 g, 0.008 mole) was refluxed with 12 ml (0.12 mole) of acetic anhydride in a 50-ml, round-bottom flask. The reaction mixture gradually turned dark brown. After refluxing for 2 hr, the excess acetic anhydride was removed under reduced pressure. The resulting brown residue was recrystallized from benzene to give a yellow solid in 70% yield (1.5 g), mp 108-110°C. After recrystallization from benzene, the light-yellow solid melted at 110-112°C; its infrared spectrum showed an intense anhydride carbonyl absorption at 1820 cm^{-1}.

Anal: Calculated for $C_7H_3NO_6S$: C, 36.60; H, 1.31; N, 6.12; S, 13.99. Found: C, 36.11; H, 1.53; N, 6.28; S, 13.68.

The recrystallized anhydride (0.29 g) was refluxed with 25 ml of water for 2 hr. After evaporation to dryness, there remained a yellow solid which melted at 133-135°C and whose infrared spectrum was identical with that of 4-nitro-2-sulfobenzoic acid. The acid number of the hydrolyzed product was found to be 2.01 (calculated value, 2.0).

By the Action of Thionyl Chloride. 4-Nitro-2-sulfobenzoic acid (3.0 g, 0.012 mole) was refluxed in a 100-ml, round-bottom flask with 30 ml (0.42 mole) of thionyl chloride for 5 hr. The resulting clear yellow solution was quenched with ice and an insoluble white solid was removed by filtration. The solid, melting at 113-115°C, was obtained in 83.5% yield (2.3 g). After

recrystallization from benzene, the solid melted at 115-117°C, and its infrared spectrum was identical with that of the anhydride whose analysis is given immediately above.

4-Amino-2-Sulfobenzoic Acid. 4-Nitro-2-sulfobenzoic acid dihydrate (10.0 g, 0.0353 mole) dissolved in 300 ml of 95% alcohol was hydrogenated in the presence of 0.106 g of 5% palladium-on-charcoal at an initial hydrogen pressure of 45 psig. After 35 min of agitation at room temperature, the hydrogen pressure had dropped to 37 psig. An additional 0.204 g of the catalyst was introduced, and the Parr bottle was again pressured with hydrogen to 45 psig. The hydrogenation was then continued for another hour, during which time the hydrogen pressure dropped to 40 psig. The total hydrogen pressure drop was 13 psig. The catalyst was removed by filtration; it weighed 6.5 g, indicating that it contained absorbed materials.

The yellow filtrate was evaporated to dryness, leaving 1.5 g of a yellow solid (a). The grey catalyst mixture was extracted three times with 100 ml of hot water; the combined brown extracts were cooled to 0°C, yielding 4.5 g of yellow crystals (b) which were removed by filtration. The reddish-brown filtrate was then evaporated to dryness and there remained 1.0 g of a pink solid. The total weight of isolated solids was 7.0 g (91.5% yield). The crude solids (a) and (b) were combined and recrystallized from hot water three times, yielding a white solid. Its infrared spectrum in Nujol showed no NO_2 absorption bands at 1540 and 1330 cm^{-1}, but the carboxyl carbonyl absorption band at 1720 cm^{-1} was still present.

Titration indicated that the product had an acid number of 1.99 (calculated value 2.0) on the basis of anhydrous 4-amino-2-sulfobenzoic acid. The recrystallized product did not melt when heated to 200°C.

Anal: Calculated for $C_7H_7NO_5S$: C, 38.71; H, 3.25; N, 6.45; S, 14.76. Found: C, 38.66; H, 3.42; N, 6.71; S, 14.83.

Catalytic Reductions of Nitro-2-Sulfobenzoic Anhydrides. *Hydrogenation of 4-Nitro-2-Sulfobenzoic Anhydride.* Recrystallized 4-nitro-2-sulfobenzoic anhydride (2.06 g, 0.009 mole) in 15 ml of N,N-dimethylacetamide was hydrogenated in the presence of 516 mg of 5% palladium-on-charcoal at 40 psig hydrogen pressure. In a few minutes, about 1 psig of hydrogen pressure was absorbed by the reaction mixture. After 1 hr, an additional 167 mg of the catalyst were introduced and the hydrogenation was continued for another hour. In about 15 min, 1 psig of hydrogen pressure drop was noted. The catalyst was removed by filtration; it weighted 0.97 g.

A 1-ml portion of the greenish-yellow filtrate (a) was quenched in ice,

and the solution was stored in the refrigerator overnight. A white solid separated. The solid was found to have an acid number of 1.96 on the basis of the dihydrate of 4-amino-2-sulfobenzoic acid (calculated value 2.0), and its infrared spectrum in potassium bromide showed an intense carboxyl carbonyl band at 1720 cm^{-1} and SO_3H absorptions at 1240 and 1080 cm^{-1}. The NH_2 absorption at the 2900-3100 cm^{-1} region was not sharp. There were no NO_2 absorptions present at 1530 and 1340 cm^{-1}. The white solid appeared to be impure 4-aminosulfobenzoic acid. On addition of 15 ml of benzene to a 1-ml portion of the filtrate (a), a greenish oil separated. However, on addition of 30 ml of dry acetone to a 1-ml portion of the filtrate (a), there precipitated a yellow solid (b) which melted partly at 120-155°C and finally completely at 210°C. Titration of a sample of solid (b) gave a neutralization equivalent which was consistent with the value expected for a mixture of dimers and trimers of 4-amino-2-sulfobenzoic anhydride.

Hydrogenation of 5-Nitro-2-Sulfobenzoic Anhydride. 5-Nitro-2-sulfobenzoic anhydride (1 g, 0.004 mole), 5% palladium-on-charcoal (0.7 g), and absolute ethanol (50 ml) were placed in a Parr bottle. The bottle was placed in the Parr apparatus, flushed three times with hydrogen, and filled with hydrogen (43 psig). This mixture was agitated at room temperature for 24 hr. The catalyst was removed by filtration, and the filtrate was evaporated to dryness. There was obtained about 0.7 g of a yellow resin.

Preparation of Ethyl 4-Amino-2-Sulfamidobenzoate

Ethyl 4-Nitro-2-Sulfamidobenzoate. 6-Nitrosaccharin (10 g, 0.044 mole) and absolute ethanol (250 ml) were placed in a 500-ml Erlenmeyer flask. The solution was saturated with hydrogen chloride and allowed to stand for 24 hr. The ethanol was evaporated at reduced pressure until a very viscous residue remained. A large volume of cold water (300 ml) was added to the residue. A white solid precipitated and was removed by filtration. The product was recrystallized from ethanol and water. There were obtained 11.5 g (93%) of a white solid, mp 134-135°C.

Anal: Calculated for $C_9H_{10}N_2O_6S$: C, 39.41; H, 3.68; N, 10.22. Found: C, 39.45; H, 3.53; N, 11.42.

Ethyl 4-Amino-2-Sulfamidobenzoate. Ethyl 4-nitro-2-sulfamidobenzoate (1 g, 0.0036 mole), 5% palladium-on-charcoal (0.5 g), and absolute ethanol (150 ml) were placed in a Parr bottle. The bottle was placed in the Parr apparatus, flushed three times with hydrogen, and filled with hydrogen (42 psig). This mixture was shaken at room temperature for 30 min. During

this time, the hydrogen pressure dropped 1.5 psig. The catalyst was removed by filtration and the filtrate was evaporated to dryness at reduced pressure. The residue was recrystallized from ethanol-water and dried. There was obtained 0.85 g (75%) of a white solid, mp 146-149°C.

Anal: Calculated for $C_9H_{12}N_2O_4S$: C, 44.26; H, 4.92; N, 11.48; S, 13.11. Found: C, 44.45; H, 5.00; N, 11.69; S, 12.90.

Preparation of Triethylammonium 6-Aminosaccharinate

6-Aminosaccharin (1 g, 0.005 mole) was dissolved in a mixture of benzene (100 ml) and ethanol (100 ml). Triethylamine (0.5 g, 0.005 mole) was added, and the solvent was evaporated at reduced pressure. There was obtained 1.3 g (87%) of a cream-colored solid, mp 177-180°C. A sample of this salt was observed to polymerize above its melting point.

Anal: Calculated for $C_{13}H_{21}N_3O_3S$: C, 52.15; H, 7.07; N, 14.04. Found: C, 52.61; H, 6.97; N, 13.68.

Attempted Nitration of N-Acetylsaccharin

Nitric acid (5.7 ml, 90%) and sulfuric acid (17.5 ml, specific gravity 1.84) were placed in a 50-ml, two-necked, round-bottom flask and cooled to 5°C in an ice bath. N-Acetylsaccharin (9.5 g, 0.042 mole) was added to the mixed acid, and the mixture was allowed to come to room temperature as the ice melted. The mixture was kept at room temperature overnight before it was poured onto crushed ice (100 g). A white solid precipitated and was removed by filtration, washed with cold water, and recrystallized from 2-butanone. There were obtained 4.3 g (46%) of a white solid, mp 170-172°C (lit. [22] N-nitrosaccharin, mp 170°C). After standing in air for several weeks, a red-brown gas had formed above the sample. The remaining white solid had a melting point of 226-227°C (lit. [23] saccharin, mp 228°C). The infrared spectrum of this compound was identical with the infrared spectrum of an authentic sample of saccharin.

Attempted Nitration of Ethyl o-Sulfamidobenzoate

Ethyl-o-sulfamidobenzoate (9.15 g, 0.04 mole) and sulfuric acid (13 ml, specific gravity 1.84) were placed in a 50-ml, three-necked, round-bottom flask equipped with a reflux condenser, a thermometer, and a dropping funnel. The flask was cooled in an ice bath and its contents were stirred magnetically. Nitric acid (5.6 ml, 90%) was added dropwise. The mixture warmed to room temperature as the ice melted and was

stirred at room temperature overnight. The nitration mixture was poured onto crushed ice (50 g). A white solid precipitated and was removed by filtration, washed with cold water, and dried. There were obtained 3.4 g (46%) of a white solid, mp 220-225°C (lit. [23] saccharin, mp 228°C). The infrared spectrum of this compound was identical to the spectrum of an authentic sample of saccharin.

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