With β-naphthalene sulfochloride, a crystalline solid melting at 185–186° was obtained. This also contained nitrogen. The corresponding glutamic acid derivative melts at 163°.

When the substance dissolved in water and mixed with aniline is acidulated with hydrochloric acid below 0°, a yellow color is formed becoming deep red with excess of acid. Similarly with α-naphthylamine a deep red color is formed.

A water solution of the substance separately mixed with a solution of the following, made just acid below 0° and then alkaline, produces colors as follows: 1,8-Amido naphthol 3,6-disulfonic (H) acid, a deep blue; 1,8-dioxynaphthaline 3,6-disulfonic acid (Chromotrope), a violet; sodium β-naphtholate a yellow color. These colors do not have the intense staining qualities of the purely aromatic azo dyes.

Discussion.

It seems probable in the light of these reactions that the isoazotate of glutamic acid is formed by the above-described process. The analytical data to establish this point conclusively is not available at this time because of the extreme difficulty attending the purification of the substance for analytical purposes.

A method is now being developed to avoid decomposition and remove the inorganic matter which unfortunately has about the same solubilities as the substance in question.

It is our purpose to present in the near future the necessary analytical data to establish the constitution of this new substance as well as additional data for derivatives and new condensations. Work is under way at this time to apply this method to other suitable aliphatic amino compounds.

The writer is indebted to Mr. H. W. LeBoutellier for assistance in this preliminary investigation.

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[CONTRIBUTION FROM THE HENRY PHIPPS INSTITUTE OF THE UNIVERSITY OF PENNSYLVANIA.]

THE PREPARATION OF HALOGEN DERIVATIVES OF CATECHOL, HONO-CATECHOL AND PYROGALLOL METHYL ETHERS AND SULFONIC ACIDS.

BY ROBERT B. KRAUSS AND EDWARD CREDE.

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Introduction.—The attention of this laboratory has been directed during recent years towards the synthesis of tetrazo and disazo dyes for the purpose of chemotherapeutic experimentation on tuberculosis.

Using benzidine and its derivatives as the base, numbers of dyes have been prepared by diazotizing them and coupling to amino and phenolic

second components. In order to extend a certain series of such dyes, it became necessary to prepare halogenated derivatives of the methyl ethers and of the sulfonic acids of the methyl ethers of hono-catechol, catechol, and pyrogallol. It was found advantageous in carrying out this work to modify the current methods of brominating phenols. A simplified method of preparing the dimethyl and trimethyl ethers of pyrogallol was developed. The methods of preparation for these various substances which we have found most suitable are described in the following paper.

Experimental.

Halogenation of Guaiacol Sulfonic Acids.—The guaiacol was obtained from beechwood creosote by fractionation, fractional separation by alkali and redistillation until all distilled at 205°.

The ortho and para sulfonic acids were made and separated according to the method of Hoffman[1] and Fabrik Heyden.[2] The isomers are separated best by means of the basic calcium salts, obtained from the neutral salt, by treatment with the calculated amount of calcium chloride and ammonium hydroxide, precipitating the para salt and leaving the ortho salt in solution. These are then transposed to the neutral salts. Both isomers give similar products on halogenation.

Dibromo-guaiacol Sulfonic Acid.—The potassium sulfonate is dissolved in ten parts of water and the calculated amount of bromine added drop by drop. A brown precipitate is formed. This is filtered off and recrystallized several times from hot water containing a little alcohol. The dibromo derivative separated in light brown crystalline crusts on cooling.

All halogen and sulfur determinations in this paper were made by the method of Carius. The methyl ether content where reported was determined by Zeisel's method.

$C_6HB_{r2}(OH)(OCH_3)SO_3K.2H_2O$.
Calculated: Br, 37.04%; S, 7.41%; H_2O, 8.02%.
Found: Br, 37.28%; S, 7.33%; H_2O, 8.02%.

Di-iodo-guaiacol Sulfonic Acid.—The iodizing of guaiacol sulfonic acids is rather difficult to accomplish. Most of the usual methods either failed to give any results or at best gave a poor yield. Best results were obtained by the method of Trommersdorff,[3] using iodine chloride. A di-iodo-guaiacol sulfonic acid was prepared in this way, the sodium salt separating as a pale yellow crystalline precipitate, difficultly soluble in cold, fairly soluble in hot water. Analysis gave the following results:

$C_6HI_2(OH)(OCH_3)SO_3Na_2H_2O$
Calculated: I, 49.41%; S, 6.23%; H_2O, 7.00%
Found: I, 49.75%; S, 6.08%; H_2O, 6.77%

[1] Ger. 109789, Friedländer V, 738.
[2] Ger. 188506, Friedländer VIII, 936.
[3] Ger. 45226, Friedländer II, 510.

Mono-bromo-creosole.—The crude fraction of creosote distilling between 218–224° C. is placed in a crystallizing dish at the bottom of a desiccator of the Hempel type. The reservoir of the desiccator is filled with moist soda-lime. A watch crystal is supported above the crystallizing dish and the calculated amount of bromine allowed to drop on the crystal slowly. The bromine vapors gradually come in contact with the creosole and are absorbed. The hydrobromic acid liberated is absorbed by the soda-lime at the top of the desiccator.

After standing about 48 hours at room temperature the mono-bromo-creosole crystallizes and can be separated by filtering on a suction filter. It is crystallized from glacial acetic acid. On recrystallizing, large colorless rhombic crystals melting at 77° were obtained. Analysis:

$CH_3C_6H_2Br(OH)(OCH_3)$
Calculated: Br, 36.87%; (OCH_3), 14.29%
Found: Br, 37.09%; (OCH_3), 14.13%

Guaiacol treated in the same manner yields dibromo-guaiacol[1] crystallizing in fine needles, m. p. 93–94°.

Pyrogallol Dimethyl Ether Sulfonic Acid.—The preparation of pyrogallol 1,3-dimethyl ether involves considerable difficulty if attempted by the usual methods. The use of an autoclave[2] and the oxidizing influence of the air[3] can be avoided by the following method:

One mol. pyrogallol is placed in a flask connected with a reflux condenser. Methyl bromide is passed into the flask by a glass tube ending in a capillary and passing through the condenser to near the bottom of the flask until the air is displaced.

Two and a half mols. metallic sodium are dissolved in twenty mols. methyl alcohol absolute. This sodium alcoholate is run into the flask together with a continuous stream of methyl bromide. The flask is heated on the water bath and the current of alkyl halide continued until the reaction is nearly neutral. The gas is rapidly absorbed and sodium bromide settles out.

The methyl ether is isolated as follows: Water is added until the sodium bromide dissolves. The methyl alcohol is then evaporated and the residue distilled in steam. Any trimethyl ether passes over in the steam. The dimethyl ether is extracted with ether after acidifying. The ether solution is evaporated and the resulting oil fractionated *in vacuo*. A colorless liquid boiling at 250° was obtained. To check the purity the methyl-ether content was determined and 40.42% : 40.31% found while the theoretical figure is 40.26%. Further methylation by the above method yields the trimethyl ether.

[1] Cousin, *Compt. rend.*, **127**, 759 (1898).
[2] Ger. 162658, Friedländer VIII, 130.
[3] Hofman, *Ber.*, **11**, 329 (1878).

The sulfonation of the dimethyl ether is accomplished by treating with an equal volume of 10% fuming sulfuric acid. Heat is developed and the liquid assumes a deep red color. Sulfonation is completed by warming on the steam bath for one hour. The barium salt can be isolated by the usual method of treating with barium carbonate. It crystallizes from water in fine needles, sparingly soluble in cold, but readily soluble in hot water. Analysis:

$(C_6H_2(OH)(OCH_3)_2(SO_3))_2Ba.3H_2O$
Calculated: Ba, 20.86%; H_2O, 8.22%
Found: Ba, 20.71%; H_2O, 8.28%

Pyrogallol Trimethyl Ether Sulfonic Acid.—The sulfonation is performed as described above for the dimethyl ether. It yields a barium salt crystallizing in fine needles fairly soluble in cold and quite soluble in hot water.

$(C_6H_2(OCH_3)_3SO_3)_2Ba.2H_2O$.
Calculated: Ba, 20.54%; H_2O, 5.40%.
Found: Ba, 20.68%; H_2O, 5.49%.

Dibromo-pyrogallol Dimethyl Ether Sulfonic Acid.—The bromination is accomplished as described under dibromo-guaiacol sulfonic acid, by adding bromine to the solution of the sodium sulfonate in water. The dibromo product formed crystallizes out on standing in needles difficultly soluble in cold and slightly soluble in hot water. Analysis:

$C_6Br_2(OH)(OCH_3)_2SO_3Na.2H_2O$
Calculated: Br, 35.56%; S, 7.01%; H_2O, 8.00%
Found: Br, 34.09%; S, 6.87%; H_2O, 7.83%

Pyrogallol trimethyl ether sulfonic acid gives a dibromo derivative by the same method. This was not analyzed.

Dibromo-pyrogallol Dimethyl Ether.—If during the bromination of the sulfonic acids described above the solution is heated on the water bath, the sulfonic acid group is split off and an oil separates out.

On pouring off the water and allowing it to stand it solidifies. Crystallizing from warm alcohol it forms four-sided prisms melting at 70°. It is insoluble in water.

$C_6HBr_2 = (OH)(OCH_3)_2$.
Calculated: Br, 51.31%; (OCH_3), 19.87%.
Found: Br, 51.78%; (OCH_3), 20.33%.

Dibromo-pyrogallol Trimethyl Ether.—Using the method given above, pyrogallol trimethyl ether sulfonic acid on treatment with bromine on the water bath yields the dibromo-pyrogallol trimethyl ether. This is a crystalline solid of m. p. 75–76°. Analysis:

$C_6HBr_2(OCH_3)_3$
Calculated: Br, 49.08%; (OCH_3), 28.53%
Found: Br, 49.79%; (OCH_3), 27.70%

Summary.

In this article are described:

1. A modified method of brominating phenols.

2. A modified method of methylating phenols to prevent oxidation.

3. The preparation of dibromo-guaiacol sulfonic acid, diiodo-guaiacol sulfonic acid, mono-bromo-creosole, pyrogallol dimethyl ether sulfonic acid, pyrogallol trimethyl-ether sulfonic acid, dibromo-pyrogallol dimethyl ether and dibromo-pyrogallol trimethyl ether.

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[CONTRIBUTION FROM THE LABORATORIES OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH.]

THE FERROUS SULFATE AND AMMONIA METHOD FOR THE REDUCTION OF NITRO TO AMINO COMPOUNDS.

BY WALTER A. JACOBS AND MICHAEL HEIDELBERGER.

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The reduction of aromatic nitro compounds to their corresponding amino derivatives has been the subject of such exhaustive treatment in the past and so many excellent methods for accomplishing this end have been devised and so thoroughly discussed in the numerous laboratory manuals that it may seem scarcely necessary to reopen the question. But to those who, like ourselves, may be engaged in investigations which require the convenient and rapid preparation of substances on a scale sufficient for further synthetic work, we feel that our experience may be of service.

In the majority of instances in which nitro compounds have been reduced tin or tin salts have perhaps been the most popular reagent. Except in the case of alkali-insoluble substances, or where the hydrochloride of the base does not form a tin double salt, the metal must be removed with hydrogen sulfide, a very time-consuming operation. And when the substances are sensitive to acids this method is to be avoided.

Of the other methods available, that of reduction by means of ferrous sulfate and ammonia has been of service in the past in the preparation of such substances as the aminocinnamic acids, aminopropiolic acid and the otherwise inaccessible *o*-aminobenzaldehyde. It has occasionally been employed with success in other isolated cases, but appears on the whole to have been comparatively neglected. Our experience with the method in reducing a great many substances of varying type would seem to warrant its more frequent employment where the properties of the substances permit. It is the object of this paper to call attention to the ease of manipulation, rapidity, and cheapness of the method, and to the good yields which accompany its proper use.

Our attention was first turned to the method in seeking for a con-