Anal. Calcd. for $C_{20}H_{15}ON_3$: N, 13.41. Found: N, 13.21.

5-Methylchrysene.—The semicarbazone (0.23 g.) was heated with a solution from 0.3 g. of sodium and 10 cc. of absolute alcohol in a sealed tube at 200° for nine hours. After dilution and acidification the product was extracted with benzene and the washed and dried solution was passed through a tower of alumina. After vacuum distillation the product was fractionally crystallized from alcohol to remove a small amount of chrysene. The 5-methyl compound then crystallized from alcohol in colorless needles, m. p. 116.8–117.6°; yield 0.03 g. (17%).

Anal. Calcd. for $C_{19}H_{14}$: C, 94.18; H, 5.82. Found: C. 94.35; H, 5.61.

The hydrocarbon shows strong blue-violet fluorescence in ultraviolet light. The substance did not depress the m. p. of a sample kindly supplied by Dr. M. S. Newman. The picrate formed red needles, m. p. 141.6–142.4°, from alcohol.

Anal. Calcd. for $C_{25}H_{17}O_7N_3$: N, 8.91. Found: N, 8.80.

Summary

Chrysene-5-carboxylic acid, obtained by the Pschorr synthesis, has been converted through the aldehyde (Sonn–Müller reaction) to the 5-methyl compound. In attempts to reduce the ester with sodium and ethanol or by high pressure hydrogenation, the aromatic nucleus was invariably attacked.

CONVERSE MEMORIAL LABORATORY
CAMBRIDGE, MASSACHUSETTS RECEIVED MARCH 12, 1940

[CONTRIBUTION NO. 220 FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Oxidation Products of Sulfanilamide

BY MARGARET K. SEIKEL[1]

Sulfanilamide (I) oxidizes with ordinary oxidizing agents either to azobenzene-4,4′-disulfonamide (II) or to azoxybenzene-4,4′-disulfonamide (III). Both II and III can be reduced to I and to hydrazobenzene-4,4′-disulfonamide (IV).[2] Oxidation of sulfanilamide with cold alkaline ferricyanide produced a 20% yield of the azo compound II.[3] A better method for preparing II, with the over-all yield of brighter colored product as high as 46%, comprises the series of reactions I→III→IV→II. II could be converted into III by heating for several hours with hydrogen peroxide in glacial acetic acid.[4]

When I was oxidized in glacial acetic acid with 30% hydrogen peroxide, the azoxy compound III was obtained in 70% yields after only half an hour's heating. The speed with which III was obtained from I in comparison with the slow conversion of II to III indicated that II is probably not an intermediate in the former reaction; likewise IV yielded mainly II by the same treatment.[5] However, with this reagent *p*-toluidine is oxidized first to the corresponding azo compound so undoubtedly the sulfonamido group affects the course of the reaction.

If I was oxidized by hydrogen peroxide in dilute sulfuric acid, the product was a mixture of II and III. If hydrochloric acid was employed as the acidifying agent, partial chlorination yielded mixtures of products. Oxidations by hydrogen peroxide in neutral or basic solutions were too slow to be practical.

Reductions of II, III or material believed to be a mixture of the two by stannous chloride in hydrochloric acid regenerated sulfanilamide in 35–50% yields.[3a] Reductions with hydrosulfite in alkaline solution produced quantitative yields of IV.

Reoxidation of IV to II occurred very readily with various oxidizing agents, but 1 *N* ferric chloride was preferable because it yielded instantaneous and quantitative results.

Sulfanilamide may be chlorinated in the cold by treatment with a great excess of hydrochloric acid and only a moderate excess of hydrogen peroxide, the previously unreported 3,5-dichloro-4-amino-benzenesulfonamide (V) separating in fair yields. The reaction undoubtedly occurs through an intermediate chloramide.

Experimental

All melting points are uncorrected and were taken by the method described in Mulliken's "Identification of

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(1) Research Associate.

(2) For biological tests on II, III and IV see *Compt. rend.*, **205**, 181 (1937).

(3) (a) Laar, *Ber.*, **14**, 1928–1934 (1881); (b) Limpricht, *ibid.*, 1356–1359; (c) Scudi, THIS JOURNAL, **59**, 1480–1483 (1937). No melting point is recorded.

(4) Compare Angeli, *Chem. Zentr.*, **81**, II, 731 (1910).

(5) Compare D'Ans and Kneip, *Ber.*, **48**, 1145 (1915).

Pure Organic Compounds," Vol. I, page 218, on a 360° thermometer immersed in a mixture of sulfuric acid and potassium acid sulfate to the 0° point. Analytical values represent averages of closely agreeing duplicate determinations.

Oxidation Procedures: Ferricyanide.—Sulfanilamide (0.85 g., 0.005 mole) dissolved in 5 ml. of water containing 1.4 g. (0.025 mole) of potassium hydroxide was treated at room temperature with an aqueous solution of 6.58 g. (0.02 mole) of potassium ferricyanide. The precipitated potassium derivative of II was filtered off after ten to thirty minutes and converted to the free amide. The 17–25% yield of tan product was most readily purified by several recrystallizations from 30–40% pyridine (its solubility in alcohol is low) from which it separated in fronds of dull apricot hair-like needles, m. p. 312° dec. after sintering above 300°.

Anal. Calcd. for $C_{12}H_{12}N_4O_4S_2$: C, 42.3; H, 3.55; N, 16.5. Found: C, 42.2; H, 3.63; N, 16.6.

It forms a vivid yellow solution in concentrated sulfuric acid and dissolves fairly readily in dilute alkali.

Hydrogen Peroxide–Acetic Acid.—A solution of 5 g. of sulfanilamide in 30 ml. of 30% hydrogen peroxide and 120 ml. of glacial acetic acid was heated for one-half hour at 100°. A 58% yield (3.0 g.) of the 6-mm. shining orange needles of III was filtered from the hot solution, and on cooling the mother liquor deposited an additional 14% yield. The same reaction occurs slowly at room temperature, a 64% yield being obtained in one day. III was easily purified by one or two recrystallizations from 30% pyridine from which it separated as yellow-orange plate-needles, m. p. 289–290° with violent evolution of gas.

Anal. Calcd. for $C_{12}H_{12}N_4O_5S_2$: C, 40.4; H, 3.39; N, 15.7. Found: C, 40.4; H, 3.49; N, 15.3.

The compound gave an orange-yellow solution in concentrated sulfuric acid. It did not free iodine from potassium iodide in acetic acid.

Hydrogen Peroxide–Sulfuric Acid.—When sulfanilamide was oxidized by 30% hydrogen peroxide in the presence of 6 *N* sulfuric acid, slower precipitation of a product occurred. After recrystallization, the vivid orange needles representing a mixture of II and III generally melted around 296° with violent evolution of gas.

Anal. Calcd. for $C_{12}H_{12}N_4O_4S_2$: C, 42.3; H, 3.55; N, 16.5. Calcd. for $C_{12}H_{12}N_4O_5S_2$: C, 40.4; H, 3.39; N, 15.7. Found: C, 41.2; H, 3.31; N, 16.0.

The mixture gave a yellow-orange solution in concentrated sulfuric acid.

Reduction Procedures: Stannous Chloride.—II, III and the mixture of the two were reduced by heating 0.25 g. of material with 1.0 g. of stannous chloride and 4 ml. of 10 *N* hydrochloric acid for ten minutes at 100°. After being made basic with bicarbonate, the reaction mixtures were evaporated to dryness by air and extracted twice with acetone. The residues obtained by evaporating the acetone were either recrystallized from or extracted with boiling water depending on the amount of high melting insoluble impurity present. From the aqueous solutions 35–50% yields of sulfanilamide melting around 160° were isolated. After further purification, material from any of the initial sources did not lower the melting point of an authentic sample.

Hydrosulfite.—Solutions of 0.10 g. of II, III and the mixture of the two in 5 ml. of 0.2 *N* sodium hydroxide were heated to boiling and treated with solid practical sodium hydrosulfite until decolorization was complete, the separation of an intermediate precipitate being disregarded. The amounts of hydrosulfite used were as follows: for II, 0.08, 0.08 g. or 0.27 g. per millimole; for III, 0.15, 0.15, 0.15 g. or 0.54 g. per millimole; for the mixture, 0.13, 0.13, 0.13 g. After boiling five minutes and cooling, the solutions deposited 100% yields of IV, m. p. 224–224.5° to a red melt which resolidified. Recrystallization from water containing a trace of hydrosulfite to prevent reoxidation produced white fronds with the melting point unchanged. Samples from the various initial materials did not lower each other's melting points.

Anal. Calcd. for $C_{12}H_{14}N_4O_4S_2$: C, 42.1; H, 4.12. Found: from II, C, 42.1; H, 4.17; from III, C, 42.1; H, 4.10; from mixture, C, 42.1; H, 3.91.

Oxidation of Hydrazo Compound IV.—When an aqueous solution of IV was heated on the steam-bath, it soon assumed a yellow tinge and in two hours the rust colored needles of II separated, m. p. 308° dec. If IV was heated with enough 30% hydrogen peroxide to dissolve it, a 70% yield of II, m. p. 311° dec., could be obtained in an hour. When hydrogen peroxide and acetic acid were used in the proportions employed in the preparation of III, a 95% yield of II, m. p. 307° dec., was obtained after five minutes of heating. The speediest reoxidation resulted when a hot aqueous solution of IV (0.10 g. in 5–7 ml.) was treated with 1.0 ml. of 1 *N* ferric chloride; 90–100% yields of II separated instantaneously.[6]

After two recrystallizations from 30% pyridine, II was obtained as pure orange opaque flat needles, m. p. 314° dec., and it did not lower the melting point of II obtained by ferricyanide oxidation of I.

Anal. Calcd. for $C_{12}H_{12}N_4O_4S_2$: C, 42.3; H, 3.55. Found: C, 42.2; H, 3.41.

Oxidation of II to III.—When II was dissolved in hot 30% hydrogen peroxide and glacial acetic acid in the proportions used for the oxidation of I, the product isolated after at least three hours of heating melted at 291° with violent evolution of gas; it did not lower the melting point of III but did lower that of II.

Chlorination.—Sulfanilamide (0.43 g., 0.0025 mole) was dissolved in 15 ml. of 6 *N* hydrochloric acid (0.08 mole) and treated with 2 ml. of 30% hydrogen peroxide (0.02 mole) at room temperature. It was found most advantageous to filter off the precipitate when the mixture first assumed a yellow tinge (thirty to forty-five minutes); the product would then be practically colorless. The 60–80% yield of V was recrystallized twice from large volumes of water (200–300 ml. per gram) producing shining colorless needles, m. p. 205–205.5°.

Anal. Calcd. for $C_6H_6Cl_2N_2O_2S$: Cl, 29.7. Found: Cl, 29.5.

The proportions of acid and peroxide suggested were

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[6] The high yields and speed of the reduction and reoxidation steps allows II to be prepared quickly and in good yields by way of III and IV. Experimentally a 46% yield, m. p. 308–309° dec., was obtained when the intermediate products were not purified.

determined empirically to be the best for a speedy reaction and a pure product.

Proof of Structure of V.—When V was desulfamidated by 75% sulfuric acid in the manner described for the analogous dibromo compound,[7] a 51% yield of 2,6-dichloroaniline, m. p. 38–39° (recorded 39°), could be steam distilled from the reaction mixture. This was acetylated with acetic acid and acetyl chloride,[8] m. p. 178.5–179°, recorded 175°, after recrystallization from 25% acetic acid.

Summary

1. On oxidation sulfanilamide yields the corresponding azo- and azoxy-benzenes which may be reduced to the hydrazo compound.

2. It can be chlorinated readily by a mixture of hydrogen peroxide and hydrochloric acid.

CAMBRIDGE, MASS. RECEIVED FEBRUARY 13, 1940

(7) Fuchs, *Monatsh.*, **36**, 125 (1915).

(8) Beilstein and Kurbatow, *Ann.*, **196**, 215, 219–220 (1879).

[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY, COLLEGE OF AGRICULTURE, UNIVERSITY OF WISCONSIN]

The Mutarotation and Rotatory Dispersion of Derivatives of Aldehydo-*d*-galacturonic Acid[1]

BY ROBERT J. DIMLER AND KARL PAUL LINK

Aldehydo tetraacetyl methyl-*d*-galacturonate and one of its ethyl hemiacetals were prepared by Link and Campbell[2] as the first derivatives of the aldehydo form of a hexuronic acid. Prior to this work on *d*-galacturonic acid Wolfrom and Morgan[3] had prepared the corresponding derivatives of the parent sugar *d*-galactose. They also reported[4,5] on the optical properties of aldehydo-*d*-galactose pentaacetate and its hemiacetals. In this communication we have extended the mutarotation and rotatory dispersion study to the aldehydo derivatives of *d*-galacturonic acid.

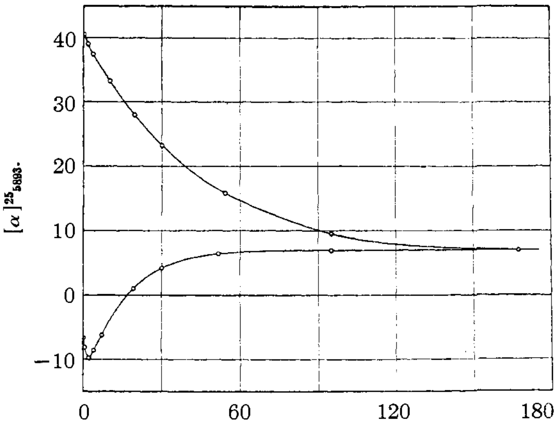
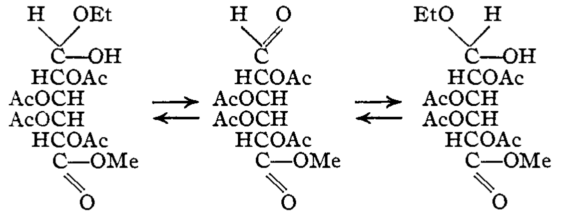


Fig. 1.—Mutarotation of α- and β-ethyl hemiacetal tetraacetyl methyl *d*-galacturonate in alcohol-free chloroform.

The isomeric α- and β-ethyl hemiacetals of tetraacetyl methyl-*d*-galacturonate have been obtained by variation of the method of preparation and fractional crystallization. This is the first member of the hemiacetal series for which both of the predictable forms have been realized. The designation of the isomers as α- and β- is based on the usage proposed by Hudson,[6] in which that derivative in the *d*-series having the more positive rotation is assigned the prefix α. The β-ethyl hemiacetal exhibits a mutarotation (Fig. 1) similar to that of the compounds of galactose studied by Wolfrom.[5] The α-ethyl hemiacetal shows a regular mutarotation without a minimum as seen in Fig. 1.

The mutarotation of the α- and β-ethyl hemiacetals involves the establishing of an equilibrium among the three compounds.



α-Hemiacetal $[\alpha]^{25}_{5893}$ +40.7° Aldehydo $[\alpha]^{25}_{5893}$ −15.6° β-Hemiacetal $[\alpha]^{25}_{5893}$ −6.7°

The minimum in the mutarotation curve for the β-ethyl hemiacetal is attributed to the primary rapid formation of the free aldehydo compound. The resulting aldehyde and alcohol recombine

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This study is part of a thesis to be submitted to the Graduate Faculty of the University of Wisconsin in partial fulfilment of the requirements for the degree of Doctor of Philosophy. R. J. Dimler is indebted to the Wisconsin Alumni Research Foundation for a fellowship in 1936–37 and to the Graduate Research Fund for an assistantship in 1937–40.

(2) Campbell and Link, *J. Biol. Chem.*, **120**, 471 (1937).

(3) Wolfrom and Morgan, THIS JOURNAL, **52**, 2464 (1930).

(4) Wolfrom, *ibid.*, **53**, 2275 (1931).

(5) Wolfrom and Morgan, *ibid.*, **54**, 3390 (1932).

(6) Hudson, *ibid.*, **31**, 66 (1909).