4. The complex situation with regard to yeast nutrilites suggests the probability that the specific vitamin (or hormone) potency of a given material may be due to several substances which perform the same function, rather than one single substance.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

A NEW METHOD FOR THE PREPARATION OF SYRINGIC ALDEHYDE[1]

BY W. M. MCCORD

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During the progress of research in the Sterling Laboratory dealing with the synthesis of some new aromatic ethers related in structure to thyroxine, it became necessary to develop a method for synthesizing syringic aldehyde, which would be free from experimental difficulties encountered in applying methods hitherto described and recommended by other investigators. Graebe and Martz[2] were the first to prepare the aldehyde by condensing 2,6-dimethoxyphenol with chloroform in alkaline solution. Their method is not productive of the aldehyde in good yields. Mauthner[3] developed later a method of synthesis by condensing 2,6-dimethoxyphenol with ethyl mesoxalate, and then converting his condensation product to syringic aldehyde by hydrolysis. Pauly and Strassberger[4] recently have improved on Mauthner's technique by substituting chloral hydrate for ethyl mesoxalate and prepared the aldehyde from 2,6-dimethoxyphenol according to the patented procedure recommended for the manufacture of vanillin.[5] Both methods of operating require a supply of 2,6-dimethoxyphenol, which is a reagent that is not easily prepared in quantity with ordinary laboratory equipment.

Späth[6] applied the Rosenmund technique[7] for a syringic aldehyde synthesis by reducing catalytically carbethoxysyringic acid chloride in the presence of palladium but here again the yield is small and the purification of the aldehyde is difficult. We now find that the Späth method can be modified and syringic aldehyde prepared easily from syringic acid without

[1] Constructed from a dissertation presented by the author in June, 1931, to the Faculty of the Graduate School of Yale University in candidacy for the degree of Doctor of Philosophy. (T. B. Johnson.)

[2] Graebe and Martz, *Ber.*, **36**, 1031 (1903).

[3] Mauthner, *Ann.*, **395**, 273 (1912).

[4] Pauly and Strassberger, *Ber.*, **62**, 2279 (1929); Pauly and Schanz, *ibid.*, **56**, 979 (1923).

[5] U. S. Patent 1,536,732 (1924).

[6] Späth, *Monatsh.*, **41**, 278 (1920).

[7] Rosenmund, *Ber.*, **51**, 598 (1918).

application of catalytic reduction as described by Späth. The changes in procedure are as follows. Gallic acid is first methylated by treatment with dimethyl sulfate in alkaline solution, and the resulting trimethyl ether converted into syringic acid by the action of sulfuric acid. This acid was then acetylated and the resulting acetylsyringic acid converted first into its acid chloride and then into the acid amide. We now find that this amide interacts smoothly with phosphorus pentachloride giving the crystalline imide chloride. When the latter was warmed in pyridine solution it was converted smoothly into the corresponding nitrile of acetylsyringic acid. The preparation of syringic aldehyde was then easily accomplished in one step by reducing this nitrile with stannous chloride in ether solution according to the method recently described by Stephen.[8] Every reaction involved in our procedure proceeds smoothly and the yields are excellent in each step of the synthesis.

Experimental Part

Acetylsyringic Acid Chloride.—Gallic acid was first methylated according to the method of Bogert and Coyne[9] and its trimethyl ether partially demethylated by the action of concentrated sulfuric acid. The resulting syringic acid was then acetylated according to the directions of Anderson and Nabenhauer[10] and converted into its acid chloride by the action of phosphorus pentachloride in chloroform solution. The acetylsyringic acid chloride was purified by crystallization from chloroform or toluene and melted at 129°, somewhat higher than the temperature reported by Bradley and Robinson.[11]

This acid chloride interacts with aniline in ether solution to give the corresponding anilide $C_{17}H_{17}O_5N$, which crystallizes from alcohol in plates melting at 146°.

Anal. Calcd.: N, 4.45. Found: N, 4.60, 4.55.

The corresponding acid amide $C_{11}H_{13}O_5N$ is obtained in a yield of 92% by bubbling ammonia gas through a chloroform solution of the acid chloride at ordinary temperature. This crystallizes from alcohol in prisms melting at 192°.

Anal. Calcd.: N, 5.86. Found: N, 5.96, 5.99.

Imide Chloride from Acetylsyringic Acid Anilide.—This is formed by interaction of the anilide of acetylsyringic acid with phosphorus pentachloride in toluene solution. It was purified by crystallization from toluene and melted at 136°.

Anal. Calcd. for $C_{17}H_{16}O_4NCl$: N, 4.2; Cl, 10.6. Found: N, 4.15, 4.18; Cl, 10.68, 10.72.

Imide Chloride from Acetylsyringic Acid Amide.—This was prepared from the corresponding acid amide by interaction with phosphorus pentachloride in toluene solution. The hydrochloride of this basic imide compound separated from toluene in crystals melting at 125°. The yield was 80%.

Anal. Calcd. for $C_{11}H_{13}O_4NCl_2$: Cl, 24.2. Found: Cl, 24.3.

Acetylsyringic Nitrile.—The above hydrochloride of the imide chloride was dissolved in five molecular proportions of technical pyridine and the resulting solution then

[8] Stephen, *J. Chem. Soc.*, **127**, 1874 (1925).

[9] Bogert and Coyne, THIS JOURNAL, **51**, 571 (1929).

[10] Anderson and Nabenhauer, *ibid.*, **48**, 2997 (1926).

[11] Bradley and Robinson, *J. Chem. Soc.*, **130**, 1553 (1928).

poured into water. The nitrile of acetylsyringic acid separated at once in the form of a colorless powder. It was purified by crystallization from hot alcohol and separated on cooling, as needles melting at 142°. The yield was 90%.

Anal. Calcd. for $C_{11}H_{11}O_4N$: N, 6.34. Found: N, 6.44, 6.22.

This acetyl compound is easily converted quantitatively into *syringic nitrile* melting at 129° by the action of dry hydrogen chloride in ether solution.

Anal. Calcd. for $C_9H_9O_3N$: N, 7.82. Found: N, 7.88, 7.80.

Syringic Aldehyde.—This aldehyde was prepared by reducing the acetylsyringic nitrile according to Stephen's method.[12] The acetyl group was removed during the reduction operation and the syringic aldehyde was produced in a yield of 70%. When allowed to crystallize slowly from a 50% alcohol solution it separated in the form of thick plates melting at 113°. The aldehyde agreed in all its properties with the description given by previous investigators, namely, Graebe and Martz, Mauthner and Pauly and Strassberger. Its semicarbazone melted at 188°.

Summary

1. A new method is described for the preparation of syringic aldehyde.

2. The nitrile of syringic acid is reduced smoothly by stannous chloride in ether solution (Stephen's method) giving this aldehyde.

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3-BENZOYLCARBAZOLE

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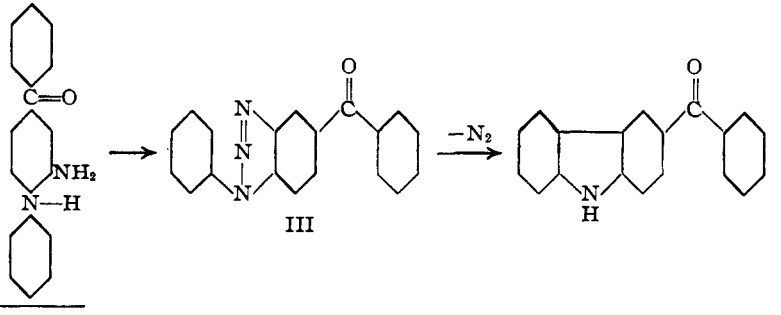
As a matter of interest in a comparison of diphenylamine and carbazole, it was decided to prepare the unknown 3-benzoyl carbazole. After several attempts at shifting the benzoyl radical of the N-benzoyl derivative into the para position, the desired substance was finally obtained by making use of the carbazole synthesis of Graebe and Ullmann,[1] the benzoyl group being introduced before the ring closure.

The steps used were as follows



[12] See also Law and Johnson, THIS JOURNAL, **52**, 3623 (1930).

[1] Graebe and Ullmann, *Ann.*, **291**, 16 (1896).