heating alone above their boiling point in a sealed tube, are decomposed into acids and unsaturated hydrocarbons,[1] and we might expect a similar behavior in the case of acetyl-trichloro-tertiary-butyl-alcohol when heated similarly. The decomposition products of acetyl chloretone when heated *alone* were not determined, but with water or acids it gave rise, in part as far as could be observed, to chloretone without the above decomposition.

DETROIT, MICH.

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF COLUMBIA UNIVERSITY, NO. 255.]

THE SYNTHESIS OF CERTAIN SUBSTITUTED SYRINGIC ACIDS.

BY MARSTON TAYLOR BOGERT AND EDWARD PLAUT.[2]

Received October 14, 1915.

Introductory.

Over a century ago, Braconnot[3] undertook an examination of various plants with particular reference to the acids they contained. Among the plants studied was the common lilac (*Syringa vulgaris*), and he called attention to the presence therein of a bitter substance, precipitable by basic lead acetate, the nature of which was not determined.

Since this early research, various chemists have made the lilac the subject of their investigations. In 1823, Robinet and Petroz[4] examined the seeds and capsules, and found therein a saccharin principle, later shown to be mannite,[5] and a bitter principle; but failed to isolate the latter in sufficient amount or purity to determine its nature.

Fifteen years later, Favrot[6] recovered an oil from the flowers.

In 1841, Bernays[7] obtained from the bark, and also from the leaves and green twigs, a crystalline substance which he believed to be analogous to salicin and phloridzin and therefore termed "syringin." At about the same time, Meillet[8] reported the discovery, in the leaves and green seed capsules, of a crystalline substance which he designated "lilacine." Bernays' article appeared in abstract in Liebig's Annalen[9] under the

[1] Lassar-Cohn, "Arbeits methoden," 3d. ed., p. 1152.

[2] The experimental work upon which this paper is based was submitted by Mr. Edward Plaut in partial fulfilment of the requirements for the degree of Doctor of Philosophy under the Faculty of Pure Science of Columbia University.

[3] *Ann. chim. phys.*, 70, 281–5 (1809).

[4] *J. Pharm.*, 9, 474 (1823); 10, 139–57 (1824).

[5] Ludwig, *Archiv. Pharm.*, [2] 91, 289–96 (1857); Kromayer, *Ibid.*, 109, 18, 216 (1862).

[6] *J. chim. med.*, 14, 212 (1838).

[7] Buchner's *Repert. d. Pharm.*, [2] 24, 349 (1841); *J. pharm. chim.*, [3] 1, 27 (1842).

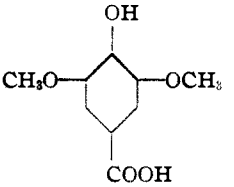
[8] *J. pharm. chim.*, [3] 1, 25 (1842).

[9] *Ann.*, 40, 320 (1841).

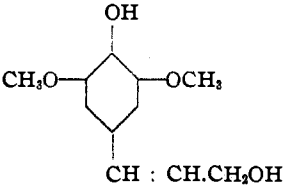
heading "Lilacin," and in Erdmann's Journal[1] under the caption "Syringin."

It appears to have been first suggested by Reinsch[2] that syringin was identical with the "ligustrin" discovered by Polex[3] in the bark of the privet (*Ligustrum vulgare*); and this surmise was later shown to be correct by the work of Kromayer.[4] It is of interest to note that, in the case of the privet also, the syringin (ligustrin) is accompanied by mannite.[5] Kromayer also discovered that syringin could be hydrolyzed to glucose and "syringenin." Further, he observed in the leaves and half-ripe fruit of the lilac a noncrystalline bitter substance, "syringopikrin," which likewise appears to be a glucoside.

Following Kromayer's investigations, Koerner[6] took up the study of syringin. His analyses established its empirical composition as $C_{17}H_{24}O_9 + H_2O$, and therefore that of syringenin as $C_{11}H_{14}O_4$. Oxidation with potassium permanganate, converted syringin into glucosyringic acid which, on hydrolysis, yielded glucose and "syringic acid." After a careful study of the latter acid and various of its derivatives, Koerner concluded that it must possess Formula I, and that syringin is therefore the glucoside of an alcohol of Formula II (sinapinic alcohol):



(I).



(II).

Subsequent work by other investigators has fully corroborated these deductions.[7]

The researches of Power[8] indicate that syringin, and possibly also glucosyringic acid, are present in the bark of *Robinia pseudacacia*.

In addition to syringic acid itself, its barium, zinc and copper salts, and its methyl ester, sundry derivatives and condensation products are mentioned in the literature.

[1] *J. prakt. Chem.*, [1] **25**, 121 (1842).

[2] *Jahrb. prakt. Pharm.*, **16**, 389–93 (1848).

[3] *Archiv. Pharm.*, [2] **17**, 75–8 (1839).

[4] *Ibid.*, [2] **109**, 18, 216 (1862); **113**, 19 (1863).

[5] Kromayer, *Archiv. Pharm.*, [2] **101**, 281–4 (1860).

[6] *Gazz. chim. ital.*, **18**, 209–19 (1888).

[7] Gadamer, *Ber.*, **30**, 2330 (1897); *Archiv. Pharm.*, **235**, 570 (1897); Graebe and Martz, *Ber.*, **36**, 216, 1031 (1903); *Ann.*, **340**, 220 (1905); Graebe and Hess, *Ann.*, **340**, 235 (1905); Mauthner, *J. prakt. Chem.*, [2] **82**, 271 (1910); **84**, 142 (1911); *Ann.*, **395**, 273 (1913); *J. prakt. Chem.*, [2] **91**, 179 (1915); Bogert and Isham, THIS JOURNAL, **36**, 519 (1915); *et al.*

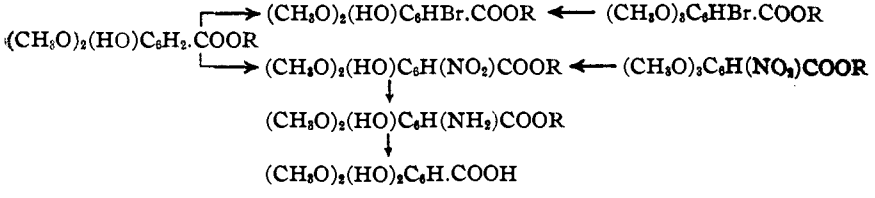
[8] *Pharm. J.*, 1901, 275.

As yet, nothing appears to have been done in the direction of preparing and studying the substitution products of this interesting acid. We have thought it desirable, therefore, to undertake an investigation along these lines, not only because of our ignorance of such substances, the accessibility of the initial material, and the occurrence of syringic compounds in nature; but also in the hope that it might open a way to the synthesis of other natural products or of compounds closely allied to them.

The subjoined experiments represent the beginning of this work, and may be summarized as follows:

Syringic acid, prepared from trimethylgallic acid by the method of Bogert and Isham,[1] was changed to its methyl ester and the acetyl derivative prepared from the latter.

From methyl syringate were obtained also the monobromo and mononitro derivatives, by reduction of the latter the corresponding amino derivative, and from the amino the hydroxy syringic acid (2,4-dihydroxy-3,5-dimethoxybenzoic acid). The bromo and nitro syringic derivatives were also produced by partial demethylation of the corresponding trimethylgallic compounds:



Methyl bromotrimethylgallate is recorded in the literature[2] as an oil, boiling at 202° under a pressure of 16 mm. We have succeeded in obtaining it as a colorless crystalline solid, melting at 90°, and in improving the method of producing it.

By the action of nitric acid upon free syringic acid, the hitherto unknown 3,4-dinitropyrogallol-2,6-dimethyl ether was secured.

Diacetyl derivatives of both the amino and hydroxy syringic acid were prepared and studied.

The work is being continued; particularly along lines leading to the production of the apionol ethers, and to the various condensation products obtainable from the amino and hydroxy syringic acids, since one of these latter acids is of anthranilic and the other of salicylic type.

Experimental.

I. Trimethylgallic Derivatives.

Methyl Trimethylgallate, $(CH_3O)_3C_6H_2.COOCH_3$, was prepared from

[1] *Loc. cit.*

[2] Hamburg, *Monatsh.*, 19, 596 (1898).

trimethylgallic acid, methyl alcohol and dry hydrogen chloride, as described by Bogert and Isham.[1] As first recorded by Powers and Moore,[2] it melts at 84° (corr.) and is volatile with steam.

Methyl Bromotrimethylgallate, $(CH_3O)_3C_6HBr.COOCH_3$ has been prepared by Hamburg[3] by the action of bromine upon methyl trimethylgallate in carbon tetrachloride solution, as an oil, b_{16} 202°, as mentioned above. On repeating Hamburg's process, our results were similar, the product being a pale yellow oil. We have succeeded, however, in bringing this oil to crystallization and, on recrystallization from ether, obtained it in practically colorless prismatic crystals, melting at 90° (corr.).

More satisfactory results were realized by carrying out the bromination in acetic anhydride solution. Ten grams of methyl trimethylgallate were dissolved in 60 g. acetic anhydride, the flask placed in a freezing mixture and a solution of 13 g. bromine in 60 cc. acetic anhydride run in gradually with constant stirring.[4] The reaction was allowed to continue for 24 hours, after which the acetic anhydride was removed by distillation under reduced pressure and the residue crystallized from ether. Nearly colorless crystals resulted, melting at 90° (corr.).

Subs. 0.4942, 0.1850: AgBr, 0.2849; CO_2, 0.2951; H_2O, 0.0719. Calc. for $C_{11}H_{13}O_6Br$: Br, 26.22; C, 43.29; H, 4.26. Found: Br, 26.27; C, 43.51; H, 4.32.

A cryoscopic molecular weight determination in benzene solution, gave the figure 309, while that calculated is 305.

Methyl Nitrotrimethylgallate, $(CH_3O)_3C_6H(NO_2).COOCH_3$.—Schiffer,[5] Thomas and Siebeling,[6] and Harding,[7] have shown that the nitration of free trimethylgallic acid by nitric acid alone, or in the presence of acetic acid, results mainly in the displacement of the carboxyl by the nitro group, with formation of 5-nitro and 5,6-dinitropyrogallol trimethyl ethers, together with but small amounts of nitrotrimethylgallic acid. In our own experiments upon trimethylgallic acid with nitric acid, in acetic acid solution, the dinitropyrogallol trimethyl ether proved to be the chief product. This ether melts at 118.4° (corr.).

Schiffer records that on nitrating ethyl triethylgallate with nitric acid, in glacial acetic solution, he obtained the corresponding mononitro derivative in fine needles, m. p. 104°; but that the action of nitric acid alone upon this, even in the cold, tended to change it to dinitropyrogallol triethyl ether.

[1] THIS JOURNAL, 36, 518 (1914).

[2] *J. Chem. Soc.*, 95, 254 (1909); see also Bogert and Isham, *Loc. cit.*

[3] *Loc. cit.*

[4] In all halogenations involving the use of free halogens in acetic anhydride solution, the unprotected hand should never be exposed over the surface of the mixture, or serious poisoning may result. Compare Bogert, THIS JOURNAL, 29, 239 (1907).

[5] *Ber.*, 25, 721 (1892).

[6] *Ibid.*, 44, 2115 (1911).

[7] *J. Chem. Soc.*, 99, 1585 (1911).

Hamburg[1] nitrated methyl trimethylgallate in acetic anhydride solution, at low temperature, and obtained the mononitro trimethylgallic ester in pale yellow crystals, m. p. 67°. Pollak and Feldscharek[2] prepared the ethyl ester of nitrotrimethylgallic acid (yellowish crystals, m. p. 68–70°) in similar manner. Thomas and Siebeling[1] nitrated methyl trimethylgallate in glacial acetic acid solution and discovered that they could obtain either mono- or dinitro (m. p. 111°) derivatives, according to the temperature of the reaction. Power and Shedden[3] found that when they nitrated ethyl triacetylgallate, they obtained ethyl dinitrodiacetylgallate, which could be converted into the triacetyl derivative by the action of acetic anhydride, or into dinitrogallic acid by hydrolysis with sulfuric acid.

Our own experience in nitrating methyl trimethylgallate with nitric acid alone, or in the presence of acetic acid, either cold or at 100°, was that the method gave but small yields of the desired nitro ester, together with considerable amounts of yellowish tar.

It was found most convenient to prepare the methyl nitrotrimethylgallate in much the same way as Hamburg,[1] operating as follows:

A solution of 30 g. methyl trimethylgallate in 120 cc. of acetic anhydride was cooled in a freezing mixture and 21 cc. nitric acid (1 cc. of fuming acid to 20 cc. concentrated) added very slowly with constant stirring. The solution was at first brownish red but, on standing overnight, changed to orange. The acetic anhydride was then distilled off under reduced pressure, and the tarry residue poured with stirring into water. What remained in the flask was dissolved out with hot alcohol, the alcoholic solution concentrated to small volume, poured into 25 volumes of cold water and salt added; the nitro derivative separated and floated to the top of the solution. The crude product was purified by crystallization from ligroin, and then melted at 67.3° (corr.). Yield, 80 per cent. It is soluble in alcohol or ether, but practically insoluble in water, and forms pale yellow, transparent prisms.

Subs. 0.2441: CO_2, 0.3695; H_2O, 0.1076. Calc. for $C_{11}H_{13}O_7N$: C, 41.32; H, 4.79. Found: C, 41.34; H, 4.9.

A nitrogen determination gave 10.5% N; calc. 10.8.

Methyl Aminotrimethylgallate, $(CH_3O)_3C_6H(NH_2).COOCH_3$ was prepared from the above nitro ester by reduction with tin and hydrochloric acid, essentially as described by Hamburg.[1] The yield of amino ester hydrochloride was 65%, and the product melted at 168° (corr.). Hamburg gives the m. p. of the hydrochloride as 167°, and of the free ester as 41°. From this hydrochloride, the free amino ester was obtained

[1] *Loc. cit.*

[2] *Monatsh.*, **29**, 139 (1907).

[3] *J. Chem. Soc.*, 81, 73 (1902).

by neutralization with sodium carbonate solution and extraction with ether. The purified ester melted at 41° (corr.).

II. Syringic Derivatives.

Syringic Acid, $(CH_3O)_2(3,5)(HO)(4)C_6H_2.COOH(1)$.—The syringic acid used in the following experiments was prepared from trimethylgallic acid and fuming sulfuric acid, by the method of Bogert and Isham,[1] which gives large yields readily and rapidly. The yield of pure acid occasionally ran as high as 98%, and actually averaged about 92% for something over 50 experiments.

The purified product formed colorless crystals, melting at 204° (corr.), in agreement with that found by Graebe and Martz,[2] and by Bogert and Isham;[1] and was soluble in chloroform, ether, alcohol, or hot water; difficultly soluble in cold water. With ferric chloride solution, it gave a reddish brown coloration, as observed by Power[3] and by Graebe and Martz.[4] At high temperatures, the acid lost CO_2, giving 1,3-dimethylpyrogallol;[5] and, on oxidation with sodium chromate and dilute sulfuric acid, yielded 3,5-dimethoxyquinone.[6]

Subs. 0.2010: CO_2, 0.4024; H_2O, 0.0949. Calc. for $C_9H_{10}O_5$: C, 54.54; H, 5.05. Found: C, 54.59; H, 5.22.

The preparation method of Graebe and Martz[1] was also tried, boiling the trimethylgallic acid with excess of concentrated hydrobromic acid (48% aqueous acid), but proved much less satisfactory, as it requires more time and does not give quite as good yields.

The **Methyl Ester** was prepared by the action of dry hydrogen chloride upon a methyl alcohol solution of the acid, as described by Bogert and Isham,[1] and melted 83–4° (corr.) in the hydrated form, and at 106–7° (corr.) in the anhydrous state.[7] It is volatile with steam.

The **Ethyl Ester,** prepared in similar manner, separated from dilute alcohol in colorless crystals, m. p. 55.8° (corr.); soluble in alcohol or ether, difficultly soluble in water. Yield, 85%.

Subs. 0.3322: CO_2, 0.7145; H_2O, 0.1855. Calc. for $C_{11}H_{14}O_5$: C, 58.40; H, 6.19. Found: C, 58.49; H, 6.21.

Isoamyl Ester.—In the preparation of this, concentrated sulfuric acid was used as the condensing agent, and the excess of the alcohol was removed by distillation under reduced pressure. The crude product was

[1] *Loc. cit.*

[2] *Ann.*, **340**, 220 (1905).

[3] *Pharm. J.*, **1901**, 275.

[4] *Ber.*, **36**, 216 (1903).

[5] Koerner, *Gazz. chim. ital.*, **18**, 209 (1888); Graebe and Hess, *Ann.*, **340**, 235 (1905).

[6] Gadamer, *Ber.*, 30, 2330 (1897); Graebe and Martz, *Ann.*, **340**, 220 (1905); Bogert and Isham, *Loc. cit.*

[7] Graebe and Martz, *Loc. cit.*; Bogert and Isham, *Loc. cit.*

crystallized from ethyl alcohol to constant m. p., and then formed fine, colorless needles, m. p. 101° (corr.).

Subs. 0.2441: CO_2, 0.5634; H_2O, 0.1537. Calc. for $C_{14}H_{10}O_5$: C, 62.68; H, 7.46. Found: C, 62.95; H, 7.01.

Methyl Acetylsyringate, $(CH_3O)_2(CH_3COO)C_6H_2.COOCH_3$.—Five g. methyl syringate dissolved in 15 g. acetic anhydride with decided rise of temperature. On standing 24 hours, some crystals separated. These were removed and an additional crop obtained from the mother liquor by dilution with water and warming. The crude product was purified by crystallization from alcohol, and then appeared in colorless crystals, m. p. 129° (corr.), soluble in alcohol, ether, or acetic anhydride (moderately), and practically insoluble in water. Yield over 95%.

Subs. 0.2136: CO_2, 0.4284; H_2O, 0.1172. Calc. for $C_{12}H_{14}O_6$: C, 52.17; H, 6.08 Found: C, 52.24; H, 6.1.

Methyl Bromosyringate, $(CH_3O)_2(HO)C_6HBr.COOCH_3$. — Attempts to brominate syringic acid directly, in various solvents, proved unsatisfactory. The same was true when an effort was made to brominate methyl syringate in alcohol, ether, chloroform or carbon disulfide solution. On the other hand, when the methyl ester was used in acetic anhydride solution, the reaction proceeded much more smoothly.

Ten g. of the ester, dissolved in 100 cc. of acetic anhydride, were cooled to 0° and treated gradually, with constant stirring, with 12 g. bromine dissolved in 60 cc. of the anhydride. After standing overnight, the excess of anhydride was distilled off under diminished pressure, the residue taken up with ether, the ether solution filtered, the solvent driven off, and the residue crystallized from dilute alcohol. Colorless crystals were obtained, m. p. 89° (corr.); soluble in alcohol, ether or benzene, practically insoluble in cold water.

Subs. 0.5335, 0.2036: AgBr, 0.3360; CO_2, 0.3054; H_2O, 0.0712. Calc. for $C_{10}H_{11}O_5Br$: Br, 27.48; C, 41.23; H, 3.78. Found: Br, 27.44; C, 40.91; H, 3.88.

The same substance was prepared by the Graebe and Martz method, heating the methyl bromotrimethylgallate with concentrated (48%) hydrobromic acid. The yield by this method was 40%, and the m. p. of the purified product 89° (corr.). A mixture of this substance with that obtained by the direct bromination method showed no change in the melting point.

The substitution of fuming sulfuric acid for hydrobromic in the above method of preparation proved unsatisfactory, since it caused too much decomposition and carbonization.

Probably for similar reasons, an attempt to apply the Juvalta process[1] to trimethylgallic acid was a failure. As fuming sulfuric acid converts trimethylgallic acid smoothly into syringic, it was thought that it might

[1] D. R. P. 50, 177, *Friedländer*, **2**, 93; Rupp, *Ber.*, **29**, 1625–34 (1896).

be possible to obtain highly halogenated syringic acids by this process; but the treatment was evidently too severe and decomposition ensued.

3,4-Dinitropyrogallol-2,6-dimethyl Ether, $(CH_3O)_2(2,6)(HO)(1)C_6H(NO_2)_2(3,4)$.—As has already been pointed out, the direct action of nitric acid upon trimethylgallic acid gives, as the main product, the dinitropyrogallol trimethyl ether.

In the case of syringic acid, the action of nitric acid causes an entirely analogous change, the chief product of the reaction being 3,4-dinitropyrogallol-2,6-dimethyl ether. The nitration was carried out by dissolving the syringic acid in glacial acetic acid, cooling the solution in a freezing mixture, adding concentrated nitric acid gradually with stirring, allowing the mixture to stand for several hours, and then precipitating by dilution with water. On purification, the ether was secured in pale yellow crystals, m. p. 154° (corr.), soluble in various organic solvents or in caustic alkali solutions, but essentially insoluble in water.

Subs. 0.3165: CO_2, 0.4758; H_2O, 0.1022. Calc. for $C_8H_8O_7N_2$: C, 41.02; H, 3.41. Found: C, 41.0; H, 3.37. Nitrogen found, 8.32; calc., 8.0.

More or less yellowish tar is apt to be formed in all these nitration reactions.

Methyl Nitrosyringate, $(CH_3O)_2(HO)C_6H(NO_2)COOCH_3$.—Eighteen grams of methyl syringate were dissolved in 100 cc. of acetic anhydride, and the solution cooled to −5° in a freezing mixture. To this were added, slowly and with constant stirring, 18 cc. of concentrated nitric acid containing a little fuming acid, maintaining the temperature below 0° throughout the operation. On standing in the ice box overnight, the reddish solution became yellow. Alcohol was then added, to convert the excess of anhydride into acetate, and the solution distilled under reduced pressure. The thick oily residue was poured, with constant stirring, into 500 cc. of water. Most of the nitro ester separated in flocculent form, rose to the top of the solution, and was filtered off. That which remained adhering to the sides of the distilling flask was dissolved out with hot alcohol. The aqueous filtrate from the precipitated nitro ester was concentrated, the alcoholic washings from the flask added, the mixture boiled for a short time, poured hot into 250 cc. of water and the solution saturated with salt. The rest of the nitro ester then separated and was filtered off. Neutralization with sodium carbonate was not found necessary.

Recrystallized from dry benzene or from absolute alcohol, the pure substance appeared in pale yellow, transparent crystals, m. p. 68.3° (corr.). Yield, 75 to 80%.

Subs. 0.2348: CO_2, 0.4031; H_2O, 0.0914. Calc. for $C_{10}H_{11}O_7N$: C, 46.69; H, 4.28. Found: C, 46.82; H, 4.33. Nitrogen found, 5.53; calc., 5.47.

The same product was obtained by heating methyl nitrotrimethylgallate with concentrated (48%) hydrobromic acid. It melted at 68° (corr.),

and no material change in the m. p. occurred when this product was mixed with some of that from the direct nitration method. The yield by this HBr method was about 30%.

As already noted, the action of nitric acid alone, or in the presence of acetic acid, upon methyl syringate, results in the formation of considerable yellowish tar and but small yields of the nitro ester.

The **Ethyl Ester,** prepared in an analogous manner, crystallizes from ligroin in nearly colorless, silky needles, m. p. 74° (corr.); soluble in alcohol, ether, ligroin or benzene; and practically insoluble in water.

Subs. 0.3112: CO_2, 0.5485; H_2O, 0.1344. Calc. for $C_{11}H_{13}O_7N$: C, 48.70; H, 4.78. Found: C, 48.66; H, 4.80.

Methyl Aminosyringate, $(CH_3O)_2(HO)C_6H(NH_2)COOCH_3$.—Ten grams methyl nitrosyringate were moistened with alcohol, and 15 g. purified tin and 50 cc. concentrated (33%) hydrochloric acid added. The flask containing the mixture was immersed in cold water until the initial vigorous reaction had somewhat abated, after which the reduction was completed by heating at 100° until the tin was all dissolved. On cooling, the double tin salt of the amino ester separated in pale yellow crystals which were filtered out, washed, suspended in dilute hydrochloric acid, and de-tinned by a current of hydrogen sulfide. The filtrate from the tin sulfide was concentrated under reduced pressure, and the concentrated solution placed in a desiccator over sulfuric acid Colorless needles of the amino ester hydrochloride separated, m. 192° (corr.); soluble in water, but practically insoluble in neutral organic solvents.

The free amino ester was recovered from its hydrochloride by (1) repeatedly boiling down its aqueous solution, the hydrochloric acid distilling off with the steam, and water being added from time to time; (2) by neutralizing its aqueous solution with sodium carbonate and extracting with ether; or (3), best, by precipitating the aqueous solution of the hydrochloride with ammonium hydroxide solution, the amino ester separating as a colorless precipitate, easily filtered out and dried. Exposed to light and air, it first turns yellow and then gradually browns. Yield, 65%. Recrystallized from dilute alcohol, in the dark, colorless crystals were secured, m. 110° (corr.).

Calc. for $C_{10}H_{13}O_5N$: C, 52.9; H, 5.7; N, 6.25. Found: C, 52.9; H, 5.98; N, 6.16.

Diacetyl Derivative.—In the first experiment, 3 g. of methyl aminosyringate hydrochloride were dissolved with 1.5 g. fused sodium acetate in 15 cc. acetic anhydride and 5 cc. glacial acetic acid, and the mixture left overnight. Water (50 cc.) was then added, and the mixture warmed for a few minutes on the water bath. This caused it to cloud, and upon cooling colorless crystals separated, which were filtered out and purified by recrystallization from ethyl acetate.

In the second experiment, 3 g. of methyl aminosyringate were warmed

with 15 cc. of acetic anhydride and 0.5 g. fused sodium acetate, and the solution set aside overnight. Water (100 cc.) was then added, and the mixture warmed for a few minutes on the water bath. The solution became cloudy, but settled well upon the addition of a little more sodium acetate. The separated crystals were filtered out, dried, and recrystallized from alcohol. Yield, 4.7 g.

The pure substance forms large, colorless crystals, m. p. 139.9° (corr.); soluble in alcohol or ether.

Better yields were realized from the free amino ester than from its hydrochloride.

Subs. 0.2050: CO_2, 0.4042; H_2O, 0.1034. Calc. for $C_{14}H_{17}O_7N$: C, 54.01; H, 5.46. Found: C, 54.00; H, 5.61.

2,4-Dihydroxy-3,5-dimethoxybenzoic Acid, (2,3,4,5-Tetrahydroxy-benzoic Acid 3,5-Dimethyl Ether), $(CH_3O)_2(HO)_2C_6H.COOH$.—Five grams of methyl aminosyringate hydrochloride were dissolved in a mixture of 10 g. concentrated sulfuric acid and 50 cc. water, and the solution diazotized by the addition of 10 g. sodium nitrite dissolved in 50 cc. water. The reaction was completed by heating for two hours at 100°. As the solution was then yellow and slightly cloudy, it was coagulated by the addition of a little acetic acid, and the precipitate filtered out and dried at 104–8°. The product was soluble in alcohol or benzene and, when purified, formed pale yellow crystals, melting with decomposition at 165°. Yield, 80%. The addition of ferric chloride to its solution colors it a rich brown.

Calc. for $C_9H_{10}O_6$: C, 50.5; H, 4.7. Found: C, 50.61; H, 4.69.

When the nitrite solution was added directly to the aqueous solution of the amino ester hydrochloride, in absence of sulfuric acid, a rich red precipitate was formed, the nature of which has not yet been determined.

What is apparently the 2,5-dimethyl ether of 2,3,4,5-tetrahydroxybenzoic acid has been prepared by Bartolotti[1] by the fusion of apiolic acid with potassium hydroxide. He describes it as a crystalline solid, melting at 147–8°.

The following preliminary experiment also was carried out: Some of the acid was heated for 40 minutes, the temperature rising finally to 220°. Gas was evolved, and the mass turned purplish. The crude product was purified by crystallization from alcohol, and the purified substance shaken with sodium hydroxide solution and dimethyl sulfate, the solution boiled for a short time, acidified, the precipitate filtered out, decolorized by boiling with boneblack in alcoholic solution, and recrystallized from the same solvent. The product was obtained in colorless, glassy needles, m. p. 89° (corr.); soluble in alcohol, ether or

[1] *Gazz. chim. ital.*, **22**, I, 562 (1892).

benzene, but not appreciably soluble in water. This experiment will be repeated with larger amounts as soon as sufficient initial material is available.

An apionol dimethyl ether has been prepared by Ciamician and Silber[1] by heating apiolic acid with potassium hydroxide and absolute alcohol. They describe it as a crystalline compound, m. p. 105–6°, b. p. 298°; soluble in hot water, in alcohol, ether, benzene or alkalies. The same authors,[2] by fusing dill oil apiolic acid with potassium hydroxide, obtained an isomeric apionol dimethyl ether as a liquid, b. p. 283°. Both of these yield, on further methylation, tetramethyl apionol, as a crystalline solid, the melting point of which is given by Ciamician and Silber as 81°, and by Boëris[3] as 89°.

It will be seen that the product of our preliminary experiment, which should be the tetramethyl apionol, agrees in its melting point with that given by Boëris for this substance.

Diacetyl Derivative.—A mixture of 10 g. of the above dihydroxy acid, 30 cc. acetic anhydride and 0.5 g. fused sodium acetate, was heated to boiling for a short time; the solution was then cooled and a dilute solution of sodium acetate added. Fine, colorless crystals separated, decomposing at 162°; soluble in alcohol, but practically insoluble in water or in dilute acids.

Subs. 0.2642: CO_2, 0.5057; H_2O, 0.1188. Calc. for $C_{13}H_{14}O_8$: C, 52.34; H, 4.69. Found: C, 52.21; H, 5.0.

Summary of Results.

1. Methyl bromotrimethylgallate is not an oil when pure, as stated in the literature, but a colorless crystalline solid, m. p. 90° (corr.). It can be most conveniently prepared by bromination of methyl trimethylgallate in acetic anhydride solution, at low temperature.

2. The following new derivatives of syringic acid have been prepared and studied; ethyl syringate, isoamyl syringate, methyl acetylsyringate, methyl bromosyringate, methyl and ethyl nitrosyringates, methyl aminosyringate, its hydrochloride and diacetyl derivative, hydroxy syringic acid (2,4-dihydroxy-3,5-dimethoxybenzoic acid) and its diacetyl derivative.

3. The action of heat upon the hydroxy syringic acid, followed by methylation, appears to yield apionol tetramethyl ether.

4. The chief product of the action of nitric acid upon syringic acid is the hitherto unknown 3,4-dinitropyrogallol-2,6-dimethyl ether.

The work is being continued.

NEW YORK, N. Y.

[1] *Ber.*, **22**, 119, 2482 (1889).
[2] *Ibid.*, **29**, 1807 (1896).
[3] *Ibid.*, **29**, 1808 (1896).