the acetate distilled, b. p. 176–177° (5 mm.); yield, 4.1 g. The viscous oil, which showed no sign of crystallizing, was allowed to stand in dry benzene (10 cc.) with phosphorus pentachloride (12 g.) for two hours, the solution turning brownish-yellow. After refluxing for one-half hour, the mixture was decomposed with ice and water and the product extracted with ether, washed with bicarbonate, dried, and distilled. After several distillations of the yellow oil a fraction was obtained boiling at 196–198° (3 mm.); yield, 2.5 g. (65%).

Anal. Calcd. for $C_{17}H_{21}Cl$: C, 78.30; H, 8.13; Cl, 13.59. Found: C, 77.87; H, 7.76; Cl, 13.19.

In an attempt to prepare the nitrile, 13 g. of the chloride was heated with 2 g. of potassium cyanide in 30 cc. of alcohol at 160–180° for twenty-four hours; repeated distillation gave a fraction boiling at 210–220° (2 mm.) and containing nitrogen (1.8 g.) but this did not solidify and gave only a small amount of oily acidic material on alkaline hydrolysis.

The unsaturated chloride (1.3 g.) absorbed hydrogen fairly rapidly in glacial acetic acid solution in the presence of Adams catalyst, and considerable hydrogen chloride was found to have been produced. The oily reaction product appeared to be a mixture; on dehydrogenation with selenium it gave a solid (0.5 g.), m. p. 59–63°, giving a picrate, m. p. 145–146°. The hydrocarbon recovered from the picrate and crystallized from alcohol formed fluorescent plates, m. p. 77.5–78°. Mixed with **2,3-dimethylphenanthrene** and its picrate, the samples showed no depression.

Dehydrogenation of the unsaturated chloride or carbinol with selenium gave a much less soluble hydrocarbon which after purification by crystallization from alcohol and from hexane formed small scales, m. p. 148–149°. The substance gives a red coloration in alcohol or benzene with picric acid, but no picrate could be isolated. The yield from the carbinol was 66% and from the chloride 35%.

Anal. Calcd. for $C_{17}H_{16}$: C, 92.69; H, 7.32. Found: C, 92.66; H, 7.31.

Summary

As a step toward a proof of the location of the ethanamine chain in the morphine alkaloids, 3,4-dimethoxy-5,6,7,8,9,10,13,14-octahydrophenanthrene-13-carboxylic acid has been synthesized for comparison with a possible degradation product of the alkaloids. The synthesis involves a diene addition to a brominated Δ^1-dihydro-α-naphthoic acid or ester obtained synthetically, the bromine being required to control the direction of cyclization and being removed in the end stages of the synthesis.

In a preliminary study of a possible lengthening of the carbon chain at C_{13}, a number of esters of substituted hexa- and octahydrophenanthrene-13-carboxylic acids have been reduced to the corresponding carbinols.

CONVERSE MEMORIAL LABORATORY
CAMBRIDGE, MASS.
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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Meso Aldehydes of Anthracene and 1,2-Benzanthracene

BY LOUIS F. FIESER AND JONATHAN L. HARTWELL[1]

Substitution reactions of polynuclear aromatic hydrocarbons have gained special interest with the observation that the most actively carcinogenic compounds of the hydrocarbon series show a high degree of susceptibility to diazo coupling[2] and to oxidation with lead tetraacetate.[3,4] Another substitution which it seemed of interest to investigate is the reaction with methylformanilide, which Vollmann, Becker, Corell and Streeck[5] recently applied with success for the conversion of pyrene into pyrene-3-aldehyde.

$$ArH + C_6H_5N(CH_3)CHO \xrightarrow{POCl_3} ArCHO + C_6H_5NHCH_3$$

Previous applications of the reaction were concerned chiefly with ortho–para substitutions of phenol ethers and amines, but the above observation shows that a sufficiently reactive hydrocarbon is capable of entering into the condensation. According to a brief report in the patent literature,[6] anthracene also reacts with methylformanilide. The present investigation of other applications of the reaction was undertaken with the idea that information might be obtained on the relative reactivities of carcinogenic hydrocarbons and in the hope of obtaining derivatives of carcinogens having the reactive aldehydic group.

By modifying slightly the procedure of Vollmann, *et al.*,[5] it was found possible to obtain the known 9-anthraldehyde in 92% yield after heating the reaction mixture for two hours on the steam-bath. 1,2-Benzanthracene reacts less readily, for under the same conditions about half of the hydrocarbon was recovered unchanged and

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(1) Research Fellow of the National Cancer Institute.

(2) Fieser and Campbell, THIS JOURNAL, **60**, 1142 (1938).

(3) Fieser and Hershberg, *ibid.*, **60**, 1893 (1938).

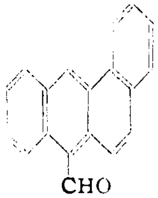
(4) Fieser and Hershberg, *ibid.*, **60**, 2542 (1938).

(5) Vollmann, Becker, Corell and Streeck, *Ann.*, **531**, 1 (1937).

(6) I. G. Farbenindustrie A.-G., English Patent 311,208 (1928).

about half converted into an aldehyde. With 1,2,5,6-dibenzanthracene no aldehyde could be isolated even under forcing conditions; after heating the reaction mixture for twenty-four hours in a sealed tube at 155°, for example, 72% of the starting material was recovered. This is a further example of the marked hindrance at both *meso* positions of the hydrocarbon,[3] and the observation shows clearly that the reaction with methylformanilide can be applied only to specific hydrocarbons at specific nuclear positions. The order of susceptibility of the three hydrocarbons to this substituting agent is: anthracene > 1,2-benzanthracene > 1,2,5,6-dibenzanthracene.

For proof of structure the new aldehyde of the 1,2-benzanthracene series was converted through the hydrazone to the corresponding hydrocarbon, which was found to be identical with 10-methyl-1,2-benzanthracene.[7] The substance, therefore, is 1,2-benzanthracene-10-aldehyde (I), the position of substitution being the same as in nitration[3] and in acetoxylation with lead tetraacetate.[3] The hydrocarbon was obtained from the aldehyde in 84% yield, and the yield of aldehyde, based on the 1,2-benzanthracene consumed, was 64%. The 10-methyl compound, which is a valuable agent for the rapid production of experimental sarcomas, thus can be obtained in a simple three-step process from a commercially available starting material in 54% yield.


I

The new aldehyde, which may be of use in the preparation of interesting conjugated compounds, is being tested for carcinogenic activity by Dr. M. J. Shear. 10-Cyano-1,2-benzanthracene, prepared in good yield by dehydration of the oxime, is of interest in connection with the observations reported by Newman.[8] The aldehyde was also converted into the corresponding 10-α-hydroxyethyl compound by reaction with methylmagnesium iodide.

Preliminary to the preparation of these and other compounds derived from the aldehyde, a few trials were made with 9-anthraldehyde. This yielded 9-methyl-, 9-cyano- and 9-α-hydroxyethylanthracene by the above methods, and it was converted also into 9-anthralmalonic acid. This acid is yellow but yields on crystallization under certain conditions an orange substance which probably is a monohydrate; it was also observed that the acid is unusually resistant to decarboxylation. Methyl-9-anthranylcarbinol when heated with potassium bisulfate yielded a colored tar from which anthracene was isolated. Application of the Tschugaeff reaction gave anthracene and 9-ethylanthracene. Bergmann and Bergmann[9] similarly obtained 9-ethylphenanthrene in certain experiments in investigating the Tschugaeff dehydration of the isomeric methylphenanthrylcarbinol. When heated with phosphorus pentoxide in benzene solution, methyl-9-anthranylcarbinol is converted into a high melting product having the composition of an ether: $[C_{14}H_9CH(CH_3)—]_2O$. It yields anthraquinone on oxidation.

Experimental Part[10]

9-Anthraldehyde.—The procedure of Vollmann, *et al.*,[6] for effecting the condensation of methylformanilide with pyrene was found satisfactory for anthracene, but their method of isolating the reaction product was not well adapted to the present case and a more generally applicable method was developed.

One hundred and thirty-five grams of phosphorus oxychloride was added slowly with external cooling to a mixture of 135 g. of methylformanilide, prepared according to Morgan and Grist,[11] and 100 cc. of dry technical *o*-dichlorobenzene, keeping the mixture at about room temperature, and 89.1 g. of anthracene (colorless, m. p. 215–216.4°) was added. The mixture was stirred mechanically and heated on the steam-bath under protection from moisture, applying heat cautiously at first. As the temperature rose the hydrocarbon gradually dissolved, the solution became deep red and hydrogen chloride was evolved. After the first vigorous reaction was over, heating on the steam-bath with stirring was continued for two hours and the viscous mass was transferred to a large flask, mixed with 1 liter of water containing 480 g. of crystalline sodium acetate and steam distilled. The *o*-dichlorobenzene distils rapidly and products other than the aldehyde are largely retained in the aqueous acetate solution. The undissolved residue consisted of a dark oil which on cooling solidified to a mass of yellow crystals. Collected, washed and crystallized from acetic acid, the aldehyde formed long, deep yellow needles, m. p. 98.4–99.4°, total yield, 94.9 g. (92%). Hinkel, Ayling and Beynon[12] give the m. p. 104–105°.

9-Methylanthracene.—The aldehyde was converted in the hydrazone by adding 2.8 g. of hydrazine hydrate in on

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[7] Fieser and Newman, THIS JOURNAL, 58, 2376 (1936).

[8] Newman, *ibid.*, 60, 1368 (1938).

[9] Bergmann and Bergmann, *ibid.*, 59, 1447 (1937).

[10] All melting points are corrected. Analyses by the Arlington Laboratories.

[11] Morgan and Grist, *J. Chem. Soc.*, 113, 690 (1918).

[12] Hinkel, Ayling and Beynon, *ibid.*, 344 (1936).

portion to a solution of 11 g. of aldehyde in 250 cc. of alcohol at 70°. After heating at the boiling point for five minutes, 10 cc. of water was added. A large crop of yellow needles, m. p. 108–110°, separated on cooling and a further amount was obtained by dilution of the mother liquor; total yield, 9.9 g. (89%). The hydrazone seems to be subject to slight hydrolysis when dissolved for recrystallization in aqueous alcohol (separation of amorphous orange material); the best sample formed orange-yellow needles, m. p. 118–119.5°, but was not analytically pure.

A mixture of 4.4 g. of the hydrazone and a solution from 0.77 g. of sodium and 25 cc. of absolute ethyl alcohol was shaken in a sealed tube until uniform and heated at 200–205° for twenty-one hours. The cooled mixture was poured into water, neutralized with acetic acid, extracted with ether and the dried solution evaporated. Crystallization of the residue from methanol gave 1.5 g. of the known 9-methylanthracene, m. p. 76.3–77.8° (lit.,[13] 79–80°, 81.5°); picrate, m. p. 133–135° (lit.,[13] 137°, dec.).

9-Cyanoanthracene.—The oxime was prepared from 15 g. of 9-anthraldehyde in 300 cc. of alcohol by the addition at 75° of a solution of 5.5 g. of hydroxylamine hydrochloride in 50 cc. of water, neutralized with sodium carbonate. Heated on the steam-bath for ten minutes, diluted with water until cloudy and cooled, the solution deposited 15 g. (93%) of yellow needles in two crops. For purification the substance was precipitated from a filtered solution in hot alkali and crystallized from alcohol, giving long yellow needles, m. p. 165–165.5° (Hinkel, Ayling and Beynon,[12] 186–187°). *Anal.* Calcd. for $C_{15}H_{11}ON$: C, 81.42; H, 4.98. Found: C, 81.72; H, 5.08. A solution of 2 g. of the oxime in 10 cc. of acetic anhydride was refluxed for fifteen minutes, and on cooling the mixture went solid with lemon-yellow needles. Washed with acetic acid and petroleum ether, the product melted at 175.5–177.5°; yield, 1.8 g. (98%). Two crystallizations from glacial acetic acid (strong blue fluorescence) raised the m. p. to 177.5–179°. Karrer and Zeller[14] give the m. p. 170–172°.

Anal. Calcd. for $C_{15}H_9N$: C, 88.61; H, 4.46. Found: C, 88.36; H, 4.54.

9-Anthraldoxime Acetate.—Since our sample of the oxime melted considerably lower than reported,[12] this further derivative was prepared for analysis. Acetyl chloride (6 cc.) was added to the oxime (2 g.) in dry ether (50 cc.), and after five minutes 10% sodium carbonate was added by drops until there was no longer a reaction; from the washed and dried ether layer there was obtained a total of 1.65 g. (70%) of crystalline product. The substance forms long lemon-yellow needles from ether, m. p. 131.5–132°.

Anal. Calcd. for $C_{17}H_{13}O_2N$: C, 77.56; H, 4.98. Found: C, 77.29; H, 4.96.

Condensation of 9-Anthraldehyde with Malonic Acid.—A mixture of 10.3 g. of the aldehyde, 6 g. of malonic acid and 0.5 cc. of pyridine was heated on the steam-bath for six hours, and the cooled mixture was extracted with sodium carbonate solution, which left a residue containing unchanged aldehyde. Acidification of the carbonate extract gave a voluminous, deep yellow precipitate (4.1 g.). Crystallization of the crude product from acetic acid–petroleum ether or from methanol–petroleum ether gave chiefly bright yellow needles of **9-anthralmalonic acid,** melting indefinitely at 240–246°, dec.

Anal. Calcd. for $C_{18}H_{12}O_4$: C, 73.97; H, 4.14; neut. equiv., 146. Found: C, 73.86; H, 4.18; neut. equiv., 138.

The **dimethyl ester,** prepared with diazomethane and crystallized from ether–petroleum ether, formed large transparent yellow prisms, m. p. 134.5–135.5° (87% yield).

Anal. Calcd. for $C_{20}H_{16}O_4$: C, 75.00; H, 5.04. Found: C, 74.97; H, 4.98.

The malonic acid is quite resistant to decarboxylation. Pyrolysis at 250° for five minutes gave a tar, and little change other than hydration (see below) occurred on refluxing the acid with an acetic–hydrochloric acid mixture. After heating in quinoline with copper bronze or basic copper carbonate at temperatures up to 245° (one hour), 22–27% of the starting material was recovered unchanged.

When the crude, deep yellow condensation product was crystallized from a mixture of methanol, ordinary ether and petroleum ether, large orange prisms were obtained, along with some yellow needles, from which they were easily separated. When heated in a capillary tube the orange material turned yellow at about 80° and showed the m. p. 246°, dec. Even at room temperature the orange prisms soon became coated yellow on the surface, and an analysis of partially transformed material is significant only in showing that the carbon and hydrogen values are lower than for the yellow material (Found: C, 71.00; H, 4.37). The neutralization equivalent determined on a fresh sample (162) is close to that required for a monohydrate (155). The orange hydrate gives the yellow needles of the anhydrous acid on crystallization from acetic acid–petroleum ether. The orange prisms on treatment with diazomethane give yellow prisms, m. p. 134.5–135.5°, identical with the dimethyl ester described above.

Methyl-9-anthranylcarbinol.—This was prepared by adding 30 g. of the aldehyde in 300 cc. of benzene to the Grignard reagent from 21.5 g. of methyl iodide and 4.05 g. of magnesium in 400 cc. of ether and refluxing for one-half hour. After adding ammonium chloride solution and working up the product there was obtained in all 29.6 g. (92%) of satisfactory material. Crystallization from ether–petroleum ether gave glistening, colorless needles having a blue fluorescence in daylight and a blue-violet fluorescence in ultraviolet light; m. p. 125–126.5°.

Anal. Calcd. for $C_{16}H_{14}O$: C, 86.46; H, 6.81. Found: C, 86.62; H, 6.62.

The only crystalline product obtained on heating the carbinol with potassium bisulfate was anthracene, and sulfuric acid of various strengths gave only colored tars. In a trial of the Tschugaeff reaction 2.5 g. of the carbinol was treated in xylene with 0.35 g. of sodium, and after refluxing for two days the dark liquid was cooled and treated with 3 cc. of carbon bisulfide, followed by 3 cc. of methyl iodide. After refluxing for about one hour the mixture turned yellow and sodium chloride precipitated. The filtered solution was then evaporated and the product distilled at 23 mm. From the distillate there was obtained a crystalline product, m. p. 215.5–217°, identified as anthracene, and a trinitrobenzene derivative, m. p. 122.5–123.5°,

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[13] Krollpfeiffer and Branshied, *Ber.*, **56**, 1617 (1923); Sieglitz and Marx, *ibid.*, **56**, 1619 (1923).

[14] Karrer and Zeller, *Helv. Chim. Acta*, **2**, 485 (1919).

found to be that of **9-ethylanthracene**. A sample of this hydrocarbon was prepared from anthrone and ethylmagnesium bromide according to Sieglitz and Marx[13] in 89% yield, m. p. 56–58°. **9-Ethylanthracene–trinitrobenzene** from this source crystallized from ether–benzene in the form of bright red needles, m. p. 125.3–125.6° (no depression with the above product).

Anal. Calcd. for $C_{16}H_{14}\cdot C_6H_3O_6N_3$: C, 63.00; H, 4.09. Found: C, 62.71; H, 4.15.

In another attempted dehydration the carbinol (14.5 g.) was refluxed in benzene (250 cc.) with excess phosphorus pentoxide for about one hour, the solution was decanted, and the residue was treated with benzene and water and extracted thoroughly with benzene. The washed and dried benzene solution was concentrated somewhat and passed through a tower of activated alumina. Material collecting in blue and deep yellow zones at the top was discarded while that adsorbed in light yellow and colorless (fluorescent) zones was washed into the filtrate with fresh benzene. The solution was filtered through a fresh tower and concentrated, giving in three crops 8.7 g. (35%) of nearly colorless needles. After further purification by repeated crystallization from benzene–ligroin the substance formed glistening, colorless needles having a blue fluorescence in ultraviolet light and melting at 247.5–248°, with some previous softening.

Anal. Calcd. for $C_{32}H_{26}O$: C, 90.11; H, 6.15. Found: C, 89.67; H, 6.30.

This substance, which evidently is an ether, yielded anthraquinone (mixed m. p.) on oxidation with chromic acid in acetic acid solution. No other crystalline product was obtained as such or as the trinitrobenzene derivative from the oily material from the mother liquor.

1,2-Benzanthracene-10-aldehyde.—The 1,2-benzanthracene employed was prepared as described by Bachmann.[15] The yellow color was removed by two treatments with lead tetraacetate[8] but the method of chromatographic adsorption of the chrysogen on activated alumina from benzene solution seemed more satisfactory for large-scale operation. Colorless material, m. p. 160.5–161°, was obtained in this way with little loss.

Phosphorus oxychloride (24.8 g.) was added at a temperature controlled to 25° to 24.8 g. of methylformanilide and 18.5 cc. of *o*-dichlorobenzene; 21 g. of 1,2-benzanthracene was introduced and the mixture heated on the steam-bath with occasional shaking until the hydrocarbon had dissolved (twenty minutes). After a total of two hours the mixture was processed as above and the solidified residue from the steam distillation crystallized from glacial acetic acid (slow cooling). Yellowish plates of the hydrocarbon and yellow prisms of the aldehyde were deposited together. A separation was accomplished most conveniently as follows. The mixture of crystals was collected, washed, dried, moistened with a little alcohol and shaken thoroughly with about 100 cc. of water. The prisms settle rapidly, leaving the plates suspended, and by decanting the suspension and repeating the flotation several times a fairly clean separation can be effected. The two crude products were dried and crystallized from glacial acetic acid (decolorizing carbon), giving in all 8.3 g. of slightly yellow hydrocarbon, the bulk of which melted at 156–159° (no depression with starting material), and 8.1 g. of aldehyde (64%, based on material consumed), m. p. 147–148°. The aldehyde on further purification formed yellow, prismatic needles, m. p. 147.5–148°.

Anal. Calcd. for $C_{19}H_{12}O$: C, 89.03; H, 4.72. Found: C, 89.00; H, 4.98.

The hydrazone was prepared by adding 1 g. of hydrazine hydrate to a solution of 2.6 g. of the aldehyde in 350 cc. of boiling alcohol and heating the mixture just below the boiling point for fifteen minutes. On cooling, the product separated almost completely in the first crop as yellow needles, m. p. 187.5–188°; yield, 2.2 g. (84%). Recrystallization from absolute alcohol did not alter the m. p.

Anal. Calcd. for $C_{19}H_{14}N_2$: C, 84.42; H, 5.22. Found: C, 84.38; H, 5.38.

10-Methyl-1,2-benzanthracene.—The hydrazone (1.9 g.) was heated in a sealed tube with the reagent from 0.27 g. of sodium and 9 cc. of absolute alcohol for ten hours at 205–210°. After dilution with water and acidification of the mixture, the nearly colorless solid when collected and dried was found to melt at 136.5–139°; yield 1.7 g. (quantitative). One crystallization from acetic acid gave faintly yellow, glistening flat needles, m. p. 139.5–140.5°, which did not depress the m. p. of a synthetic sample,[7] m. p. 140.2–140.8°.

1,2-Benzanthracene-10-aldoxime.—A mixture of 2 g. of the aldehyde, 250 cc. of alcohol, 3.13 g. of sodium acetate crystals and 0.93 g. of hydroxylamine hydrochloride was heated just below boiling for fifteen minutes, and the solution was filtered and cooled. The product which separated (1.7 g.) on recrystallization from absolute alcohol formed crusts of light yellow needles melting at 203.5–204.5°, and remelting at 231–232.5°, dec.

Anal. Calcd. for $C_{19}H_{13}ON$: C, 84.11; H, 4.83. Found: C, 83.82; H, 4.90.

10-Cyano-1,2-benzanthracene.—After refluxing the oxime (1.35 g.) with acetic anhydride for fifteen minutes, the solution set to a thick paste of yellow crystals of the nitrile on cooling; m. p. 188–189.5°, yield, 1.25 g. (99%). Recrystallized from glacial acetic acid, it formed light yellow blades, m. p. 188.5–189.5°.

Anal. Calcd. for $C_{19}H_{11}N$: C, 90.09; H, 4.38. Found: C, 90.47; H, 4.40.

Methyl-10-benzanthranylcarbinol.—Prepared as above from 1,2-benzanthracene-10-aldehyde and methylmagnesium iodide, this carbinol was obtained in a satisfactory crystalline condition from ether–petroleum ether in 56% yield. Recrystallized from methanol it formed nearly colorless prisms, m. p. 148–150°.

Anal. Calcd. for $C_{20}H_{16}O$: C, 90.27; H, 5.92. Found: C, 90.55; H, 5.51.

Summary

Methylformanilide in the presence of a condensing agent reacts less readily with 1,2-benzanthracene than with anthracene, and does not react with 1,2,5,6-dibenzanthracene even under considerably more drastic conditions. The prod-

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[15] Bachmann, *J. Org. Chem.*, **1**, 349 (1936).

uct from 1,2-benzanthracene is the 10-aldehyde, and this on Wolff–Kishner reduction affords the carcinogenic 10-methyl compound. The 10-nitrile and 10-α-hydroxyethyl derivatives have also been prepared and various reactions of 9-anthraldehyde investigated.

CONVERSE MEMORIAL LABORATORY
CAMBRIDGE, MASS.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

The Preparation of α- and β-Gentiobiose Octaacetates

BY DELBERT DANIEL REYNOLDS AND WILLIAM LLOYD EVANS[1]

Recent investigations in this Laboratory gave rise to a need for considerable quantities of β-gentiobiose octaacetate. The five most important methods for its preparation are as follows: (1) isolation from gentian root,[2] (2) the action of emulsin on glucose to form gentiobiose, which is then connected to β-gentiobiose octaacetate,[3,4] (3) the catalytic hydrogenolysis of amygdalin followed by acetylation,[5] (4) separation from the commercial mother liquors ("Hydrol") obtained in the manufacture of glucose[6] and (5) the condensation of acetobromoglucose with β-*d*-glucose-1,2,3,4-tetraacetate by means of the Königs-Knorr reaction.[7]

The inferior quality of most gentian root renders the first method undesirable. The second method proved objectionable for two reasons, namely, (1) from ten to twelve weeks are required to complete the synthesis, and (2) emulsin is not readily available. The third method has not been tried in this Laboratory because of the relatively high cost of amygdalin. Since the percentage of gentiobiose in "Hydrol" varies greatly, this method leaves much to be desired.

A yield of 23.4% of the theoretical value has been reported for the fifth method.[7] This low yield may be attributed to numerous possible side reactions. The most probable of these is the reaction of acetobromoglucose with water in the presence of silver oxide to form β-*d*-glucose-2,3,4,6-tetraacetate, silver bromide and water. The water formed in this reaction may react with more acetobromoglucose, thus setting up a series of changes which would continually use up the acetobromo compound. Moreover, the β-*d*-glucose-2,3,4,6-tetraacetate may react with acetobromoglucose in the presence of silver oxide to form a trehalose octaacetate and more water. Accordingly, the yield of the β-gentiobiose octaacetate would be greatly lowered.

It was the purpose of this work to make the latter method a practical one for the preparation of β-gentiobiose octaacetate by reducing these side reactions to a minimum. This may be accomplished only if the reaction is carried out under anhydrous conditions. Such conditions are realized by (1) ensuring complete absence of water at the beginning of the reaction and (2) removal of the water from the reaction mixture as rapidly as it is formed, thus keeping the concentration of water in the reaction mixture relatively small at any given time. A preliminary stirring of the tetraacetate, silver oxide and chloroform with a large excess of Drierite assures complete absence of water when the reaction is begun. The addition of a chloroform solution of acetobromoglucose over a considerable period of time, as opposed to adding it in one large portion, permits only a small amount of water to be formed at any given time. The water formed during the reaction may be removed by employing an effective internal desiccant. Studies in this Laboratory[8] have shown that anhydrous calcium sulfate (Drierite) is an excellent substance for this purpose. Other investigators[9] have used powdered calcium chloride in similar reactions. By proceeding with the foregoing facts in mind, β-gentiobiose octaacetate has been obtained in yields as high as 82% of the theoretical value.

After β-gentiobiose octaacetate had been obtained in good yields, it seemed reasonable to believe that α-gentiobiose octaacetate might be prepared by the same method even though α-*d*-glucose-1,2,3,4-tetraacetate could be obtained

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(1) Presented at the Milwaukee Meeting of the American Chemical Society, September 8, 1938.

(2) E. Bourquelot and H. Herissey, *Compt. rend.*, **132**, 571 (1901); *Bull. Soc. chim.*, [3] **29**, 363 (1903).

(3) E. Bourquelot, H. Herissey and J. Coirre, *Compt. rend.*, **157**, 732 (1913).

(4) J. F. Leete, Ph.D. Dissertation, The University of Greifswald, Greifswald, 1929.

(5) M. Bergmann and W. Freudenberg, *Ber.*, **62**, 2783 (1929).

(6) H. Berlin, THIS JOURNAL, **48**, 2627 (1926).

(7) B. Helferich and W. Klein, *Ann.*, **450**, 219 (1926).

(8) L. C. Kreider and W. L. Evans, THIS JOURNAL, **58**, 797 (1936).

(9) B. Helferich, E. Bohm and S. Winkler, *Ber.*, **63**, 990 (1930).