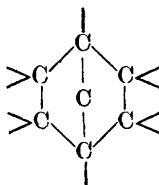


CIII.—*A New Synthesis of Phloroglucinol.*

By DAVID SMILES JERDAN, B.Sc.

RECENT researches in the terpene series, and especially investigations into the nature of camphor, have led to the development of various formulæ to represent the constitution of the latter. Especially prominent within the last few years have been the formulæ proposed by Tiemann and others, in which camphor is represented as containing two variously substituted pentamethylene rings, which have three carbon atoms in common. The proposed formulæ may also be described as consisting of a substituted hexamethylene ring in which two carbon atoms in the *para* position are united by single bonds to a seventh carbon atom in the following way :—



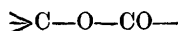
At the suggestion of the late Professor Victor Meyer, the author

made various experiments with a view to the synthesis of a substance of analogous constitution. Although, unfortunately, the end in view was not attained, the experiments resulted in a new synthesis of phloroglucinol from ethylic acetonedicarboxylate, and thus added another to the many known methods of passing from the fatty to the aromatic series. Phloroglucinol itself has already been prepared synthetically from another member of the fatty series by Baeyer (*Ber.*, 1885, 18, 3457) who, by heating the monosodium derivative of ethylic malonate, obtained the ethylic salt of phloroglucinoltricarboxylic acid. The ethereal salt, when melted with potash, yielded phloroglucinol.

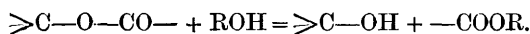
An attempt to condense ethylic acetonedicarboxylate in benzene solution with ethylene chlorhydrin or ethylene dibromide by means of finely-divided sodium, yielded a solid, well-defined substance, which analysis showed to possess the composition  $C_{12}H_{10}O_7$ . Its empirical formula and properties seemed at first so inexplicable that it was resolved to examine into its constitution, and only after this had been determined did it become clear that the new substance must result from the action of sodium on ethylic acetonedicarboxylate alone. Experiment fully bore out this conclusion. The new substance may be easily prepared in quantity by this reaction, as will be described in detail later.

The results of the following experiments made the mode of formation of the new substance, and its constitution, clear.

(1) Since the substance  $C_{12}H_{10}O_7$  showed an acid reaction, and liberated carbon dioxide from alkaline carbonates, an attempt was made to obtain an ethereal salt according to Fischer's method, namely, by boiling it with methylic alcohol containing 3 per cent. of hydrogen chloride. This reaction yielded a substance which, on analysis, proved to have the composition  $C_{13}H_{14}O_8$ , being formed from the original substance by addition of a molecule of methylic alcohol. The substance  $C_{12}H_{10}O_7$  must therefore contain the lactone group



which on etherification would act in accordance with the equation



In what follows, therefore, the substance  $C_{12}H_{10}O_7$  will be referred to as "the lactone."

In order to confirm the above result, an exactly parallel experiment was made with ethylic alcohol, and an exactly analogous substance was obtained, having the composition  $C_{14}H_{16}O_8$ , and resulting from the addition of a molecule of alcohol to the lactone.

(2) When a chloroform solution of the lactone was treated with a chloroform solution of bromine, substitution at once took place, and a

new substance was formed in which two atoms of hydrogen were replaced by two of bromine.

(3) When an acetic acid solution of the lactone was mixed with an acetic acid solution of phenylhydrazine, a hydrazone crystallised out which, on analysis, proved to contain one hydrazine residue.

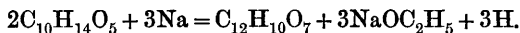
(4) When the lactone was hydrolysed by being boiled with barium hydrate solution, four products were obtained which finally explained its constitution. In the first place, it was shown that barium carbonate was formed in the hydrolysis, and a quantitative determination showed that one molecule of lactone gave one molecule of carbon dioxide.

Further, after a quantity of the lactone had been boiled with excess of baryta water for some hours, a quantity of liquid was distilled off, which, after repeated fractionation, yielded a liquid boiling at  $78^{\circ}$ , and possessing all the properties of ethylic alcohol.

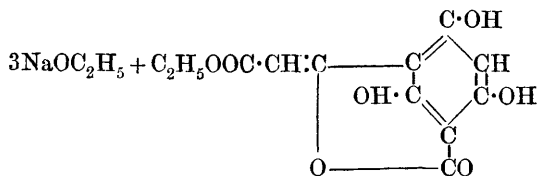
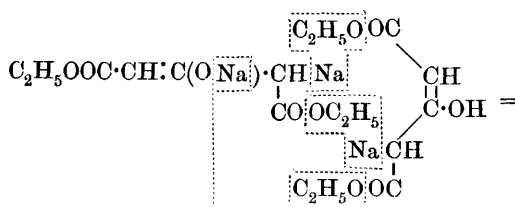
The precipitate formed during the hydrolysis, after being decomposed by hydrochloric acid, yielded a solid, crystalline acid which melted at  $131.5^{\circ}$ , and gave, on further heating, acetic acid and carbon dioxide. The acid possessed the composition  $C_3H_4O_4$ , and was in every respect identical with malonic acid.

The filtrate from the precipitate, after removal of the greater portion of the barium, was made just acid, and extracted with ether. The ethereal solution, on evaporation, yielded a substance which crystallised well from water and possessed the composition  $C_6H_{10}O_5$ . It was found to contain two molecules of water of crystallisation, which it gave off at  $105^{\circ}$ . The dry substance, which analysis showed to have the composition  $C_6H_6O_3$ , melted about  $210^{\circ}$ , coloured a piece of pine wood moistened with hydrochloric acid cherry-red, and in short possessed the composition and properties of phloroglucinol, the (1:3:5) symmetrical trihydroxybenzene.

The following equations may be suggested as probably representing the formation of the lactone  $C_{12}H_{10}O_7$  from ethylic acetonedicarboxylate by the action of sodium. Two molecules of the ethereal salt react with three atoms of sodium, thus—



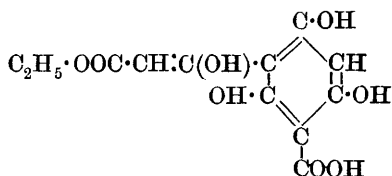
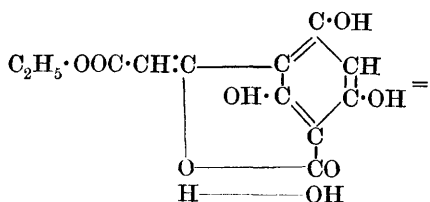
Graphically, the reaction is best represented by supposing a mono-sodium derivative of the ethereal salt to react with a disodium derivative, with elimination of three molecules of sodium ethylate:—



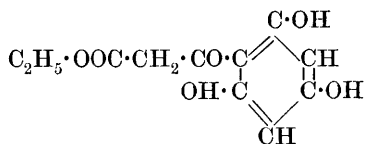
The immediate product of the reaction is, of course, a sodium salt, which, on addition of sulphuric acid, yields the lactone.

This formula explains most of the reactions shown by the substance  $\text{C}_{12}\text{H}_{10}\text{O}_7$ , the chief uncertainty lying in the satisfactory disposal of the possible "ketonic" and "enolic" forms.

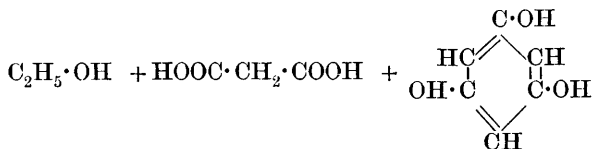
The presence of a lactone group accounts for the anomaly noticed in the attempt to prepare an ethereal salt. The formation of a hydrazone containing only one hydrazine residue may be accounted for by the oxygen atom which binds together the carbon atoms of the lactone group being replaced by the residue  $\text{:N}\cdot\text{NHC}_6\text{H}_5$ . The production of carbon dioxide, alcohol, malonic acid, and phloroglucinol from the lactone by hydrolysis may be represented as follows. The lactone first takes up a molecule of water with formation of the corresponding acid.



The acid thus formed gives up carbon dioxide in presence of barium hydrate, and passes in all probability into the following "ketonic" form—



which will again react with two molecules of water, giving alcohol, malonic acid, and phloroglucinol, thus :—



The fact that both malonic acid and phloroglucinol are very readily acted on by bromine explains the fact that the two available hydrogen atoms in the lactone are so easily replaced.

#### EXPERIMENTAL.

##### *Preparation of the Lactone* $\text{C}_{12}\text{H}_{10}\text{O}_7$ .

Twenty grams of pure distilled ethylic acetonedicarboxylate (2 mols.) are dissolved in 100 grams of dry benzene, and 3·5 grams (3 atoms) of finely-divided sodium are then added. The sodium is reduced to the required condition according to the usual method, by shaking the weighed quantity of the metal with petroleum in a small flask at 120°. The petroleum is poured off when cold, and the globules of sodium are washed with benzene before use. The sodium immediately dissolves in the mixture of the ethereal salt with benzene, giving a clear, yellowish solution. This is then boiled on the water bath with a reflux condenser, until the liquid is full of a yellow, gummy mass, which no longer increases in quantity. The reaction is then at an end. About 300 c.c. of water are poured into the flask, and the whole is well shaken: the water dissolves the sodium derivative of the new substance, and the yellow, aqueous solution is separated from the benzene by means of a separating funnel. On addition of excess of sulphuric acid to the aqueous solution, it becomes milky, and after a short time deposits a considerable precipitate; this is collected, well washed with water, and finally with a small quantity of ether, and the product is dried at 100°.

The yield under favourable conditions is from 8 to 9 grams, that is to to say, between 60 and 70 per cent. of the theoretical quantity.

The crude product is then crystallised from glacial acetic acid, and is obtained either in small, glistening leaflets, or in star-like aggregates, the former modification being deposited preferentially from strong, hot, and impure solutions. Neither form is stable; on stirring the crystals with the mother liquor, they become opaque and quickly yield a cryptocrystalline powder. After several crystallisations from glacial acetic acid, an almost white product is obtained, which melts sharply at  $188^{\circ}$ .\* If the sulphuric acid in the melting point apparatus has been mixed with a few drops of nitric acid, the melting point tube acquires a peculiar purple colour. Three separately prepared samples of this substance gave the following results on analysis:

- I. 0.1191 gave 0.2372  $\text{CO}_2$  and 0.0404  $\text{H}_2\text{O}$ . C = 54.32; H = 3.77.
  - II. 0.1481 „ 0.2930  $\text{CO}_2$  „ 0.0498  $\text{H}_2\text{O}$ . C = 53.95; H = 3.74.
  - III. 0.1485 „ 0.2940  $\text{CO}_2$  „ 0.0506  $\text{H}_2\text{O}$ . C = 54.00; H = 3.78.
- $\text{C}_{12}\text{H}_{10}\text{O}_7$  requires C = 54.06; H = 3.76 per cent.

The lactone dissolves easily in alcohol, in hot glacial acetic acid, and in boiling chloroform, but is only sparingly soluble in ether, and insoluble in ligroin. It possesses an extremely bitter taste, gives an acid reaction with litmus, and dissolves in sodium carbonate solution with effervescence, giving, when pure, a colourless solution, from which it may be reprecipitated by acids. An alcoholic solution of the lactone gives, with ferric chloride, a deep purple coloration.

*Preparation of the Methylic and Ethylic Salts of the Corresponding Acid.*

The lactone was boiled for 5 hours in a flask provided with a reflux condenser with five times its weight of methylic alcohol containing 3 per cent. of hydrogen chloride. Water was then added, when the ethereal salt separated out on the sides of the flask in oily drops which soon solidified. The solid was collected, and crystallised once from alcohol and twice from benzene. It formed nearly white, prismatic crystals melting at  $128^{\circ}$ — $130^{\circ}$ .

- 0.1309 gave 0.2513  $\text{CO}_2$  and 0.0559  $\text{H}_2\text{O}$ . C = 52.35; H = 4.75.
- $\text{C}_{12}\text{H}_{10}\text{O}_5(\text{OH})(\text{COOCH}_3)$  requires C = 52.35; H = 4.70.

The ethereal salt dissolves readily in alcohol, ether, benzene, chloroform, and acetic acid, but is insoluble in ligroin.

The ethylic salt was made in exactly the same way, using ethylic alcohol instead of methylic alcohol. It was found to melt at  $90^{\circ}$ , and to be more readily soluble in alcohol, ether, and benzene than the methylic salt.

\* The melting points given are uncorrected.

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0.1280 gave 0.2547  $\text{CO}_2$  and 0.0590  $\text{H}_2\text{O}$ .  $\text{C} = 54.26$ ;  $\text{H} = 5.12$ .

$\text{C}_{12}\text{H}_{10}\text{O}_5(\text{OH})(\text{COOC}_2\text{H}_5)$  requires  $\text{C} = 53.85$ ;  $\text{H} = 5.12$  per cent.

Both salts give with fuming nitric acid a deep purple-red coloration which quickly fades.

*Action of Bromine on the Lactone and the Methylic Salt.*

A quantity of the lactone was dissolved in boiling chloroform, and a solution of bromine in chloroform was added until the mixture became permanently coloured. Much hydrogen bromide was evolved on boiling, and on cooling, a plentiful crop of small, needle-shaped crystals was deposited. These were filtered off and crystallised from glacial acetic acid. The substance was finally obtained in short, delicate, colourless needles, which on rapid heating melted with decomposition at  $220^\circ$ , but on slower heating decomposed about  $208^\circ$ .

0.2553 gave 0.2264 AgBr.  $\text{Br} = 37.73$ .

$\text{C}_{12}\text{H}_8\text{O}_7\text{Br}_2$  requires  $\text{Br} = 37.74$  per cent.

When the methylic salt,  $\text{C}_{12}\text{H}_{10}\text{O}_5(\text{OH})(\text{COOCH}_3)$ , was dissolved in chloroform and treated with a chloroform solution of bromine, a mixture of two substances was obtained, which were separated by treatment with boiling ligroin, in which one substance only was soluble. The hot ligroin solution was filtered, and on cooling, deposited white, microscopic crystals which melted at  $139\text{--}140^\circ$ .

0.1003 gave 0.0824 AgBr.  $\text{Br} = 35.06$ .

$\text{C}_{12}\text{H}_8\text{Br}_2\text{O}_5(\text{OH})(\text{COOCH}_3)$  requires  $\text{Br} = 35.09$  per cent.

This substance was therefore a dibromo-substitution product of the methylic salt.

The residue undissolved by the ligroin, which constituted the greater part of the product, crystallised well from glacial acetic acid in needles melting and decomposing at  $219^\circ$ .

0.0984 gave 0.0874 AgBr.  $\text{Br} = 37.79$ .

$\text{C}_{12}\text{H}_8\text{O}_7\text{Br}_2$  requires  $\text{Br} = 37.74$  per cent.

The second product is thus identical with the bromine substitution product of the lactone; methylic alcohol must therefore have been eliminated from the ethereal salt during the bromination.

*Preparation of a Phenylhydrazone.*

A hot solution of the lactone in glacial acetic acid was mixed with excess of phenylhydrazine likewise dissolved in glacial acetic acid. In a few minutes, the phenylhydrazone crystallised out in beautiful

needles, which, after recrystallisation from glacial acetic acid, melted sharply at  $243^{\circ}$ .

0.1549 gave 10.6 c.c. nitrogen at  $19.5^{\circ}$  and 752 mm.  $N = 7.77$ .

$C_{12}H_{10}O_6 \cdot N \cdot NHC_6H_5$  requires  $N = 7.86$  per cent.

### *Hydrolysis of the Lactone.*

A preliminary experiment showed that the lactone dissolved easily in baryta water, but that, on gently warming the solution, a precipitate appeared which dissolved in dilute acids with effervescence. In order to estimate the amount of carbon dioxide thus formed, a weighed quantity of the lactone was boiled for 3 hours with excess of a filtered solution of barium hydrate in a flask fitted with a reflux condenser, to the top of which was attached a tube filled with soda-lime, to prevent the access of carbon dioxide from the air. When the precipitation of barium carbonate was complete, the flask was fitted with a rubber stopper with three holes. Through these passed, first a dropping funnel containing dilute hydrochloric acid, then a long tube dipping below the surface of the liquid in the flask to admit a stream of air, and lastly a tube to convey the gases to the absorption apparatus. The hydrochloric acid was allowed to run into the flask until the contents were strongly acid, and the evolved gas was carried over by a stream of air free from carbon dioxide, first through drying tubes containing sulphuric acid, and lastly into a weighed potash bulb apparatus. 0.5495 lactone gave 0.0945  $CO_2$ ; that is, 1 molecule of the lactone gave 1.04 molecule of carbon dioxide.

The other products of the hydrolysis were found, after some preliminary experiments, to be best isolated in the following way. Eight grams of the lactone were boiled with a solution of 50 grams of barium hydrate in a flask attached to a reflux condenser. After seven hours, the condenser was reversed and 50 c.c. of liquid were distilled off. The distillate was submitted several times to fractionation, the more volatile portion in each case being alone collected, until at last about 2 c.c. of a liquid were obtained, which, on treatment with potassium carbonate, separated into two layers. The upper layer, when distilled, boiled between  $78^{\circ}$  and  $80^{\circ}$ , possessed a spirituous smell, burned with a faintly luminous flame, and with iodine and sodium carbonate yielded iodoform. It was therefore ethylic alcohol.

The mixture left after separating the alcohol was filtered, and the precipitate washed. The latter was then dissolved in the necessary quantity of hydrochloric acid, and the solution evaporated to dryness on the water bath. The residue was washed with ether until nothing further was dissolved. The ethereal solution was evaporated and yielded some two grams of a beautifully crystalline acid, which, after



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being several times crystallised from water, was obtained in colourless plates. The acid melted at  $131\cdot5^{\circ}$ , and at a higher temperature decomposed, yielding carbon dioxide and an acid liquid which boiled between  $110$ — $120^{\circ}$  and gave the characteristic odour of ethylic acetate when heated with ethylic alcohol and sulphuric acid.

$0\cdot1575$  gave  $0\cdot2012$   $\text{CO}_2$  and  $0\cdot0548$   $\text{H}_2\text{O}$ .  $\text{C} = 34\cdot84$ ;  $\text{H} = 3\cdot86$ .

$\text{C}_3\text{H}_4\text{O}_4$  requires  $\text{C} = 34\cdot61$ ;  $\text{H} = 3\cdot84$ .

The substance therefore possesses the composition and shows all the properties of malonic acid.

The filtrate from the precipitate of barium carbonate and malonate still contained much barium hydrate. This was precipitated by a stream of carbon dioxide, and the barium carbonate filtered off. The filtrate was concentrated by evaporation, rendered slightly acid with acetic acid, and extracted with ether until the ether gave no residue on evaporation. On boiling off the ether, a yellow solid remained, which, after treatment with animal charcoal and repeated crystallisation from hot water, was obtained in glistening plates.

$0\cdot1346$  gave  $0\cdot2199$   $\text{CO}_2$  and  $0\cdot0733$   $\text{H}_2\text{O}$ .  $\text{C} = 44\cdot55$ ;  $\text{H} = 6\cdot05$ .

$\text{C}_6\text{H}_{10}\text{O}_5$  requires  $\text{C} = 44\cdot44$ ;  $\text{H} = 6\cdot10$  per cent.

It was found that at  $100^{\circ}$  this substance lost a large quantity of water, the crystals at the same time becoming opaque. The loss of water was determined by drying the crystals in the air bath at  $105^{\circ}$ .

$0\cdot1149$  gave  $0\cdot0253$   $\text{H}_2\text{O}$ .  $\text{H}_2\text{O} = 22\cdot02$ .

$1\cdot0514$  „  $0\cdot2351$   $\text{H}_2\text{O}$ .  $\text{H}_2\text{O} = 22\cdot39$ .

$\text{C}_6\text{H}_{10}\text{O}_5 - 2\text{H}_2\text{O}$  requires loss =  $22\cdot22$  per cent.

The substance therefore contains 2 molecules of water of crystallisation, and when anhydrous must have the composition  $\text{C}_6\text{H}_6\text{O}_3$ . The dried substance gave the following result on analysis:

$0\cdot1361$  gave  $0\cdot2891$   $\text{CO}_2$  and  $0\cdot0555$   $\text{H}_2\text{O}$ .  $\text{C} = 56\cdot53$ ;  $\text{H} = 4\cdot53$ .

$\text{C}_6\text{H}_6\text{O}_3$  requires  $\text{C} = 57\cdot14$ ;  $\text{H} = 4\cdot76$  per cent.

It melted about  $210^{\circ}$ , although much lower if slowly heated, and gave a cherry-red coloration with pinewood moistened with hydrochloric acid. With ferric chloride, it gave only a very faint purple coloration. The substance is thus identical in every respect with phloroglucinol, the symmetrical trihydroxybenzene.

UNIVERSITY CHEMICAL LABORATORY,  
HEIDELBERG.