Summary

Dimesityl triketone ($C_9H_{11}COCOCOC_9H_{11}$) has been prepared by the oxidation of di-(β-isoduryloyl)-methane with selenium dioxide, and by the action of heat or of alkali on dimesityl tetraketone ($C_9H_{11}COCOCOCOC_9H_{11}$).

The triketone reacts with semicarbazide to give the semicarbazone of mesitylglyoxal, and with alkali to give a mixture of dimesityl diketone, carbon dioxide, mesitylglycolic acid and β-isodurylic acid.

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The Synthesis of Long-Chain Aliphatic ω,ω'-Dicarboxylic Acids

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The preparation of aliphatic ω,ω'-dicarboxylic acids with a long chain containing more than ten carbon atoms became an interesting problem as the investigations of Ruzicka and co-workers[1] on the constitution and synthesis of natural musk revealed the structural relationships between this substance, which is a ketone containing a ring system of fifteen carbon atoms, with the *n*-hexadecane-ω,ω'-dicarboxylic acid. Since Ruzicka demonstrated that by dry distillation of different metal salts of this acid and of other long-chain aliphatic ω,ω'-dicarboxylic acids, ketones of olfactive character could be obtained, the problem of a better method for the preparation of acids of this kind became important. Ruzicka and his co-workers prepared the acids used in their investigations by the reaction of aliphatic ω,ω'-dihalides with sodium malonic acid esters, saponification and subsequent splitting off of two carboxylic groups from the resulting bis-malonic acids. This way of synthesis is a very long one because the above-mentioned dihalides must be prepared step by step from a shorter chain dibasic acid.

In 1896 Baeyer and Oehler[2] described a method for the preparation of the 2,6-dimethyl-3-octanone-1-carboxylic acid by the oxidation of 3-menthone, and this reaction has often been used for the preparation of acids from other cyclohexanones and the corresponding hexanols.[3] As it seemed to be possible to reduce the ketone group in this acid by the Clemmenssen method, opening thus a way for the preparation of long-chain carbonic acids, the Baeyer method was applied to the 1,6-di-(2-hydroxy-4-methylcyclohexyl)-hexane IV in which the two cyclohexane rings are connected through an aliphatic chain which is attached to each of the cyclohexane rings in the ortho position to the hydroxy groups. The oxidation of this compound through rupture of both of the rings gives the 2,15-dimethyl-5,12-hexadecanedione-1,16-dicarboxylic acid V with a long aliphatic chain. The reduction of this diketo acid can be carried out easily by the Clemmenssen method and yields the 2,15-dimethylhexadecane-1,16-dicarboxylic acid VI.

The starting material can best be prepared by the hydrogenation of the corresponding diphenol III which, as other similar diphenols, is available by different methods.

We used the Fries–Nencki rearrangement[4] in the form given to it by Rosenmund and Schnurr,[5] starting with the phenol esters of appropriate aliphatic dicarboxylic acids with a shorter chain. Thus the hexane IV, which was used in our investigation, has been made from the corresponding 1,6-di-(2-hydroxy-4-methylphenyl)-hexane-1,6-dione II, which was obtained by rearrangement of the adipic acid di-ester of *m*-cresol with aluminum chloride. The dione was reduced by the Clemmenssen method to the corresponding 1,6-di-

$$\begin{array}{ll}
MeC_6H_4OCO(CH_2)_4COOC_6H_4Me & \text{I} \\
\downarrow \text{rearrangement} & \\
MeC_6H_3(OH)CO(CH_2)_4CO(OH)C_6H_3Me & \text{II} \\
\downarrow \text{reduction} & \\
MeC_6H_3(OH)(CH_2)_6(OH)C_6H_3Me & \text{III} \\
\downarrow \text{hydrogenation} & \\
MeC_6H_{10}(OH)(CH_2)_6(OH)C_6H_{11}Me & \text{IV} \\
\downarrow \text{oxidation} & \\
HOOCCH_2CH(CH_3)CH_2CH_2CO(CH_2)_6COCH_2CH_2CH(CH_3)CH_2COOH & \text{V} \\
\downarrow \text{reduction} & \\
HOOCCH_2CH(CH_3)(CH_2)_{12}CH(CH_3)CH_2COOH & \text{VI}
\end{array}$$

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(1) Ruzicka and co-workers, *Helv. Chim. Acta*, **9**, 230, 249, 715 (1926); **10**, 695 (1927).

(2) Baeyer and Oehler, *Ber.*, **27**, 1914 (1894).

(3) More recently the same reaction has been utilized by Drs. Niederl and Smith for the synthesis of a long-chain monocarboxylic acid (paper presented before the Organic Division at the St. Petersburg meeting of the American Chemical Society, March, 1934). Also see R. Kuhn and H. Brockmann, *Ber.*, **67**, 885 (1934).

(4) Fries, Nencki and Sieber, *J. prakt. Chem.*, [2] **23**, 149 (1881); Heller, *Ber.*, **46**, 418 (1912); Eykman, *ibid.*, **34**, 1798 (1901).

(5) Rosenmund and Schnurr, *Ann.*, **460**, 79 (1927).

(2-hydroxy-4-methylphenyl)-hexane III from which, by hydrogenation, resulted the 1,6-di-(2-hydroxy-4-methylcyclohexyl)-hexane IV mentioned above.

Experimental Part

(1) ***m*-Cresyladipic Ester.**—One mole of adipic acid was mixed with 2 moles of freshly distilled *m*-cresol and then heated in a 1-liter round-bottomed flask to which a condenser was attached. The temperature of the oil-bath in which the reaction flask was immersed was about 150°. After the acid had dissolved in the molten cresol, one mole of phosphorus oxychloride was added in small amounts into the reaction mixture by means of a dropping funnel. As soon as a vigorous reaction set in, the oil-bath was removed and the temperature inside the reaction flask was kept at about 120° by cautious addition of the phosphorus oxychloride. When the reaction had ceased the molten ester floated above the black residue containing phosphorus, and could be decanted easily. The ester solidified to a cake which is best powdered and then washed with water. Finally it was crystallized from 95% ethanol. After recrystallization from benzine (b. p. 120–130°) the product had a melting point of 85–87°.

(2) **1,6-Di-(2-hydroxy-4-methylphenyl)-hexane-1,6-dione.**—Thirty grams of the ester from (1) was mixed with 30 g. of finely powdered sublimed aluminum chloride and placed in a round-bottomed flask which was provided with a long air condenser. The flask was placed in a molten metal bath at a temperature of approximately 100° and then quickly brought to 165°. The mixture became reddish-brown and expanded. Heating was continued for an additional fifty minutes. After cooling, the cake-like reaction material was powdered and mixed with ice water to which some hydrochloric acid had been added. The undissolved crystals were recrystallized from ethanol, acidified with a little hydrochloric acid, m. p. 122–123°.

Anal. Calcd. for $C_{20}H_{22}O_4$: C, 73.58; H, 6.80. Found: C, 73.85; H, 6.81.

(3) **1,6-Di-(2-hydroxy-4-methylphenyl)-hexane.**—Twenty grams of the diketone from (2) was boiled in a mixture of 400 cc. of glacial acetic acid and 400 cc. of concd. hydrochloric acid with 300 g. of zinc wool, which previously had been activated with a mercuric chloride solution. It was necessary to heat almost for one day until all the zinc was dissolved; m. p. 102–103°.

Anal. Calcd. for $C_{20}H_{26}O_2$: C, 80.48; H, 8.79. Found: C, 80.53; H, 8.81.

(4) **1,6-Di-(2-hydroxy-4-methylcyclohexyl)-hexane.**—Twenty grams of the substance from (3) was dissolved in 150 cc. of methylcyclohexane. After addition of 5 g. of a usual nickel catalyst the hydrogenation was carried out at 230° and a pressure of about 100 atm. The distillation in vacuum of the reaction mixture gave a clear colorless oil with a boiling point of 205–208° (1.5 mm.).

(5) **2,15-Dimethylhexadecane-5,12-dione-1,16-dicarboxylic Acid.**—15.5 grams of the cyclohexanol from (4) was added dropwise to a solution of 20 g. of chromic acid in 20 cc. of water and 130 cc. of glacial acetic acid cooled by ice and thoroughly stirred. The temperature did not rise above 20°. After cessation of the reaction, the material was heated for half an hour by a steam-bath until the chromic acid had disappeared completely. The acetic acid was now distilled off *in vacuo* as much as possible and the residue taken up with diluted sulfuric acid and extracted with ether. From this ether solution, which first was washed with water, the acid product was extracted with 5% sodium hydroxide solution. In the ether remained the neutral reaction products which could be added to the next oxidation batch. The alkaline solution was washed with ether, acidified with diluted sulfuric acid, and again extracted with ether. The ethereal solution was washed with water and then evaporated, finally *in vacuo*. The residue was partially crystalline and had to stand for some time to finish crystallization. The crystals were spread on porous tile to remove the adhering oil and then dissolved in methanol, from which the acid was precipitated with water. After recrystallization from benzine the melting point of the substance was 70–71°.

Anal. Calcd. for $C_{20}H_{34}O_6$: C, 64.81; H, 9.25. Found: C, 65.31; H, 9.07.

Using only 8.5 g. of chromic acid for 21.7 g. of the substance from (4) the 1,6-di-(2-keto-4-methylcyclohexyl)-hexane could be obtained by appropriate isolation, distilling as an oil at 180–205° (0.3 mm.). It crystallized after standing for a while and gave crystals from petroleum ether of melting point 60–65°. It was not absolutely pure.

Anal. Calcd. for $C_{20}H_{34}O_2$: C, 78.35; H, 11.19. Found: C, 78.68; H, 11.43.

(6) **2,15-Dimethylhexadecane-1,16-dicarboxylic Acid.**—One gram of the acid from (5) was boiled with 30 cc. of concd. hydrochloric acid, 10 cc. of water and 15 g. of zinc wool, activated previously with a mercuric chloride solution, until all the zinc had been dissolved. On cooling, the reaction product solidified and was then recrystallized twice from methanol and water, m. p. 64–68°.

Anal. Calcd. for $C_{20}H_{38}O_4$: C, 70.11; H, 11.19. Found: C, 70.67, 70.63; H, 11.3.

Summary

A five-step synthesis of a long-chain (20 carbon atoms) dicarboxylic acid is described, starting with a substituted diphenol and utilizing the methods of Baeyer, Fries–Nencki and Clemmenssen.

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