

XXXII.— *$\alpha\delta$ -Derivatives of Adipic and  $\beta$ -Methyladipic Acids, and the Preparation of Muconic and  $\beta$ -Methylmuconic Acids.*

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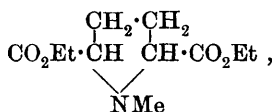
THE experiments on  $\alpha\delta$ -derivatives of adipic and  $\beta$ -methyladipic acids, of which a short account has appeared (P., 1912, **28**, 95), have been continued, and have led finally to some interesting results. The work of Markovnikov (*J. Russ. Phys. Chem. Soc.*, 1903, **35**, 381), and also the process discovered by the Farbenfabriken vorm. Friedr. Bayer & Co. (D.R.-P. 221849), have made adipic and  $\beta$ -methyladipic acids accessible. It was desirable to prepare from these acids, on the one hand,  $\alpha\delta$ -diaminoadipic and  $\alpha\delta$ -diamino- $\beta$ -methyladipic acids, and on the other, muconic and  $\beta$ -methylmuconic acids.

Considerable quantities of adipic and  $\beta$ -methyladipic acids have been prepared by oxidising *cyclohexanone* and 4-methyl*cyclohexanone* respectively with nitric acid (D 1'4), and the acids thus obtained have been brominated.

The bromination of these acids was carried out by the usual Hell-Volhard method, with the difference that thionyl chloride was used for the preparation of the acid chlorides. The use of this reagent leads to the formation of very pure acid chlorides. The product from the bromination was treated with anhydrous formic acid or alcohol according as the free acid or ester was required; and in this way we have prepared the  $\alpha\delta$ -dibromo-acids and esters. These dibromo-esters have also been described by Le Sueur (T., 1909, **95**, 273).

The displacement of the two bromine atoms in the above  $\alpha\delta$ -dibromo-compounds by the amino-group was found to be a matter of considerable experimental difficulty. The action of ammonia, both aqueous and alcoholic, leads to the formation of pyrrolidinedicarboxylic esters or acids. It was therefore thought that the treatment of the dibromo-esters with potassium phthalimide, and the subsequent hydrolysis of the diphthalimino-compounds might lead to a satisfactory result. This proved to be correct especially in the case of the  $\alpha\delta$ -dibromoadipic esters; but the  $\alpha\delta$ -dibromo- $\beta$ -methyladipic esters were found to react with potassium phthalimide with great difficulty, and only small quantities of the diphthalimino-compounds could be obtained.

The preparation of muconic and  $\beta$ -methylmuconic acids by removing two molecules of hydrogen bromide from the corresponding dibromo-esters was also one of considerable difficulty. In this connexion, Willstätter and Lessing (*Ber.*, 1902, **35**, 2065) found that when ethyl  $\alpha\delta$ -dibromoadipate was treated with methylamine in benzene solution, ethyl 1-methylpyrrolidine-2:5-dicarboxylate was produced.



Le Sueur (*loc. cit.*) has also observed a similar reaction in an attempt to obtain the unsaturated ester from the same dibromo-ester, by treating the latter with mono- or di-ethylaniline, obtaining, however, the corresponding *N*-pyrrolidine compounds, analogous to that obtained by Willstätter and Lessing (*loc. cit.*). In our experiments we have studied the action of trimethylamine in alcoholic solution (33 per cent.), and triethylamine in dry benzene, on methyl and ethyl  $\alpha\delta$ -dibromoadipates and  $\alpha\delta$ -dibromo- $\beta$ -methyladipate respectively, and have succeeded in isolating the corresponding unsaturated esters which on hydrolysis led to the acids. The yields obtained by these methods are small, due to the same tendency of ring formation, and here again the results obtained are more satisfactory in the case of the dibromo-adipic esters than with the homologue. As a further attempt to obtain the unsaturated compounds, we have treated the dibromo-esters with quinoline, but only very small quantities of unsaturated esters could be isolated.

The diacetoxy-compounds of ethyl  $\alpha\delta$ -dibromoadipate and ethyl  $\alpha\delta$ -dibromo- $\beta$ -methyladipate have also been prepared by heating the above esters with fused potassium acetate in glacial acetic acid.

## EXPERIMENTAL.

*Bromination of Adipic Acid.*

In order to brominate the adipic acid obtained as stated above, 100 grams of the acid were treated with 190 grams of thionyl chloride, an excess of 20 per cent. being used. The mixture was warmed on the steam-bath until the whole had assumed the liquid state, and there was no further evolution of hydrogen chloride, which requires about one hour for completion. Pure bromine (240 grams) was then added gradually during a period of forty-eight hours, and the whole continuously heated on the steam-bath until evolution of hydrogen bromide had ceased.

*Methyl  $\alpha\delta$ -dibromoadipate*,  $\text{CO}_2\text{Me}\cdot\text{CHBr}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CHBr}\cdot\text{CO}_2\text{Me}$ .

This ester was obtained by carefully adding methyl alcohol to the bromo-acid chloride prepared above, until the somewhat violent reaction had subsided. On cooling, the bromo-ester was poured into water, extracted several times with ether, the ethereal extract washed with a dilute solution of sodium hydrogen sulphite, and finally several times with water; on removal of the ether a semi-solid mass remained, which was distilled under diminished pressure. The ester (yield, 175 grams from 100 grams of adipic acid) obtained boils at  $182^\circ/10$  mm., and is a colourless liquid, which on cooling partly solidifies to a white, crystalline solid.

This, after being separated from the liquid portion by pouring the mixture on a porous plate, was crystallised from ethyl alcohol, and obtained in white needles, which melted at  $75^\circ$ . The ester is soluble in methyl or ethyl alcohols, ether, benzene, or chloroform.

*Ethyl  $\alpha\delta$ -dibromoadipate*,  $\text{CO}_2\text{Et}\cdot\text{CHBr}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CHBr}\cdot\text{CO}_2\text{Et}$ .

This was obtained in an analogous way to the methyl ester. It also exhibited the same semi-solid state, and the solid modification of the ester was crystallised from ethyl alcohol and obtained in white needles melting at  $65^\circ$ . The ester distils at  $195^\circ/10$  mm.; the solubility was the same as for the methyl ester, and the yield was 180 grams from 100 grams of adipic acid.

 *$\alpha\delta$ -Dibromo- $\beta$ -methyladipic Acid*,  
 $\text{CO}_2\text{H}\cdot\text{CHBr}\cdot\text{CHMe}\cdot\text{CH}_2\cdot\text{CHBr}\cdot\text{CO}_2\text{H}$ .

$\beta$ -Methyladipic acid (160 grams: 1 mol.) was brominated as described above. The bromo-acid chloride was converted into the free acid by the addition of anhydrous formic acid until the reaction

had ceased. A viscid, yellow oil was obtained, from which after several weeks crystals of  $\alpha\delta$ -dibromo- $\beta$ -methyladipic acid separated. When recrystallised from anhydrous formic acid it is obtained in large, white, rhombic prisms, which melt at  $138^\circ$ . The acid is soluble in the usual organic solvents, and sparingly so in hot water:

0.2148 gave 0.2101  $\text{CO}_2$  and 0.0599  $\text{H}_2\text{O}$ .  $\text{C}=26.6$ ;  $\text{H}=3.1$ .

0.1665 „ 0.1941  $\text{AgBr}$ .  $\text{Br}=49.9$ .

$\text{C}_7\text{H}_{10}\text{O}_4\text{Br}_2$  requires  $\text{C}=26.4$ ;  $\text{H}=3.1$ ;  $\text{Br}=50.3$  per cent.

*Methyl  $\alpha\delta$ -Dibromo- $\beta$ -methyladipate,*  
 $\text{CO}_2\text{Me}\cdot\text{CHBr}\cdot\text{CH}_2\cdot\text{CHMe}\cdot\text{CHBr}\cdot\text{CO}_2\text{Me}.$

This was obtained from the bromo-acid chloride on treatment with methyl alcohol. It is a colourless liquid boiling at  $167\text{--}168^\circ/12$  mm., and could not be prepared in the solid form; a yield of 64 per cent. of the acid used was obtained.

*Ethyl  $\alpha\delta$ -Dibromo- $\beta$ -methyladipate,*  
 $\text{CO}_2\text{Et}\cdot\text{CHBr}\cdot\text{CH}_2\cdot\text{CHMe}\cdot\text{CHBr}\cdot\text{CO}_2\text{Et}.$

This was prepared in an analogous manner to the above; it is a colourless liquid, which distils at  $180^\circ/10$  mm., and also does not solidify; a yield of 72 per cent. of the acid used was obtained. Even when these esters were prepared by esterification of the solid  $\alpha\delta$ -dibromo- $\beta$ -methyladipic acid they could not be obtained in the solid state.

*Ethyl  $\alpha\delta$ -Diacetoxyadipate,*  
 $\text{CO}_2\text{Et}\cdot\text{CH}(\text{OAc})\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CH}(\text{OAc})\cdot\text{CO}_2\text{Et}.$

This ester was obtained by heating in an oil-bath 36 grams of ethyl  $\alpha\delta$ -dibromoadipate with twice the theoretical quantity of fused potassium acetate (40 grams) in a large excess of glacial acetic acid, at  $160^\circ$  for eight hours. The product was poured into water, the ester extracted several times with ether, and the ethereal solution shaken several times with dilute sodium carbonate solution to remove traces of acetic acid, washed with distilled water, and dried. On removal of the ether the ester was distilled, and a colourless liquid boiling at  $195^\circ/10$  mm. was obtained; this, on cooling, gave a white solid, which crystallised from ethyl alcohol in small, white needles, melting at  $73^\circ$ . (Yield, 15 grams.) The pure diacetate can be distilled without decomposition under the ordinary pressure:

0.1466 gave 0.2861  $\text{CO}_2$  and 0.0898  $\text{H}_2\text{O}$ .  $\text{C}=53.2$ ;  $\text{H}=6.5$ .

$\text{C}_{14}\text{H}_{22}\text{O}_8$  requires  $\text{C}=52.7$ ;  $\text{H}=6.8$  per cent.

*Ethyl  $\alpha\delta$ -Diacetoxy- $\beta$ -methyladipate,*  
 $\text{CO}_2\text{Et}\cdot\text{CH}(\text{OAc})\cdot\text{CHMe}\cdot\text{CH}_2\cdot\text{CH}(\text{OAc})\cdot\text{CO}_2\text{Et}.$

This was obtained in the same way as the previous compound. It is a white solid, which crystallises from ethyl alcohol in white needles melting at  $66^\circ$ , and boiling at  $182^\circ/10$  mm.:

0.1022 gave 0.2031  $\text{CO}_2$  and 0.0647  $\text{H}_2\text{O}$ .  $\text{C}=54.3$ ;  $\text{H}=7.04$ .

$\text{C}_{15}\text{H}_{24}\text{O}_8$  requires  $\text{C}=54.2$ ;  $\text{H}=7.2$  per cent.

Both diacetoxy-compounds, like the corresponding dibromo-compounds, occur in two modifications, namely, as liquids and solids.

*Ethyl  $\alpha\delta$ -Diphthaliminoadipate,*  
 $\text{CO}_2\text{Et}\cdot\text{CH}\left(\text{N}\begin{smallmatrix} \text{CO} \\ \diagup \diagdown \end{smallmatrix}\text{C}_6\text{H}_4\right)\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CH}\left(\text{N}\begin{smallmatrix} \text{CO} \\ \diagup \diagdown \end{smallmatrix}\text{C}_6\text{H}_4\right)\cdot\text{CO}_2\text{Et}.$

This ester was obtained by heating 50 grams of ethyl  $\alpha\delta$ -dibromoadipate with 70 grams of potassium phthalimide, using a quarter of a molecule excess of the latter, in xylene in an oil-bath at  $135$ — $140^\circ$  for twenty-four hours, the xylene being gradually distilled from the product during the last hour of the heating. The crude product obtained, which was a deep honey-yellow, semi-solid cake, was then poured into water and distilled in a current of steam to remove remaining traces of xylene. On cooling, the product was extracted with carbon disulphide, which separates the excess of phthalimide from the condensation product, only the latter being soluble in carbon disulphide. The extract was then dried, the carbon disulphide removed by distillation, and the oily residue submitted to distillation under diminished pressure. A pale yellow liquid boiling at  $200$ — $210^\circ/10$  mm. was obtained, and it solidified on cooling to a white solid, which crystallised from ethyl alcohol in colourless needles melting at  $115^\circ$ . It is soluble in methyl or ethyl alcohols, and very soluble in carbon disulphide:

0.1731 gave 0.3976  $\text{CO}_2$  and 0.0739  $\text{H}_2\text{O}$ .  $\text{C}=62.77$ ;  $\text{H}=4.77$ .

0.1701 „ 7.4 c.c.  $\text{N}_2$  at  $18^\circ$  and 754 mm.  $\text{N}=5.58$ .

$\text{C}_{26}\text{H}_{24}\text{O}_8\text{N}_2$  requires  $\text{C}=63.3$ ;  $\text{H}=4.8$ ;  $\text{N}=5.7$  per cent.

*$\alpha\delta$ -Diphthaliminoadipic Acid,*  
 $\text{CO}_2\text{H}\cdot\text{CH}\left(\text{N}\begin{smallmatrix} \text{CO} \\ \diagup \diagdown \end{smallmatrix}\text{C}_6\text{H}_4\right)\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CH}\left(\text{N}\begin{smallmatrix} \text{CO} \\ \diagup \diagdown \end{smallmatrix}\text{C}_6\text{H}_4\right)\cdot\text{CO}_2\text{H}.$

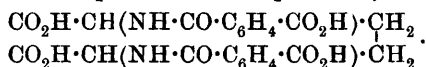
This acid was obtained from the above ester by (a) hydrolysis of the ester with an excess of a glacial acetic acid solution of hydrogen bromide at the ordinary temperature, or (b) by hydrolysis of the ester with the necessary quantity of alcoholic potassium hydroxide. In the first case (a), the acid was obtained directly as a solid on

addition of water to the glacial acetic acid solution. In the other case (b), the free acid was obtained from the alkaline solution on addition of hydrochloric acid in the cold. It is a pale yellow, crystalline powder, which does not melt at  $270^\circ$ , and is soluble in glacial acetic acid, from which it can be crystallised. It is insoluble in water, but sparingly soluble in ethyl alcohol:

0.2016 gave 0.4434  $\text{CO}_2$  and 0.0724  $\text{H}_2\text{O}$ .  $\text{C}=60.00$ ;  $\text{H}=3.96$ .

$\text{C}_{22}\text{H}_{16}\text{O}_8\text{N}_2$  requires  $\text{C}=60.5$ ;  $\text{H}=3.7$  per cent.

*$\alpha\delta$ -Diphthalaminoadipic Acid,*



Twenty-four grams of ethyl  $\alpha\delta$ -diphthalaminoadipate were treated with a solution of 20 grams of potassium hydroxide dissolved in its own weight of water; a vigorous reaction set in, and when this had subsided the mixture was heated on the steam-bath for some time until a clear solution had been obtained. The solution was then cooled on ice and carefully neutralised with the exact quantity of 5*N*-hydrochloric acid. A solid separated, which was washed free from potassium chloride with water, and crystallised from hot water. It was obtained as a fine, crystalline powder, which when dried at the ordinary temperature contains two molecules of water of crystallisation:

0.1960 gave 0.3804  $\text{CO}_2$  and 0.0736  $\text{H}_2\text{O}$ .  $\text{C}=52.3$ ;  $\text{H}=4.7$ .

0.7510 lost 0.0532 at  $100^\circ$ .  $\text{H}_2\text{O}=7.08$ .

$\text{C}_{22}\text{H}_{20}\text{O}_{10}\text{N}_2\cdot 2\text{H}_2\text{O}$  requires  $\text{C}=52.00$ ;  $\text{H}=4.7$ ;  $\text{H}_2\text{O}=7.08$  per cent.

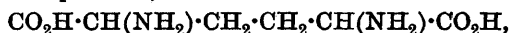
A sample of the acid dried at  $100^\circ$  gave the following results:

0.1252 gave 0.2570  $\text{CO}_2$  and 0.0516  $\text{H}_2\text{O}$ .  $\text{C}=55.3$ ;  $\text{H}=4.3$ .

$\text{C}_{22}\text{H}_{20}\text{O}_{10}\text{N}_2$  requires  $\text{C}=55.9$ ;  $\text{H}=4.2$  per cent.

The acid after being dried at  $100^\circ$  is insoluble in hot water, but soluble in sodium carbonate solution, from which it is again precipitated in the insoluble form on addition of hydrochloric acid. On fusion the acid begins to decompose at  $119^\circ$  with evolution of carbon dioxide.

*$\alpha\delta$ -Diaminoadipic acid,*



was obtained by treating the above acid with concentrated hydrochloric acid, the free acid being obtained by neutralising the solution of the hydrochloride with dilute aqueous ammonia.

The crude acid was converted into the copper salt by boiling with an aqueous suspension of copper hydroxide, filtering, and

allowing the copper salt to crystallise. It is obtained in this way in blue, crystalline plates:

0.5840 gave  $\text{Cu} = 22.7$ .

0.4527 lost 0.0591 at  $110^\circ$ .  $\text{H}_2\text{O} = 13.02$ .

$\text{C}_6\text{H}_{10}\text{O}_4\text{N}_2\text{Cu}, 2\text{H}_2\text{O}$  requires  $\text{Cu} = 23.2$ ;  $\text{H}_2\text{O} = 13.05$  per cent.

The dried copper salt is insoluble in water. These observations are in agreement with those of Sørensen and Andersen (*Zeitsch. physiol. Chem.*, 1908, **56**, 266).

*The Action of Trimethylamine and Triethylamine on Methyl and Ethyl  $\alpha\delta$ -Dibromoadipates, and Methyl and Ethyl  $\alpha\delta$ -Dibromo- $\beta$ -methyladipates respectively.*

Methyl  $\alpha\delta$ -dibromoadipate (64 grams) was heated in sealed tubes with a slight excess over the theoretical quantity of a 33 per cent. alcoholic solution of trimethylamine for thirty-eight hours at  $100$ – $105^\circ$ . The product was diluted with anhydrous ether in order to separate trimethylamine hydrobromide, filtered, and the filtrate poured into water, extracted with a further quantity of ether, and the ethereal extract washed several times with dilute hydrochloric acid. The dried ethereal extract was evaporated, and the residue submitted to distillation under diminished pressure.

A colourless liquid began to distil at  $185^\circ/12$  mm., and solidified on cooling to a white, crystalline solid, which was unsaturated and free from bromine; after crystallisation from ethyl alcohol it melted at  $158^\circ$ , which is the melting point of methyl muconate (*Ber.*, 1902, **35**, 1148). The yield was about 3 grams of solid ester, which was hydrolysed by means of methyl-alcoholic potassium hydroxide to the free acid. This was crystallised from hot water, and a white, crystalline powder melting and decomposing at  $298^\circ$  was obtained.

Replacing the methyl ester by the ethyl ester made no difference in the actual yield of muconic acid. The ethyl ester of muconic acid distilled at  $200^\circ/12$  mm.

In a similar way ethyl and methyl  $\alpha\delta$ -dibromoadipates were heated with triethylamine diluted with dry benzene in a sealed tube for the same time at  $110^\circ$ . The same unsaturated esters were obtained, but the yield did not improve.

The washings obtained by treating the ethereal extract with hydrochloric acid were evaporated nearly to dryness with animal charcoal, filtered, and then evaporated to dryness under diminished pressure; a white, crystalline solid was obtained, which on treatment with moist silver oxide gave the characteristic odour of trimethylamine. After removing the silver chloride formed, the filtrate was concentrated in a vacuum, and a viscid, syrupy liquid

remained, which, however, did not distil, and nothing of definite composition could be isolated.

*Ethyl  $\beta$ -methylmuconate*,  $\text{CO}_2\text{Et}\cdot\text{CH}\cdot\text{CMe}\cdot\text{CH}\cdot\text{CH}\cdot\text{CO}_2\text{Et}$ , was obtained in a similar way to that stated above when ethyl  $\alpha\delta$ -dibromo- $\beta$ -methyladipate was treated with trimethylamine in 33 per cent. alcoholic solution, or with triethylamine in dry benzene. As in the previous case, the yields were very poor, and the substitution of the methyl ester caused no alteration in the result. A basic substance was apparently removed, as in the case of the adipic compound, on washing the ethereal extract with hydrochloric acid; but on similar treatment no compound of definite composition could be isolated. The ethyl ester is a colourless liquid boiling at  $175^\circ/10$  mm., which showed a tendency to crystallise, but remained in a semi-solid condition.

*Methyl  $\beta$ -methylmuconate*,  $\text{CO}_2\text{Me}\cdot\text{CH}\cdot\text{CMe}\cdot\text{CH}\cdot\text{CH}\cdot\text{CO}_2\text{Me}$ , obtained by the same method as in the case of the ethyl ester described above, is a colourless liquid boiling at  $145^\circ/9$  mm. It could not be obtained in the solid state.

In some experiments we have found that ethyl-alcoholic barium hydroxide also gave very good results when used to hydrolyse these unsaturated esters, especially in the case of the esters of  $\beta$ -methylmuconic acid. The two esters above were hydrolysed with alcoholic barium hydroxide, and the free  $\beta$ -methylmuconic acid was obtained by precipitating the barium salt with dilute hydrochloric acid.

*$\beta$ -Methylmuconic acid*,  $\text{CO}_2\text{H}\cdot\text{CH}\cdot\text{CMe}\cdot\text{CH}\cdot\text{CH}\cdot\text{CO}_2\text{H}$ , is a white solid which crystallises from hot water as a crystalline powder; it may also be crystallised from acetic acid, and melts and decomposes at  $235^\circ$ :

0.1054 gave 0.2077  $\text{CO}_2$  and 0.0486  $\text{H}_2\text{O}$ .  $\text{C}=53.74$ ;  $\text{H}=5.12$ .

$\text{C}_7\text{H}_8\text{O}_4$  requires  $\text{C}=53.84$ ;  $\text{H}=5.12$  per cent.

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