XIV.—*The Interaction of Ethyl Sodiomethylmalonate and Mesityl Oxide.*

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EXPERIMENTS undertaken with the object of synthesising dihydrocamphoric acid (Trans., 1898, 73, 5, 23) have already been described by the author (Trans., 1899, 75, 771). Although non-success has attended further efforts to prepare this acid, several new and interesting substances have been encountered, and are described in the present communication (compare Proc., 1900, 16, 90), of which the main object was the preparation of a ketonic acid of the formula

It was then intended to add on the elements of hydrogen cyanide to the ketonic group, ultimately obtaining a substituted adipic acid.

Vorländer (*Annalen*, 1897, 294, 317) has shown that several of the substituted dihydroresorcinols undergo hydrolysis, with rupture of the ring, when treated with either barium hydroxide or dilute mineral acids. For example, phenyldihydroresorcinol gives rise to β -phenyl- γ -acetobutyric acid when treated in this manner:

It seemed possible, therefore, that the ketonic acid just mentioned might be obtained by hydrolysis of trimethyldihydroresorcinol (2:6-diketo-3:4:4-trimethylhexamethylene):

This substance may be readily prepared in large quantities by hydrolysing the compound formed by the condensation of ethyl sodio-methylmalonate and mesityl oxide :

That this substance, I, has the constitution ascribed to it, is proved, not only by its method of formation, but also by the facts that it gives the characteristic reactions of substituted resorcinols, and is converted on oxidation with sodium hypobromite into $\alpha\beta\beta$ -trimethylglutaric acid :

Up to the present, however, it has not been possible to hydrolyse this substance and produce the desired ketonic acid by splitting the ring. It may, for example, be recovered quantitatively after boiling for 16 hours with excess of barium hydroxide. On boiling with dilute sulphuric acid, it appears to suffer some change, and the question of its hydrolysis is still being investigated.

Like the dihydroresorcinols already described (Merling, *Annalen*, 1894, 278, 20 ; Vorländer, *ibid.*, 1897, 294, 302), 2 : 6-diketo-3 : 4 : 4-trimethylhexamethylene behaves in some respects as a diketone, giving, for example, a well-defined dioxime :

It may also react as Δ^6 -6-hydroxy-2-keto-3 : 4 : 4-trimethylhexamethylene (and this appears to be its most usual form) :

when, for example, it yields a silver salt, and this on treatment with ethyl iodide gives an ethyl ether :

Towards phosphorus pentachloride, however, it behaves as $\Delta^{3,6}$ -2 : 6-

dihydroxy-3:4:4-trimethyldihydroresorcinol (formula I), giving rise to $\Delta^{2,8}$ -2:6-dichloro-3:4:4-trimethyldihydrobenzene (formula II), where both oxygen atoms have been removed as hydroxyl groups.

This behaviour is peculiar, as apparently no derivatives of dihydroresorcinol or substituted dihydroresorcinols have been described in which these compounds react as though they contained two hydroxyl groups.

Dihydroresorcinol gives a monoacetyl derivative,

but Merling states (*loc. cit.*, 23) that he was unable to obtain a diacetyl derivative. On this account, the action of the phosphorus haloids and other reagents towards substituted dihydroresorcinols is being thoroughly investigated.

The unsaturated nature of diketotrimethylhexamethylene (hydroxy-ketonic form) is shown by its behaviour towards bromine, when it takes up two atomic proportions forming *dibromohydroxyketotrimethylhexamethylene* (formula III.). This is a highly unstable compound, readily losing hydrogen bromide to form 1-bromo-2:6-diketo-3:4:4-trimethylhexamethylene (formula IV), from which, conversely, it may be prepared by the direct addition of the elements of hydrogen bromide.

When treated with an insufficient amount of sodium hypobromite for complete oxidation, diketotrimethylhexamethylene is converted into a dibromo-derivative to which the following constitution is assigned:

because when treated with potash alone it is converted into $\alpha\beta\beta$ -trimethylglutaric acid and monobromodiketotrimethylhexamethylene (formula IV), and when oxidised with sodium hypobromite is quantitatively changed into $\alpha\beta\beta$ -trimethylglutaric acid and bromoform.

EXPERIMENTAL.

Ethyl 2:6-Diketo-3:4:4-trimethylhexamethylene-3-carboxylate,

Ethyl methylmalonate was first prepared by pouring ethyl malonate into a solution of 5 per cent. more than the theoretical quantity of sodium in absolute alcohol, cooling the whole, and then gradually adding a slight excess of methyl iodide. After working up in the usual manner, the liquid was submitted to careful fractionation, and the portion boiling between 198—200° used in these experiments. As the context shows (see page 142), however, this liquid must have contained considerable quantities of unaltered ethyl malonate.

Twenty-three grams of sodium were dissolved in 275 c.c. of absolute alcohol, 185 grams of ethyl methylmalonate added, and after cooling, 98 grams of mesityl oxide. The mixture, which turned a light reddish-brown and became warm, was heated on the water-bath for 10 hours, when water was added, the alcohol evaporated, and the alkaline liquid extracted * twice with ether. On distilling off the ether, 30 grams of a dark red-brown liquid, A, smelling of peppermint were obtained. The whole was then acidified with dilute sulphuric acid, and again extracted with ether, the ethereal solution washed with water, dried over calcium chloride, and the ether evaporated. The residual clear yellow oil (207 grams) set almost immediately to a semi-solid mass which was spread on a porous plate. After drying, it weighed 120 grams, B, and on extracting the porous plate with ether 65 grams of a dark brown, oily liquid, C, were obtained.

A. This material has not yet been fully investigated, but, most probably, it consists of condensation products of mesityl oxide. Claisen and Ehrhardt (*Ber.*, 1889, 21, 1013) have shown that sodium ethoxide acts on mesityl oxide with production of several complicated condensation products. Probably these compounds are formed during the course of the above reaction, despite the fact that excess of ethyl malonate was always employed for the express purpose of avoiding the presence of free sodium ethoxide.

B. This substance was purified by rapid crystallisation from a mixture of chloroform and light petroleum (b. p. 40—60°), when it was obtained as a microcrystalline powder melting at 93·5—94·5° (uncorr.).

0·1172 gave 0·2730 CO₂ and 0·0842 H₂O. C = 63·53; H = 7·98.

C₁₂H₁₈O₄ requires C = 63·71; H = 7·96 per cent.

* Unless the alkaline liquid is treated in this manner, the final products are difficult to obtain in a pure crystalline condition.

Ethyl diketotrimethylhexamethylenecarboxylate dissolves only slightly in hot water or light petroleum, but is readily soluble in other ordinary organic solvents. When slowly crystallised from a mixture of chloroform and light petroleum, it comes down in large, six-sided prisms, but is most readily obtained pure as described above. The yield (53 per cent. of the theoretical) cannot well be compared with that of the ester obtained by condensing ethyl malonate and mesityl oxide, for it is impossible to say how much unchanged ethyl malonate was contained in the ethyl methylmalonate employed.

The ester may be distilled under diminished pressure with but very slight decomposition, and boils at 190° under 31 mm. Its aqueous solution is coloured violet-red by addition of ferric chloride.

When treated in alcoholic solution with an acetic acid solution of semicarbazide, it yields a *semicarbazone* separating from dilute ethyl alcohol in crystalline nodules, melting at 206° with decomposition and evolution of gas.

0.1594 gave 20.4 c.c. moist nitrogen at 14° and 760 mm. $N = 15.06$.

$C_{13}H_{21}O_4N_3$ requires $N = 14.84$ per cent.

C. This thick, dark-coloured oil showed no signs of solidifying after standing in a vacuum for many weeks, so it was hydrolysed with alcoholic potash, acidified with sulphuric acid, extracted with ether, and the residue left after evaporation of the ether distilled in a vacuum. Two main fractions were obtained, boiling respectively at 140 — 150° and 170 — 175° under 41 mm. pressure, and a considerable residue remained which, on cooling, set to a red resin (compare Trans., 1899, 75, 773).

The fraction boiling at 140 — 150° under 41 mm. pressure smelt strongly of fatty acids, and on distilling in air separated into two portions, boiling about 118° and 140° respectively and although not further investigated, evidently consisted of acetic and propionic acids, produced by the hydrolysis of unaltered ethyl malonate and ethyl methylmalonate.

The fraction boiling at 170 — 175° under 41 mm. pressure solidified completely, and by repeated crystallisation from a mixture of chloroform and light petroleum two compounds were isolated melting at 148° (with production of a red film) and 100° . These are the melting points respectively of 2:6-diketo-4:4-dimethylhexamethylene (dimethyldihydroresorcinol) and 2:6-diketo-3:4:4-trimethylhexamethylene (see page 143), the occurrence of the former being due to the presence of ethyl malonate in the ethyl methylmalonate employed in the condensation experiment.

2:6-Diketo-3:4:4-trimethylhexamethylene (2:6-Dihydroxy-3:4:4-trimethyldihydroresorcinol), $(\text{CH}_3)_2\text{C} \begin{array}{c} \text{CH}(\text{CH}_3) \cdot \text{CO} \\ \text{CH}_2 \text{---} \text{CO} \end{array} \text{CH}_2$.

One hundred and fifteen grams of ethyl 2:6-diketo-3:4:4-trimethylhexamethylene-3-carboxylate were hydrolysed by heating for 12 hours with 170 grams of pure potassium hydroxide dissolved in alcohol. Water was then added, the alcohol evaporated, and the whole acidified with dilute sulphuric acid. A small amount of material separated, which was insoluble in water or ether, but on boiling with water, carbon dioxide was evolved, and diketotrimethylhexamethylene remained, so the substance probably consisted of *diketotrimethylhexamethylenecarboxylic acid*. The acidified solution was then extracted with ether, &c., when 75 grams (calculated 78) of a solid were obtained, which was purified by crystallisation from a mixture of chloroform and light petroleum (b. p. 40—60°) and analysed:

0.1172 gave 0.3012 CO_2 and 0.0970 H_2O . C = 70.08; H = 9.19.

$\text{C}_9\text{H}_{14}\text{O}_2$ requires C = 70.13; H = 9.09 per cent.

Diketotrimethylhexamethylene is sparingly soluble in water or light petroleum, but dissolves readily in the ordinary organic solvents. It crystallises from the above mixture in radiating clusters of needles melting at 99.5—100°. When heated in a capillary tube above its melting point, it does not give rise to a red film like the dimethyl derivative, but at 200—210° evolves gas, becomes light brown in colour, and does not resolidify on cooling. Its aqueous solution has an intensely acid reaction, effervesces with sodium hydrogen carbonate, and gives a violet-red coloration with ferric chloride.

The *silver salt*, $\text{C}_9\text{H}_{13}\text{O}_2\text{Ag}$, prepared in the usual manner, is a white, flocculent precipitate almost insoluble in water.

0.2402 gave, on ignition, 0.0990 Ag. Ag = 41.21.

$\text{C}_9\text{H}_{13}\text{O}_2\text{Ag}$ requires Ag = 41.38 per cent.

The *dioxime*, $\text{C}_9\text{H}_{16}\text{O}_2\text{N}_2$, was obtained by adding the calculated quantities of hydroxylamine hydrochloride and sodium hydroxide, dissolved in the smallest possible quantity of water, to an alcoholic solution of the ketone. On standing, the solution became violet and gradually deposited crystals, which were filtered off, treated with animal charcoal, and recrystallised from dilute ethyl alcohol, from which solvent they separate in colourless, four-sided pyramids melting at 167°. It is insoluble in chloroform or benzene, but readily soluble in methyl or ethyl alcohol on warming.

0.1994 gave 27 c.c. moist nitrogen at 17° and 760 mm. N = 15.71.

$\text{C}_9\text{H}_{16}\text{O}_2\text{N}_2$ requires N = 15.22 per cent.

The *ethyl ether*, $(\text{CH}_3)_2\text{C} \begin{smallmatrix} \text{CH}(\text{CH}_3) - \text{CO} \\ \text{CH}_2 \cdot \text{C}(\text{OC}_2\text{H}_5) \end{smallmatrix} \text{CH}$, was prepared by heating the dry silver salt suspended in dry ether with the calculated amount of ethyl iodide in a reflux apparatus for 3 hours. The oil obtained by evaporating the filtered ethereal solution did not solidify even after long standing. It was therefore purified by distillation and analysed:

0.1182 gave 0.3127 CO_2 and 0.1036 H_2O . $\text{C} = 72.16$; $\text{H} = 9.74$.

$\text{C}_{11}\text{H}_{18}\text{O}_2$ requires $\text{C} = 72.52$; $\text{H} = 9.90$ per cent.

The ether is a faintly yellow, thick, oily liquid boiling at 265° under 750 mm. pressure. It is insoluble in cold sodium carbonate solution, and when hydrolysed with alcoholic potassium hydroxide is quantitatively reconverted into diketotrimethylhexamethylene.

Action of Phosphorus Pentachloride on $\Delta^{2.6.2} : 6$ -Dihydroxy-3 : 4 : 4-trimethyldihydroresorcinol.

Five grams of the resorcinol were mixed with 14 grams of phosphorus pentachloride. A moderate action at once set in with formation of a yellow solution, which was heated on a water-bath for half an hour to complete the reaction, during which time remarkable colour changes took place. The yellow solution first changed to olive-green, and then successively to brown, green, indigo-blue, nearly black, and finally reddish-brown. The whole was then slowly poured into water and extracted with ether, the ethereal solution washed with water, dried over calcium chloride, and the ether evaporated, when a thick brown liquid was obtained which rapidly deposited crystals. These were drained off,* purified by crystallisation from methyl alcohol, and analysed:

0.1400 gave 0.2914 CO_2 and 0.0740 H_2O . $\text{C} = 56.77$; $\text{H} = 5.90$.

0.1504 „ 0.2260 AgCl . $\text{Cl} = 37.17$.

$\text{C}_9\text{H}_{12}\text{Cl}_2$ requires $\text{C} = 56.54$; $\text{H} = 6.28$; $\text{Cl} = 37.17$ per cent.

$\Delta^{2.6.2} : 6$ -Dichloro-3 : 4 : 4-trimethyldihydrobenzene,

thus obtained, is insoluble in water, but very soluble in the cold in benzene, light petroleum, or acetone, and in methyl or ethyl alcohol on warming. From the last-named solvent it crystallises in beautiful, long, flattened, glistening needles melting at 77° .

* The filtrate from these crystals boils undecomposed at 120 — 125° under 31 mm. pressure, but its properties have not yet been further examined.

Action of Bromine on Diketotrimethylhexamethylene.

To a solution of diketotrimethylhexamethylene in dry chloroform, a solution of bromine in dry chloroform was added in the dark, until the colour of the bromine was no longer destroyed, when hydrogen bromide was freely evolved. The whole was placed in a vacuum over potassium hydroxide, when it slowly solidified. After purification by spreading on porous plates and crystallisation from benzene, the substance was analysed :

0.2366 gave 0.1899 AgBr. Br = 34.15.

$C_9H_{13}O_2Br$ requires Br = 34.33 per cent.

1-Bromo-2:6-diketo-3:4:4-trimethylhexamethylene,

is insoluble in light petroleum, moderately soluble in hot water or benzene, and very soluble in alcohol, acetone, or ethyl acetate. It crystallises from benzene in stellar aggregates of colourless, transparent, glistening plates melting at 151.5° with decomposition and evolution of gas. When dissolved in dilute aqueous potassium hydroxide and treated with sodium amalgam, it is quantitatively reconverted into diketotrimethylhexamethylene melting at 100° , and when oxidised with sodium hypobromite it is converted into $\alpha\beta\beta$ trimethylglutaric acid (see p. 147).

If during the addition of bromine the whole is cooled in ice, comparatively little hydrogen bromide is evolved, and after standing for some time a white, crystalline powder is deposited, which on exposure to air rapidly evolves hydrogen bromide. It was therefore filtered off by the aid of a pump, washed with light petroleum, dried as rapidly as possible, and the bromine determined :

0.1986 gave 0.2450 AgBr. Br = 52.41.

$C_9H_{14}O_2Br_2$ requires Br = 50.95 per cent.

Additional bromine determinations in separate preparations gave :

Br = 53.34, 52.21, and 52.95 per cent.

The amount of hydrogen bromide evolved on keeping the substance in a vacuum over potassium hydroxide was also determined, but was always in excess of that calculated :

1.8530 lost 0.5266 HBr. HBr = 28.42.

1.8304 „ 0.5225 HBr. HBr = 28.54.

Calculated loss of HBr = 25.80 per cent.

Although the numbers obtained do not agree either with the calcu-

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lated amount or with one another, they are sufficiently close to point to the fact that this substance is a dibromide formed by the direct addition of two atomic proportions of bromine to the hexamethylene derivative.

1 : 6-Dibromo-6-hydroxy-2-keto-3 : 4 : 4-trimethylhexamethylene,

is a white, crystalline powder melting sharply at 87—88°. It cannot be obtained pure because it only separates from a solution containing excess of hydrogen bromide, and on attempting to crystallise it from any solvent, hydrogen bromide is evolved, and the above described monobromo-derivative melting at 151·5° separates out. It seemed probable, therefore, that this dibromide would be formed by the direct addition of hydrogen bromide to monobromodiketotrimethylhexamethylene, which proved to be the case, for if the latter is dissolved in dry chloroform and the solution after cooling in ice is saturated with hydrogen bromide, on standing a crystalline powder separates melting at 87—88° and having identical properties with the above dibromoderivative.

Action of Sodium Hypobromite on 2 : 6-Diketo-3 : 4 : 4-trimethylhexamethylene.

Fifty grams of bromine were poured into 300 c.c. of water cooled to 0°, and a strong solution of sodium hydroxide was then slowly added until the colour of the bromine had disappeared. A solution of 12 grams of diketotrimethylhexamethylene in sodium hydroxide (14 grams NaOH in 80 c.c. of water) was then poured in and the whole allowed to stand for 2½ hours. The solution, after separation from carbon tetrabromide and bromoform, was acidified with hydrochloric acid, when a copious white precipitate (10 grams) was formed which was collected (filtrate = A), purified by crystallisation from alcohol, and analysed :

0·1560 gave 0·1883 AgBr. Br = 51·34.

0·1554 „ 0·1868 AgBr. Br = 51·15.

$\text{C}_9\text{H}_{12}\text{O}_2\text{Br}_2$ requires Br = 51·28 per cent.

1 : 1-Dibromo-2 : 6-diketo-3 : 4 : 4-trimethylhexamethylene,

is readily soluble in cold chloroform, acetone, or ethyl acetate, but less so in hot alcohol, light petroleum, or water. It crystallises from alcohol in well-formed white needles melting at 112·5° without any sign of decomposition, and resolidifies at 110°. When boiled with aqueous potassium hydroxide, it dissolves and bromoform separates.

On acidifying the filtered solution with hydrochloric acid, a white solid separates which was collected (filtrate = B) and purified by crystallisation from benzene, when it was found to melt at 151.5° with decomposition and evolution of gas, and had properties identical with monobromodiketotrimethylhexamethylene (see page 145).

A portion of the dibromo-derivative (m. p. 151.5°) was then further treated with sodium hypobromite. The resulting liquid, separated from bromoform, gave no precipitate on acidification with hydrochloric acid, but after evaporation and extraction with ether, &c., $\alpha\beta\beta$ -trimethylglutaric acid melting at 87° was obtained.

The filtrates A and B, on evaporation and extraction with ether, gave further quantities of the same glutaric acid.

If when treating the hexamethylene derivative with sodium hypobromite the above quantities are slightly varied (the proportions which give the best results are: 80 grams of bromine in 1000 c.c. of water, decolorised with sodium hydroxide; and 20 grams of diketotrimethylhexamethylene in a solution of 30 grams of sodium hydroxide in 150 c.c. of water), then on acidifying with hydrochloric acid no solid separates. On evaporation and extraction with ether, &c., a solid substance is obtained which dissolves completely in water with a very acid reaction, and on saturating the solution with hydrogen chloride, crystallises out in beautiful leaflets melting at $87-88^{\circ}$.

0.1109 gave 0.2231 CO_2 and 0.0802 H_2O . $\text{C} = 54.86$; $\text{H} = 8.03$.

$\text{C}_8\text{H}_{14}\text{O}_4$ requires $\text{C} = 55.17$; $\text{H} = 8.04$ per cent.

In order to further compare this substance with the $\alpha\beta\beta$ -trimethylglutaric acid described by Perkin and Thorpe (Trans., 1899, 75, 65), it was converted into the anhydride and this into the anilic acid, which crystallised from dilute methyl alcohol in stout needle-shaped crystals melting at 150° .

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