XLI.—*Dimethylketohexamethylene.*

By F. STANLEY KIPPING, Ph.D., D.Sc.

SOME years ago, when engaged in studying the action of phosphoric anhydride on fatty acids (Trans., 1890, **57**, 532 and 980; 1893, **63**, 452), a few experiments were made with various dicarboxylic acids, amongst others $\alpha\alpha'$ -dimethylpimelic acid, a compound which happened to be under investigation at the time (Kipping and Mackenzie, Trans., 1891, **59**, 569), and which has formed the subject of a recent communication (this vol., p. 139).

It was then observed that this acid, when heated with phosphoric anhydride, yielded an oil having an odour of peppermint,* but further experiments were necessarily postponed owing to lack of material.

Subsequent researches having necessitated the preparation of a considerable quantity of dimethylpimelic acid for further examination in other directions, the study of its behaviour with phosphoric anhydride was also resumed, but the results were not satisfactory, the yield of the oil in question being very small. Under these circumstances, and as it seemed probable that the product would prove to be dimethylketohexamethylene, $\text{CH}_2 < \begin{smallmatrix} \text{CH}_2 \cdot \text{CHMe} \\ \text{CH}_2 \cdot \text{CHMe} \end{smallmatrix} > \text{CO}$, a different method of preparation was resorted to, and the calcium salt of the acid was submitted to dry distillation, a process which had been previously employed with satisfactory results in the preparation of suberone from suberic acid, and, more recently, in the conversion of several other dicarboxylic acids into cycloid ketones (Semmler, Ber., 1891, **25**, 3517; v. Baeyer, Ber., 1892, **26**, 231; Wislicenus, Annalen, 1893, **275**, 309).

In this case, also, the method proved applicable, and the crude dimethylketohexamethylene (Proc., **121**, 68) in the distillate was finally obtained in a state of purity by converting it into the crystalline oxime, and decomposing the latter with hydrochloric acid.

Dimethylketohexamethylene has the strong peppermint-like smell which seems to be characteristic of the saturated cycloid ketones of this class, whereas its oxime has an odour very similar to that of camphoroxime; the general properties of the ketone resemble those of its homologues. On oxidation with nitric acid it is probably first

* Not an odour of turpentine as originally stated (Kipping and Mackenzie, *loc. cit.*); a reference to the author's note-book has shown that this misstatement arose in writing the paper, as in the notes of the experiment the oil is described as having "a strong odour of peppermint."

converted into α -methylglutaric acid, $\text{COOH}\cdot\text{CHMe}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{COOH}$; but this compound undergoes further oxidation, yielding $\alpha\alpha$ -hydroxymethylglutaric acid, $\text{COOH}\cdot\text{CMe}(\text{OH})\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{COOH}$ (or the lactonic acid $\text{COOH}\cdot\text{CMe}\langle\text{O}-\text{CO}\rangle_{\text{CH}_2\cdot\text{CH}_2}$), just as β -methyladipic acid, $\text{COOH}\cdot\text{CH}_2\cdot\text{CHMe}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{COOH}$, is converted into $\beta\beta$ -hydroxymethyladipic acid, $\text{COOH}\cdot\text{CH}_2\cdot\text{CMe}(\text{OH})\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{COOH}$ (or the lactonic acid $\text{COOH}\cdot\text{CH}_2\cdot\text{CMe}\langle\text{O}-\text{CO}\rangle_{\text{CH}_2\cdot\text{CH}_2}$), on oxidation with potassium permanganate (Semmler, *loc. cit.*).

Preparation of Crude Dimethylketoexamethylene.

The material employed in these experiments consisted of a sample of liquid dimethylpimelic acid, which had been purified by distillation under reduced pressure, and from which, after keeping for several months, the crystalline acid had been separated by filtration; this liquid, therefore, was probably a mixture of the two stereoisomeric modifications of the acid, free from any appreciable quantity of impurity (compare this vol., p. 139).

The calcium salt was prepared by dissolving the liquid acid in hot water, adding excess of precipitated calcium carbonate to the boiling solution, and filtering; on evaporation, the filtrate yielded the readily soluble salt in the form of a pasty mass, which was first heated at about 120° until it became hard and brittle, and then intimately mixed with an equal weight of dry, powdered, soda-lime. This mixture, in quantities of about 8 grams, was then submitted to dry distillation in small, hard-glass retorts, under a pressure of about 400 mm.; at first, it became pasty and frothed up, but, on continued heating, an oil began to collect in the receiver, and the residue in the retort gradually changed to a hard, grey mass. The dark brown and slightly fluorescent, oily distillate was dissolved in ether, the solution shaken with dilute potassium carbonate, dried over anhydrous potassium carbonate, filtered, and evaporated; the weight of the residue, when practically free from ether, amounted to about 40 per cent. of that of the calcium salt employed.

When distilled under ordinary pressure, the oil began to boil at about 150° , but the temperature rapidly rose to 165° , and the principal portion of the product passed over between 165° and 185° ; above this, only a small quantity was collected, and, although the thermometer subsequently rose to 250° , a thick, brown oil still remained in the distilling flask. The fraction 165 — 185° was now redistilled and collected in two principal portions, boiling at 170 — 175° and 175 — 179° respectively; both of these were almost colourless, and had a strong odour of peppermint.

An analysis of the fraction boiling at 175—179°, which was the larger of the two, gave results agreeing well with those required by dimethylketoexamethylene.

0·1737 gave 0·4876 CO₂ and 0·1733 H₂O. C = 76·5; H = 11·1.

C₈H₁₄O requires C = 76·2; H = 11·1 per cent.

Dimethylketoexamethylene Oxime.

In order to obtain the ketone in a state of purity, without the unavoidable loss which would have attended further fractional distillation, the two portions just referred to were dissolved in methylic alcohol, and the solution mixed with a slight excess of hydroxylamine hydrochloride in aqueous solution and about four times the theoretical quantity of concentrated soda; after warming gently for a short time, this mixture was left to evaporate at the ordinary temperature. The oxime, which was slowly deposited in colourless crystals, was separated by filtration, washed with water, and spread on porous earthenware to free it from oil; it was then recrystallised from hot dilute alcohol, dried over sulphuric acid, and analysed.

0·1387 gave 0·3460 CO₂ and 0·1344 H₂O. C = 68·03; H = 10·76.

C₈H₁₄·NOH requires C = 68·08; H = 10·64 per cent.

Dimethylketoexamethylene oxime crystallises from warm dilute alcohol and from other solvents in long, colourless prisms, melting at 114—115°; it dissolves freely in cold acetone, ether, and chloroform, but is only moderately easily soluble in cold alcohol, and insoluble, or nearly so, in water and also in concentrated soda; on the other hand, it is readily soluble in warm, moderately strong hydrochloric acid, by which it is decomposed (see below). The oxime has a very peculiar and somewhat unpleasant smell, very like that of camphor oxime; it is volatile in steam, and distils under ordinary atmospheric pressure without visibly decomposing if heated in small quantities at a time. Crystals of the oxime suitable for goniometrical measurement were not obtained; those deposited from alcoholic solution belonged apparently to the anorthic system.

As the oxime can be easily obtained in a state of purity, and is readily reconverted into the ketone by the action of hydrochloric acid, it afforded a convenient means of preparing pure dimethylketoexamethylene. For this purpose, the crystalline compound was gently warmed with moderately concentrated hydrochloric acid, in which, at first, it rapidly dissolved; in a very short time, however, the solution became turbid, owing to the separation of a colourless oil, and, on

distilling in a current of steam, the ketone quickly passed over. The distillate was extracted with ether, the ethereal extract dried over calcium chloride, and evaporated; on distilling the residual oil under atmospheric pressure, the thermometer rose at once to 174° , and practically the whole of the ketone passed over at 174 — 176° , only a few drops remaining in the distilling flask.

This preparation, therefore, consisted of pure dimethylketo-hexamethylene, and, as analyses of the oxime and of the less pure ketone had already established its composition, another combustion was deemed superfluous.

Dimethylketo-hexamethylene is a colourless, mobile liquid, specifically lighter than water at 16° , and readily volatile in steam; it has a very strong and pure odour of peppermint. It is practically insoluble in water, but is miscible with alcohol, ether, and other organic liquids in all proportions; its melting point is doubtless very low, as it showed no signs of crystallising when cooled to 0° . Attempts to prepare a crystalline additive compound by shaking the ketone with a strong solution of sodium hydrogen sulphite were unsuccessful; on the other hand, it was readily acted on by phenylhydrazine in warm acetic acid solution, giving a yellowish, oily hydrazone.

Although there could be little doubt, considering its method of formation and its general properties, that this ketone has the constitution assigned to it above, its behaviour on oxidation was investigated in the hope of obtaining confirmatory evidence of this view. The pure ketone, prepared from the oxime, was therefore slowly added to a considerable quantity of warm nitric acid of sp. gr. 1.2, whereupon a vigorous action occurred, showing that, like ketopentamethylene (W. Hentzschel and Wislicenus, *Annalen*, 1893, 275, 312), the compound was very readily oxidised. As, however, the oil did not readily pass into solution, and brown fumes continued to be evolved even after warming for some time, the mixture was heated on a sand bath until oxidation appeared to be at an end; on then evaporating to a syrup and adding a little water, a very small quantity of a crystalline substance (see below) was deposited, but after separating this by filtration and again evaporating, the bulk of the oxidation product remained as a colourless syrup. As this syrup did not solidify even when, after keeping for some days over sulphuric acid, it was rubbed with a crystal of α -methylglutaric acid—an acid which might well have been obtained as an oxidation product of the ketone—it appeared probable that oxidation had proceeded beyond this stage and that the α -methylglutaric acid, which it may be assumed had been produced in the first instance, had been partially converted into $\alpha\alpha$ -hydroxymethylglutaric acid, in the same way as the β -methyladipic acid

obtained by Semmler as an oxidation product of methylketopentamethylene may be transformed into $\beta\beta$ -hydroxymethyladipic acid (*Ber.*, 1892, **25**, 3513). For this reason the syrup was again heated with concentrated nitric acid, as it seemed probable that further oxidation would lead to a more homogeneous, and possibly crystalline product. This supposition proved to be well founded, since, on again evaporating until free from nitric acid and then keeping the residual syrup over sulphuric acid, it was slowly converted into a colourless, crystalline mass, which was freed from adherent oil with the aid of porous earthenware. When purified in this way, the compound melted, not very sharply, at $65-68^\circ$, had an acid reaction, and dissolved in cold sodium carbonate solution with effervescence; it charred when distilled under ordinary atmospheric pressure, giving an oily distillate which soon solidified and which, as far as could be ascertained, was identical with the original substance. As the oxidation product was so very readily soluble in water, alcohol, ether, &c., the small quantity at disposal could not be purified by recrystallisation, and, partly for this reason, it was not analysed. There is little doubt, however, judging from its method of preparation and properties, that it is the lactone of $\alpha\alpha$ -hydroxymethylglutaric acid and identical with the compound described by Brecht (*Annalen*, 1881, **208**, 62; *Ber.*, 1881, **14**, 1780) and by Kreckeler, Tollens and Block (*Annalen*, 1887, **238**, 287).

This view was confirmed by an analysis of the silver salt; a portion of the acid was dissolved in dilute ammonia and the neutral solution precipitated with silver nitrate; the precipitate was collected with the aid of the pump, and dried first on porous earthenware over sulphuric acid, and finally at 100° , at which temperature it did not appreciably darken.

0.3111 gave 0.2176 CO_2 , 0.0659 H_2O and 0.1796 Ag. C = 19.0; H = 2.4; Ag = 57.6 per cent.

$\text{C}_8\text{H}_8\text{O}_5\text{Ag}_2$ requires C = 19.2; H = 2.1; Ag = 57.4 per cent.

This result, as will be seen, agrees well with that required for the silver salt of a hydroxymethylglutaric acid, and the properties of the salt were the same as those of the compound described by Brecht; it was very sparingly soluble in water, and appeared to be amorphous when examined under the microscope.

The crystalline oxidation product of the ketone, referred to above, proved to be a mixture, as, on recrystallising it from dilute alcohol, very long flat plates or needles and small compact crystals were deposited side by side; these two compounds were separated, partly mechanically, partly by fractional crystallisation, and eventually obtained in a state of purity, but in quantities so small that analyses were out of the question.

The long, flat plates melted at 113—114°, and probably belonged to the anorthic system; they were at first thought to be crystals of methylsuccinic acid, the melting point of which is 112°; they were, however, insoluble in water, or nearly so, whereas methylsuccinic acid is readily soluble.

The other crystalline oxidation product melted at 108—109° and was also insoluble, or nearly so, in water; it formed orthorhombic octahedra, and was therefore not identical with the substance melting at 113—114°.

Unfortunately the nature of these two acids remained undetermined, owing to the very small quantities which were produced; as, however, the ketone which was submitted to oxidation must have been of a high degree of purity, having been prepared from the pure oxime, these products can hardly have been derived from any extraneous source, and their formation is therefore of some interest.

*Chemical Department,
City and Guilds of London Institute,
Central Technical College.*