343. *2 : 2 : 4- and 2 : 4 : 4-Trimethylcyclopentanone and Some Related Compounds.*

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During the synthesis of 1 : 1 : 3-trimethyl*cyclo*pentane, pure specimens of 2 : 2 : 4- and 2 : 4 : 4-trimethyl*cyclo*pentanone and of their parent acids, $\alpha\alpha\gamma$- and $\alpha\gamma\gamma$-trimethyladipic acids, have been isolated and characterised unambiguously. Published information about these compounds is often unsatisfactory. 2 : 2 : 4- and 2 : 4 : 4-Trimethyl*cyclo*pentanol, 1 : 4 : 4- and 3 : 3 : 5-trimethyl*cyclo*pentene, and two 1 : 2 : 4-trimethyl*cyclo*pentanes are also described.

IN connection with an investigation into the composition of Iranian naphthas, pure samples of the isomeric trimethyl*cyclo*pentanes were required. The general method adopted for the preparation of substituted *cyclo*pentanes is by cyclisation of the corresponding adipic acid followed by conversion of the resultant ketone into the hydrocarbon through the carbinol and olefin. As starting point for the 1 : 1 : 3-isomer, *iso*phorone was selected since this is now commercially available and can be readily converted into the corresponding 3 : 3 : 5-trimethyl*cyclo*hexanol by catalytic reduction. This *cyclo*hexanol on oxidation with nitric acid yields a mixture of acids in which the major products are $\alpha\alpha\gamma$- and $\alpha\gamma\gamma$-trimethyladipic acids. The acids of lower molecular weight formed simultaneously illustrate well the strong resistance to oxidation shown by the *gem*-dimethyl group. From the trimethyladipic acid fraction two acids were obtained which melted at 100° and 69° respectively. Since the higher-melting of these showed a strong tendency to form a monoester and monoanilide under conditions in which the other acid readily yielded a diester and dianilide, it was thought probable that this acid possessed the $\alpha\alpha\gamma$-structure.

Qudrat-i-Khuda and Ghosh (*J. Indian Chem. Soc.*, 1939, **16**, 287) describe $\alpha\alpha\gamma$-trimethyladipic acid prepared by two distinct synthetic methods, and give its melting point as 80°. We therefore repeated one of these syntheses and obtained an acid melting at 98°. This value was not raised by recrystallisation but derivatives were obtained which were identical with those from the higher-melting acid from the oxidation products. This identified the acid as $\alpha\alpha\gamma$-trimethyladipic acid. $\alpha\gamma\gamma$-Trimethyladipic acid was also synthesised by a method which in its

earlier stages followed work by Qudrat-i-Khuda (*J.*, 1929, 201), and melted at 69°. It was indistinguishable from the corresponding acid from *iso*phorone both in itself and in its derivatives.

Dry distillation of these acids with barium hydroxide gave good yields of the corresponding *cyclo*pentanones. 2 : 2 : 4-Trimethyl*cyclo*pentanone had been described by Wallach (*Annalen*, 1915, **408**, 207; 1924, **437**, 193) from preparations giving no proof of structure, by Qudrat-i-Khuda and Ghosh (*loc. cit.*), and by Sargent (*J. Org. Chem.*, 1942, **7**, 154), and adequately characterised by Sargent. 2 : 4 : 4-Trimethyl*cyclo*pentanone had also been described by Wallach (*Annalen*, 1918, **414**, 332), Dey and Linstead (*J.*, 1935, 1063), and Voitila (*Ann. Acad. Sci. Fennicae*, 1938, **49**, *A*, No. 1, p. 110), but was prepared in each case by methods involving molecular rearrangements.

The trimethyl*cyclo*pentanols obtained from the corresponding ketones by catalytic reduction were dehydrated by activated alumina at 300—325°. Fractional distillation through 40-plate columns showed that the products were mixtures of olefins. Of these one was found to be common to both products and was therefore presumed to be 3 : 3 : 5-trimethyl*cyclo*pentene. This structure was confirmed by oxidation to *ααγ*-trimethylglutaric acid with permanganate.

The product from 2 : 4 : 4-trimethyl*cyclo*pentanol consisted of 3 : 3 : 5-trimethyl*cyclo*-pentene mixed with a second olefin. Both yielded 1 : 1 : 3-trimethyl*cyclo*pentane on catalytic hydrogenation; the second should therefore have been 1 : 4 : 4-trimethyl*cyclo*pentene.

From 2 : 2 : 4-trimethyl*cyclo*pentanol a mixture of three olefins was obtained, of which more than half was 3 : 3 : 5-trimethyl*cyclo*pentene. The remaining two olefins on hydrogenation gave stereoisomeric forms of 1 : 2 : 4-trimethyl*cyclo*pentane and were therefore isomeric forms of 1 : 2 : 4-trimethyl*cyclo*pentene.

After the work described above had been completed (1944) further papers appeared describing 2 : 4 : 4-trimethyl*cyclo*pentanone (Naves, *Helv. Chim. Acta*, 1944, **27**, 51; Qudrat-i-Khuda and Mukherji, *J. Indian Chem. Soc.*, 1946, **23**, 435; Chakravarti, *J.*, 1947, 1028). Values quoted for the melting point of the semicarbazone of this ketone still varied from 159° to 168° and, since other discrepancies appeared between our work and that of some of these authors, it was decided to repeat the synthesis of 2 : 4 : 4-trimethyl*cyclo*pentanone described by Chakravarti (*loc. cit.*). The properties of the product obtained agreed quite well with those of our previous preparation. It was observed that the semicarbazones of all the samples examined tended to decompose below the melting points which consequently were dependent on the rate of heating. If this was sufficiently rapid, the value could be as high as 167—168° but was, under normal conditions, in the region of 161—165°. The 2 : 4-dinitrophenylhydrazone was found to be a more reliable derivative for characterisation.

Qudrat-i-Khuda and Mukherji (*loc.c it.*) also described *αγγ*-trimethyladipic acid giving a melting point of 71°.

EXPERIMENTAL.

Analyses are by Drs. Weiler and Strauss, Oxford. All m. p.s and b. p.s are corrected.

3 : 3 : 5-*Trimethyl*cyclo*hexanol.*—Technical *iso*phorone was hydrogenated in a high-pressure autoclave at 150°, with Raney nickel as catalyst. The yield after distillation under reduced pressure was almost theoretical.

Oxidation of 3 : 3 : 5-*Trimethyl*cyclo*hexanol.*—3 : 3 : 5-Trimethyl*cyclo*hexanol was oxidised by the method given in *Org. Synth.*, Coll. Vol. I., 2nd edn., p. 19, note 5. The molten alcohol was run from a heated funnel into the nitric acid. After removal of nitric acid and water the entire yield of acids was converted into ethyl esters by refluxing it with ethanol in the presence of sulphosalicylic acid. These were then fractionally distilled at 10 mm. through a 25-plate column. Sharply defined fractions were obtained which were identified as shown in the table.

Fraction.	Wt. (%) of crude ester.	B. p./10 mm.	n_D^{20}.	Compound.
1	1·3	80°	1·4175	Ethyl dimethylmalonate.
2	3·7	98	1·4212	Ethyl *αα*-dimethylsuccinate.
3	9·0	111	1·4275	Ethyl *ααγ*-trimethylglutarate.
4	70	127—128	1·4326	Ethyl trimethyladipates.
Residue	16	>128	—	Monoethyl trimethyladipates.

The mixed esters were hydrolysed with alcoholic potash and the mixed acids recovered in the usual way.

Separation of aaγ- and aγγ-trimethyladipic acids. The two trimethyladipic acids were separated by fractional crystallisation. They showed a strong tendency to form two liquid phases in aqueous solutions, which was largely avoided by the use of dilute formic acid as a solvent. Although the higher-melting *ααγ*-trimethyladipic acid was less soluble and crystallised out more readily than its isomer, complete separation was not easily effected. For characterisation the acids were recrystallised to constant m. p. from di*iso*propyl ether, or from chloroform–*iso*pentane.

$\alpha\alpha\gamma$-Trimethyladipic acid melts at 100·1—100·5° (Found : C, 57·4; H, 8·4%; equiv., 94·1. Calc for $C_9H_{16}O_4$: C, 57·4; H, 8·6%; equiv., 94·0). Qudrat-i-Khuda and Ghosh (*loc. cit.*) and Qudrat-i-Khuda and Mukherji (*loc. cit.*) give m. p. 79—80°. The acid (1 g.), heated in aniline (2 g.) for 2 hours, yields mainly a *monoanilide*, m. p. 160·6—161·0° (Found : C, 68·3; H, 7·9; N, 5·2. $C_{15}H_{21}O_3N$ requires C, 68·4; H, 8·0; N, 5·3%), with a little *dianilide* m. p. 169·4—169·8° (Found : C, 74·2; H, 7·6; N, 8·4. $C_{21}H_{26}O_2N_2$ requires C, 74·5; H, 7·7; N, 8·3%). Its diethyl ester has b. p. 123°/9 mm., n_D^{20} 1·4322, d^{20} 0·9694 (Found : C, 64·0; H, 9·9. Calc. for $C_{13}H_{22}O_4$: C, 63·9; H, 9·9%).

$\alpha\gamma\gamma$-Trimethyladipic acid melts at 68·6—69·2° (Found : C, 57·2; H, 8·5%; equiv., 93·8). Qudrat-i-Khuda and Mukherji (*loc. cit.*) give m. p. 71°. It forms a *dianilide*, m. p. 162·8—163·3° (Found : C, 74·5; H, 7·5; N, 8·4%), and a diethyl ester, b. p. 124°/9 mm., n_D^{20} 1·4330, d^{20} 0·9703 (Found : C, 64·0; H, 9·9%).

Synthesis of aaγ-Trimethyladipic Acid.—The synthetic method used to confirm the structure of the $\alpha\alpha\gamma$-trimethyladipic acid was one employed by Qudrat-i-Khuda and Ghosh (*loc. cit.*), involving condensation of ethyl mesitonate with ethyl cyanoacetate, reduction of the product to ethyl α-cyano-$\alpha\gamma\gamma$-trimethyladipate, and acid hydrolysis of the latter. In all but the final stage our results agreed well enough with those of Qudrat-i-Khuda and Ghosh. During the hydrolysis of the cyano-ester with hydrochloric acid a small quantity of volatile oil separated, which proved to be 2 : 2 : 4-trimethyl*cyclo*pentanone. Some cyclisation of the ester must have occurred at an earlier stage, probably during the reduction with amalgamated aluminium. The acid product from the hydrolysis after two recrystallisations from water had m. p. 98°, which was not raised by a further recrystallisation (Found : C, 57·6; H, 8·5%). A mixture of this with the acid from *iso*phorone (melting at 100°) melted at 99°. Refluxing with aniline gave a mono- and a di-anilide, identical with those from the other sample (m. p. and mixed m. p.).

Synthesis of a$\gamma\gamma$-Trimethyladipic Acid.—This acid was prepared by a method which also followed in its earlier stages work by Qudrat-i-Khuda (*loc. cit.*). 3 : 3-Dimethyl-5-hexanolactone ($CO_2H = 1$) was prepared from γ-acetyl-$\beta\beta$-dimethylbutyric acid by catalytic reduction; the physical constants of the lactone showed an unusual agreement with the values quoted by Qudrat-i-Khuda. Attempts to condense it with potassium cyanide according to Blaise's method (*Bull. Soc. chim.*, 1905, **33**, 899) were unsuccessful. The keto-acid (180 g.) was therefore converted *via* the cyanohydrin by von Auwers's method (*Annalen*, 1896, **292**, 222) into 3 : 3-dimethyl-5-hexanolactone-5-carboxylic acid. The total acid product from the reaction was esterified with methanol and a little hydrochloric acid, and the ester mixture fractionally distilled. After removal of a low-boiling fraction a viscous ester was obtained of b. p. 100°/1·8 mm., n_D^{20} 1·4547, believed to be the methyl ester of the lactonic acid. Hydrolysis of this ester gave the lactonic acid, which after two recrystallisations from benzene–light petroleum melted at 97·2—97·6° (Found : C, 58·1; H, 7·6. Calc. for $C_9H_{14}O_4$: C, 58·2; H, 7·6%). In the subsequent paper by Qudrat-i-Khuda and Mukherji (*loc. cit.*), the same compound was described as melting at 81°. We have repeated their method of preparation and obtained a product melting at 96·7—97·4° after four recrystallisations from ethyl acetate (Found : C, 58·2; H, 7·6%).

3 : 3-Dimethyl-5-hexanolactone-5-carboxylic acid (3 g.) was reduced by heating it under reflux with syrupy phosphoric acid (11 ml.), hydriodic acid (2 ml.), potassium iodide (0·35 g.), and red phosphorus (1 g.). After 12 hours, water (30 ml.) was added and the whole thoroughly extracted with ether. The extract was washed with sodium pyrosulphite solution to remove iodine, then with water, dried, and evaporated. The residue (2 g.) was recrystallised twice from water; the $\alpha\gamma\gamma$-trimethyladipic acid obtained melted at 68·5—69·5°, and did not depress the m. p. of the corresponding acid from *iso*phorone (Found : C, 57·5; H, 8·6. Calc. for $C_9H_{16}O_4$: C, 57·4; H, 8·6%). It formed a dianilide which was identical with that derived from *iso*phorone (m. p. and mixed m. p.).

Cyclisation of the Trimethyladipic acids.—The trimethyladipic acids were converted into the corresponding cyclic ketones by the procedure described in *Org. Synth.*, Coll. Vol. I, 2nd edn., p. 192, involving dry distillation with 10% (by wt.) of barium hydroxide. The yield was 90%. Pure specimens of the ketones were obtained by fractional distillation at atmospheric pressure through 40-plate fractionating columns, the estimate of purity being determined from the f. p. curves. It was found that some condensation with elimination of water and formation of high-boiling residue always occurred on distillation.

2 : 2 : 4-*Trimethyl*cyclo*pentanone*.—This ketone had b. p. 155·6°/760 mm., n_D^{20} 1·4294, d^{20} 0·8730, f. p. —40·6° (purity 99·7 mole-%) (Found : C, 76·1; H, 11·3. Calc. for $C_8H_{14}O$: C, 76·1; H, 11·2%). The semicarbazone had a more consistent m. p. (170·4—171·1°) than had its isomer (Found : C, 59·3; H, 9·2; N, 22·6. Calc. for $C_9H_{17}ON_3$: C, 59·0; H, 9·3; N, 22·9%). The 2 : 4-*dinitrophenylhydrazone* melts at 164·0—164·6° (Found : C, 55·2; H, 6·0; N, 18·5. $C_{14}H_{18}O_4N_4$ requires C, 54·9; H, 5·9; N, 18·3%). The *p*-nitrobenzylidene derivative melts at 101·2—101·5°; Sargent (*loc. cit.*) gives 99·3—99·5°. The ketone formed as a by-product in the last stage of the synthesis of $\alpha\alpha\gamma$-trimethyladipic acid gave a semicarbazone melting at 169·5—170° (uncorr.) (Found : C, 59·2; H, 9·4; N, 22·4. Calc. for $C_9H_{17}ON_3$: C, 59·0; H, 9·3; N, 22·9%). This did not depress the m. p. of the semicarbazone of 2 : 2 : 4-trimethyl*cyclo*pentanone.

2 : 4 : 4-*Trimethyl*cyclo*pentanone*.—This had b. p. 161·5°/760 mm., n_D^{20} 1·4313, d^{20} 0·8765, f. p. —25·6° (purity 99·6 mole-%) (Found : C, 76·3; H, 11·3%). The semicarbazone had m. p. 160—168° depending on heating rate, the 2 : 4-dinitrophenylhydrazone, m. p. 160·6—160·9° (Found : C, 54·9; H, 5·7; N, 17·4%), in excellent agreement with the value given by Naves (*loc. cit.*), and the *p*-nitrobenzylidene derivative, m. p. 122—123·5° (decomp.)

2 : 4 : 4-Trimethyl*cyclo*pentanone was synthesised by Chakravarti's method (*loc. cit.*) with some variations in detail. Dimedone (5 : 5-dimethyl*cyclo*hexane-1 : 3-dione) was oxidised with sodium hypochlorite to $\beta\beta$-dimethylglutaric acid. The anhydride of this acid was reduced catalytically (copper chromite) to $\beta\beta$-dimethylvalero-δ-lactone. This was converted *via* the bromo- and cyano-esters into $\beta\beta$-dimethyladipic acid which was converted by means of sodium into ethyl 2-keto-4 : 4-dimethyl*cyclo*-

pentanecarboxylate. The latter was methylated either without separation from the reaction mixture or after purification, the resulting ethyl 2-keto-1 : 4 : 4-trimethyl*cyclo*pentanecarboxylate being hydrolysed and decarboxylated by refluxing with acid to yield the required ketone.

The best sample of 2 : 4 : 4-trimethyl*cyclo*pentanone from this synthesis boiled at 160·1—160·4° and had n_D^{20} 1·4318—1·4320 (Found : C, 76·4; H, 11·4%). The 2 : 4-dinitrophenylhydrazone had m. p. 160·1—160·6° (Found : C, 55·0; H, 5·9; N, 18·1%).

A further sample of 2 : 4 : 4-trimethyl*cyclo*pentanone was obtained by the Dieckmann condensation of ethyl a$\gamma\gamma$-trimethyladipate (from *iso*phorone) with sodium followed by hydrolysis of the 2-keto-1 : 4 : 4-trimethyl*cyclo*pentanecarboxylate [2 : 4-dinitrophenylhydrazone, m. p. 160·6—160·9° (Found : C, 55·2; H, 5·9; N, 17·8%)].

Mixed m. p.s showed that the three samples of 2 : 4 : 4-trimethyl*cyclo*pentanone gave identical 2 : 4-dinitrophenylhydrazones; the derivative of 2 : 2 : 4-trimethyl*cyclo*pentanone depressed their m. p.s.

*Oxidation of the Trimethyl*cyclo*pentanones.*—The structures of the two ketones were finally checked by oxidation with acid dichromate (140 g. of potassium dichromate per l. of 16% sulphuric acid). By a quantity of oxidising agent equiv. to 2 atoms of oxygen per mole of ketone, 2 : 2 : 4-trimethyl*cyclo*pentanone was oxidised partly to a$a\gamma$-trimethylglutaric acid (m. p. and mixed m. p.). 2 : 4 : 4-Trimethyl*cyclo*pentanone was oxidised completely to a liquid product which was esterified. The ester gave a semicarbazone, m. p. 112°, and a 2 : 4-dinitrophenylhydrazone, m. p. 55·5°, which did not depress the m. p.s of the corresponding derivatives of ethyl γ-acetyl-$\beta\beta$-dimethylbutyrate. These results were in complete agreement with the expected structures.

*2 : 2 : 4- and 2 : 4 : 4-Trimethyl*cyclo*pentanols.*—These were obtained in almost theoretical yields by catalytic reduction of the ketones in a high-pressure autoclave at 95—140°, with Raney nickel as catalyst. Both products appeared to be mixtures of geometrical isomers, and no attempt was made to separate these. 2 : 2 : 4-*Trimethyl*cyclo*pentanol boiled at 113—116·3°/149 mm. and had n_D^{20} 1·4461 (Found : C, 74·7; H, 12·7. $C_8H_{16}O$ requires C, 74·9; H, 12·6%). 2 : 4 : 4-*Trimethyl*cyclo*pentanol boiled at 115—118·5°/152 mm. and had n_D^{20} 1·4439 (Found : C, 74·7; H, 12·8%).

*Dehydration of 2 : 2 : 4- and 2 : 4 : 4-Trimethyl*cyclo*pentanols.*—This was accomplished by passing the carbinols over activated alumina (10—14 mesh) at 300—325° at a rate of about 0·2 v./v./hour.

The product obtained from 2 : 2 : 4-trimethyl*cyclo*pentanol contained about 60% of one olefin and 10—15% of each of two higher-boiling olefins. That obtained from 2 : 4 : 4-trimethyl*cyclo*pentanol contained about 35% of an olefin which proved to be identical with the lowest-boiling from the other isomer, and about 55% of another. The olefin common to both products was shown to be 3 : 3 : 5-trimethyl*cyclo*pentene by oxidation with potassium permanganate solution to a$a\gamma$-trimethylglutaric acid (m. p. and mixed m. p.). On refractionation through a 60-plate precision column it boiled at 95·2°/760 mm. (uncorr.) and had n_D^{20} 1·4160, d^{20} 0·7506, and f. p. —107·95°. The purity estimated from the freezing-point curve was 99·5 mole-%.

The second olefin from 2 : 4 : 4-trimethyl*cyclo*pentanol also possessed the 1 : 1 : 3-structure, since on subsequent hydrogenation it yielded a hydrocarbon indistinguishable from that from 3 : 5 : 5-trimethyl*cyclo*pentene, and although on oxidation only aa-dimethylsuccinic acid was obtained, it could certainly be regarded as 1 : 4 : 4-trimethyl*cyclo*pentene. The best sample obtained, of purity estimated to be 98·8 mole-%, boiled at 103·4°/760 mm. (uncorr.) and had n_D^{20} 1·4253, d^{20} 0·7687, and f. p. —113·14°. The two remaining olefins from 2 : 2 : 4-trimethyl*cyclo*pentanol yielded on hydrogenation two isomers of 1 : 2 : 4-trimethyl*cyclo*pentane. It was therefore evident that rearrangement involving a methyl group occurs during the dehydration of this carbinol, as might have been expected from the work of Whitmore (*J. Amer. Chem. Soc.*, 1932, **54**, 3274). The two olefins were therefore regarded as isomeric 1 : 2 : 4-trimethyl*cyclo*pentenes, b. p. 111° (uncorr.), n_D^{20} 1·4308, and b. p. 118° (uncorr.), n_D^{20} 1·4390.

*1 : 1 : 3- and 1 : 2 : 4-Trimethyl*cyclo*pentanes.*—The samples of 3 : 5 : 5- and 1 : 4 : 4-trimethyl*cyclo*pentene were hydrogenated separately in a high-pressure autoclave over Raney nickel. The hydrocarbon products were passed through columns of activated silica gel to remove traces of olefins and finally fractionally distilled through a 100-plate precision column. The product, which was identical from both olefins, formed a glass at its f. p. and did not crystallise. It had b. p. 104·70°/752 mm., d^{20} 0·7483, d^{25} 0·7437, n_D^{20} 1·4111, n_{6563}^{20} 1·4090, n_{5461}^{20} 1·4129, n_{4861}^{20} 1·4163, n_{4358}^{20} 1·4205, n_D^{25} 1·4087, n_{6563}^{25} 1·4066, n_{5461}^{25} 1·4106, n_{4861}^{25} 1·4138, and n_{4358}^{25} 1·4181. Rossini *et al.* (*J. Res. Nat. Bur. Stand.*, 1949, **43**, 473; 1947, **38**, 53) give b. p. 104·893°/760 mm., d^{20} 0·74825, d^{25} 0·74392, n_D^{20} 1·41119, n_D^{25} 1·40870, and f. p. —142·44°.

The higher-boiling olefins obtained from 2 : 2 : 4-trimethyl*cyclo*pentanol were treated in the same manner, and the product on distillation yielded two saturated hydrocarbons, b. p. 108·95°/751 mm., n_D^{20} 1·4106, d^{20} 0·7471, and b. p. 116·55°/751 mm., n_D^{20} 1·4184, d^{20} 0·7634. The physical properties of these hydrocarbons correspond with those of *cis-trans-cis-* and the *cis-cis-trans-*1 : 2 : 4-trimethyl*cyclo*pentanes respectively. Recently published data (Rossini *et al.*, *loc. cit.*) for these two compounds are : *cis-trans-cis*, b. p. 109·290°/760 mm., n_D^{20} 1·41060, d^{20} 0·74727; *cis-cis-trans*, b. p. 116·731°/760 mm., n_D^{20} 1·41855, d^{20} 0·76345.

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