247. *The Supposed Isolation of a Second Form of ββ-Dimethyl*cyclo*-
hexanone.   Ring Rearrangement during Clemmensen Reduction.*

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THREE claims have recently been made of the isolation of simple isomeric cyclohexane derivatives corresponding to the two multiplanar (Sachse) forms of the ring.   Khuda (*J. Ind. Chem. Soc.*, 1931, **8**, 277) announced the isolation of four forms of 4-methylcyclohexane-1-acetic-2-carboxylic acid, but this has been corrected by Goldschmidt and Gräfinger (*Ber.*, 1935, **68**, 279).   Zelinsky and Tarassowa (*Annalen*, 1934, **508**, 115) obtained what appeared to be two acetylcyclohexanes, but the possibility that one of these is an acetyl-methylcyclopentane is not excluded by the experimental evidence and is, indeed, quite reasonable, for the ketone was formed by a reaction involving the use of aluminium chloride. There remains the statement of Khuda (*Nature*, 1933, **132**, 210) that ββ-dimethylcyclohexanone exists in two forms.

The well-known form of this ketone (semicarbazone, m. p. 195°), first prepared from ββ-dimethylpimelic acid, was obtained by Crossley and Renouf (J., 1907, **91**, 63) by an indirect reduction of dimethyldihydroresorcinol.   Khuda reduced this substance directly by the Clemmensen method to an isomeric monoketone (semicarbazone, m. p. 162°). No details of this work have appeared, and as the Clemmensen reduction of cyclic 1 : 3-diketones was under study in these laboratories for synthetic purposes, it became necessary to re-examine these substances.

We find that dimethyldihydroresorcinol is reduced by Crossley's and Khuda's procedures to two different saturated monocyclic ketones, $C_8H_{14}O$, the semicarbazones of which melt at 195° and 168°.   Crossley's ketone is undoubtedly 3 : 3-dimethylcyclohexanone, and its oxidation to ββ-dimethyladipic acid has been confirmed.   The Clemmensen reduction yielded the new ketone, together with a fully reduced hydrocarbon as by-product.   Both the ketone and the hydrocarbon had lower b. p.'s, densities, and refractive indices than the authentic cyclohexane isomerides (see table), and the differences were so large as to suggest that the new compounds contained a smaller ring.

The second ketone was oxidised by potassium permanganate to αα-dimethylsuccinic acid, and by nitric acid to a mixture of this and ααα'-trimethylglutaric acid.   No dimethyl-adipic acid could be detected.   This suggested that the ketone was 2 : 4 : 4-trimethylcyclopentanone, which had been made by Wallach (*Annalen*, 1918, **414**, 331), and the close agreement between the properties of the two ketones supports the suggestion.

Ketone.	B. p.	$d_{4°}^{18°}$.	$n_D^{18°}$.	M. p. of semicarbazone.
3 : 3-Dimethylcyclohexanone	175°/757 mm.	0·907 *	1·448 *	195° (decomp.)
2 : 4 : 4-Trimethylcyclopentanone † ...	160—161	0·8785	1·433	171—173°
" Clemmensen ketone "	160/768 mm.	0·879	1·433	168 (no decomp.)

* v. Auwers and Lange, *Annalen*, 1913, **401**, 325.   † Wallach (*loc. cit.*).

(The experimental figures have been corrected for temperature to facilitate comparison.)

Conclusive proof of structure was provided by the oxidation of the " Clemmensen ketone " by Beckmann's mixture to γ-acetyl-ββ-dimethylbutyric acid (cf. Wallach, *loc. cit.*), which was identified by a comparison of its semicarbazone with a synthetic sample. The keto-acid was synthesised for this purpose by adding malonic ester to mesityl oxide, and hydrolysing and decarboxylating the product.   Hence the Clemmensen reduction of

dimethyldihydroresorcinol is accompanied by a molecular rearrangement, and the ketonic product is 2 : 4 : 4-trimethyl*cyclo*pentanone.

There is therefore no satisfactory evidence for the existence of isomeric *cyclo*hexane compounds derived from the " C " and from the " Z " form of the ring. It appears that the energy required for the interconversion of such forms is so small (Mills) that their isolation as separate individuals under ordinary conditions is not possible, and the number of isolable isomerides is that which would be expected if the ring were planar. The isolation of a greater number than this (cf., *e.g.*, Desai and Hunter, *Nature*, 1935, **135**, 434) must therefore be viewed with caution both on theoretical grounds and in the light of the present work and that of Goldschmidt and Gräfinger.

The positive result of this work—the discovery that the carbon skeleton of a diketone can be rearranged during reduction—is new, although the change of the *cyclo*hexane into the methyl*cyclo*pentane system is well established through the work of Hantzsch, Zincke, Wallach, Zelinsky, Nenitzescu, and others. It is intended to investigate further the structural factors necessary for this change, which has some formal resemblance to the pinacone–pinacolin and the Wagner–Meerwein rearrangement.

EXPERIMENTAL.

3 : 3-Dimethyl*cyclo*hexanone, prepared by Crossley and Renouf's method (*loc. cit.*), yielded a semicarbazone which crystallised from dilute methanol in thin needles, m. p. 195—196° (charring). From this, the ketone was regenerated in good yield, b. p. 174—175°/757 mm. The pure ketone (2·50 g.) was oxidised on the steam-bath under reflux with 450 c.c. of 3% potassium permanganate, added during 41 hrs. The crude dimethyladipic acid was isolated following Crossley and Renouf, and purified by extraction with cold chloroform and several crystallisations from water. If formed bold, transparent prisms, m. p. 88°, alone or admixed with an authentic sample. It gave Crossley and Renouf's colour reaction with resorcinol, and yielded 3 : 3-dimethyl-*cyclo*pentanone on cyclisation [semicarbazone, m. p. 177—178°; Blanc (*Bull. Soc. chim.*, 1908, **3**, 778) gives 178—179°].

Clemmensen Reduction.—Dimethyldihydroresorcinol (25 g.) was refluxed for 6 hours with 100 g. of amalgamated zinc and 150 c.c. of concentrated hydrochloric acid. The solution, at first clear, became opalescent, then dirty-green, and finally an oily layer separated. This was removed with ether, and the extract washed successively with ammonium sulphate solution, dilute alkali, and water, dried, and distilled. Practically all the material was contained in two fractions, b. p. 95—130° and 160—175°. The first fraction after two distillations boiled at 110°/754 mm.; it was washed with sodium bisulphite, dried (potassium carbonate), and distilled over sodium. It then had b. p. 106—107°/767 mm., $n_D^{18\cdot0°}$ 1·4240, $d_{4°}^{18\cdot0°}$ 0·7764, $[R_L]_D$ 36·84 (Calc., 36·94). [For 1 : 1-dimethyl*cyclo*hexane, v. Auwers and Lange (*Annalen*, 1915, **409**, 150) give b. p. 125°/761 mm.; $n_D^{17°}$ 1·4310, $d_{4°}^{17°}$ 0·7851. For 1 : 1 : 3-trimethyl*cyclo*pentane, Zelinsky and Uspenski (*Ber.*, 1913, **46**, 1470) give b. p. 115—116°/760 mm., $n_D^{20°}$ 1·4223, $d_{4°}^{20°}$ 0·7703.]

The second fraction was distilled twice, and boiled almost completely at 159—162°. This fraction (2·83 g.) had $n_D^{14\cdot1°}$ 1·4365, $d_{4°}^{14\cdot1°}$ 0·8839, $[R_L]_D$ 37·30 (Calc., 36·96) (Found : C, 76·0; H, 10·8. Calc. for $C_8H_{14}O$: C, 76·1; H, 11·2%).

It did not decolorise bromine in chloroform, or neutral or acid permanganate. The smell was stronger and more peppermint-like than that of Crossley's ketone. The semicarbazone, m. p. (crude) 164°, formed glistening leaflets from dilute methanol, m. p. 168°. It was much more soluble in alcohol than Crossley's semicarbazone and, unlike the latter, did not decompose on melting. Addition of light petroleum to its ethereal solution precipitated it as a crystalline powder (Found : C, 58·9; H, 9·4; N, 22·9. Calc. for $C_9H_{17}ON_3$: C, 59·0; H, 9·3; N, 22·9%). From it, by means of oxalic acid, the ketone was regenerated almost quantitatively, b. p. 160°/768 mm., $n_D^{15\cdot6°}$ 1·4347, $d_{4°}^{15\cdot6°}$ 0·8813, $[R_L]_D$ 37·31 (Found : C, 76·1; H, 11·2. Calc. : C, 76·1; H, 11·2%). This yielded the same semicarbazone (m. p. 167°).

Oxidation.—(1) 1·4 G. of the ketone were warmed with a mixture of 12·5 c.c. each of concentrated nitric acid and water. After the vigorous reaction had subsided, the mixture was warmed for ½ hr. (steam-bath) under reflux, and then evaporated to dryness. The residue was extracted with chloroform, and the extract left in a vacuum desiccator. The sticky solid obtained from the extract was triturated with small amounts of light petroleum. Evaporation of the petroleum left a hard solid, which crystallised from hydrochloric acid in clusters of transparent, flattened

needles, which melted sharply at 98°, depressed the m. p. of ββ-dimethylglutaric acid, and had the properties of ααα'-trimethylglutaric acid (Found : C, 54·7; H, 8·0. Calc. : C, 55·2; H, 8·1%). The residue insoluble in light petroleum was crystallised from hydrochloric acid and boiled with a little benzene. The insoluble portion was identified as αα-dimethylsuccinic acid (m. p. and mixed m. p.).

(2) 3·15 G. of ketone were oxidised during 45 hrs. with 700 c.c. of warm 3% potassium permanganate, added in small portions. The product was filtered, decolorised with sulphur dioxide, evaporated to dryness, and the residue acidified with concentrated hydrochloric acid and extracted first with ether and then with acetone. The residue from the ethereal extract, which smelt strongly of acetic acid, was ground with light petroleum and left on a porous tile. The hard solid (1·85 g.) was boiled with benzene (in which it was sparingly soluble) and crystallised from water, αα-dimethylsuccinic acid being obtained, m. p. and mixed m. p. 142°. Only a trace of lower-melting and more soluble material could be isolated. The acetone extract gave the same acid (1·2 g.).

(3) The ketone was oxidised with Beckmann's mixture, following Wallach (*loc. cit.*). The ethereal solution of the product was extracted with dilute alkali, acidified, and again extracted with ether. The residue from the ether gave the semicarbazone of γ-acetyl-ββ-dimethylbutyric acid in excellent yield, as glassy prismatic aggregates, m. p. 172° alone or admixed with synthetic material (below).

Synthesis of γ-Acetyl-ββ-dimethylbutyric Acid.—This substance has been made by Khuda (J., 1929, 206) by the interaction of ethyl cyanoacetate or cyanoacetamide and mesityl oxide. The preparation by the use of malonic ester proceeds equally well. A mixture of mesityl oxide (98 g.), malonic ester (160 g.), sodium ethoxide (from 2·3 g. sodium and 25 c.c. of alcohol), and ether (100 c.c.) was refluxed for 24 hrs. The product was neutralised with the calculated quantity of alcoholic hydrogen chloride, and the solvents removed under reduced pressure. On distillation, the residue yielded 50% of ethyl α-carbethoxy-γ-acetyl-ββ-dimethylbutyrate, b. **p.** 160°/20 mm. (Khuda, *loc. cit.*) (Found : C, 60·2; H, 8·4. Calc. : C, 60·5; H, 8·5%). This was converted through the malonic acid into γ-acetyl-ββ-dimethylbutyric acid, the semicarbazone of which melted at 172° (Found : C, 50·1, 50·0; H, 7·8, 7·7; N, 18·8. Calc. : C, 50·2; H, 7·3; N, 19·5%).

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