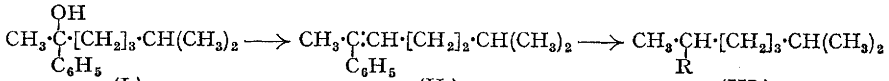
# **12.** *The Synthesis of* 2-cyclo*Hexyl*-6-*methylheptane.*

By D. H. Hey and D. S. Morris.

2-cyclo*Hexyl*-6-*methylheptane* has been prepared by the catalytic reduction of 2-*phenyl*-6-*methylhept*-2-*ene*, which was obtained from the action of phenylmagnesium bromide on methylheptanone. The action of *cyclo*hexylmagnesium halides on methylheptanone appears to result in the self-condensation of the ketone. *cyclo*Hexylmagnesium halides effect the self-condensation of ethyl phenylacetate to give ethyl αγ-diphenylacetoacetate; the action of bromine on the latter gives *αγ-diphenyltetronic acid.*

2-cyclo*Hexyl*-6-*methylheptane* (III, R = *cyclo*hexyl) has been prepared from 6-methylheptan-2-one, which reacted with phenylmagnesium bromide to give *phenylmethyl*iso*hexylcarbinol* (I); dehydration of this with formic acid gave an unsaturated hydrocarbon regarded as 2-*phenyl*-6-*methylhept*-2-*ene* (II), which was catalytically reduced at room temperature and pressure to 2-*phenyl*-6-*methylheptane* (III, R = $C_6H_5$). The further catalytic reduction of the latter under more drastic conditions gave 2-*cyclo*hexyl-6-methylheptane (III, R = *cyclo*hexyl).



$$CH_3\cdot\underset{C_6H_5}{\overset{OH}{C}}\cdot[CH_2]_3\cdot CH(CH_3)_2 \longrightarrow CH_3\cdot\underset{C_6H_5}{C}{:}CH\cdot[CH_2]_2\cdot CH(CH_3)_2 \longrightarrow CH_3\cdot\underset{R}{CH}\cdot[CH_2]_3\cdot CH(CH_3)_2$$

(I.) (II.) (III.)

The pure 6-methylheptan-2-one required in the above work was prepared by the method of Verley (*Bull. Soc. chim.*, 1899, **17**, 176), whereby methylheptenone, obtained from citral by boiling under reflux with aqueous sodium carbonate, is hydrogenated to the saturated ketone (cf. Wallach, *Annalen*, 1911, **381**, 86). It was not found practicable to obtain the pure ketone in quantity by the method of Clarke (*J. Amer. Chem. Soc.*, 1909, **31**, 107), using *iso*amyl halides and the sodium derivative of ethyl acetoacetate followed by ketonic hydrolysis. The ketone obtained by this method showed the correct boiling point, but invariably gave derivatives having low melting points, thus indicating the presence of mixtures. This is probably due to the presence of isomerides in the *iso*amyl alcohol used as one of the starting materials. Although Clarke claimed it to be unnecessary to purify the alcohol it is significant that he did not report the preparation of any ketonic derivatives in order to establish the purity of his product. It was found that pure methylheptanone could be obtained by this method only after a tedious fractional crystallisation of the semicarbazone followed by hydrolysis.

Attempts to obtain 2-*cyclo*hexyl-6-methylheptane by the direct action of *cyclo*hexylmagnesium chloride on methylheptanone, followed by dehydration and hydrogenation of the double bond, were unsuccessful, since the Grignard reagent appeared to bring about self-condensation of the methylheptanone. Hickinbottom and Schlüchterer (*Nature*, 1945, **155**, 19) have recently drawn attention to the fact that certain Grignard reagents, such as *tert.*-butylmagnesium chloride, ethylmagnesium bromide, and phenylmagnesium bromide, will effect the self-condensation of methyl *tert.*-butyl ketone. More recently Shine and Turner (*Nature*, 1946, **158**, 170) have reported the formation of 2 : 4 : 8-trimethylnon-4-en-6-one from *iso*propylmagnesium bromide and methyl *iso*butyl ketone. *iso*Propylmagnesium bromide readily effects the self-condensation of ethyl phenylacetate and ethyl *p*-chlorophenylacetate (Conant and Blatt, *J. Amer. Chem. Soc.*, 1929, **51**, 1227; Ivanov and Spasov, *Bull. Soc. chim.*, 1931, **49**, 375). It is now shown that *cyclo*hexylmagnesium halides will also bring about the self-condensation of ethyl phenylacetate to give ethyl αγ-diphenylacetoacetate in good yield. Before the identity of the latter compound was known it was subjected to the action of bromine in glacial acetic acid solution. In the resulting reaction hydrogen bromide was evolved and a crystalline acidic product was obtained. Dimroth and Eble (*Ber.*, 1906, **39**, 3928) have reported the isolation of α-phenyltetronic acid from the product of the action of bromine on ethyl α-phenylacetoacetate and, by analogy, the above-mentioned acidic product is regarded as *αγ-diphenyltetronic acid*, which is in agreement with the analytical figures.

## Experimental.

6-*Methylheptan*-2-*one*.—(a) *From citral.* Using the conditions given by Verley (*loc. cit.*), citral (250 g.) was boiled under reflux with 10% aqueous potassium carbonate (2,500 c.c.) for 12 hours and subsequently distilled with steam. The methylheptanone was extracted from the distillate, dried, and distilled (120 g., b. p. 80—84°/26 mm.; semicarbazone, m. p. 135—136°). After hydrogenation at room temperature and pressure in presence of platinum oxide catalyst and subsequent distillation through a 12-inch Fenske column, methylheptanone was obtained (92 g., b. p. 164—164·5°/757 mm., $n_D^{19°}$ 1·4144; semicarbazone, m. p. 154—155°; 2 : 4-dinitrophenylhydrazone, m. p. 77°).

(b) *From ethyl* iso*amylacetoacetate.* *iso*Amyl alcohol was fractionally distilled with a 12-inch Dufton column and the fraction, b. p. 130—131°/763 mm., collected. This fraction was converted into the iodide by the method of Clarke (*loc. cit.*), into the bromide using either phosphorus tribromide (*Org. Synth.*, 1933, **13**, 20) or hydrobromic acid and sulphuric acid (*ibid.*, Coll. Vol. I, 27), and into the chloride by the method of Whitmore, Karnatz, and Popkin (*J. Amer. Chem. Soc.*, 1938, **60**, 2540). The three halides were separately treated with ethyl acetoacetate and sodium by the method of Conrad and Limpach (*Annalen*, 1878, **192**, 153). The chloride did not react but the bromide and iodide gave crude ethyl *iso*amylacetoacetate in good yield (b. p. 117—119°/16 mm.). The esters thus obtained were treated with cold 5% aqueous sodium hydroxide and then acidified with 50% sulphuric acid (cf. *Org. Synth.*, Coll. Vol. I, 351). The crude ketones thus obtained were dried and fractionated twice with a 12-inch Fenske column. The final product had b. p. 165—165·5°/760 mm., $n_{\mathrm{D}}^{19^\circ}$ 1·4173 (Clarke, *loc. cit.*, records b. p. 165°, and Wallach, *loc. cit.*, $n_{\mathrm{D}}^{19^\circ}$ 1·4144), but the semicarbazone melted at 148—149° after repeated crystallisation (Wallach, *loc. cit.*, records m. p. 157—158°), and the 2 : 4-dinitrophenylhydrazone at 66—67° (Allen, *J. Amer. Chem. Soc.*, 1930, **52**, 2955, records m. p. 77°). The ketones were converted into semicarbazones, and fractional crystallisation from ethyl alcohol gave a product, m. p. 154—155°, both alone and on admixture with an authentic specimen prepared by method (a). The pure semicarbazone (63 g.) was hydrolysed by boiling it under reflux with a solution of oxalic acid (60 g.) in water (300 c.c.) for 30 minutes, and the liberated ketone was removed in steam. The resulting methylheptanone, which was obtained in almost quantitative yield, had the same constants as those recorded above for the product obtained by method (a).

*Phenylmethyl*iso*hexylcarbinol.*—Methylheptanone (30 g.) in ether (30 c.c.) was slowly added to a well-cooled solution of phenylmagnesium bromide, prepared from bromobenzene (74 g.), magnesium (11·4 g.), and ether (150 c.c.). The mixture was boiled gently under reflux for 4 hours and, after standing overnight, was worked up in the usual manner. The resulting oil was collected at 125—143°/7—10 mm. (46 g.), and on redistillation the *carbinol* was obtained as a colourless oil (36 g.), b. p. 128—132°/5 mm. (Found : C, 82·5; H, 10·3. $C_{14}H_{22}O$ requires C, 81·5; H, 10·7%).

2-*Phenyl*-6-*methylhept*-2-*ene.*—The carbinol (36 g.) was shaken with 98% formic acid (25 c.c.) and allowed to stand for 24 hours. The product was washed with water and with aqueous sodium carbonate. Distillation of the dried product gave 2-*phenyl*-6-*methylhept*-2-*ene* (26·4 g.) as a colourless oil, b. p. 252—254°, $n_{\mathrm{D}}^{16^\circ}$ 1·5213 (Found : C, 89·3; H, 10·4. $C_{14}H_{20}$ requires C, 89·4; H, 10·6%). Oxidation with a warm solution of chromic anhydride in acetic acid gave acetophenone, identified as the 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 244—245°.

2-*Phenyl*-6-*methylheptane.*—The heptene (5·6 g.) in ethyl alcohol (25 c.c.) was hydrogenated at atmospheric pressure and temperature over platinum oxide (0·1 g.). After absorption of one molecular equivalent of hydrogen the product was distilled, and 2-*phenyl*-6-*methylheptane* (4·9 g.) was collected as a colourless oil, b. p. 235—238°, $n_{\mathrm{D}}^{16^\circ}$ 1·4893 (Found : C, 88·4; H, 11·4. $C_{14}H_{22}$ requires C, 88·4; H, 11·6%)

2-cyclo*Hexyl*-6-*methylheptane.*—2-Phenyl-6-methylheptane (33 g.) in glacial acetic acid (250 c.c.) was hydrogenated over platinum oxide (2·5 g.) at 100° and 100—135 atmospheres for 24 hours. Distillation of the product gave 2-cyclo*hexyl*-6-*methylheptane* (30 g.) as a colourless liquid, b. p. 240—245°, $n_{\mathrm{D}}^{17^\circ}$ 1·4569 (Found : C, 85·5; H, 14·3. $C_{14}H_{28}$ requires C, 85·7; H, 14·3%).

*Action of* cyclo*Hexylmagnesium Chloride on Methylheptanone.*—A solution of methylheptanone (23 g.) in ether (25 c.c.) was slowly added to a well-cooled solution of *cyclo*hexylmagnesium chloride, prepared from *cyclo*hexyl chloride (23·7 g.), magnesium (5·35 g.), and ether (90 c.c.). The preparation of the Grignard reagent was found to be adversely affected to a marked degree by the presence of traces of aluminium in the magnesium. The solution was boiled under reflux for 30 minutes, and after standing overnight the product was worked up in the usual manner. An oil (36·7 g.) was obtained which boiled with some decomposition at 6 mm., but by distillation at 1 mm. the major fraction (22·1 g.) was collected at 125—128° as a colourless oil. Dehydration with 98% formic acid, as described above, gave a product, b. p. 50—80°/3—4 mm., which showed an equivalent of 120 on titration with pyridine sulphate dibromide, as described by Rosenmund (*Z. angew. Chem.*, 1924, **37**, 58). The equivalent for 2-*cyclo*hexyl-6-methylhept-2-ene is 97, and that for the condensation product resulting from two molecules of methylheptanone by loss of water is 119.

*Action of* cyclo*Hexylmagnesium Halides on Ethyl Phenylacetate.*—A solution of ethyl phenylacetate (13·5 g.) in ether (15 c.c.) was slowly added to a well-cooled solution of *cyclo*hexylmagnesium chloride, prepared from *cyclo*hexyl chloride (23·7 g.), magnesium (5·35 g.), and ether (90 c.c.). The mixture was boiled under reflux for 45 minutes and allowed to stand overnight. On working up in the usual manner, evaporation of the ether deposited ethyl αγ-diphenylacetoacetate as a crystalline solid (7·9 g., m. p. 71—72°), which crystallised from light petroleum (b. p. 40—60°)-benzene in colourless needles, m. p. 77—78° (Found : C, 76·8; H, 6·4. Calc. for $C_{18}H_{18}O_3$ : C, 76·6; H, 6·4%). Conant and Blatt (*loc. cit.*) record m. p. 78° for ethyl αγ-diphenylacetoacetate. The same product was obtained when *cyclo*hexyl bromide was used in place of the chloride.

*Action of Bromine on Ethyl αγ-Diphenylacetoacetate.*—A solution of bromine (3·2 g.) in glacial acetic acid (20 c.c.) was added to a solution of the ester (5·7 g.) in the same solvent (70 c.c.). Hydrogen bromide was evolved and a crystalline deposit (4 g., m. p. 201—205°) separated on removal of most of the acetic acid under reduced pressure. The product was soluble in aqueous alkalis, but insoluble in acids. Recrystallisation from acetic acid gave *αγ-diphenyltetronic acid* in prisms, m. p. 204—205° [Found : C, 75·9; H, 4·8; equiv. (by silver salt), 253. $C_{16}H_{12}O_3$ requires C, 76·2; H, 4·8%; equiv., 252].

British Schering Research Institute,
Alderley Edge, Cheshire.

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