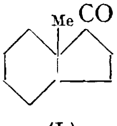
148. 2 : 2-*Dimethyl*cyclo*hexylacetic Acid.*

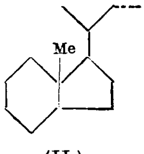
By G. H. Elliott and R. P. Linstead.

In connection with the synthesis of compounds containing a side chain similar to that present in the bile acids, 2 : 2-dimethyl*cyclo*hexanone has been treated with ethyl bromoacetate and magnesium, and 2 : 2-dimethyl*cyclo*hexylidene- and 2 : 2-dimethyl*cyclo*hexyl-acetic acids prepared. The former yields 2 : 2-dimethyl*cyclo*hexanone on oxidation, hence no molecular rearrangement occurs during the preparation. The latter acid is identical with that prepared by Adamson, Marlow, and Simonsen (preceding paper).

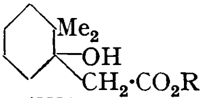
8-Methyl-1-hydrindanone (I) appeared a convenient starting point for the preparation of substances containing the carbon skeleton (II), which would serve as models for the synthesis of bile acids and similar compounds. Before employing this valuable ketone it seemed advisable to carry out parallel experiments on the more easily accessible 2 : 2-dimethyl*cyclo*hexanone, which also contains a quaternary carbon atom adjacent to a cyclic carbonyl group. What particularly interested us was whether it would be possible to dehydrate the hydroxy-ester (III, R = Et), obtained by the Reformatsky reaction, or the corresponding acid, without a retropinacolic change. The danger of this was indicated by Meerwein's well-known demonstration (*Annalen*, 1914, **405**, 142) that 2 : 2-dimethyl*cyclo*hexanol gave, *inter alia*, 1 : 2-dimethyl*cyclo*hexene on dehydration. By analogy, the dehydration product of (III) might be a 1 : 2-dimethyl*cyclo*hexenyl-1-acetic acid derivative.



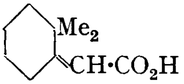
(I.)



(II.)



(III.)



(IV.)

To avoid this, the crystalline hydroxy-acid (III, R = H) was dehydrated with acetic anhydride, following Wallach (*Annalen*, 1909, **365**, 261). This yielded 2 : 2-*dimethyl*-cyclo*hexylideneacetic acid* (IV) as a crystalline solid, the structure of which was proved by its oxidation to 2 : 2-dimethyl*cyclo*hexanone.

At this stage in our work, Professor Simonsen informed us of his parallel experiments, described in the preceding paper. To unite the two pieces of work we reduced our αβ-unsaturated acid (IV). The 2 : 2-dimethyl*cyclo*hexylacetic acid so obtained melted rather higher than the material prepared by Adamson, Marlow, and Simonsen (preceding paper), but the identity of the products was proved by comparison of the crystalline *p*-phenylphenacyl esters.

We also examined the reaction between 2 : 2-dimethyl*cyclo*hexanone and ethyl α-bromopropionate under Reformatsky conditions, but the yield was poor, and such reactions on ketones containing shielded carbonyl groups do not at the moment appear particularly promising for synthetic purposes.

EXPERIMENTAL.

Crude 2 : 2-dimethyl*cyclo*hexanone (Cornubert, Borrel, and Le Bihan, *Bull. Soc. chim.*, 1931, **49**, 1381) was purified through the 6-carboxylic ester as follows: A mixture of 200 g. of the crude ketone (b. p. 68—73°/21 mm.) with 250 g. of ethyl oxalate was treated at −10° during 2 hours with sodium ethoxide (34 g. of sodium and 520 c.c. of absolute alcohol). The product was kept for 2 days at 0° and for a day at room temperature, moisture being excluded, and then poured into a slight excess of dilute acid. The material extracted by ether was washed with water, dried (sodium sulphate), freed from solvent and low-boiling substances, and heated under reflux at 200° until no more carbon monoxide came off. Two fractionations of the product gave 103 g. of the 6-carboxylic ester, b. p. 125—128°/20 mm. This was hydrolysed and decarboxylated at the b. p. with an equal weight of baryta dissolved in 10 parts of water. 2 : 2-Dimethyl*cyclo*hexanone, isolated by means of ether, boiled at 67°/19 mm. (49 g.) and yielded a semicarbazone, m. p. 203° (Meerwein, *loc. cit.*, gives 201°).

18 G. of the pure ketone were warmed with ethyl bromoacetate (38 g.) and magnesium (5 g.) in 75 c.c. of dry benzene. After the vigour of the reaction had abated the mixture was refluxed for an hour, and the hydroxy-ester isolated in the usual manner. This was hydrolysed without purification with 80 c.c. of 20% aqueous potassium hydroxide in the cold for 24 hours and the crude acid, freed from neutral material, was esterified with 100 c.c. of 7% alcoholic sulphuric acid (6 hours at the b. p.). The *ethyl* 1-*hydroxy*-2 : 2-*dimethyl*cyclo*hexyl*-1-*acetate* (III, R = Et) (5·5 g.) was isolated by distillation, b. p. 136—140°/16 mm. (Found: C, 66·9; H, 10·3. $C_{12}H_{22}O_3$ requires C, 67·3; H, 10·4%). This procedure separates the hydroxy-ester from auto-condensation products of the ketone. Hydrolysis of the pure ester with cold alcoholic potash yielded the corresponding *acid* (III, R = H), which immediately solidified; it formed rhombs from benzene–petrol, m. p. 99—100° (Found: C, 64·7; H, 9·9. $C_{10}H_{18}O_3$ requires C, 64·5; H, 9·7%).

The hydroxy-acid (3·2 g.) was refluxed for 3 hours with 8 c.c. of acetic anhydride. The unsaturated acid, isolated from the product by distillation in steam and extraction with ether, rapidly solidified. Yield, 2·0 g. 2 : 2-*Dimethyl*cyclo*hexylideneacetic acid* (IV) formed needles, m. p. 91—92°, from dilute acetic acid (Found: C, 71·3; H, 9·7. $C_{10}H_{16}O_2$ requires C, 71·4; H, 9·6%). In keeping with the αβ-position of the double bond, a solution of the acid in aqueous sodium bicarbonate did not decolourise one of iodine in potassium iodide.

The unsaturated acid (1 g.), dissolved in a little water containing sodium bicarbonate (0·8 g.), was treated slowly with 55 c.c. of 3% aqueous potassium permanganate. After an hour the product was distilled in steam. The ketone was isolated by means of ether and identified as 2 : 2-dimethyl*cyclo*hexanone by conversion into the semicarbazone, m. p. and mixed m. p. 202—203°.

The acid (250 mg.) was reduced over Adams's catalyst in acetic acid, the theoretical quantity of hydrogen being absorbed within 24 hours. The solvent was removed at 60°, and the product, isolated by means of ether, crystallised immediately. 2 : 2-Dimethyl*cyclo*hexylacetic acid formed fern-shaped aggregates of needles, m. p. 45° (crude), 47° after crystallisation from dilute acetic acid. The *p*-phenylphenacyl ester, after crystallisation from ethyl alcohol, melted at 86—87°, alone or in admixture with a specimen kindly supplied by Professor Simonsen.

Condensation of 2 : 2-dimethyl*cyclo*hexanone with ethyl α-bromopropionate and magnesium under various conditions gave poor yields of hydroxy-ester. In one series of experiments 18 g. of the ketone yielded 5 g. of crude hydroxy-ester after hydrolysis and re-esterification by the method described above. This boiled at 100—140°/18 mm. and on hydrolysis yielded a gummy acid, which on dehydration with acetic anhydride gave 2 g. of an acid volatile in steam, which failed to solidify (Found: equiv., 187. $C_{11}H_{18}O_2$ requires equiv., 182·1).

We are indebted to Professor J. L. Simonsen, F.R.S., for the opportunity of comparing the products made by the two routes.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,
LONDON. S.W. 7.

[*Received, April 6th*, 1938.]