189. *A Synthesis of* cis- *and* trans-dl-1 : 1-*Dimethyl*-2-γ-*ketobutyl*cyclo*propane*-3-*carboxylic Acids.*

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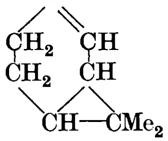
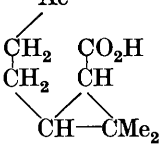
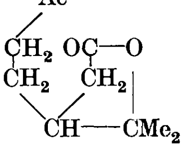
THE constitutional formulæ which have been assigned to the two dicyclic hydrocarbons, *d*-Δ^3-carene and *d*-Δ^4-carene, are based in part on their degradation by oxidation to a number of *cyclo*propane acids, of which only the simplest, caronic acid, has been synthesised. We now describe the synthesis of the *cis*- and *trans*-modifications of dl-1 : 1-*dimethyl*-2-γ-*ketobutyl*cyclo*propane*-3-*carboxylic acid* (II), a dextrorotatory form of which was obtained by the oxidation of Δ^4-carene (I) with potassium permanganate (J., 1922, **121**, 2292).


(I.)


(II.)

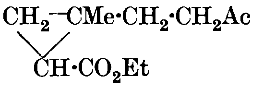

(VII.)

The methods which are available for the synthesis of *cyclo*propane acids with long side chains are somewhat limited, but we have found that the ethyl ester of the required keto-acid can be prepared readily by the condensation of methylheptenone with ethyl diazoacetate in the presence of copper-bronze.* As is now well established, methylheptenone is not homogeneous, but is a mixture of the two ketones represented by (III) and (IV), in which the former largely predominates. It was therefore anticipated that the condensation product might be a mixture of the structurally isomeric esters (V) and (VI).

(III.) $CMe_2{:}CH{\cdot}CH_2{\cdot}CH_2Ac$

(V.)

(IV.) $CH_2{:}CMe{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2Ac$



(VI.)

No evidence of the presence of an ester having the structure (VI) was however obtained. Hydrolysis of the crude condensation product gave a mixture of a liquid and a crystalline acid which could be readily separated by the fractional crystallisation of their semicarbazones, m. p. 193—194° and 223—224° respectively. By hydrolysis of the semicarbazones the corresponding acids were obtained, that from the higher-melting being crystalline, m. p. 78—79°, whilst the lower-melting gave a liquid keto-acid. The two acids must be the stereoisomeric modifications of dl-1 : 1-*dimethyl*-2-γ-*ketobutyl*cyclo*propane*-3-*carboxylic acid* (II), since they both on hydration with dilute sulphuric acid yield *dl*-homoterpenyl methyl ketone (VII), and in accordance with the usual convention the higher-melting acid is assumed to have the *trans*-configuration, although no direct proof of this has been obtained. The hydration of these two keto-acids to the keto-lactone is the first synthesis of this important degradation product of α-terpineol and α-pinene and the identity of the lactone itself and of its semicarbazone was established by direct comparison with specimens prepared from *dl*-pinonic acid. We found the semicarbazone to have a somewhat higher m. p. 206—207° than that recorded by Wallach (*Annalen*, 1896, **291**, 343).

By oxidation with sodium hypobromite the two keto-acids were converted into the corresponding dibasic acids, cis- and trans-dl-3-*carboxy*-1 : 1-*dimethyl*cyclo*propane*-2-*propionic acids*, m. p. 131—132° and 107—108°, the constitutions of which were confirmed by their hydration to homoterpenylic acid.

Since the keto-acid and the corresponding dibasic acid obtained

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* This condensation was first investigated by Dr. K. N. Menon at the Indian Institute of Science in 1927. We desire to thank him for his assistance.

by the oxidation of *d*-Δ^4-carene were dextrorotatory, no direct proof of their structural identity with the synthetic acids described in this paper can be offered. There would, however, appear to be little doubt that they are the dextrorotatory modifications of the *cis*-acid and it is proposed to confirm this by the resolution of the synthetic acids.

During the hydrolysis of the condensation ester referred to above with methyl-alcoholic potassium hydroxide solution a sparingly soluble potassium salt separated. From this a crystalline acid was obtained, decomp. 286°, which analysis and a molecular weight determination of the *methyl* ester showed to be a tetrabasic acid, $C_4H_4(CO_2H)_4$. There can be little doubt that the acid is cyclo*butane*-1 : 2 : 3 : 4-*tetracarboxylic acid* formed by the decomposition and interaction of four molecules of ethyl diazoacetate.

EXPERIMENTAL.

Condensation of Methylheptenone and Ethyl Diazoacetate.—To methylheptenone (60 g.) and copper-bronze (2 g.), ethyl diazoacetate (20 g.) was gradually added, the mixture being gently warmed on the water-bath to start the condensation, which proceeds smoothly at 45—50°. (If this temperature is exceeded, the reaction may proceed with explosive violence.) After the evolution of nitrogen had ceased (6 hours), the product from two such condensations was distilled under diminished pressure (17 mm.); after removal of unchanged methylheptenone (93 g.), a fraction (40 g.), b. p. 90—150°, was obtained. This was mixed with methyl-alcoholic potassium hydroxide solution (KOH, 15 g.) and heated under reflux for 2 hours; a small quantity of a sparingly soluble potassium salt (A) then separated. This was collected, and the filtrate distilled in steam to remove unchanged methylheptenone. The residue from the steam distillate was concentrated and acidified, and the solution extracted with ether; the ethereal extract was washed with sodium carbonate solution, dried, and evaporated, leaving a small quantity of methylheptenone. The sodium carbonate washings were acidified and the oil which separated was extracted with ether, the solution dried, and the solvent removed. The viscid brown oil (19 g.) obtained partly crystallised on keeping. The solid acid (14 g.) was freed as far as possible from the oil (4 g.) by filtration and the two fractions were converted separately into the semicarbazones. By crystallisation from methyl alcohol two semicarbazones, m. p. 180—183° (5·1 g.) and 201—205° (17·4 g.), were obtained.

dl-trans-1 : 1-*Dimethyl*-2-γ-*ketobutyl*cyclo*propane*-3-*carboxylic acid semicarbazone.* When the more sparingly soluble and higher-melting *semicarbazone* was recrystallised from methyl alcohol, it separated in prisms, decomp. 223—224° (Found : C, 54·8; H, 7·9. $C_{11}H_{19}O_3N_3$ requires C, 54·8; H, 7·9%). For the preparation of the acid, the semicarbazone (5 g.) was heated with sulphuric acid (70 c.c.; 5%) on the water-bath for 4 hours. The cooled solution, after saturation with ammonium sulphate, deposited a crystalline acid; this was dissolved in ether, the ethereal solution dried and evaporated, and the solid residue recrystallised from hot water. dl-trans-1 : 1-*Dimethyl*-2-γ-*ketobutyl*cyclo*propane*-3-*carboxylic acid* crystallised in leaflets which, under the microscope, were seen to consist of bayonet-shaped needles, m. p. 78—79° (Found : C, 64·9; H, 8·9; *M*, 185·2. $C_{10}H_{16}O_3$ requires C, 65·2; H, 8·7%; *M*, 184).

The *oxime* crystallised from hot water in rosettes of stout prismatic needles, m. p. 114° (Found : C, 60·1; H, 8·8. $C_{10}H_{17}O_3N$ requires C, 60·3; H, 8·5%).

dl-trans-3-*Carboxy*-1 : 1-*dimethyl*cyclo*propane*-2-*propionic acid.* A solution of the keto-acid (5 g.) in aqueous sodium hydroxide (NaOH, 1·5 g.) was added all at once to a well-cooled solution of sodium hypobromite (275 c.c.; NaOH, 15 g.; Br_2, 20 g.). The solution immediately became cloudy and after remaining at room temperature for 2 hours the bromoform was separated, the excess of hypobromite removed with sulphur dioxide, and the solution acidified, saturated with ammonium sulphate, and repeatedly extracted with ether. On removal of the dried solvent an oil remained which rapidly solidified. It was purified by two crystallisations from hot water, from which it separated in conglomerates of hard prisms, m. p. 131—132°, sintering slightly below this temperature. The *acid* was readily soluble in hot water and benzene, more sparingly in the cold solvents, very readily in alcohol, acetic acid, formic acid, very sparingly in *cyclo*hexane. Its aqueous solution gave a sparingly soluble copper salt on the addition of copper acetate (Found : C, 58·4; H, 7·6; *M*, 186·1. $C_9H_{14}O_4$ requires C, 58·0; H, 7·5%; *M*, 186).

cis-dl-1 : 1-*Dimethyl*-2-γ-*ketobutyl*cyclo*propane*-3-*carboxylic acid semicarbazone.* The lower-melting and more soluble *semicarbazone* (p. 1426) was somewhat sparingly soluble in ethyl alcohol and crystallised therefrom in prismatic needles, decomp. 193—194° (Found : C, 54·6; H, 8·2. $C_{11}H_{19}O_3N_3$ requires C, 54·8; H, 7·9%).

On hydrolysis with dilute sulphuric acid the keto-acid was obtained as a colourless viscid oil, which was further characterised by the preparation of the *oxime.* This was a gum, which solidified after some weeks and then crystallised from water in small plates, m. p. 102° (Found : C, 60·4; H, 8·3. $C_{10}H_{17}O_3N$ requires C, 60·3; H, 8·5%).

cis-dl-3-*Carboxy*-1 : 1-*dimethyl*cyclo*propane*-2-*propionic acid*, prepared from the keto-acid by oxidation with sodium hypobromite under the same conditions as those used for the preparation of the *trans*-acid, crystallised from hot water, in which it was readily soluble, in prisms, m. p. 107—108°, sintering at 105°. It was readily soluble in the ordinary organic solvents except light petroleum. Its aqueous solution gave with copper acetate a sparingly soluble copper salt (Found: C, 57·8; H, 7·8; *M*, 187·2. $C_9H_{14}O_4$ requires C, 58·0; H, 7·5%; *M*, 186).

Conversion of cis- *and* trans-dl-1 : 1-*Dimethyl*-2-γ-*ketobutyl*cyclo*propane*-3-*carboxylic Acids into* dl-*Homoterpenyl Methyl Ketone*.—Since both forms of the keto-acid gave homoterpenyl methyl ketone on treatment with mineral acids, only one experiment need be described. The *trans*-acid (0·5 g.) was digested with sulphuric acid (15 c.c.; 20%) for 6 hours. The solution darkened somewhat and an oil separated. After being cooled and saturated with ammonium sulphate, the solution was extracted with chloroform, the extract dried, and the solvent removed. The residual oil was triturated with sodium carbonate solution, and the insoluble portion, which partly crystallised, redissolved in chloroform. After removal of the solvent the brown oil (0·3 g.) was mixed with semicarbazide acetate; the semicarbazone, which separated immediately, was collected, washed with ether to remove an oily impurity, and recrystallised from methyl alcohol, forming rhombs, decomp. 206—207°. This decomposition point was not depressed on admixture with an authentic specimen of *dl*-homoterpenyl methyl ketone semicarbazone (Found: C, 54·8; H, 8·1. Calc. for $C_{11}H_{19}O_3N_3$: C, 54·8; H, 7·9%).

A portion of the semicarbazone was hydrolysed with dilute sulphuric acid, and the resulting ketone recrystallised from water; *dl*-homoterpenyl methyl ketone then separated in prismatic needles, m. p. 63—64°, both alone and in admixture with a specimen prepared from *dl*-pinonic acid (Found: C, 65·0; H, 8·8. Calc. for $C_{10}H_{16}O_3$: C, 65·2; H, 8·7%).

Conversion of cis- *and* trans-dl-3-*Carboxy*-1 : 1-*dimethyl*cyclo*propane*-3-*propionic Acids into Homoterpenylic Acid*.—The *cis*-acid (0·5 g.), in concentrated hydrochloric acid (5 c.c.), was heated at 100° in a sealed tube for 5 hours. After removal of the mineral acid the residual brown oil was dissolved in hot water and filtered from insoluble matter (charcoal), and the water evaporated. A solid remained, which crystallised from ether in prisms, m. p. 99—100°. Its identity with homoterpenylic acid was confirmed by titration (Found: *M*, monobasic, 186. Calc., 186).

The *trans*-acid, when treated with hydrobromic acid (saturated at 0°), also gave homoterpenylic acid.

The sparingly soluble potassium salt (A) (p. 1426) was dissolved in water, the solution acidified and extracted with ether, the ethereal solution dried, and the solvent evaporated; a crystalline acid, mixed with a little oil, remained (1·5 g. from 224 g. of ethyl diazoacetate). The solid was collected, washed with ether, and recrystallised from hot water, in which it was somewhat sparingly soluble and from which it separated in serrated prisms, decomp. 287° (Found: C, 41·9; H, 3·8. $C_8H_8O_8$ requires C, 41·4; H, 3·4%). The *silver* salt, which separated from an ammoniacal solution of the acid as a white powder on the addition of silver nitrate (Found: C, 14·8; H, 0·8. $C_8H_4O_8Ag_4$ requires C, 14·6; H, 0·6%), was dried and converted into the methyl ester by digestion with methyl iodide in benzene solution. *Methyl* cyclo*butane*-1 : 2 : 3 : 4-*tetracarboxylate* crystallised from methyl alcohol in needles, m. p. 103° [Found: C, 50·1, 50·2; H, 5·8, 5·7; *M* (Rast), 279·8. $C_{12}H_{16}O_8$ requires C, 50·0; H, 5·6%; *M*, 288].

The authors are indebted to the Government Grants Committee of the Royal Society and to the Chemical Society for grants which have in part defrayed the cost of this investigation; they desire also to make acknowledgment to Imperial Chemical Industries. A maintenance grant from the Department of Scientific and Industrial Research has enabled one of them (J. O.) to take part in the investigation.

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[*Received, March 8th*, 1932.]