3. The synthesis of 2-hydroxy-4,6,3′,4′-tetramethoxy-3-phenylcoumarin is described.

4. The synthesis of tetramethyl-acacatechin previously described by the author and since then contested by Freudenberg has been repeated.

5. The chroman nucleus in pentamethyl-acacatechin is shown to undergo fission by the interaction of alkali and methylating reagents when β,γ-2,4,6,3′,4′-heptamethoxy-α,α-diphenylpropane is produced.

6. β,γ,2,4,6,3′,4′-Heptamethoxy-α,α-diphenylpropane has been synthesized.

7. The production of the α,α-diphenylacetic acid derivatives from acacatechin is emphasized, thus showing that the α,α,-diphenylpropane structure is the normal structure of acacatechin.

8. It is shown that 2-hydroxy-4,6,3′,4′-tetramethoxy-3-phenylcoumarin obtained from tetramethyl-acacatechin and 4,6,3′,4′-tetra-acetoxy-3-phenylcoumarin prepared by the action of acetic anhydride on maclurin yield the same substance when reacted on with hydriodic acid.

9. These observations confirm the formula assigned to acacatechin by the author.

BRISTOL, ENGLAND

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF OTAGO]

EXPERIMENTS ON THE SYNTHESIS OF APOFENCHOCAMPHORIC ACID. PREPARATION OF ALPHA, ALPHA-DIMETHYL-GAMMA-CARBOXYADIPIC ACID

BY KENNETH CHARLES ROBERTS

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Recent literature on the dicyclic terpenes contains several references[1] to a dibasic acid of the formula $C_9H_{14}O_4$. This acid is isomeric with apocamphoric acid, and has been named apofenchocamphoric acid. All the papers cited appear to regard it as having the constitution 4,4-dimethylcyclopentane-1,3-dicarboxylic acid but, since the constitutions of the substances from which the acid is obtained can in no case be regarded as definitely established, this tentative structure still remains to be proved. It has been the aim of the present investigation to synthesize 4,4-dimethylcyclopentane-1,3-dicarboxylic acid and thus prove, if possible, its identity with apofenchocamphoric acid.

By analogy with Perkin and Thorpe's synthesis of camphoric acid, it was thought that, if α,α-dimethyl-γ-carboxyadipic acid could be prepared, this could then be readily closed up to a five-carbon ring, and the resulting cyclic keto acid transformed into the required 4,4-dimethylcyclopentane-

[1] Nametkin and Chuchrikovaia, *J. Chem. Soc.*, **108**, 701 (1915). Komppa and Roschier, *ibid.*, **112**, 398 (1917); **122**, 1167 (1922). Roschier, *ibid.*, **116**, 408 (1919).

1,3-dicarboxylic acid. The synthesis of α,α-dimethyl-γ-carboxyadipic acid has, therefore, been carried through, the steps being the following.

(a) Ethyl-α,α-dimethylacetone dicarboxylate was condensed by means of its monosodium derivative, with chloro-acetic ester.

$$C_2H_5OOC.C(CH_3)_2.CO.CHNa.COOC_2H_5 \longrightarrow C_2H_5OOC.C(CH_3)_2.CO.CH\ (CH_2COOC_2H_5).COOC_2H_5$$

(b) The resulting ester was reduced, first to the corresponding hydroxy ester, and, finally, hydrolyzed and reduced to the corresponding dimethyl-carboxyadipic acid, $HOOC.(CH_3)_2.CH_2.CH(CH_2.COOH).COOH$. Only a very small yield was obtained, however, and it will be necessary to prepare the acid at considerably less expense before an attempt is made to carry the synthesis further. This work is now in hand.

Experimental Part

First Condensation. Preparation of Ethyl-α,α-dimethylacetone Dicarboxylate ($C_{11}H_{18}O_5$)

The method described by Perkin and Smith[2] was adopted, namely, condensation of ethyl acetate and ethyl dimethylmalonate with powdered sodium, but it was found possible to double the yield by introducing the two following modifications. (a) Instead of ethyl acetate, a synthetic mixture of absolute alcohol and anhydrous ethyl acetate[3] was used. This was found to increase the yield by one-half. (b) A steady stream of carbon dioxide was passed through the reaction mixture. This prevented loss of ester by alkaline hydrolysis during the condensation, and resulted in a further material increase in the yield.

The above two modifications may prove to be of general applicability in increasing the efficiency of condensations of this type.

Second Condensation. Preparation of Ethyl-α,α-dimethyl-β-keto-γ-carbethoxyadipate ($C_{15}H_{24}O_7$)

$C_{11}H_{18}O_5$ (above) was converted in the usual way into its monosodium derivative, care being necessary to avoid the formation of appreciable quantities of the di-derivative. The semi-solid contents of the flask were then refluxed with a 25% excess of chloro-acetic ester until the product was no longer alkaline (three to four hours), and the ester separated in the usual way. Distillation of the residue after removal of ether, alcohol and unchanged chloro-acetic ester gave a good yield of a colorless oil which gave an intense red coloration with ferric chloride, b. p., 150–160° (14 mm.); n_D, 1.4400.

Anal. Calcd. for $C_{15}H_{24}O_7$: C, 57.0; H, 7.6. Found: C, 56.9; H, 7.8.

In one instance a small amount of the di-derivative, $C_2H_5OOC.C(CH_3)_2.CO.C(CH_2.COOC_2H_5)_2.COOC_2H_5$, giving no coloration with ferric chloride, was isolated; b. p., 170–180° (14 mm.); n_D, 1.4458.

Anal. Calcd. for $C_{19}H_{30}O_9$: C, 56.7; H, 7.5. Found: C, 56.9; H, 7.8.

[2] Perkin and Smith, *J. Chem. Soc.*, **83**, 12 (1903).

[3] Compare *Chem. Ind.*, **43**, 295T–297T (1924).

Reduction of Ethyl-α,α-dimethyl-β-keto-γ-carbethoxyadipate in Two Stages

I. Formation of Ethyl-α,α-dimethyl-β-hydroxy-γ-carbethoxyadipate ($C_{15}H_{26}O_7$).—The reduction of the keto group to a secondary alcohol group was carried through in the ordinary way, using 4% sodium amalgam and a 1:16 solution of the ester in aqueous alcohol. To separate the ester after reduction, the liquid was freed from mercury and solid bicarbonate, neutralized with dil. hydrochloric acid, and heated on a water-bath to remove alcohol. The ester separated and was extracted with ether. The hydrolyzed portion, amounting to about 15%, was recovered from the combined residues by acidifying, evaporating nearly to dryness and extracting with ether. The sirupy hydroxy acid (or lactone?) thus recovered was added to the reduced ester, and the combined product treated as described in II.

II. Hydrolysis and Reduction to α,α-Dimethyl-γ-carboxyadipic Acid ($C_9H_{14}O_6$).—

(a) A preliminary attempt at hydrolysis and reduction of the hydroxy ester ($C_{15}H_{26}O_7$), using red phosphorus and hydriodic acid (d., 1.69), resulted in the isolation of crystals; m. p., 146°.

Neutr. eq. Calcd. for the γ-lactone, $C_9H_{12}O_6$: 108. Found: 110.5, 110.3.

Anal. Calcd. for $C_9H_{12}O_6$: C, 50.0; H, 5.56. Found: C, 50.0, 49.5; H, 5.96, 5.87.

(b) Finally, the hydroxy ester was treated with red phosphorus and fuming hydriodic acid (d., 1.93) in the cold. When the mixture had stood for some time, the ethyl iodide resulting from hydrolysis was removed, and the mixture then refluxed for nine hours. To separate the organic acid, the hydriodic acid was distilled off in a vacuum, the residue washed onto a filter with ether, the filtrate freed from iodine and water in the usual way and the ether then removed. Crystals, m. p. 139–141°, were deposited on standing in a vacuum desiccator overnight, but no solvent was found from which they could be recrystallized.

Neutr. eq. (titration with $Ba(OH)_2$. Calcd. for $C_9H_{14}O_6$: 72.7. Found: 73.2, 73.6.

Anal. Calcd. for $C_9H_{14}O_6$: C, 49.5; H, 6.4. Found: C, 49.6; H, 6.6.

The yield from this reduction was only about half of that calculated.

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DUNEDIN, NEW ZEALAND