300. *The αα'-Di*cyclo*hexylsuccinic Acids.*

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The preparation of simple monobasic and dibasic acids containing two substituents such as the *cyclo*hexyl group cannot be achieved by the simple condensation reactions which can be used in other cases. These acids are, however, possible starting materials for investigating interesting problems of isomerism and isomeric change. Hence an electrolytic method of preparing αα'-di*cyclo*hexylsuccinic acid has been attempted and has proved successful. The two possible stereoisomeric forms of that acid have been obtained, and their properties show that the *cyclo*hexyl group has a very large steric effect; for example, the anhydride which one of them forms is only attacked slowly by boiling alcoholic potash.

αα'-Di*cyclo*HEXYLSUCCINIC acid, αβ-di*cyclo*hexylpropionic acid, and their derivatives might serve as useful intermediate substances for the preparation of compounds which could be used for studying the many possibilities of isomerism and geometrical isomerism of unsaturated substances containing two alicyclic rings, a problem about which little is known, and which is becoming of increasing interest. Attempts to obtain either of these acids by ordinary condensation reactions from *cyclo*hexylmethyl bromide or *cyclo*hexyl bromide were unsuccessful, and consequently the experiments described here were undertaken to see whether a general method of preparing symmetrically disubstituted dibasic acids with alicyclic substituents could be found in the electrolysis of the salts of the half esters of compounds of the type of *cyclo*hexylmalonic acid. Conditions were eventually found under which potassium ethyl *cyclo*hexylmalonate can be converted into a mixture of the *racemic* and the meso-*form* of *ethyl αα'-di*cyclo*hexylsuccinate*, but the yield is not good, being only 17% under the most favourable conditions.

The electrolytic method of preparing succinic acids was discovered by Crum Brown and Walker (*Annalen*, 1891, **261**, 107), and was applied by them to the preparation of dimethyl-, diethyl-, tetramethyl- and tetraethyl-succinic acids. They showed that the yield is improved by working at high salt concentration and with an anode of small area. Since then the conditions that determine the formation of succinic acid from potassium ethyl malonate have been studied by Robertson (J., 1925, **127**, 2057), who found that with an anode of gold or platinised platinum no succinic ester is formed, but that grey or smooth platinum can be used. The mechanism of the synthesis has been discussed in detail by Fichter and his co-workers (*Helv. Chim. Acta*, 1935, **18**, 445, 704). The cell used in this work is described in the experimental section. Its main features were that: (1) the anode, a small loop of platinum wire, could be rotated rapidly to ensure efficient cooling in the region of the anode; (2) a streaming mercury cathode was used in order to remove from the cell the liberated potassium, and to avoid the accumulation of hydroxyl ions in the solution. Without the latter precaution the current is carried mainly by the hydroxyl ions and the yield of the desired ester falls; such a cathode makes it unnecessary to introduce a diaphragm (Meyer and Hofer, *Ber.*, 1895, **28**, 2427), which increases the total resistance and thus lengthens the time of electrolysis. A stationary mercury cathode has been used for the same purpose by Fairweather (*Proc. Roy. Soc. Edin.*, 1924, **45**, 31). Repetition of Crum Brown's synthesis of adipic ester from potassium ethyl succinate with our cell gave a yield of 50% of theory, as compared with the 35% yield which he obtained. Fichter and Heer (*Helv. Chim. Acta*, 1935, **18**, 704) obtained 60%, but gave no details of their procedure.

Electrolysis of potassium ethyl *cyclo*hexylmalonate at first gave only an oil which consisted essentially of ethyl hydrogen *cyclo*hexylmalonate, set free from its potassium salt, most probably by acids formed in anodic oxidation. In very concentrated solution, however, the ethyl esters of the two stereoisomeric $\alpha\alpha'$-di*cyclo*hexylsuccinic acids were formed in small amounts. The two esters differ widely in m. p., and can be separated because the higher-melting ester is almost insoluble in cold alcohol. They are both very difficult to hydrolyse and are only slowly attacked by boiling alcoholic potash. In this they resemble the tetramethyl- and tetraethyl-succinic esters (Crum Brown and Walker, *Annalen*, **1893**, **274**, 41), and differ from the dimethyl-, diethyl- and diphenyl-succinic esters, all of which can be conveniently hydrolysed with alcoholic potash. The steric effect of one *cyclo*hexyl group seems to be much greater than that of a simple alkyl or aryl group. The most convenient reagent for the hydrolysis of both esters was found to be a mixture of sulphuric acid, acetic acid, and water at 140°. Under these conditions both esters give the same products, an *acid* of high m. p. and a very stable *anhydride*; the latter was shown to be related to a lower-melting *acid*, so both stereoisomeric acids are obtained from either ester, and interconversion of the isomers takes place under the vigorous conditions needed for the hydrolysis. The product of the slow alkaline hydrolysis is, as would be expected, also a mixture of the two acids, which can be separated by means of their barium salts. The higher-melting ester was, however, shown to be that of the higher-melting acid by esterification of that acid through its silver salt. The anhydride is only slowly attacked by aqueous or alcoholic potash, and the product is again a mixture of the two acids. It reacts readily, however, with anilinomagnesium iodide to give an anilic acid. The stability of the anhydride resembles that of tetraethyl- and tetraphenyl-succinic anhydrides (Walker and Walker, J., **1905**, **87**, 961; Crichton, J., **1906**, **89**, 929), and again shows the large steric effect of a *cyclo*hexyl group. Which of the two acids is the racemic and which the *meso*-form can only be settled by the optical resolution of one, but the consistent analogies in anhydride formation, solubilities of the barium salts, and the m. p.'s of the acids and their esters with the corresponding properties of the two dimethyl- (Werner and Basyrin, *Ber.*, **1913**, **46**, 3229), diethyl- (Wren and Haller, this vol., p. 230), and diphenyl-succinic acids (Wren and Still, J., **1915**, **107**, 444), in all of which cases one acid has been resolved, make it very probable that the lower-melting acid is the racemic form. Attempts to convert either acid into di*cyclo*hexylethylene by electrolysis of their salts have so far proved unsuccessful.

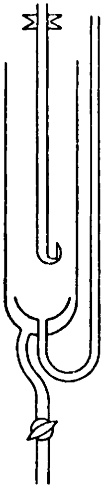
EXPERIMENTAL.

The following condensations were attempted under a variety of conditions, but in no case could the desired products be obtained: *cyclo*hexylmethyl bromide with the sodium derivatives of *cyclo*hexyl-malonic or -cyanoacetic ester or *cyclo*hexenylmalonic ester; *cyclo*hexyl bromide with the disodium derivative of ethanetetracarboxylic ester; *cyclo*hexylchloromalonic ester with sodio*cyclo*hexylmalonic ester; the action of iodine on sodio*cyclo*hexylmalonic ester.

Ethyl *cyclo*hexylmalonate was prepared by the reduction of the *cyclo*hexenyl ester (Kon and Speight, J., 1926, 2730) on palladised strontium carbonate, from *cyclo*hexylcyanoacetic ester (Vogel, J., 1928, 2023), or, most conveniently, from *cyclo*hexyl bromide and malonic ester (Hiers and Adams, *J. Amer. Chem. Soc.*, 1926, **48**, 2385). The yield obtained by the last method was 40% of theory, and attempts to improve it by using benzene as solvent or potassium carbonate in place of sodium were unsuccessful; the yield is seriously diminished if the reaction mixture is not stirred continuously.

Potassium ethyl *cyclo*hexylmalonate is best obtained by isolating the half ester. Ethyl *cyclo*hexylmalonate (143 g.) in 1200 c.c. of absolute alcohol was treated with potassium hydroxide (16 g.) in 10 c.c. of water and 400 c.c. of alcohol. When the alkaline reaction had disappeared (2—3 days), most of the alcohol was removed on the water-bath, and the residue treated with 80 c.c. of water and thoroughly extracted with ether to remove unchanged ester. The dissolved ether was removed in a stream of air, and the solution cooled in ice and acidified with phosphoric acid; ethyl hydrogen *cyclo*hexylmalonate separated as an oil, some samples of which solidified to colourless crystals, m. p. 44—45°. The compound boils at 163°/15 mm. with partial decomposition to ethyl *cyclo*hexylacetate. In most experiments the oil was neutralised with concentrated aqueous potassium hydroxide, and the solution diluted to the desired extent.

Two cells were used for the electrolysis, one holding 90 c.c. and the other 15 c.c.; the general design of both is shown in the figure. Mercury flows down the narrow side tube from a tap-funnel, wells up in the cup at the bottom of the cell, and drains away through the bottom tap; electrical connection is made to this mercury by a wire sealed through the side tube. The anode is a loop of platinum wire of surface area 0·35 sq. cm., and is rotated rapidly; the cell is surrounded by a large inverted bell-jar containing ice and water frequently renewed. The current was taken from a 100-volt D.C. supply, and regulated by a sliding resistance. In a series of trials with different concentrations of electrolyte and different current strengths, it was found that if the volume of electrolyte exceeded 28 c.c. for each 10 g. of the salt, the product was an oil which consisted of ethyl hydrogen *cyclo*hexylmalonate. When the oil was distilled, it partly decomposed and gave two fractions: (i) b. p. 100—105°/15 mm., shown to be ethyl *cyclo*hexylacetate by hydrolysis and conversion of the acid into its amide; (ii) b. p. 163—165°/15 mm., which was ethyl hydrogen *cyclo*hexylmalonate, as shown by hydrolysis and the mixed m. p. of the acid so obtained with an authentic sample of *cyclo*hexylmalonic acid. With more concentrated solutions, a solid separated during the electrolysis, and this proved to contain the esters of the two desired di*cyclo*hexylsuccinic acids. Alteration of current strength showed that if it exceeded 5 amps., complete anodic oxidation took place and no organic product could be isolated. The best current was found to be 1 amp.; if it were smaller, the time of electrolysis became inconveniently long.



After many trials the procedure for obtaining the best yields of the desired esters seemed to be the following. 90 C.c. of a solution containing 61 g. of potassium ethyl *cyclo*hexylmalonate were electrolysed with a current of 1 amp.; after 4 hours the current was stopped, the solid formed removed, and the solution extracted with ether. The aqueous layer was acidified with phosphoric acid, 21 g. of ethyl hydrogen *cyclo*hexylmalonate separating. This was converted into the potassium salt, and electrolysed at the same concentration for a further 3 hours. In this way electrolysis of a dilute solution was avoided. The resulting solution was extracted with ether, and then on acidification gave 12 g. of the half ester. Thus 46·8 g. of the potassium salt have disappeared; the combined yield of the two di*cyclo*hexylsuccinic esters was 5·3 g., so that this, the best yield obtained, is 17% of the theoretical.

The ether was removed from the extracts, the residual oil combined with the solid which had been formed, and the whole treated with a little cold alcohol. The solid which separated on standing was recrystallised from light petroleum and formed colourless needles, m. p. 120° (3 g.), of (?)meso-*ethyl di*cyclo*hexylsuccinate* (Found: C, 70·8; H, 10·2. $C_{20}H_{34}O_4$ requires C, 71·0; H, 10·1%). The alcoholic filtrate was distilled under reduced pressure and gave 9·6 g. of a mixture of ethyl hydrogen *cyclo*hexylmalonate and ethyl *cyclo*hexylacetate (b. p. 100—160°/15 mm.) and 2·3 g. of a viscous oil (b. p. 203—210°/15 mm.), which solidified on standing; it was recrystallised from aqueous acetic acid and formed odourless crystals, m. p. 60°, soluble in cold alcohol. This is (?) r-*ethyl di*cyclo*hexylsuccinate* (Found: C, 71·2; H, 10·1%). Attempts to improve the yield by adding a little alcohol to the solution in the cell or by adding a little mercuric cyanide were completely unsuccessful. Mercuric cyanide, which acts as an inhibitor for the decomposition of hydrogen peroxide on the surface of the electrodes, was found by Glasstone and Hickling (J., 1934, 1878) to improve the yield of ethane in the electrolysis of acetates, but it has a definitely harmful effect in the present case.

Hydrolysis of the Esters.—The higher-melting ester is not completely hydrolysed by refluxing with excess of alcoholic potash for 10 hours. The product obtained (m. p. 140—145°) is a mixture of the two stereoisomeric acids, which cannot be separated by crystallisation from aqueous alcohol or by crystallisation of the potassium salts from water. Addition of barium chloride to a solution of the mixed potassium salts gave a white precipitate of a sparingly soluble barium salt; this yielded an acid which could be crystallised from aqueous acetic acid and melted at 147° on rapid heating. This is (?)r-*di*cyclo*hexylsuccinic acid* (Found: C, 68·0; H, 9·2. $C_{16}H_{26}O_4$ requires C, 68·1; H, 9·2%). It is insoluble in light petroleum and benzene, and easily soluble in cold alcohol. Even below its m. p. the acid loses water to give an *anhydride*, m. p. 62·5°, recrystallised from aqueous acetic acid or light petroleum (Found: C, 72·7, 73·2; H, 9·1, 9·1. $C_{16}H_{24}O_3$ requires C, 72·7; H, 9·1%). Acidification of the filtrate from the sparingly soluble barium salt gave the higher-melting acid, (?)meso-*di*cyclo*hexylsuccinic acid*, which, recrystallised from aqueous acetic acid, melted at 225° [Found (micro), after drying in high vacuum: C, 68·6; H, 9·2%]. The acid forms a *dihydrate* when crystallised from aqueous solvents (Found: loss of weight on drying, 11·0. $C_{16}H_{26}O_4,2H_2O$ requires $2H_2O$, 11·3%)

and is insoluble in cold alcohol. Its silver salt, heated with ethyl iodide, gave an ester, m. p. 120°, identical (mixed m. p.) with the higher-melting ester formed in the electrolysis.

The ester of higher m. p. is unattacked by boiling with 30% sulphuric acid, but can be hydrolysed by heating for 2 hours with a mixture of sulphuric and acetic acids and water (46 : 26 : 18, by vol.). The product consists of the higher-melting acid and the anhydride of the lower-melting acid; the two can be separated with aqueous sodium carbonate. When the proportion of sulphuric acid was increased, and heating continued for 6 hours at 165°, the product was a mixture of the anhydride and the lower-melting acid (mixed m. p. with acid from less soluble barium salt, 146°). Acid hydrolysis of the lower-melting ester at 140° gave only a small quantity of the higher-melting acid, and a 67% yield of the anhydride.

When heated with resorcinol and sulphuric acid, (?)*r*-di*cyclo*hexylsuccinic anhydride gives a compound which is fluorescent in alkaline solution. The anhydride reacts with anilinomagnesium iodide (Bodroux, *Compt. rend.*, 1904, **138**, 1427; cf. Hardy, J., 1936, 398) in warm ether to give the *half-anilide* of di*cyclo*hexylsuccinic acid which was recrystallised from alcohol, m. p. 225° (Found: C, 74·3; H, 8·7; N, 4·0. $C_{22}H_{31}O_3N$ requires C, 74·0; H, 8·7; N, 3·9%). The anhydride is insoluble in aqueous caustic alkalis, and is slowly hydrolysed by boiling alcoholic potash to give a mixture of the two acids, similar to that formed in the alkaline hydrolysis of the esters.

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