(b) **From the Condensation of Di-*n*-hexylcadmium and Cyclohexanecarboxyl Chloride.**—This alternate synthesis is a modification of a procedure reported by Cason.[5]

To the Grignard reagent prepared from 82.5 g. (0.5 mole) of *n*-hexyl bromide and 12.2 g. (0.5 mole) of magnesium was added, over a 5-minute period, 45.9 g. (0.25 mole) of $CdCl_2$ and the mixture was stirred under reflux for one hour. The ether was removed by distillation, and 100 ml. of benzene was added. Another 15 ml. of distillate was removed, and 200 ml. of benzene was added. The stirred solution was heated to boiling, and 73.3 g. (0.5 mole) of cyclohexanecarboxyl chloride was added as fast as the exothermic reaction would permit (5–10 minutes). The mixture was stirred for one hour and poured into a slurry of ice and dilute H_2SO_4. The benzene and water layers were separated, and the water layer was extracted three times with benzene. The benzene portions were combined and the product was washed successively with water, saturated Na_2CO_3 solution, water and saturated NaCl solution. It was then dried by filtration through anhydrous Na_2SO_4. Distillation through a 10-in. Vigreux column gave 26 g. of material boiling 110–116° at 3 mm. A 2,4-dinitrophenylhydrazone from the material melted at 63.5° after two recrystallizations from ethanol. As mentioned before, a mixed melting point of this derivative and the 2,4-dinitrophenylhydrazone of the ketone prepared by method (a) showed no depression.

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ORONO, MAINE

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

The Synthesis of Higher Aliphatic α,ω-Dicarboxylic Acids[1]

BY ALGIRD KREUCHUNAS

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A general synthetic procedure has been developed for the preparation of higher α,ω-dicarboxylic acids. The method involves the reaction between half ester acid chlorides of certain lower α,ω-dicarboxylic acids and the cadmium reagents formed from α,ω-dibromoalkanes to yield long chain diketodiesters. The final product is obtained by saponification of the diketodiester and subsequent reduction of both carbonyl groups. The acids from C_{14} through C_{22} have been prepared.

The aliphatic α,ω-dicarboxylic acids having more than ten carbon atoms are not readily accessible. In general, three synthetic methods have been employed for their preparation.

The first two methods require the use of an α,ω-dibromoalkane which can be prepared by the reduction of the corresponding α,ω-dicarboxylic acid ester to the diol followed by treatment with hydrogen bromide. Further treatment of the α,ω-dibromoalkane with potassium cyanide followed by hydrolysis leads to an α,ω-dicarboxylic acid having two more carbon atoms than the parent compound[2]; treatment, instead, with diethyl sodiomalonate and subsequent saponification and decarboxylation leads to an α,ω-dicarboxylic acid having four more carbon atoms than the parent compound.[3,4] These methods can be repeated again and again to build chains of considerable length. However, such processes are tedious and inefficient.

The third general method, known as the Crum Brown–Walker reaction, is the electrolytic coupling between two molecules of a half ester metal salt of an α,ω-dicarboxylic acid with the elimination of two molecules of carbon dioxide.[5,6] Usually only acids containing an even number of carbon atoms can be prepared in this way.

Recently, a fourth method has been disclosed which utilizes the condensation between 2,6-dimethoxyphenyllithium and α,ω-dibromoalkanes followed by demethylation, treatment with sodium amalgam to open the ring and reduction of the carbonyl groups to give α,ω-dicarboxylic acids in low over-all yield.[7]

This paper describes a new method for preparing higher aliphatic α,ω-dicarboxylic acids containing from fourteen to twenty-two carbon atoms.

The most effective method found involved the reaction between an α,ω-alkylene cadmium compound and a half ester acid chloride to yield a diketodiester. Subsequent saponification and reduction of the carbonyl groups of the diketodicarboxylic acid by means of the Wolff–Kishner reaction yielded the α,ω-dicarboxylic acid.

$$[\cdot Cd(CH_2)_m\cdot] + 2ROOC(CH_2)_nCOCl \xrightarrow{\text{benzene}} ROOC(CH_2)_nCO(CH_2)_mCO(CH_2)_nCOOR$$

This approach is an extension of the reaction between dialkyl cadmium compounds and half ester acid chlorides.[8]

For most practical purposes terminal bifunctional aliphatic compounds are limited to those having ten or less carbon atoms. Granting this restriction any single coupling reaction involving two molecules would be limited to the preparation of compounds having a maximum of twenty carbon atoms. In addition, single coupling usually leads to the formation of compounds with an even number of carbon atoms.

By achieving a simultaneous two-way coupling with three molecules (A + B + A → ABA), a method became available for the preparation of higher homologs through to the C_{30} compound inclusive.

Work done on the preparation of di-Grignard reagents by earlier investigators[3,9–11] indicated that

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(1) Taken from the thesis of A. Kreuchunas, submitted in partial fulfillment of the requirements for the Ph.D. Degree at the Massachusetts Institute of Technology, June, 1950.

(2) P. Chuit and J. Hausser, *Helv. Chim. Acta*, **12**, 850 (1929).

(3) P. Chuit, *ibid.*, **9**, 264 (1926).

(4) N. L. Drake, H. W. Carhart and R. Mozingo, THIS JOURNAL, **63**, 617 (1941).

(5) L. Ruzicka, M. Stoll and H. Schinz, *Helv. Chim. Acta*, **11**, 1174 (1928).

(6) G. M. Bennett and H. Gudgeon, *J. Chem. Soc.*, 1679 (1938).

(7) H. Lettre and A. Jahn, *Ber.*, **85**, 346 (1952).

(8) J. Cason, *Chem. Revs.*, **40**, 15 (1947).

(9) S. Hilpert and G. Gruttner, *Ber.*, **47**, 177 (1914).

(10) J. von Braun and W. Sobecki, *ibid.*, **44**, 1918 (1911).

(11) R. Brown and W. E. Jones, *J. Chem. Soc.*, 781 (1946).

they could be prepared in reasonable yield. This was subsequently confirmed by the preparation of the di-Grignard reagents from 1,5-dibromopentane, 1,6-dibromohexane, 1,9-dibromononane and 1,10-dibromodecane; although certain modifications had to be made to ensure good yields.

For example, Hilpert and Gruttner[9] and several other investigators[10,11] reported that in order to minimize coupling, it was necessary to carry out the preparation of di-Grignard reagents in *wet*[12] ether.

When the *wet* ether technique was tried using 1,5-dibromopentane, the reaction went only to 65.9% completion and contained 57.6% organometallic product. The experiment was repeated in every detail except that anhydrous ether was used instead of *wet* ether. The reaction went to 88.5% completion and contained 77.5% of the organometallic compound. The preparation of the di-Grignard reagents is summarized in Table I.

TABLE I

DATA FOR THE PREPARATION OF DI-GRIGNARD REAGENTS

α,ω-Dibromoalkane (0.2 mole)	Hours of refluxing	% bromide[a] reacted	% organometallic formed[b]
1,5-Dibromopentane	3	65.9	57.5[c]
1,5-Dibromopentane	3	88.5	77.5
1,6-Dibromohexane	3	97.5	96.3
1,9-Dibromononane	5	96.9	100.0
1,10-Dibromodecane[d]	5	95.0	90.0

[a] Titration for bromide ion was made with 0.1 N silver nitrate solution followed by a back-titration with 0.1 N potassium thiocyanate solution in the presence of ferric iron. [b] Titration for organometallic compound was made by titrating with an excess of 0.1 N sulfuric acid followed by a back-titration with 0.1 N sodium hydroxide solution. Phenolphthalein was used as the indicator. [c] Made by the *wet* ether technique. [d] Obtained from du Pont, redistilled, b.p. 138–140° (3 mm.).

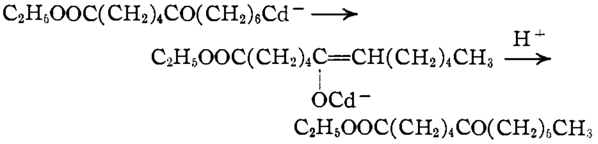
The conversion of the di-Grignard reagents to the corresponding alkylene cadmium compounds was carried out without difficulty. The alkylene cadmium reagents are heavy, taffy-like compounds which required the use of a special stirrer that is described in the experimental section. This conversion has been described in detail by Cason[8,13] in papers reporting on the use of dialkyl cadmium compounds.

The optimum conditions for the general synthetic method were worked out by intensive study of the reaction between the cadmium reagent prepared from 1,6-dibromohexane and ethyl ω-(chloroformyl)-valerate to yield diethyl 6,13-diketoöctadecane-1,18-dioate. Certain difficulties which were encountered will be discussed briefly.

(1) **Sludge Formation.**—The addition of a benzene solution of an acid chloride to the taffy-like cadmium reagents causes a marked thickening to occur. At times, the reaction mixture set to a hard, refractory mass. In an attempt to eliminate this erratic setting action, reactions were conducted in xylene, toluene and β,β'-dichloroethyl ether. Toluene was the best choice; however, Cason, *et al.*,[14] caution against heating cadmium alkyls too high since thermal cracking is very likely to occur. For this reason another approach was worked out using benzene (see under 2).

(2) **Side Reactions.**—Enolization under the conditions of this reaction can always be considered a potential side reaction.[8] Cason[15] reported that the reaction between 1-chloro-2-hexanone and di-*n*-butylcadmium yielded 70% butane. This example illustrates the striking enolizing power of a cadmium reagent.

Ethyl 6-ketododecanoate was isolated as the ketoacid and identified by analysis. It is postulated that it was formed in the following manner



$$C_2H_5OOC(CH_2)_4CO(CH_2)_6Cd^- \longrightarrow C_2H_5OOC(CH_2)_4\underset{\substack{|\\ OCd^-}}{C}{=}CH(CH_2)_4CH_3 \xrightarrow{H^+} C_2H_5OOC(CH_2)_4CO(CH_2)_5CH_3$$

This same phenomenon was observed in the preparation of the other acids; however, the monoketocarboxylic acids were not identified.

To minimize the enolization, the order of addition of reagents was reversed. The cadmium reagent slurry was added to a very rapidly stirred solution of acid chloride in benzene. This change was made to decrease the enolizing effect of large excesses of cadmium reagent and magnesium halide on freshly formed ketoester. A slight increase in yield was obtained.

Another modification was made at this time to reduce the tendency toward agglutination. High speed stirring was employed (2000 r.p.m.). This technique was very successful. Although benzene was used as the solvent, the cadmium complex did not thicken or agglutinate as it had in the earlier work.

(3) **Reduction of the Diketodicarboxylic Acids.**—The Wolff–Kishner reduction[16] proceeded smoothly except for the C_{14} (4-6-4) (see Table III) and C_{17} (4-9-4) compounds. Both of these compounds have γ-carbonyl groups. This is not true of the other compounds. Purification of these products was difficult and the yields were low. Especially significant is the action of the C_{17} (6-5-6) diketodicarboxylic acid which is reduced to the same compound, 1,17-heptadecanedioic acid, as the abnormal C_{17} (4-9-4) diketodicarboxylic acid. The C_{17} (6-5-6) diketodicarboxylic acid contains ϵ-carbonyl groups and is reduced in 83.1% yield. This indicates that the position of the carbonyl group with respect to the carboxylic acid group is very important. Cason, *et al.*,[14] report that difficulties arising in certain Huang-Minlon reductions are associated with the γ-position of the carbonyl group and postulate an unsaturated lactam as the by-product.

Experimental[17]

General Method for α,ω-Dibromoalkanes.—The apparatus used for the preparation of α,ω-dibromoalkanes consisted of a long Pyrex tube (3.5 × 70 cm.) fitted on the bottom with a stopcock and on the top with an outer 24/40 standard taper Pyrex joint. This served as the reaction chamber. It was enclosed for its entire length by another Pyrex tube (5.0 × 70 cm.) on which was wound a heating

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(12) *Wet* ether was considered to contain 0.1% water.

(13) J. Cason and F. S. Prout, *Org. Syntheses*, **28**, 75 (1948).

(14) J. Cason, G. Sumrell and R. S. Mitchell, *J. Org. Chem.*, **15**, 850 (1950).

(15) J. Cason, THIS JOURNAL, **68**, 2078 (1946).

(16) Huang-Minlon, *ibid.*, **68**, 2487 (1946).

(17) All melting points are corrected; boiling points are uncorrected.

coil (15 ohms). The entire apparatus was enclosed by a third Pyrex tube (7.5 × 70 cm.). Extending to the bottom of the reaction chamber was a removable gas-inlet tube which was perforated at the end. A thermometer was fastened to the wall of the reaction chamber.

The glycol (1.0 mole) was placed in the reaction chamber, heated to 100° and treated with a slow stream of anhydrous hydrogen bromide for six hours. The product was separated from the hydrobromic acid layer, cooled, washed with concentrated sulfuric acid, 5% aqueous sodium carbonate solution and water and dried over sodium sulfate. The pure material was obtained by distillation under reduced pressure.

1,5-Dibromopentane.—1,5-Pentanediol (du Pont), 208 g., 2.0 moles, b.p. 133–134° (10 mm.), n^{25}D 1.4500, was converted as described above and yielded 292 g. of product, b.p. 93–94° (10 mm.), n^{25}D 1.5101, 63.4%; reported 92–93° (10 mm.),[18] n^{20}D 1.5146.[19]

1,6-Dibromohexane.—1,6-Hexanediol (du Pont), 118 g., 1.0 moles, m.p. 36–39°, was converted as described above and yielded 187 g. of product, b.p. 112–113° (12 mm.), n^{25}D 1.5048, 76.6%; reported b.p. 115–116° (12 mm.),[20] n^{15}D 1.5111.[19]

1,9-Dibromononane.—1,9-Nonanediol, 160 g., 1.0 mole (preparation follows), was converted as described above and yielded 165.5 g. of product, b.p. 145–150° (9 mm.), n^{25}D 1.4945, 49%; reported b.p. 147–149° (9 mm.).[8]

Diethyl Azelate.—Azelaic acid (Emery Industries), 564 g., 3.0 moles, m.p. 90–96°, was converted in the same manner as described by Micovic[21] for the preparation of diethyl adipate and yielded 603 g. of product, b.p. 145–150° (5 mm.), n^{25}D 1.4323, 82.3%; reported b.p. 154–155° (8 mm.),[8] n^{20}D 1.43509.[22]

1,9-Nonanediol.—Diethyl azelate, 300 g., 1.23 moles, was converted in the same manner described by Lazier, Hill and Amend[23] for the high pressure catalytic reduction of diethyl adipate to 1,6-hexanediol and yielded 186.8 g. of product, b.p. 138–142° (2 mm.), 68.4%; reported b.p. 147–150° (2 mm.).[24]

Methyl Hydrogen Succinate.—Succinic anhydride, 500 g., 5 moles, m.p. 115–116°, was converted by the method of Bone, Sudborough and Sprankling[25] (see also ref. 26) and yielded 614 g. of product, m.p. 52–57°, 93.0%. A small sample was recrystallized twice from an ether–carbon disulfide mixture, m.p. 58–59°; reported m.p. 58°.[26]

Methyl Hydrogen Glutarate.—This compound was made by a modification of the method described by Swann, Oehler and Buswell[27] for the preparation of ethyl hydrogen sebacate. From glutaric acid, 164 g., 1.24 moles, m.p. 97–99°; dimethyl glutarate, 115.2 g., 0.72 mole, b.p. 96–97° (10 mm.); di-*n*-butyl ether, 62 ml.; concentrated hydrochloric acid, 37.2 g., and methanol, 52 g., 1.61 moles, was obtained 116.7 g. of methyl hydrogen glutarate, b.p. 146–151° (10 mm.), n^{25}D 1.4365, 64.4%; reported b.p. 150–151° (10 mm.),[28] n^{18}D 1.4392.[28] It was found that if the residue which remains after the product has been removed by distillation was added to subsequent preparations the yield of product was increased. A second preparation of methyl hydrogen glutarate using the residue from the first preparation gave a yield of 79.9%.

Ethyl Hydrogen Adipate.—This compound was made by a modification of the method described for the preparation of ethyl hydrogen sebacate.[27] From adipic acid, 292 g., 2 moles, m.p. 150–153°; diethyl adipate, 243 g., 1.16 moles, b.p. 129° (13 mm.), n^{24}D 1.4268; di-*n*-butyl ether, 100 ml.; concentrated hydrochloric acid, 70 g., and absolute ethanol, 124 g., 2.7 moles, was obtained 219 g. of ethyl hydrogen adipate, b.p. 159–164° (7 mm.), 62.9%; reported b.p. 155–157° (7 mm.).[27] By adding the high boiling residues to succeeding preparations of ethyl hydrogen adipate, the yield was increased to 273 g., 77.7%.

Methyl ω-(Chloroformyl)-propionate.—Methyl hydrogen succinate, 614 g., 4.65 moles,[29] was converted by the method of Ruggli and Maeder[30] (see also ref. 26) and yielded 598 g. of product, b.p. 90–91° (18 mm.), n^{25}D 1.4380, 85.2%; reported b.p. 93° (18 mm.).[31]

Methyl ω-(Chloroformyl)-butyrate.—Methyl hydrogen glutarate, 116.7 g., 0.8 mole, was converted by the method of Ruggli and Maeder[30] and yielded 134 g. of product, b.p. 107–109° (20 mm.), n^{25}D 1.4440, 91.5%; reported b.p. 98° (10 mm.).[32]

Ethyl ω-(Chloroformyl)-valerate.—Ethyl hydrogen adipate, 273 g., 1.57 moles, was converted by the method of Ruggli and Maeder[30] and yielded 282 g. of product, b.p. 116–117° (9 mm.), n^{25}D 1.4434, 93.2%; reported b.p. 124° (15 mm.).[33]

General Procedure for α,ω-Dicarboxylic Acids. A. Preparation of Diketodiesters.—Magnesium powder (9.6 g., 0.4 gram atom) was placed in a dried, 1.5-l., three-necked, round-bottomed flask fitted with a stirrer[34] and a reflux condenser closed with a calcium chloride drying tube. The flask was swept out with nitrogen and 200 ml. of anhydrous ether (dried over sodium wire) was added. The α,ω-dibromoalkane (0.2 mole) was added together with a small crystal of iodine. The reaction usually began within five minutes; no external cooling was required. External heating was applied after 30 minutes and refluxing was continued for a time dependent on which di-Grignard reagent was being prepared (see Table I). The reaction mixture was cooled in an ice-bath under an atmosphere of nitrogen. The stirrer was stopped to permit the heavy oily Grignard reagent to settle out. A 1-ml. aliquot portion was taken from each layer and analyzed for bromide and hydroxide ions.[35] For analytical data see Table I.

To the rapidly stirred, cooled di-Grignard reagent was added in one portion 40.3 g. (0.22 mole, 100 mesh) anhydrous cadmium chloride.[36] After five minutes, the ice-bath was removed. The mixture was allowed to warm to room temperature (10 minutes), then refluxed for 45 minutes on a steam-bath.[37]

The flask was fitted with a second condenser directed for distillation. The ether was removed by distillation until a thick paste remained. Anhydrous benzene (200 ml., dried over sodium wire) was added and distillation was continued until 50 ml. more of liquid was removed. An additional 150 ml. of anhydrous benzene was added; the second condenser was removed and the reaction mixture was refluxed for several minutes.

While the above distillation was being completed, a second flask was prepared to carry out the remaining part of the reaction. Anhydrous benzene (100 ml.) was placed in a 1-l., three-necked, round-bottomed, creased flask[39] fitted

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[18] R. Lespieau, *Bull. soc. chim.* (*France*), [4] **37**, 421 (1925).

[19] R. Dionneau, *Ann. chim.*, [9] **3**, 236 (1915).

[20] J. von Braun and C. Muller, *Ber.*, **39**, 2018 (1906).

[21] V. M. Micovic, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 264.

[22] A. Karvonen, *Ann. Acad. Sci. Fennicae*, **A10**, No. 5, 1 (1916), "Beilstein," Vol. 2, 1929, p. 290, 1st supplement.

[23] W. A. Lazier, J. W. Hill and W. J. Amend, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 325.

[24] R. H. Manske, *ibid.*, p. 154.

[25] W. A. Bone, J. J. Sudborough and C. H. G. Sprankling, *J. Chem. Soc.*, **85**, 534 (1904).

[26] J. Cason, *Org. Syntheses*, **25**, 19 (1945).

[27] S. Swann, Jr., R. Oehler and R. J. Buswell, *ibid.*, **19**, 45 (1939).

[28] E. Fourneau and S. Sabetay, *Bull. soc. chim.* (*France*), [4] **45**, 834 (1929).

[29] Crude and purified methyl hydrogen succinate have been used in this preparation. The final product in either case had the same physical constants.

[30] P. Ruggli and A. Maeder, *Helv. Chim. Acta*, **25**, 936 (1942).

[31] G. M. Robinson and R. Robinson, *J. Chem. Soc.*, **127**, 175 (1925).

[32] R. F. Naylor, *ibid.*, 1106 (1947).

[33] F. Fichter and S. Lurie, *Helv. Chim. Acta*, **16**, 885 (1933).

[34] A special heavy-duty stirrer was required. It consisted of two sections; one part was a $^3/_8$ × 18″ stainless steel shaft threaded at one end; the other was a $^1/_8$ × ½ × 7 bar of stainless steel formed to fit the inner contour of the reaction flask and tapped in the center. When the bar was in place in the flask, the shaft was inserted through a slip seal and joined firmly to the bar by means of the threaded end.

[35] The double Grignard reagents: C_5, C_6, C_9 and C_{10}, are increasingly soluble in ether, in that order. The C_{10} compound does not form a separate layer.

[36] Anhydrous cadmium chloride was prepared by heating the hydrate to 120° to constant weight,[8] grinding and passing through a 100-mesh screen and reheating briefly. 10% excess was used.

[37] At this point the reaction mixture was checked for remaining traces of Grignard reagent by means of the Michler ketone test; see ref. 38.

[38] H. Gilman and F. Schulze, THIS JOURNAL, **47**, 2002 (1925).

[39] A. A. Morton and L. M. Redman, *Ind. Eng. Chem.*, **40**, 1190 (1948).

with a high-speed stirrer.[39] Half ester acid chloride (0.36 mole, 90% of theoretical) was added and the solution was heated to refluxing.

The stirrer was stopped in the first reaction flask and raised out of the mixture. The two flasks were joined by a 10-mm. glass transfer tube which extended to the bottom of the first flask. By means of low pressure nitrogen, the heavy slurry of the cadmium reagent was transferred to the rapidly stirred solution (2000 r.p.m.) of acid chloride over a period of 15 minutes. Inevitably some of the slurry remained behind on the walls of the first flask. This was removed by washing with four 50-ml. portions of benzene; a flow of nitrogen was maintained throughout. Heating and stirring were continued for two hours. The reaction mixture was allowed to remain undisturbed overnight.

The complex was decomposed by the addition of 100 g. of chopped ice, followed by dilute sulfuric acid (5 g. of concentrated sulfuric acid, 25 g. of ice). The clear yellow benzene layer was removed. The aqueous portion was extracted with 100 ml. of benzene. The benzene portions were combined, filtered, washed successively with 200 ml. of water, 200 ml. of 5% aqueous sodium carbonate solution and 200 ml. of water and dried by filtration through sodium sulfate.

Two procedures were developed for the final separation: procedure A for diketodiesters from C_{14} through C_{19}; procedure B for diketodiesters from C_{19} through C_{22}.

Procedure A.—The benzene was removed by distillation under reduced pressure (water aspirator). The residue was distilled at 1 mm. by means of a mechanical pump to remove the lower boiling monoketomonoester (see Table II). The residue consisted of the crude diketodiester which was purified further after saponification.

TABLE II

DATA FOR DIKETODIESTERS TREATED BY PROCEDURE A

		Combination[a]	Top distillation temp., °C. (1 mm.)	Low boiling material, g.	High boiling material, g.
1	C_{14}	4-6-4	110	11.2	31.7
2	C_{15}	5-5-5	120	18.0	20.0
3	C_{16}	5-6-5	135	10.0	39.8
4	C_{17}	6-5-6	145	29.3	33.0
5	C_{17}	4-9-4	150	16.5	38.5
6	C_{18}	6-6-6	155	17.0	48.2
7	C_{19}	5-9-5	160	18.0	42.0

[a] The first and third figures indicate the number of carbon atoms in the acid chloride; the second figure represents the number of carbon atoms in the cadmium reagent.

Procedure B.—The benzene solution was concentrated by evaporation to approximately 100 ml. of solution. Much of the product crystallized. Petroleum ether (400 ml.) was added. The product was collected by filtration, washed with 100 ml. of petroleum ether and recrystallized as indicated in Table III.

TABLE III

DATA FOR DIKETODIESTERS TREATED BY PROCEDURE B

			Recrystallization data	M.p., °C.	Wt. g., crude	Yield, %
1	C_{19}	5-9-5	Twice from 250 ml. of methanol	89–91.5	15.0	21.7
2	C_{20}	5-10-5	Twice from 300 ml. of ligroin, then from 300 ml. of methanol	87.2–88.4	21.3	29.7
3	C_{21}	6-9-6	Twice from 300 ml. of ethanol, then from 300 ml. of ligroin	64–66	17.0	21.4
4	C_{22}	6-10-6	Twice from 500 ml. of ligroin, then from 500 ml. of ethanol	69.4–71.6	32.0	39.1

B. Saponification of Diketodiesters.—Sodium hydroxide (6.4 g., 0.16 mole) was dissolved in 500 ml. of water and 0.035 to 0.040 mole of the crude diketodiester was added. The mixture was refluxed for a period of time depending on the compound being saponified; see Table IV. The hot solution was passed through a fluted filter to remove the small quantity of oil which was usually present. The well stirred filtrate was then acidified by the slow addition of 15 ml. (0.18 mole) of concentrated hydrochloric acid. A voluminous, colorless precipitate formed. The mixture was digested for one-half to one hour to ensure complete conversion to the free acid and to modify the precipitate to permit easier filtration. The mixture was cooled and the product was separated by filtration. The well washed product was treated as specified in Table IV.

TABLE IV

DATA FOR THE SAPONIFICATION OF DIKETODIESTERS

			Time, hr.	Recrystallization data	M.p., °C.	Over-all yield, %
1	C_{14}	4-6-4	6	Twice from 500 ml. of water, then 100 ml. of methanol, then 200 ml. ligroin	154.8–158	24.8
2	C_{15}	5-5-5	6	Once from 500 ml. of water	134–137	12.2
3	C_{16}	5-6-5	6	Two extractions with 1 l. of boiling water	142.5–146	38.3
4	C_{17}	6-5-6	6	Three extractions with 1 l. of boiling water	130–134.5	23.7
5	C_{17}	4-9-4	6	Three extractions with 1 l. of boiling water; esterification with methanol, recry. from ligroin–benzene, then methanol; saponification	150.6–151.6	24.9
6	C_{18}	6-6-6	6	Five extractions with 1 l. of boiling water	135–137	38.8
7	C_{19}	5-9-5	6	Five extractions with 3 l. of boiling water, then from methanol twice	141–142.5	30.2
8	C_{19}	5-9-5	6	Saponification of purified	142.5–145	18.2
9	C_{20}	5-10-5	10	ester[a]	145.8–148.4	29.1
10	C_{21}	6-9-6	12	Saponification of purified	138–140.5	21.3
11	C_{22}	6-10-6	24	ester[a]	138.5–141.4	35.7

[a] No further purification was required for these compounds prior to reduction.

C. Reduction of the Diketodicarboxylic Acids.[16]—A mixture of 0.017 mole of diketodicarboxylic acid, 6.6 g. (0.118 mole) of potassium hydroxide, 5 ml. of 85% hydrazine hydrate and 50 ml. of diethylene glycol (redistilled, b.p. 124–128° (8 mm.)) was refluxed for one hour. The condenser was removed until the temperature of the reaction mixture reached 200° by the slow evaporation of water. The reflux condenser was replaced and refluxing was continued at the increased temperature for three hours. The mixture was cooled to about 100° and poured into 300 ml. of water. To this was added with stirring dilute hydrochloric acid (15 ml. of concentrated hydrochloric acid and 250 ml. of water). A thick, gelatinous, colorless solid separated which was digested for one hour, separated by filtration, washed with water and dried in a vacuum desiccator. A crude yield of 90% or better was obtained except for the C_{14} (4-6-4) and the C_{17} (4-9-4) diketodicarboxylic acids (discussed in previous paragraphs). During the first recrystallization from benzene (100 ml.), the solution was treated with small amounts of Florex[40] which acted as an effective decolorizing agent. The subsequent treatment of each acid is listed separately in Table V.

6-Ketododecanoic Acid.—To an aqueous solution prepared by dissolving 6 g. (0.15 mole) of sodium hydroxide in 100 ml. of water was added 13.3 g. of ethyl 6-ketodo-

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(40) Sold by the Floridin Co., Warren, Pennsylvania.

TABLE V

SUMMATION OF ANALYTICAL DATA, MELTING POINTS AND OVER-ALL YIELDS FOR α,ω-DICARBOXYLIC ACIDS AND RELATED INTERMEDIATE COMPOUNDS

		Compound	Molecular formula	Calcd.		Found		Neut. equiv.		M.p., °C.	Recrystallization data	Yield red'n, %	Over-all[u] yield, %
				C	H	C	H	Calcd.	Found				
1	C_{14}	Dimethyl 4,11-diketotetradecane-1,14-dioate	$C_{16}H_{26}O_6$	61.13	8.34	61.32	8.48	...	...	59.5–60.5	Twice from methanol		
2		4,11-Diketotetradecane-1,14-dioic acid	$C_{14}H_{22}O_6$	58.72	7.74	59.03	7.91	143.2	146.2	160.5–161.5	Twice from methanol		
3		1,14-Tetradecanedioic acid	$C_{14}H_{26}O_4$	65.08	10.14	64.90	9.97	129.1	128.7	124.2–125.5[a,b]	Benzene, then 50 MeOH–H_2O	62.2	15.2
4	C_{15}	Dimethyl 5,11-diketopentadecane-1,15-dioate	$C_{17}H_{28}O_6$	62.17	8.59	62.40	8.67	...	...	76.5–77.5	Three times from methanol		
5		5,11-Diketopentadecane-1,15-dioic acid	$C_{15}H_{24}O_6$	59.98	8.05	60.18	8.08	150.2	150.2	136.4–138.0	Water and twice from methanol		
6		1,15-Pentadecanedioic acid	$C_{15}H_{28}O_4$	66.14	10.36	66.15	10.53	136.2	136.0	113.4–114.4[c]	Benzene, ligroin, then gl. HOAc	70.3	8.6[t]
7	C_{16}	Dimethyl 5,12-diketohexadecane-1,16-dioate	$C_{18}H_{30}O_6$	63.13	8.85	63.18	8.97	...	...	73.5–74.5[d]	Twice from methanol		
8		5,12-Diketohexadecane-1,16-dioic acid	$C_{18}H_{26}O_6$	61.13	8.34	61.39	8.44	157.2	157.8	142.2–143.4[e]	H_2O, acetone and digest. lig.		
9		1,16-Hexadecanedioic acid	$C_{16}H_{30}O_4$	67.10	10.56	66.97	10.58	143.2	143.2	123.5–124.5[f,g]	Twice from benzene	76.0	29.1
10	C_{17}	Diethyl 6,12-diketoheptadecane-1,17-dioate	$C_{21}H_{36}O_6$	65.59	9.44	65.69	9.51	...	...	52.8–53.4	Ethanol–water, then petr. ether		
11		6,12-Diketoheptadecane-1,17-dioic acid	$C_{17}H_{28}O_6$	62.17	8.59	62.04	8.78	164.2	165.3	132.6–134.8	Twice from methanol		
12		1,17-Heptadecanedioic acid	$C_{17}H_{32}O_4$	67.96	10.74	67.93	10.65	150.2	150.5	117.5–118.6[h]	Three times from benzene	83.1	19.7
13	C_{17}	Dimethyl 4,14-diketoheptadecane-1,17-dioate	$C_{19}H_{32}O_6$	64.02	9.05	63.96	9.12	...	...	73.0–73.5	Twice from methanol		
14		4,14-Diketoheptadecane-1,17-dioic acid	$C_{17}H_{28}O_6$	62.17	8.59	61.87	8.59	164.2	164.5	150.6–151.6	Saponification of ester		
15		1,17-Heptadecanedioic acid[s]	$C_{17}H_{32}O_4$	67.96	10.74	...	...	150.2	149.1	117.8–119.1[i]	Methyl esterification, methanol, saponification	36.9	9.2
16	C_{18}	Diethyl 6,13-diketoöctadecane-1,18-dioate	$C_{22}H_{38}O_6$	66.30	9.61	66.46	9.78	...	...	61.5–62.0	Once from methanol		
17		6,13-Diketoöctadecane-1,18-dioic acid	$C_{18}H_{30}O_6$	63.13	8.83	63.17	8.75	171.2	170.8	138.5–139.5	Three times from water, digested with chloroform		
18		1,18-Octadecanedioic acid	$C_{18}H_{34}O_4$	68.75	10.90	68.54	11.18	157.2	157.7	126.5–127.0[j]	Twice from benzene	86.8	33.7
19	C_{19}	Dimethyl 5,15-diketononadecane-1,19-dioate	$C_{21}H_{36}O_6$	65.59	9.44	65.84	9.57	...	...	96.5–97.5	Twice from methanol		
20		5,15-Diketononadecane-1,19-dioic acid	$C_{19}H_{32}O_6$	64.02	9.05	64.02	9.17	178.3	178.6	142–144	Twice from methanol		
21		1,19-Nonadecanedioic acid	$C_{19}H_{36}O_4$	69.47	11.05	69.62	11.18	164.2	165.8	121–121.6[k,l,m]	Twice from benzene, then ligroin	89.6	27.1
22	C_{20}	Dimethyl 5,16-diketoeicosane-1,20-dioate	$C_{22}H_{38}O_6$	66.30	9.61	66.31	9.60	...	...	93.0–93.5	Twice from methanol		
23		5,16-Diketoeicosane-1,20-dioic acid	$C_{20}H_{34}O_6$	64.84	9.25	64.78	9.38	185.3	184.7	147.5–149.5	Methyl ethyl ketone–acetic acid		
24		1,20-Eicosanedioic acid	$C_{20}H_{38}O_4$	70.13	11.18	70.38	11.29	171.3	171.3	125.4–126.6[n]	Twice from benzene	73.3	21.3
25	C_{21}	Diethyl 6,16-diketoheneicosane-1,21-dioate	$C_{25}H_{44}O_6$	68.14	10.07	68.20	10.09	...	...	65–66	Three times from ethanol		
26		6,16-Diketoheneicosane-1,21-dioic acid	$C_{21}H_{36}O_6$	65.59	9.44	65.61	9.73	192.3	193.6	137.6–139.8	Methanol then acetic acid		
27		1,21-Heneicosanedioic acid	$C_{21}H_{40}O_4$	70.74	11.31	71.05	11.45	178.3	178.1	121.8–123.2[o,p]	Twice from benzene, then methanol, acetone, methanol	51.6	11.0
28	C_{22}	Diethyl 6,17-diketodocosane-1,22-dioate	$C_{26}H_{46}O_6$	68.68	10.20	68.65	10.20	...	...	74–75	Twice from ethanol		
29		6,17-Diketodocosane-1,22-dioic acid	$C_{22}H_{38}O_6$	66.30	9.61	66.34	9.62	199.2	201.6	138.8–141.4	Methanol then acetic acid		
30		1,22-Docosanedioic acid	$C_{22}H_{42}O_4$	71.30	11.43	71.71	11.47	185.3	184.8	125.6–126.8[q,r]	Twice from benzene, digested with ligroin; acetic acid	73.8	26.3

[a] Reported m.p. 123–124°, L. Ruzicka, M. Stoll and H. Schinz, *Helv. Chim. Acta*, 9, 249 (1926). [b] Reported m.p. 126.5°, D. A. Fairweather, *Proc. Roy. Soc. Edin.*, **46**, 71 (1926). [c] Reported m.p. 114.6–114.8°, ref. 3. [d] Reported m.p. 74°, ref. 7. [e] Reported m.p. 141–141.5°, ref. 7. [f] Reported m.p. 124–124.2°, ref. 3. [g] Reported m.p. 123°, ref. 7. [h] Reported m.p. 118°, ref. 3. [i] Reported m.p. 118°, ref. 3. [j] Reported m.p. 124.6–124.8°, ref. 3. [k] Reported m.p. 119°, L. Ruzicka, M. Stoll and H. Schinz, *Helv. Chim. Acta*, 11, 670 (1928). [l] Reported m.p. 119.2°, ref. 3. [m] Obtained by remelting a sample which originally melted at 116.4–121.4°, successive recrystallizations from benzene, ligroin and acetone did not change the range. [n] Reported m.p. 124–125°, ref. 5. [o] Reported m.p. 118–120°, see ref. 5. [p] Reported m.p. 123°, ref. 2. [q] Reported m.p. 123–124°, ref. *k*. [r] Reported m.p. 123.75°, see ref. under *b*. [s] Mixed m.p. with compound obtained above (12) did not depress. [t] Prepared by the *wet* ether method. The yield could be improved using anhydrous ether. [u] Calcd. on basis of acid chloride.

decanoate.[41] The mixture was refluxed for six hours, cooled and acidified with 20 ml. of concentrated hydrochloric acid. A gelatinous, colorless precipitate formed immediately which was separated by filtration, washed with water and air dried. The crude material (5 g.) was recrystallized twice from ligroin and once from petroleum ether, yielding 3.0 g., m.p. 60.5–61.5°. This represented a 7.7% over-all yield.

Anal. Calcd. for $C_{12}H_{22}O_3$: C, 67.25; H, 10.35; neut. equiv., 214.3. Found: C, 67.25; H, 10.26; neut. equiv., 215.2.

Cambridge, Mass.

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[41] This material was formed during the preparation of diethyl 6,13-diketoöctadecane-1,18-dioate. It was obtained in the preliminary purification of the C_{18} diketodiester by Procedure A as the liquid fraction boiling below 155° (1 mm.). See Table II.

[Contribution from the Department of Chemistry of The Ohio State University]

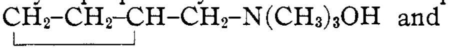
The Synthesis and Properties of Methylenecyclopropane[1]

By James T. Gragson, Kenneth W. Greenlee, John M. Derfer and Cecil E. Boord

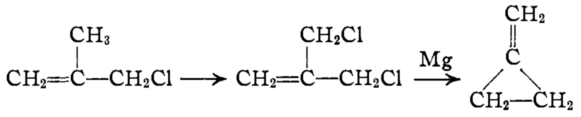
Received June 13, 1952

Methylenecyclopropane has been synthesized and isolated for the first time. Some physical and chemical properties of this hydrocarbon were determined, and its infrared absorption spectrum was measured. Methylcyclopropane was prepared for use in identification work, and improved physical properties are reported for it. Evidences of interaction between the double bond and the ring of methylenecyclopropane are noted.

The synthesis of methylenecyclopropane has been attempted with little success by several workers. Merezhkovskii[2] reported that the treatment of 1,2,3-tribromo-(2-bromomethyl)-propane with zinc in 80% alcohol gave a gaseous mixture, which on oxidation with 1% potassium permanganate produced products to be expected from isobutene, as well as some oxalic acid. He postulated that the oxalic acid was derived from methylenecyclopropane; however, 1,3-butadiene, which may have been present, would also give oxalic acid. Dechlorination of a mixture of 3-chloro-(2-chloromethyl)-1-propene and its isomer 1,3-dichloro-2-methyl-1-propene with zinc in alcohol[3] also gave isobutene (75% yield) rather than methylenecyclopropane.

Dem'janov and Dojarenko[4] attempted to prepare methylenecyclopropane by the thermal decomposition of  $\underbrace{CH_2\text{–}CH_2\text{–}CH}\text{–}CH_2\text{–}N(CH_3)_3OH$ and obtained very little hydrocarbon, most of which was 1,3-butadiene. Whitmore[5] wrote that "all attempts to prepare methylenecyclopropane have failed."

In the present work, 3-chloro-(2-chloromethyl)-1-propene, prepared by chlorination of 2-methylallyl chloride, was treated with zinc dust in molten acetamide,[6] because it was thought that this solvent, being less polar than ethanol, might alter the course of the reaction sufficiently to allow formation of methylenecyclopropane; however, isobutene (38% yield) was the only product found. The dechlorination was then attempted with magnesium in dry tetrahydrofuran at the reflux temperature of the mixture. A 17% yield of a hydrocarbon which was subsequently shown to be methylenecyclopropane was obtained by fractional distillation of the reaction product.



The physical properties of the sample of the new hydrocarbon, estimated cryoscopically to have a purity of 93 mole %, were compared with the properties of the only known unsaturated hydrocarbons (1,2-butadiene and 1-butyne) with similar boiling points (Table I). Although these two hydrocarbons are virtually eliminated on the basis of their other physical properties, it was definitely shown that the new hydrocarbon was not 1,2-butadiene by comparison of its infrared spectrum (Fig. 1) with that of authentic 1,2-butadiene[7]; that it was not 1-butyne was shown when it did not yield a yellow

Table I

Physical Properties of Methylenecylopropane and Related Hydrocarbons

	Methylene-cyclopropane	1,2-Buta-diene[a]	1-Butyne[b]
B.p., °C. (749 mm.)	8.34	....	.....
B.p., °C. (760 mm.)	8.8[d]	10.9	8.07
M.p., °C.	−138.7[e]	−136.20	−125.720
ΔM.p., °C./mole % impurity	0.32	0.244	0.286
Ref. index (n^0D)	1.415	....	.....
Density (d^{20}_4)	0.718 (at 0°)	0.652[c]	0.65[c]
Purity, %	93	....	.....

[a] F. D. Rossini, *et al.*, *J. Research Natl. Bur. Standards*, **39**, 321 (1947). [b] F. D. Rossini, *et al.*, *ibid.*, 41, 323 (1948). [c] F. D. Rossini, *et al.*, "Selected Values of Properties of Hydrocarbons," N.B.S. Circular C461, U. **S**. Gov. Printing Office, Washington, D. C., Tables 11a and 12a. [d] Corrected from the b.p. at 749 mm. and a d*t*/d*p* value of 0.04°/mm. [e] The m.p. for the 100% pure product was calculated from this and other cryoscopic data to be −136°.

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[1] This paper was abstracted largely from the dissertation submitted in 1951 by J. T. Gragson to the Graduate School of The Ohio State University in partial fulfillment of the requirements for the degree of Doctor of Philosophy. It was presented before the Organic Division of the American Chemical Society, in Buffalo, March, 1952. The investigation was sponsored by the American Petroleum Institute in coöperation with The Ohio State University Research Foundation.

[2] B. K. Merezhkovskii, *J. Russ. Phys. Chem. Soc.*, **45**, 2072 (1913).

[3] I. A. D'yakanov, *J. Gen. Chem.* (*U.S.S.R.*), **10**, 402 (1940).

[4] N. J. Dem'janov and Marie Dojarenko, *Ber.*, **56B**, 2208 (1923).

[5] F. C. Whitmore, "Organic Chemistry," 2nd edition, D. Van Nostrand Co., New York, N. Y., 1951, p. 530.

[6] H. B. Hass, E. T. McBee, G. E. Hinds and E. W. Glusenkamp, *Ind. Eng. Chem.*, **28**, 1178 (1936).

[7] Catalog of Infrared Spectral Data, American Petroleum Institute Research Project 44, F. D. Rossini, Director, Carnegie Institute of Technology.