

SYNTHESIS OF DERIVATIVES OF DIMETHYLCYCLOPENTANONE, $\beta\beta$ -DIMETHYLADIPIC ACID, AND $\alpha\beta\beta$ -TRIMETHYLADIPIC ACID.¹

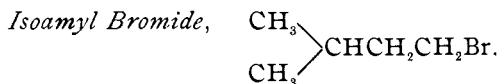
BY W. A. NOYES.

Received April 29, 1901.

SOME time since, the author reported on the synthesis of 2.33-trimethylcyclopentanone,² and its identification with a ketone previously obtained from camphoric acid by a series of easily interpreted reactions. As the study of this ketone and of related compounds, seems likely to prove of some importance in the further development of the chemistry of camphor and of the terpenes, it appears desirable to give in greater detail the methods used in their preparation.

The investigation of some of the derivatives of cyclopentanone involved has also led to the discovery that some of them decompose in a manner which is, so far as I am aware, quite new.

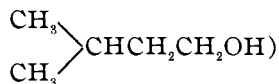
Phosphorus Tribromide.—Fifty grams of yellow phosphorus were dissolved in 100 grams of carbon disulphide in a flask, the lip of which had been cut off. The flask was connected with an upright condenser by means of a piece of rubber tubing slipped over both. A little more than the theoretical amount of bromine (about 125 cc.) was measured into a drop-funnel which was then hung in the top of the condenser. The bromine was then allowed to drop as rapidly as possible without the escape of carbon disulphide or bromine vapors. The carbon disulphide boils from the heat of the reaction and, condensing above, dilutes the bromine as it flows down. The whole of the bromine may usually be added in forty to fifty minutes. The completion of the change of the phosphorus to the tribromide, is indicated sharply by a change from yellow to a reddish color. The solution is then distilled from a Ladenburg bulb till a temperature of 165° is reached. The residue is sufficiently pure for use. A small additional amount may be obtained by distilling, in the same manner, the portion which passes over, and the yield is then almost quantitative.



¹ An account of the results of this investigation was given at the Chicago meeting of the Society but some details completed since then are included in the present paper.

² *Am. Chem. J.*, **23**, 128; *Ber. d. chem. Ges.*, **33**, 54.

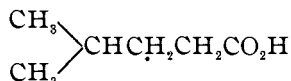
480 grams of fusel oil (boiling-point 128° – 132° and consisting mainly of methyl-3-butanol,



were put in a flask and 437 grams of the phosphorus tribromide were added in portions, with constant cooling, the whole being added within half an hour. The mixture was allowed to stand over night and was then warmed for a couple of hours on the water-bath, a little water being added from time to time to prevent much evolution of hydrobromic acid. The evolution of hydrobromic acid indicates that the reaction takes place in part with the formation of esters of phosphorous acid, but the hydrobromic acid formed may, if retained, still react with the esters or with amyl alcohol. The mixture separated into two layers. The lower layer was separated and distilled slowly, with the addition of some pieces of porous tile to prevent bumping, till a temperature of 140° was reached by a thermometer in the liquid.

The distillate was mixed with the portion of isoamyl bromide previously separated, and the whole shaken twice with sulphuric acid which had been diluted with an equal volume of water, to remove hydrobromic acid, twice with concentrated sulphuric acid, to remove amyl alcohol, then with water and with a solution of sodium carbonate, and finally with dry sodium sulphate to dry and clear it. After filtering, it is sufficiently pure for the present use. Yield, 636 grams, or 88 per cent. of the theory.

Isocaproic Acid,

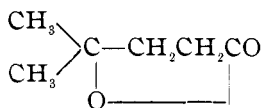


(methyl-4-pentanoic acid).—The only method of preparing isoamyl cyanide given by Beilstein, is from isoamyl chloride. The use of the bromide gives, in my experience, at least, very much better yields. For the preparation of isocaproic acid, the separation of the cyanide is not necessary. 280 grams of potassium cyanide were dissolved in 300 cc. of hot water, 1250 cc. of alcohol, and 636 grams of amyl bromide were added, and the whole boiled on a water-bath in a flask connected with an upright condenser for twenty-four hours. The solution was then poured from the potassium bromide, which separated, into a second flask

containing 350 grams of caustic potash, and the boiling continued for twenty-four hours longer. The solution was transferred to a large porcelain dish and evaporated with the addition of water, till the alcohol was removed. The residue was transferred to a flask containing 400 cc. of dilute sulphuric acid (1:1 by volume), and the isocaproic acid, which separated, was distilled. The acid solution was extracted once with ligroin. The yield was 401 grams, or 82 per cent. of the theory.

The method here given for the preparation of isocaproic acid may be used with advantage in the preparation of other acids and especially in the preparation of propionic acid, but requires some modification in details.

Isocapro lactone,



(4-methyl-1.4-pentanolide).—300 grams of isocaproic acid and 150 grams of sodium hydroxide were dissolved in 900 cc. of water, the solution was cooled, and 4.5 liters of a 10 per cent. slightly warm solution of potassium permanganate were added in portions of 500 cc. at a time, at intervals of one-half hour to one hour. Considerable heat is produced by the reaction and external heating is not necessary. A temperature of 50°–60° seems to be most desirable. The final decolorization of the permanganate may be hastened by warming on the water-bath. The filtrate and washings from the oxides of manganese were concentrated to about 600 cc. and poured into 350 cc. of dilute sulphuric acid (1:1 by volume). The mixture of isocaproic acid and lactone was separated from the acid solution and the latter was distilled with steam till about a liter had passed over. The mixture of acid and lactone was shaken with the distillate in portions of 300 cc. at a time, separating the aqueous solution each time, and then with water in the same manner till 4 or 5 liters have been used. By this treatment the lactone gradually passes into the aqueous solution, while most of the unchanged isocaproic acid remains behind. If an emulsion forms, a little ligroin can be added to clear the solution and does not seem to interfere with the extraction of the lactone by the water.

If desired, the amounts of acid and lactone in the successive

aqueous extracts can be followed approximately by titrating with tenth-normal caustic potash, with phenolphthalein as an indicator. The direct titration of the cold solution gives the amount of acid; then on adding an excess of the alkali, warming in a covered flask on the water-bath for a few minutes, and titrating back with tenth-normal acid, the difference between the excess of alkali added and the acid used, corresponds to the amount of lactone present.

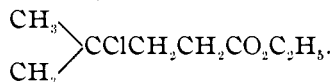
The residual isocaproic acid is distilled to a temperature of 190° to remove the ligroin, and may then be used for a new oxidation.

The aqueous solution is then made strongly alkaline with sodium hydroxide, making sure enough is present to combine with all of the lactone, and warming the solution at first in a flask to avoid loss. It is then evaporated to a volume of 200 cc. or less, poured into dilute sulphuric acid, the mixture of acid and lactone separated, and the solution extracted several times with ether.

The mixture of lactone and acid is then exactly neutralized with a 30 per cent. solution of potassium hydroxide, added in portions, the mixture being shaken and cooled quickly after each addition. Fifteen to 20 grams of dry potassium carbonate are added and the solution is extracted repeatedly with ether. After extraction the alkaline solution is acidified, the isocaproic acid, which separates, is added to the mixture of lactone and acid obtained by a new oxidation, and the aqueous solution is also distilled with steam to recover some of the lactone which it retains.

The ethereal solutions are dried with a little sodium sulphate and distilled. If enough potassium carbonate was used to remove all of the isocaproic acid a pure lactone is obtained by one distillation. The boiling-point is 208° – $208^{\circ}.5$ and the melting-point 10° . Bredt and Fittig give the boiling-point as $207^{\circ}1$ and melting-point as 7° – 8° .² The yield is 35 to 40 per cent. of the portion of the isocaproic acid oxidized. Bredt and Fittig obtained a yield of 25 to 30 per cent.

γ-Chloroisocaproic Ester,³



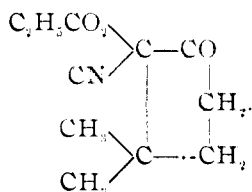
¹ *Ann. Chem* (Liebig). **208**, 56.

² *Ibid.*, **200**, 260.

³ Bredt : *Ber. d. chem. Ges.*, **19**, 514.

In the original synthesis of trimethylcyclopentanone the γ -bromisocaproic ester was used. It has been found that better yields are obtained by the use of the corresponding chlorine derivative. Fifty grams of the lactone were mixed with 150 cc. of absolute alcohol and the solution in a bottle, surrounded with cold water, was saturated with hydrochloric acid gas, from 90 to 100 grams being required. After standing over night the solution was poured on crushed ice, the ester, which separated, washed two or three times with a little salt water, dried with sodium sulphate and filtered. The aqueous solution was extracted two or three times with low boiling ligroin, the ligroin being distilled away under diminished pressure. The yield is 71 to 73 grams, or 90 to 93 per cent. of the theory.

Dimethylcyanocarboxethylcyclopentanone.



The preparation¹ of this substance and proof of its structure² have been given. In its further preparation, 250 grams of bromisocaproic ester gave 25 grams of the pure, crystallized substance. Better yields could probably be obtained by the use of the chlorisocaproic ester, but this has not been tried.

When the substance is boiled with dilute hydrochloric acid, it decomposes very slowly with evolution of carbon dioxide. In sealed tubes, at 150°–160°, the decomposition is more rapid, but still requires two or three hours. The products of decomposition are *acetic acid*, *isocapro lactone*, and *carbon dioxide*. The lactone boiled at 206°–209° and was analyzed, giving 62.83 per cent. of carbon and 8.62 per cent. of hydrogen. Theory requires 63.16 and 8.77 per cent. The silver salt gave 44.92 per cent. silver. Theory requires 45.19 per cent.

When saponified with alcoholic potash, *malonic acid*, melting at 133°, and *isocapro lactone*, boiling at 208°–209° and melting at 10°, were obtained.

The decomposition here described is, of course, related to the

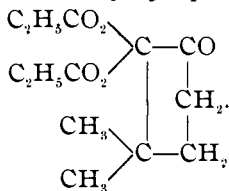
¹ *Am. Chem. J.*, **22**, 259.

² *Ibid.*, **23**, 135.

"acid decomposition" of acetacetic ester and its derivatives, but I do not recall any other case in which a carbon atom is removed from a ring and replaced by oxygen in this manner. A similar case will, however, be described further on, and the decomposition will, undoubtedly, be found typical for bodies of similar structure.

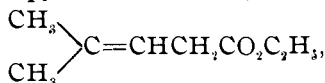
So far as the purpose of the experiments in working toward a synthesis of camphoric acid is concerned, the result was, of course, disappointing. At the end of a considerable amount of work, the original lactone was obtained instead of the dimethyl-carboxethylcyclopentanone, which had been sought.

3,3-Dimethyl 2,2-dicarboxethyl cyclopentanone,



115 grams of sodium were dissolved in 130 cc. of absolute alcohol, 85 grams of *pure* malonic ester were added and 89 grams of the γ -chloroisocaproic ester. The mixture was heated on the water-bath from four to six hours; most of the alcohol was then distilled by heating on the water-bath under diminished pressure. The residue was cooled, water added, and the oil which separated was dried with sodium sulphate and fractioned under diminished pressure, the lower boiling portions being distilled twice. The aqueous solution was also extracted once or twice with ether.

The portion boiling below 80° under a pressure of 20 mm., consists mainly of pyroterebinic ester,



that from 90° to 100° of malonic ester with some chlorisocaproic ester, and that from 170° – 180° of the dimethyldicarboxethylcyclopentanone. The yield of the last compound was about 20 per cent of the weight of the chlorisocaproic ester used.

¹ When malonic ester is prepared by the method described in this Journal, 18, 1105 (1896), it contains considerable amounts of cyanacetic ester, and the conversion to malonic ester is not complete after many hours' heating of the acid-alcoholic solution. The ester prepared by Claissen's method, *Ann. Chem.* (Liebig), 218, 131, would probably contain some of the same impurity. For the present purpose a pure ester prepared from calcium malonate is required.

The pyroterebinic ester may be saponified with alcoholic potash, the pyroterebinic acid converted into isocapro lactone by boiling for a short time with dilute sulphuric acid (1 : 1 by volume) and the latter purified by treatment with potassium hydroxide and potassium carbonate as before. The recovered malonic ester may, of course, be used repeatedly.

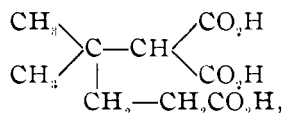
Dimethyldicarboxethylcyclopentanone is a nearly colorless oil which boils at 167°–169° under a pressure of 14 mm.

0.1831 gram gave 0.1328 gram water and 0.4086 gram carbon dioxide.

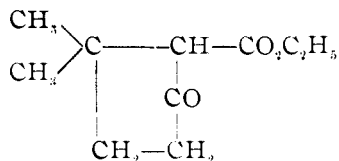
0.2208 gram gave 0.1594 gram water and 0.4892 gram carbon dioxide.

	Calculated for C ₁₂ H ₂₀ O ₄ .	Found.	
		I.	II.
Carbon.....	60.94	60.83	60.43
Hydrogen.....	7.77	8.06	8.02

When dimethyldicarboxethylcyclopentanone is saponified by warming with an excess of alcoholic potash or soda, it breaks down in the same manner as dimethylcyclohexanedicarboxethylcyclopentanone (p. 396), giving malonic and hydroxy isocaproic acids. In some cases, by careful saponification in a cold solution, there was obtained a small amount of the tribasic acid

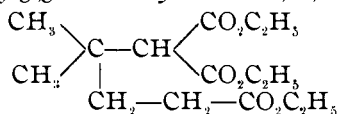


and at one time it was thought that this acid was formed by the saponification of the cyclic compound. A further study of the matter, however, makes it very probable that the tribasic acid was formed chiefly, if not altogether, from a small amount of the ester of that acid which had failed to condense to the cyclic compound. In one case, a considerable amount of dimethyladipic acid was found among the products of the saponification. This indicates that the cyclic compound had, in part, undergone the ketonic decomposition, giving the compound



This would then saponify to $\beta\beta$ -dimethyladipic acid. It is also possible, however, that the ester of the tribasic acid decomposes partly on distillation, forming the ester of dimethyladipic acid.

Triethyl Ester of 3,3-Trimethylhexanoic, 1,2',6 Acid,



When 8.5 grams of sodium are dissolved in 140 cc. of absolute alcohol and the solution is dropped slowly, during two or three hours, into a mixture of 66 grams of chlorisocaproic ester and 75 grams of pure malonic ester, the ester of the tribasic acid is formed and its condensation to the cyclic ester is largely prevented. After heating for an hour longer, the product was treated as described above under the cyclic compound. Ten grams of the ester boiling at 150° – 172° , under a pressure of 15 mm., were obtained. The boiling-point is apparently very nearly the same as that of the dimethyldicarboxethylcyclopentanone. Analysis I, below, was made with the ester prepared as described, and distilled but once. Analysis II was with an ester prepared from the pure crystallized acid by treatment with alcohol and hydrochloric acid as usual.

I. 0.2467 gram gave 0.1865 gram water and 0.5374 gram carbon dioxide.

II. 0.1612 gram gave 0.1276 gram water and 0.3521 gram carbon dioxide.

Calculated for $\text{C}_{15}\text{H}_{26}\text{O}_6$.	I.	II.
$\text{C}_{15} = 180 = 59.60$	59.00	59.58
$\text{H}_{26} = 26 = 8.61$	8.40	8.80
$\text{O}_6 = 96 = 31.79$		
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3,3-Trimethylhexanoic-1,2',6 Acid, obtained from the ester by saponification, crystallizes from water in compact crystals which melt at 165° – 175° with decomposition, the temperature of melting being dependent on the rate of heating. The acid is very difficultly soluble in ether, and rather difficultly soluble in cold water.

0.2791 gram gave 0.1629 gram water and 0.5047 gram carbon dioxide.

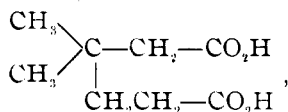
	Calculated for $\text{C}_9\text{H}_{14}\text{O}_6$.	Found.
Carbon	49.54	49.32
Hydrogen	6.42	6.49

The *calcium salt*, $\text{Ca}_3(\text{C}_9\text{H}_{11}\text{O}_6)_2 + 5\text{H}_2\text{O}$, was prepared by dissolving the acid in ammonia, adding calcium chloride and heating the solution on the water-bath. The salt which separated was filtered off, dissolved in cold water and the salt precipitated a second time by warming and evaporating the solution. The salt

is moderately soluble in cold water, and much less soluble in hot water. The portion which separates on warming the solution dissolves on cooling, while the calcium salt of dimethyladipic acid, which separates on warming, does not redissolve on cooling. These facts may be used to advantage in separating mixtures of the two acids.

The salt dried over sulphuric acid lost 13.69 per cent. water. Theory requires for $5\text{H}_2\text{O}$ 14.06 per cent. The dry salt gave 21.79 per cent. calcium. Theory requires 21.81 per cent.

ββ-Dimethyladipic Acid,



is formed quantitatively, when the acid last mentioned is heated for a short time to 200° . The acid is easily soluble in hot water and in ether, difficultly soluble in cold water, and almost insoluble in ligroin. It crystallizes from water in small plates. It melts at 102° .

0.2052 gram gave 0.1490 gram water and 0.2160 gram carbon dioxide.

0.1934 gram gave 0.1401 gram water and 0.3926 gram carbon dioxide.

	Calculated for $\text{C}_8\text{H}_{14}\text{O}_4$.	I.	Found.	II.
Carbon.....	55.17	55.29		55.36
Hydrogen.....	8.05	8.07		8.05

0.1136 gram of the acid took 13.13 cc. tenth-normal caustic potash. Theory requires 13.05 cc.

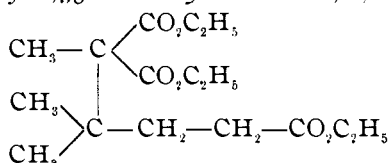
The *calcium salt*, $\text{Ca}(\text{C}_8\text{H}_{12}\text{O}_4) + n\text{H}_2\text{O}$, is most easily prepared by dissolving the acid in ammonia, adding calcium chloride and boiling the solution. No precipitate forms till the solution is warmed. The salt, when once formed, is difficultly soluble but may be crystallized by evaporating its solution, when it is deposited in pearly scales. The salt prepared in this manner lost 21.99 per cent. of water at 140° , while that prepared by precipitation lost only 6.18 per cent. The dried salts gave, respectively, 18.72 and 19.16 per cent. of calcium. Theory requires 18.87 per cent.

The *silver salt* was prepared by adding silver nitrate to a solution of the calcium salt. It is almost entirely insoluble in water. The analysis gave 55.38 per cent. silver. Theory requires 55.67 per cent.

The *copper salt* is precipitated as a green powder on adding copper acetate to an aqueous solution of the acid.

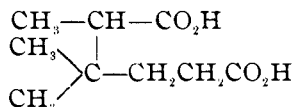
Some time ago Tiemann¹ obtained from ionone an acid which he supposed to be $\beta\beta$ -dimethyladipic acid and which melted at 87° . The $\alpha\alpha$ -dimethyladipic acid which he describes melts at the same temperature.² Baeyer³ has also obtained a dimethyladipic acid which melts at 87° - 88° by the oxidation of tetrahydroeucarvone. He seems to imply that his acid is the $\beta\beta$ -acid but does not make a definite statement to that effect. Since $\beta\beta$ -dimethyladipic acid contains no asymmetric carbon atom, stereoisomerism is extremely improbable and no evidence of its existence has appeared in my study of the body. It would seem, therefore, that if the acids obtained by Tiemann and Baeyer were pure, they must possess another structure than that ascribed to them.

Triethyl Ester of 2,33-Trimethylhexanoic 1,2',6 Acid,



The preparation of this compound by the condensation of γ -bromoisocaproic ester with the diethyl ester of methyl malonic acid has been described.⁴ It has been found that to obtain a pure product, the methyl malonic acid must be purified by crystallization from water⁵ and so freed from malonic acid, which it will contain if prepared by the condensation of malonic ester with methyl iodide. The yield is improved somewhat by the use of γ -chlorisocaproic ester in place of the bromine derivative but it is always poor. A better method of preparation consists in the condensation of the triethyl ester of the trimethyl hexanoic acid described above (p. 399) with methyl iodide by means of sodium ethylate.

$\alpha\beta\beta$ -Trimethyladipic Acid,



¹ *Ber. d. chem. Ges.*, **31**, 860, 884.

² *Ibid.*, **31**, 883.

³ *Ibid.*, **31**, 2074.

⁴ *Am. Chem. J.*, **23**, 128.

⁵ Perkin: *J. Chem. Soc. (London)*, **45**, 510.

This acid is formed when the 3,3-trimethylhexanoic-1,2',6 acid is heated for a short time to 200°. It appears to exist in two forms, a fumaroid and a maleinoid form. Only the former has thus far been obtained pure. The acid was purified by crystallization from water and from ether. It is difficultly soluble in cold water and in ether, almost insoluble in ligroin. It crystallizes from water or from ether in leaflets which melt at 136°.

0.1637 gram of the acid gave 0.1286 gram water and 0.3424 gram carbon dioxide.

	Calculated for $C_9H_{16}O_4$	Found.
Carbon	57.44	57.04
Hydrogen.....	8.57	8.73

ROSE POLYTECHNIC INSTITUTE, TERRE
HAUTE, IND., April 25, 1901.

[CONTRIBUTION FROM THE CHEMICAL DIVISION, U. S. DEPARTMENT OF
AGRICULTURE, NO. 41.—SENT BY H. W. WILEY.]

A NEW INDICATOR FOR USE IN DETERMINING TOTAL ACIDITY OF WINES.¹

BY E. G. RUNYAN.

Received May 11, 1901.

IN maintaining a chemical control of a beet sugar house, it is often necessary to determine by some rapid method the excess of alkali in the juices, sirups, and massecuites. The usual method is to titrate the material with a standard acid solution. As these products vary in color from a light amber to a dark brown, or nearly black, the ordinary indicators often give very unsatisfactory results, or fail entirely, on account of the difficulty of noting the end reaction.

To meet this difficulty, a French chemist, L. Lachaux, in 1892, proposed a mixture of corallin and malachite green² prepared as follows:

Three and one-tenth grams of corallin or commercial rosolic acid are dissolved in 150 cc. of 90 per cent. alcohol, neutralized and mixed with 0.5 gram malachite green dissolved in 50 cc. of alcohol. With this mixture, alkalies give a purple color, which is changed to a green by acids.

Malachite green dissolves in alcohol yielding a greenish blue

¹ Read before the Washington Section of the American Chemical Society, March 14, 1901.

² The zinc-double-chloride of tetramethyl-di-*p*-amidotriphenyl-carbinol. $(C_{15}H_{15}N_2Cl_2)_2 + 2ZnCl_2 + 2H_2O$.