TABLE I

ARYLIDENE DERIVATIVES OF *o*-AMINOPHENOL

Aldehyde	Appearance	Yield, %	M. p., cor., °C.	Formula	Analyses, % N Calcd.	Analyses, % N Found
m-Tolualdehyde	Pale yellow leaflets	52	105	$C_{14}H_{13}NO$	6.63	6.67
p-Tolualdehyde	Pale yellow leaflets	81	108.5	$C_{14}H_{13}NO$	6.63	6.64
o-Chlorobenzaldehyde	Yellow leaflets	48	94	$C_{13}H_{10}NOCl$	6.05	6.15
2-Chloro-5-nitrobenzaldehyde	Bright yellow needles	56	164	$C_{13}H_9N_2O_3Cl$	10.12	10.12

condensed with *o*-aminophenol. Senier and Clarke[4] carried out the same reaction with *o*-nitrobenzaldehyde, obtaining the condensation product. Levi[1] studied the same reaction and arrived at a similar conclusion. While differences in melting points were reported, the spread was never more than four degrees. Beilstein apparently overlooked Möhlau and Adam's statement, as all of the compounds are listed as azomethines.

In order to clear up this situation the three nitrobenzaldehydes were allowed to react with *o*-aminophenol under five different sets of conditions: (1) in the cold without a solvent; (2) on the steam-bath without a solvent; (3) in hot alcohol; (4) in hot glacial acetic acid; (5) the hydrochloride of *o*-aminophenol used instead of the free base. For each of the three nitrobenzaldehydes all five procedures led to the same compound as evidenced by melting point and mixed melting point determinations. Nitrogen analysis gave the following results: *o*-nitrobenzylidene-*o*-aminophenol, m. p. 104.5°, 11.59% N; *m*-nitrobenzylidene-*o*-aminophenol, m. p. 132°, 11.54% N; *p*-nitrobenzylidene-*o*-aminophenol, m. p. 161°, 11.51% N. Since calculation shows 11.56% N for the azomethine compound and 10.77% N for the addition compound, this is considered positive proof that the compounds prepared are azomethines.

During the course of this work four new aldehyde condensation products of *o*-aminophenol have been prepared. These are described in Table I.

Summary

1. Attention is called to errors in the literature.
2. The reactions of *o*-aminophenol with the three nitrobenzaldehydes have been studied. Our results show the products of these reactions to be azomethine compounds.
3. Four new arylidene-*o*-aminophenols have been prepared and described.

GAINESVILLE, FLORIDA RECEIVED JUNE 10, 1940

---

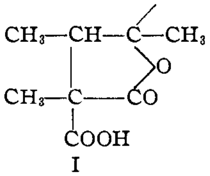
[4] Senier and Clarke, *J. Chem. Soc.*, **105**, 1917 (1914).

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

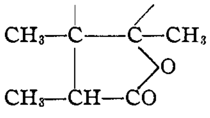
Structure of Monocrotaline. IV. Monocrotalic Acid[1]

BY ROGER ADAMS AND R. S. LONG[2]

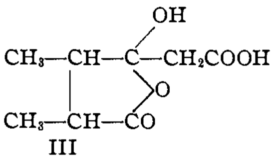
Monocrotalic acid, obtained by catalytic hydrogenation of the alkaloid monocrotaline,[3] was assigned three possible structural formulas I, II and III of which I was selected as the most probable. Monocrotalic acid in the presence of alkali is decarboxylated to monocrotic acid (IV) which was postulated as dimethyllevulinic acid on the basis of its oxidation with sodium hypobromite to meso and racemic dimethylsuccinic acids. Dimethyllevulinic acid has been prepared previously; it is an oil, the *p*-nitrophenylhydrazone of which is reported as a solid.[4] However, no *p*-nitrophenylhydrazone of monocrotic acid could be obtained. α,β-Dimethyllevulinic acid, therefore,



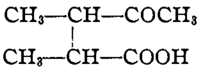
I



II



III



IV

---

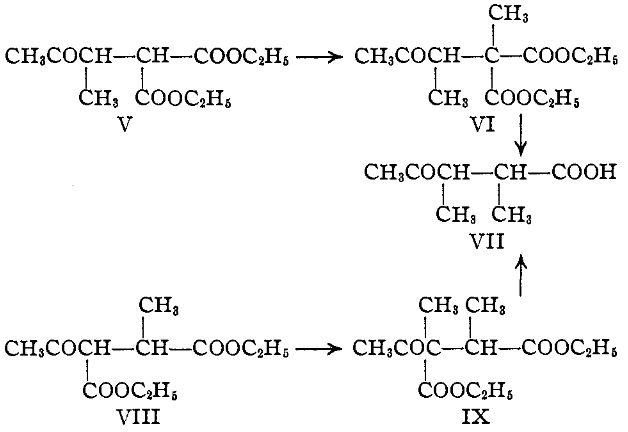
[1] For previous paper see Adams, Rogers and Long, THIS JOURNAL, **61**, 2822 (1939).

[2] An abstract of a thesis submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Chemistry.

[3] Adams and Rogers, THIS JOURNAL, **61**, 2815 (1939).

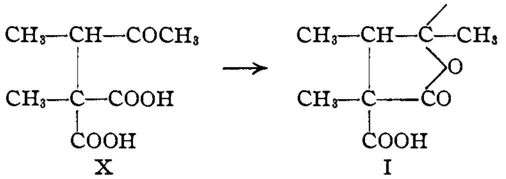
[4] Willstätter and Brossa, *Ber.*, **44**, 2191 (1911).

has been synthesized again (by two different procedures) in order to determine how to characterize the molecule effectively. The first method of synthesis consisted in condensing methyl α-bromoethyl ketone with malonic ester to ethyl α-carbethoxy-β-methyllevulinate (V) followed by methylation to ethyl α-carbethoxy-α,β-dimethyllevulinate (VI) and saponification to α,β-dimethyllevulinic acid (VII). The second procedure was to condense ethyl α-bromopropionate with ethyl acetoacetate to ethyl β-carbethoxy-α-methyllevulinate (VIII) followed by methylation to ethyl β-carbethoxy-α,β-dimethyllevulinate (IX) and saponification to α,β-dimethyllevulinic acid (VII).



It was found impossible to isolate a solid *p*-nitrophenylhydrazone of the synthetic product. A satisfactory solid derivative for identification purposes proved to be the 2,4-dinitrophenylhydrazone of the methyl ester of the acid. A 2,4-dinitrophenylhydrazone was reported previously for methyl monocrotate[5] but the earlier results were in error; it was described as an orange, crystalline compound, m. p. 95–96°, whereas it has been found now to consist of a difficultly separated mixture of two dinitrophenylhydrazones, m. p. 108–109° and 121–122°. Each of the two samples of synthetic methyl α,β-dimethyllevulinate gave two dinitrophenylhydrazones of the same melting points and were shown to be identical with the methyl monocrotate derivatives by means of mixed melting points. Whether the two hydrazones are derived from the two theoretically possible methyl dimethyllevulinates or are *syn-* and *anti-*forms of the hydrazone of a single methyl dimethyllevulinate has not been determined.

The establishment of the structure of monocrotic acid as α,β-dimethyllevulinic acid and its formation from monocrotalic acid by loss of carbon dioxide limits very definitely the possible structures of the latter. The detailed reasons for proposing structure I for monocrotalic acid[1] as the most probable formula will not be repeated here. An approach to its synthesis was begun using as an intermediate compound VI prepared in the synthesis of α,β-dimethyllevulinic acid. By acid hydrolysis, it was hoped that a malonic acid derivative (X) would be formed first which might then spontaneously isomerize to monocrotalic acid (I).



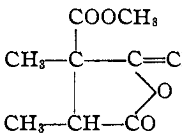
Acid has been shown in previous cases to cause this type of isomerization especially in polysubstituted γ-keto acids.[6] Acid hydrolysis of compound VI, however, resulted in an acid which lost carbon dioxide to form α,β-dimethyllevulinic acid. In contrast to this is monocrotalic acid, which is stable to boiling hydrochloric acid without loss of carbon dioxide. Alkaline saponification of compound VI followed by acidification gave an oily acid (X), which was titrated and shown to be dibasic, thus indicating no lactonization and which upon heating to 80° was decarboxylated to α,β-dimethyllevulinic acid. Similarly ethyl α-carbethoxy-β-methyllevulinate (V) saponifies with alkali to a dibasic acid which in this instance was a solid and obtained in crystalline state. Monocrotalic acid, on the other hand, loses carbon dioxide in alkaline solution even at room temperature to give α,β-dimethyllevulinic acid. The results of these experiments introduce doubts concerning the correctness of the postulated structure of monocrotalic acid as I.

One of the pertinent reasons for not favoring structure II for monocrotalic acid was that the predicted properties of the corresponding anhydro ester (XI) did not coincide entirely with the experimental facts. The anhydro ester was very difficult to reduce, requiring high pressures, and this would not be expected of such a structure as

---

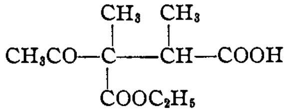
[5] Adams, Rogers and Sprules, THIS JOURNAL, **61**, 2819 (1939).

[6] Rothstein and Shoppee, *J. Chem. Soc.*, 531 (1927); Pandya and Thorpe, *ibid.*, **123**, 2852 (1923); Bredt, *Ann.*, **236**, 228 (1886); **256**, 338 (1890).



XI

XI. The presence of a methylene group in the compound has been demonstrated now as unlikely by application of the method of Doeuvre,[7] which consists in ozonolysis and determination of the formaldehyde liberated by means of the color obtained with the Grosse–Bohle reagent.[8] No formaldehyde was obtained. In spite of these facts, a study was made of ethyl β-carbethoxy-α,β-dimethyllevulinate (IX) a structure which upon hydrolysis of the ester groupings might give a compound of formula II. Upon alkaline saponification of compound IX, carbon dioxide was lost and α,β-dimethyllevulinic acid was isolated. Boiling hydrochloric acid gave similar results. However, cold hydrochloric acid yielded the half ester, unquestionably of structure XII.

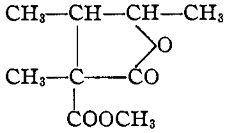


$$\mathrm{CH_3CO{-}\underset{COOC_2H_5}{\overset{CH_3}{C}}{-}\overset{CH_3}{C}H{-}COOH}$$

XII

The acid XII gave a normal neutral equivalent, thus apparently showing no tendency to isomerize to a cyclic molecule. Methyl monocrotalate, on the other hand, hydrolyzes by means of hydrochloric acid to monocrotalic acid which is stable in this medium and does not lose carbon dioxide.

In contrast to the instability of monocrotalic acid to alkali and the stability to acid, is the acid obtained by hydrolysis of the methyl ester of hydrogenated anhydromonocrotalic acid, which was assigned[1] formula XIII. This ester hydrolyzes



XIII

either with boiling acid or alkali to the corresponding acid which shows no tendency to lose carbon dioxide.

With the failure to synthesize a compound of structure I or II, attempts are being made now to prepare a compound of structure III as well as of structure XIII. The latter, if identical with the methyl ester of dihydroanhydromonocrotalic acid, would limit the possible formulas of monocrotalic acid much more rigidly than merely the degradation to α,β-dimethyllevulinic acid which has been positively identified.

Experimental

Ethyl α-Carbethoxy-β-methyllevulinate.—To a suspension of 12.2 g. of powdered sodium in 200 cc. of dry ether was added slowly 130 g. of diethyl malonate. The reaction started immediately but it was necessary to stir overnight to complete the precipitation of the sodium salt which separated as a white, gelatinous precipitate. After 400 cc. of dry ether had been added to permit more efficient stirring, 80 g. of methyl α-bromoethyl ketone was added rapidly enough to keep the ether refluxing gently. The gelatinous precipitate of diethyl sodio-malonate was gradually replaced by a more finely divided precipitate of sodium bromide. The mixture was refluxed gently with stirring for twenty-four hours. Water containing a few cubic centimeters of hydrochloric acid was added to dissolve the sodium bromide. The ether layer was washed twice with water and dried over anhydrous sodium sulfate. The ether was removed by distillation from the steam-bath and the residue was distilled *in vacuo;* colorless liquid, b. p. 120–125° (3 mm.); $n^{20}{}_{\mathrm{D}}$ 1.4321; $d^{20}{}_{4}$ 1.0394; yield, 85 g. (74%).

Anal. Calcd. for $C_{11}H_{18}O_5$: C, 57.39; H, 7.83. Found: C, 56.99; H, 7.99.

This compound was prepared in approximately the same yield using toluene or a mixture of toluene and ethanol as the solvent.

The 2,4-dinitrophenylhydrazone was prepared by refluxing 0.2 g. of the ester with an equivalent amount of 2,4-dinitrophenylhydrazine in 10 cc. of ethanol containing 0.2 cc. of concentrated hydrochloric acid for about ten minutes. Upon cooling, the product separated as a yellow, crystalline precipitate. Recrystallized from ethanol it gave fine yellow crystals, m. p. 118–119° (cor.); yield, 85%.

Anal. Calcd. for $C_{17}H_{22}O_8N_4$: C, 49.76; H, 5.37; N, 13.66. Found: C, 49.91; H, 5.34; N, 13.49.

The possibility that methyl α-bromoethyl ketone in reacting with diethyl sodio-malonate had first dehydrohalogenated to methyl vinyl ketone followed by addition of the malonic ester in the β-position to the keto group was excluded. The 2,4-dinitrophenylhydrazone of the product that would be obtained thus is reported to melt at 55°.[9]

Hydrolysis of Ethyl α-Carbethoxy-β-methyllevulinate.—A solution of 15 g. of ethyl α-carbethoxy-β-methyllevulinate and 15 g. of potassium hydroxide dissolved in 200 cc. of ethanol was refluxed for ten hours. The ethanol was distilled under reduced pressure and the residue was dissolved in sufficient dilute hydrochloric acid to render the solution acidic to congo red. The aqueous solution was extracted with ether, the ether solution was dried, and the ether was distilled, the last traces being removed under reduced pressure. The residue solidified rapidly to give 9.8 g. (84%) of a tan, somewhat oily solid. The color was removed with Darco in ether solution, petroleum ether (b. p. 30–60°) was added to incipient cloudiness,

---

(7) Doeuvre, *Bull. soc. chim.*, [5] **3**, 612 (1936).

(8) Doeuvre, *ibid.*, [4] **45**, 146 (1929).

(9) Harradence and Lions, *J. Proc. Roy. Soc. N. S. Wales*, **72**, 233 (1939).

and the solution was cooled in the ice box until crystallization was complete. The product, α-carboxy-β-methyllevulinic acid, separated in small clusters of pure, white crystals, m. p. 127–128° (cor.) with decomposition; yield, 2.5 g.

Anal. Calcd. for $C_7H_{10}O_5$: C, 48.28; H, 5.75; neut. equiv., 87. Found: C, 48.68; H, 5.94; neut. equiv., 88.6.

The filtrate from the crystallization was evaporated to dryness and the residue, which consisted of an oily solid, was heated at 130 to 140° until decarboxylation was complete. The β-methyllevulinic acid which remained had a b. p. 115–118° (3 mm.); n^{17}_D 1.4446; yield, 3.5 g. The value previously reported for the refractive index is n^{17}_D 1.4443.[10]

The *p*-nitrophenylhydrazone of β-methyllevulinic acid was prepared by adding 0.1 g. of β-methyllevulinic acid to an equivalent amount of *p*-nitrophenylhydrazine dissolved in the minimum amount of 50% acetic acid. The product separated almost at once and after recrystallization from dilute ethanol formed yellow crystals, m. p. 160–162° (cor.); previously reported m. p. 168–169°.[10]

Anal. Calcd. for $C_{12}H_{15}O_4N_3$: C, 54.34; H, 5.66. Found: C, 54.19; H, 5.48.

Ethyl α-Carbethoxy-α,β-dimethyllevulinate.—To a suspension of 2 g. of powdered sodium in 200 cc. of dry ether was added 20 g. of ethyl α-carbethoxy-β-methyllevulinate. The formation of the sodium derivative began immediately but it was necessary to stir overnight in order to bring the sodium completely into solution. The sodium salt which had precipitated was brought partially into solution by the addition of 30 cc. of absolute ethanol and then 20 g. of methyl iodide was added rapidly. The precipitation of sodium iodide began at once and after three hours of refluxing with stirring the solution was neutral to moist litmus paper. Water was added to dissolve the sodium iodide, the ether layer was separated, washed twice with water, and dried over anhydrous sodium sulfate. The ether was distilled from the steam-bath and the residue was distilled *in vacuo:* colorless liquid, b. p. 116–117° (2.5 mm.); n^{20}_D 1.4421; d^{20}_4 1.0668; yield, 16 g. (76%).

Anal. Calcd. for $C_{12}H_{20}O_5$: C, 59.02; H, 8.19; M_D 60.95. Found: C, 59.14; H, 8.14; M_D 60.55.

The same compound was prepared in approximately the same yield using absolute ethanol or a mixture of toluene and absolute ethanol as the solvent, and in somewhat lower yield using benzene as the solvent. The refractive index was occasionally slightly lower due to the presence of a small amount of unmethylated ester.

It was also prepared from diethyl methylmalonate and methyl α-bromoethyl ketone by a procedure similar to that used for ethyl α-carbethoxy-β-methyllevulinate but the yield was much lower and the product distilled over a wide range.

An attempt to prepare the 2,4-dinitrophenylhydrazone of the above compound by a procedure identical with that used for ethyl α-carbethoxy-β-methyllevulinate was unsuccessful, no reaction taking place.

α,β-Dimethyllevulinic Acid.—A solution of 10 g. of ethyl α-carbethoxy-α,β-dimethyllevulinate and 5 g. of potassium hydroxide dissolved in 75 cc. of ethanol was refluxed gently for twelve hours. The ethanol was distilled under diminished pressure and the residue was dissolved in a small amount of water. The solution was acidified to congo red with concentrated hydrochloric acid and then extracted six times with 20-cc. portions of ether. After drying over anhydrous sodium sulfate, the ether was removed completely *in vacuo.* The residue was an extremely viscous acidic liquid, α-carboxy-α,β-dimethyllevulinic acid; yield, 6 g. (78%). When 4 g. of this crude acid was heated at 120° in a 5-cc. modified Claisen distilling flask, decarboxylation took place. Distillation of the residue *in vacuo* gave a small forerun of neutral material followed by 2.5 g. (83%) of α,β-dimethyllevulinic acid, b. p. 117–122° (4 mm.); n^{20}_D 1.4470. The indices of refraction reported for monocrotic acid are $n^{17.5}_D$ 1.4449 and n^{19}_D 1.4480.[3] The discrepancy in the values is very probably due to the presence of α,β,γ-trimethylangelicalactone, which appears to form to a certain extent when α,β-dimethyllevulinic acid is distilled.

Anal. Calcd. for $C_7H_{12}O_3$: C, 58.31; H, 8.33; neut. equiv., 144. Found: C, 58.14; H, 8.35; neut. equiv., 154.

The high value for the neutral equivalent is due to the formation of a small amount of α,β,γ-trimethylangelicalactone during distillation. A similar value is obtained for monocrotic acid.

The neutral by-product in the decarboxylation described above is probably α,β,γ-trimethylangelicalactone as it could be further saponified with alkali to give α,β-dimethyllevulinic acid.

Methyl α,β-Dimethyllevulinate 2,4-Dinitrophenylhydrazone.—To a solution of the above acid in ether was added an excess of diazomethane. The ether solution was dried over anhydrous sodium sulfate and the ether was evaporated by a stream of air. The residual methyl α,β-dimethyllevulinate was treated with 2,4-dinitrophenylhydrazine in the usual manner. The dinitrophenylhydrazone separated first as a yellow solid, m. p. 85–105°. Four recrystallizations from methanol gave light orange needles, m. p. 121–122° (cor.). The mixed melting point with an authentic sample of methyl monocrotate 2,4-dinitrophenylhydrazone, m. p. 121–122° (cor.), was the same.

Anal. Calcd. for $C_{14}H_{18}O_6N_4$: C, 49.70; H, 5.33. Found: C, 49.72; H, 5.27.

The mother liquors from the four recrystallizations were evaporated to dryness and the residue was recrystallized slowly from ether-petroleum ether (b. p. 30–60°). The two crystalline forms which were obtained were separated by the procedure given for methyl monocrotate 2,4-dinitrophenylhydrazone; orange, prismatic crystals, m. p. 107–109° (cor.); light orange needles, m. p. 121–122°, identical with the product obtained above from methanol. Neither form depressed the melting point of the corresponding hydrazone of methyl monocrotate.

Methyl α,β-Dimethyllevulinate.—A cold ether solution of 2 g. of α,β-dimethyllevulinic acid was treated with a slight excess of an ether solution of diazomethane. The ether solution was dried over anhydrous sodium sulfate and distilled: colorless liquid, b. p. 97–98° (20 mm.); n^{25}_D 1.4257; yield, 1.6 g. The refractive index did not change upon redistillation. The value reported for methyl monocrotate is n^{25}_D 1.4273.[5]

---

(10) Pauly, Gilmour and Will, *Ann.*, **403**, 119 (1914).

Anal. Calcd. for $C_8H_{14}O_3$: C, 60.75; H, 8.93. Found: C, 60.53; H, 8.91.

Methyl Monocrotate 2,4-Dinitrophenylhydrazone.—To a solution of 2 g. of methyl monocrotate in 100 cc. of methanol was added 2.5 g. of 2,4-dinitrophenylhydrazine. The mixture was heated to boiling, 2 cc. of concentrated hydrochloric acid was added, and the solution was refluxed gently for five minutes. After standing at room temperature overnight, 1.62 g. of product separated in two different crystalline forms, orange prisms and fine yellow needles. A rough separation was effected by hand-picking and the crude prismatic form was purified by two or more slow crystallizations from ether–petroleum ether (b. p. 30–60°); m. p. 108–109° (cor.).

Anal. Calcd. for $C_{14}H_{18}O_6N_4$: C, 49.70; H, 5.33. Found: C, 49.98; H, 5.51.

The mother liquor from the original precipitate was concentrated to 60 cc. and allowed to stand at room temperature until precipitation was complete. The product, 1.44 g. was again a mixture of both forms. Mechanical separation gave 0.85 g. of the yellow needles which, after two or more slow recrystallizations from ether–petroleum ether (b. p. 30–60°) melted at 121–122° (cor.).

Anal. Calcd. for $C_{14}H_{18}O_6N_4$: C, 49.70; H, 5.33. Found: C, 49.75; H, 5.22.

The melting point of a mixture of the two forms was 91–97°.

Hydrolysis of **Ethyl α-Carbethoxy-α,β-dimethyllevulinate.**—The saponification of ethyl α-carbethoxy-α,β-dimethyllevulinate to give α-carboxy-α,β-dimethyllevulinic acid was attempted a number of times using varying strengths of ethanolic potassium hydroxide and aqueous sodium hydroxide, but in no case could a crystalline acid be isolated. The product was in every instance an extremely viscous, acidic liquid, which upon heating to about 80° was decarboxylated. The substance thus formed boiled at 80–120° (2 mm.) and was partially insoluble in alkali. This neutral product was evidently a mixture of α,β,γ-trimethylangelicalactone and ethyl α,β-dimethyllevulinate, since further saponification with alkali gave α,β-dimethyllevulinic acid. The amount of neutral material varied and was reduced to the minimum when more concentrated alkali was used.

Hydrolysis of ethyl α-carbethoxy-α,β-dimethyllevulinate by refluxing with concentrated hydrochloric acid resulted in decarboxylation during hydrolysis with the formation of α,β-dimethyllevulinic acid.

Ethyl β-Carbethoxy-α-methyllevulinate.—This compound was prepared by the procedure used by Bischoff.[11] The product was a colorless liquid, b. p. 107° (2 mm.); n^{20}_D 1.4341; yield, 75%.

The 2,4-dinitrophenylhydrazone was prepared by refluxing 0.2 g. of the above ester with an equivalent amount of 2,4-dinitrophenylhydrazine in 10 cc. of ethanol containing 0.2 cc. of concentrated hydrochloric acid for ten minutes. The product separated on cooling as a yellow, crystalline solid. Recrystallized from ethanol it gave fine, light yellow needles, m. p. 99–100° (cor.).

Anal. Calcd. for $C_{17}H_{22}O_8N_4$: C, 49.76; H, 5.37. Found: C, 49.77; H, 5.56.

Ethyl β-Carbethoxy-α,β-dimethyllevulinate.—The procedure used by Hardtmuth[12] was followed with slight modification. To a suspension of 6.5 g. of powdered sodium in 100 cc. of dry benzene was added 65 g. of ethyl β-carbethoxy-α-methyllevulinate. The formation of the sodium derivative began rapidly but it was necessary to reflux with stirring on the steam cone for one hour to complete the reaction. Methyl iodide in slight excess was added slowly. There was no reaction at first but after about fifteen minutes sodium iodide started to precipitate. The mixture was stirred overnight and then refluxed with stirring for one hour. Water was added to dissolve the sodium iodide and the benzene layer was taken up with ether. The ether extract was washed well, dried over anhydrous sodium sulfate and distilled. The product was a colorless liquid, b. p. 110–115° (2 mm.); n^{20}_D 1.4409; d^{20}_4 1.0599; yield, 43 g. (62%).

Anal. Calcd. for $C_{12}H_{20}O_5$: C, 59.02; H, 8.19; M_D, 60.95. Found: C, 58.59; H, 8.22; M_D, 60.77.

The same compound was prepared in slightly lower yield using dry ether as the solvent. It was also prepared in approximately the same yield by refluxing an alcoholic solution of the sodium salt of ethyl β-carbethoxy-α-methyllevulinate with a slight excess of methyl iodide for ten hours. In each case the value obtained for the refractive index was n^{20}_D 1.4410. In addition, it was prepared from ethyl α-methylacetoacetate and ethyl α-bromopropionate by a procedure similar to that used for ethyl β-carbethoxy-α-methyllevulinate. In this case, however, a large amount of starting material was recovered and the yield was only 25%.

Ethyl α-Methylacetoacetate 2,4-Dinitrophenylhydrazone.—This compound was prepared in order to check on the purity of the ethyl α-methylacetoacetate used in the above synthesis. A solution of 0.5 g. of the ester and 0.7 g. of 2,4-dinitrophenylhydrazine in 25 cc. of ethanol containing 0.5 cc. of concentrated hydrochloric acid was refluxed for ten minutes. The product separated on cooling as orange needles; yield, 82%. Recrystallized from ethanol it gave fine, yellow-orange needles, m. p. 56–57° (cor.).

Anal. Calcd. for $C_{13}H_{16}O_6N_4$: C, 48.15; H, 4.91. Found: C, 48.58; H, 5.01.

β-Carbethoxy-α,β-dimethyllevulinic Acid.—A solution of 13.5 g. of ethyl β-carbethoxy-α,β-dimethyllevulinate in 50 cc. of concentrated hydrochloric acid was allowed to shake at room temperature for twenty-four hours. The solution was then concentrated under reduced pressure at slightly above room temperature to about three-fourths of its original volume and made alkaline with sodium hydroxide. After extracting the small amount of oil which separated with ether, the aqueous layer was acidified to congo red with concentrated hydrochloric acid and extracted three times with ether. The ether extract was dried over anhydrous sodium sulfate and distilled. A forerun of 3 g., b. p. 135–154° (2.5 mm.), consisting of a mixture of β-carbethoxy-α,β-dimethyllevulinic acid and α,β-dimethyllevulinic acid, was obtained, and then 6.5 g. of pure β-carbethoxy-α,β-dimethyllevulinic acid, b. p. 154–158° (2.5 mm.). For analysis, the second fraction was redistilled and a sample taken near the end of the distillation; n^{20}_D 1.4578.

---

[11] Bischoff, *Ann.*, **206**, 320 (1881).

[12] Hardtmuth, *ibid.*, **192**, 142 (1878).

Anal. Calcd. for $C_{10}H_{16}O_5$: C, 55.56; H, 7.41; neut. equiv., 216. Found: C, 55.46; H, 7.51; neut. equiv., 221.7.

This compound was identified by saponification with 40% aqueous potassium hydroxide. In addition to dimethyllevulinic acid a solid acid was obtained which was recrystallized from water and identified by a mixed melting point determination as *meso*-dimethylsuccinic acid.

Hydrolysis of Ethyl β-Carbethoxy-α,β-dimethyllevulinate to α,β-Dimethyllevulinic Acid.—A mixture of 24.4 g. of ethyl β-carbethoxy-α,β-dimethyllevulinate and 100 cc. of 10% aqueous sodium hydroxide solution was refluxed for twelve hours. The alkaline solution was extracted twice with ether to remove traces of unsaponified ester and then acidified to congo red with concentrated hydrochloric acid. The addition of hydrochloric acid was accompanied by a vigorous evolution of carbon dioxide. The milky solution which resulted was extracted five times with ether, the ether solution was dried over anhydrous sodium sulfate, and the ether was distilled from the steam-bath. The residue, a yellow viscous liquid, was distilled *in vacuo:* colorless oil, b. p. 117–118° (3.5 mm.); n^{20}_D 1.4451; yield, 10.4 g. (72%). The refractive index did not change upon redistillation.

Anal. Calcd. for $C_7H_{12}O_3$: neut. equiv., 144. Found: neut. equiv., 142.7.

The residue in the distilling flask solidified near the end of the distillation. It was pressed dry on a clay plate and washed with a small amount of dry ether to give 0.54 g. of a white crystalline acid. After purification by recrystallization from water the melting point was 190–192° (cor.) with decomposition. It proved to be *meso*-dimethylsuccinic acid.

Anal. Calcd. for $C_6H_{10}O_4$: neut. equiv., 73. Found: neut. equiv., 73.7.

Saponification of this compound with either alkali or boiling hydrochloric acid resulted in direct formation of α,β-dimethyllevulinic acid. Evidence for this was obtained by the precipitation of potassium carbonate from the reaction mixture when alcoholic potassium hydroxide was used and by the precipitation of barium carbonate when the exit gases were passed into a solution of barium hydroxide when hydrochloric acid was used as the hydrolytic agent.

Methyl α,β-Dimethyllevulinate 2,4-Dinitrophenylhydrazone.—To a cold solution of 2 g. of α,β-dimethyllevulinic acid, obtained by alkaline hydrolysis of ethyl β-carbethoxy-α,β-dimethyllevulinate in a small amount of ether was added a slight excess of a cold, ethereal solution of diazomethane. The ether was removed by distillation, 100 cc. of methanol and 2.5 g. of 2,4-dinitrophenylhydrazine were added, the mixture was heated to boiling, and 2 cc. of concentrated hydrochloric acid introduced. After refluxing gently for five minutes, the solution was filtered and allowed to cool. The yellow solid which separated was resolved into two forms, deep orange prisms, m. p. 107–109° (cor.), and light orange needles, m. p. 121.5–122.5° (cor.), according to the procedure given for methyl monocrotate 2,4-dinitrophenylhydrazone. Neither form depressed the melting point of the corresponding 2,4-dinitrophenylhydrazone obtained from methyl monocrotate.

Hydrolysis of Methyl Monocrotalate.—A solution of 0.2 g. of methyl monocrotalate and 5 cc. of concentrated hydrochloric acid after refluxing for five hours, was evaporated by means of a stream of air. The residue (0.13 g.) was monocrotalic acid identified by a mixed melting point with an authentic sample.

A mixture of 7 g. of methyl monocrotalate and a solution of 6 g. of sodium hydroxide in 20 cc. of water was refluxed for five hours. The solution was diluted with a little water, acidified to congo red with concentrated hydrochloric acid, and extracted continuously with ether for ten hours. A vigorous evolution of carbon dioxide accompanied the acidification. The product, 3 g., b. p. 95–110° (2 mm.), consisted of α,β-dimethyllevulinic acid contaminated with a small amount of α,β,γ-trimethylangelicalactone.

Hydrolysis of Methyl Dihydroanhydromonocrotalate.—Acid hydrolysis of this compound has been shown to yield the corresponding acid, m. p. 131–132° (cor.); $[\alpha]^{30}_D$ + 3.80.[1]

Alkali saponification was not clean-cut but in no case was carbon dioxide eliminated in the reaction.

Summary

Ethyl α-carbethoxy-α,β-dimethyllevulinate was prepared and hydrolyzed. Alkali gave the corresponding malonic acid and acid caused the direct formation of α,β-dimethyllevulinic acid.

Ethyl β-carbethoxy-α,β-dimethyllevulinate was also synthesized and hydrolyzed. With both acid and alkali α,β-dimethyllevulinic acid was obtained.

These results lead to the conclusion that two of the previously proposed structures for monocrotalic acid are probably incorrect since monocrotalic acid loses carbon dioxide when treated with alkali and is stable to acid.

α,β-Dimethyllevulinic acid has been synthesized by the two methods indicated above and has been shown to be identical with monocrotic acid. This was done by comparing and showing to be identical the 2,4-dinitrophenylhydrazones of the methyl esters of the natural and synthetic acids.

URBANA, ILLINOIS RECEIVED JUNE 17, 1940