Anal. Calcd. for $C_{18}H_{17}ON_3$: C, 74.23; H, 5.89; N, 14.43. Found: C, 74.21; H, 5.75; N, 14.52.

Resolution of N-acetyl-DL-tryptophan. With 95% L-lysine. *N*-Acetyl-DL-tryptophan (12.3 g., 0.050 mole) was stirred into a solution of 95% L-lysine (7.3 g., 0.062 mole) in water (18.7 g.) and, when it had dissolved, methanol (50 ml.) was added. The solution was seeded with pure L-lysine *N*-acetyl-L-tryptophanate (0.5 g., 0.002 mole), then gently stirred for 3.5 hr. at 25°. During this period the solution turned slowly into a thick slurry. This slurry was poured into a 3-cm., coarse-grained, sintered glass funnel and filtered under vacuum. The product, after washing with 75% methanol-water and drying, weighed 4.9 g. (0.013 mole, 27% conversion). It had a specific rotation, $[\alpha]^{22}D$ +17.17 (*c*, 3.6, water). This compared with $[\alpha]^{22}D$ values of +3.45 (*c* 2.8, water) for L-lysine *N*-acetyl-DL-tryptophanate and +20.47 (*c* 5, water) for L-lysine *N*-acetyl-L-tryptophanate and indicates that the salt had an optical purity of 90.0%.

With 100% L-lysine. At 25°. Pure L-lysine (11.2 g., 0.095 mole) was dissolved in water (19.8 g.). *N*-Acetyl-DL-tryptophan (12.3 g., 0.050 mole) was dissolved in the lysine solution, and the L-lysine *N*-acetyl-DL-tryptophanate solution so formed was diluted with methanol (78 ml.), seeded with L-lysine *N*-acetyl-L-tryptophanate (*ca.* 1 mg.), then stirred at 25° for 2.25 hr. At the end of this period, the solution was passed through a sintered glass filter, and the solid so obtained was washed with a mixture of methanol (22 ml.) and water (4 ml.). The resolution salt after drying over calcium chloride overnight weighed 6.39 g. (0.0175 mole, 35% conversion). This salt was found to be 90.0% pure L-lysine *N*-acetyl-L-tryptophanate ($[\alpha]^{22}D$ +16.8, *c* 4.7, water).

At 45°. To a solution of L-lysine (8.0 g., 0.068 mole) in water (21.8 g.) were added successively *N*-acetyl-DL-tryptophan (12.3 g., 0.050 mole), methanol (75 ml.), a finely triturated slurry of L-lysine *N*-acetyl-L-tryptophanate (0.5 g., 0.001 mole) in methanol (10 ml.), and, lastly, an additional amount of methanol (5 ml.). The suspension so obtained was stirred at 45° for 6.67 hr. and then filtered. The filter cake was washed first with 92% methanol–water (25 ml.) and then with 96% methanol–water (25 ml.). The salt obtained in this resolution (6.25 g., 0.0175 mole, 34% conversion) was shown to be 96.0% pure L-lysine *N*-acetyl-L-tryptophanate ($[\alpha]^{22}D$ +19.27, *c* 2.9, water).

Isolation of N-acetyl-L-tryptophan from L-lysine N-acetyl-L-tryptophanate. For this separation a sample of L-lysine *N*-acetyl-L-tryptophanate having a specific rotation, $[\alpha]^{22}D$ +17.2 (*c* 2.8, water) and an optical purity of 91% was used. A sample (5.8 g., 0.016 mole) of this product was dissolved in 50% methanol–water (100 ml.) and then poured through a bed of washed Dowex 50-8X resin (50 ml., H^+ form, 20–50 mesh). After the L-lysine *N*-acetyl-L-tryptophanate solution had been run through the bed, the resin was washed with water (50 ml.). After standing overnight, the effluent and the wash solution deposited crystals of *N*-acetyl-L-tryptophan which were collected by filtration. Concentration of the filtrates by evaporation under vacuum produced an additional quantity of product. The total yield obtained was 2.9 g. (0.012 mole, 79% yield). The material had a specific rotation, $[\alpha]^{29}D$ +21.2 (*c* 0.85, ethanol) and on optical purity of 91.0%.

An equally effective way of separating the amino acid components of L-lysine *N*-acetyl-L-tryptophanate was to run a solution of the salt over Dowex 50 (NH_4^+ form) resin. In this case the effluent consisted of a solution of ammonium *N*-acetyl-L-tryptophanate. *N*-Acetyl-L-tryptophan was filtered from the solution after acidification.

In both of the above examples, the L-lysine component of the resolution salt was absorbed on the resin and could be recovered by elution by 20% ammonium hydroxide (100 ml. in each case). The ammonium hydroxide eluate was evaporated to remove the ammonia, and the L-lysine reused.

Hydrolysis of N-acetyl-L-tryptophan. *N*-Acetyl-L-tryptophan (10 g., 0.040 mole) was boiled under reflux with 2 *N* hydrochloric acid (50 ml.) for 2 hr., then cooled, diluted with an equal volume of methanol, and poured down a 2 × 80 cm. column of Amberlite IR-45 resin (OH^- form). The resin was washed first with methanol (300 ml.) and then with hot water (200 ml.). The effluent and wash solution were mixed and evaporated to dryness at about 50° to give L-tryptophan (7.4 g., 0.036 mole, 89%). The optical purity of this product was 96.0%.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF MIAMI]

Studies of Thermal Decarboxylation of Iron Carboxylates. I. Preparation of Symmetrical Aliphatic Ketones[1,2]

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The thermal decarboxylation of iron carboxylates has been demonstrated to be an excellent method for the preparation of symmetrical, straight chain, aliphatic ketones. Some anomalous results are also reported.

The intermolecular decarboxylation of alkaline earth salts of carboxylic acids is frequently cited as a general method useful for the preparation of carbonyl compounds. A recently published critique[3] of this reaction presents evidence that yields are low and the expected carbonyl compounds are mixed with a variety of homologous compounds. Easterfield and Taylor[4] reported the syntheses of symmetrical ketones in yields of 60–80% by the reaction of straight chain fatty acids with iron filings, followed by distillation. They worked successfully with carboxylic acids of eighteen to thirty carbon atoms, but reported negative results

(1) Abstracted in part from the M.S. thesis of Robert Davis, University of Miami (1961).

(2) Presented before the 140th Meeting of the American Chemical Society, Chicago, Ill., Sept. 3–8, 1961.

(3) H. Schultz and J. Sickels, *J. Chem. Educ.*, **38**, 300 (1961).

(4) T. Easterfield and C. Taylor, *J. Chem. Soc.*, **99**, 2298 (1911).

from such simple acids as ethanoic acid, butanoic acid, and phenylethanoic acid. Ruzicka *et al.*,[5] later reported the preparation of 1,20-henicosadiene-11-one in good yield from 10-undecenoic acid.

The purpose of this paper is to report the successful syntheses of symmetrical ketones from the iron salts of the lower molecular weight fatty acids, as well as a study of the influence of certain substituents upon the reaction.

In essence, it was demonstrated that when fatty acids were refluxed with iron powder, hydrogen was evolved and the iron(II) carboxylates formed. When heated, the iron(II) carboxylates decomposed to yield symmetrical ketones, ferrous oxide, and carbon dioxide.

$$2\ \mathrm{RCOOH} + \mathrm{Fe} \longrightarrow (\mathrm{RCO\bar{O}})_2\mathrm{Fe}^{++} + \mathrm{H}_2$$

$$(\mathrm{RCO\bar{O}})_2\mathrm{Fe}^{++} \longrightarrow \mathrm{RCOR} + \mathrm{FeO} + \mathrm{CO}_2$$

Salt formation occurred very rapidly with ethanoic and propanoic acids; butanoic acid and higher members of the series reacted at lower but relatively constant rates with iron powder, evolution of hydrogen beginning at 80–140°.

The iron carboxylates were deduced to be ferrous in nature. This deduction was based upon a number of observations. It was noted that as salt formation progressed, the material assumed the light green color characteristic of iron compounds in which iron exists in the iron(II) oxidation state. If the cooled salts were exposed to air, the surface would immediately turn dark brown; however, cool iron carboxylates covered with dry nitrogen exhibited no change in the light green color. Also, the crude distillates from iron salts of butanoic through heptanoic acids all had light green colors while protected from air; all gave positive tests for iron(II) ion (precipitation of Prussian blue on addition of potassium ferricyanide solution); all turned from light green to light brown on contact with air, and on redistillation, the crude yields left a trace of brown ferric oxide. (Only the acids cited above gave iron salts of a sufficiently high vapor pressure to distil in detectable quantities into the crude yield). Hexanoic acid gave a yield of 70% of ketone with little tar formation when treated with one equivalent of iron. The dry, nonmagnetic, black powder remaining as a residue after destructive distillation of the iron(II) hexanoate was protected from air with dry nitrogen; this residue of iron(II) oxide was treated with an equivalent of hexanoic acid, refluxed, and again destructively distilled to give 63% of pure ketone. The black residue from the second reaction was also without tar and was not magnetic. The oxide was scraped from the flask, finely powdered, and dried in air several days. At this point the black iron oxide residue was strongly magnetic. It was again treated with a third portion of an equivalent of hexanoic acid to yield only 2% of ketone. Commercial iron(II,III) oxide (magnetic iron oxide) gave only 4% of ketone when treated with hexanoic acid. Commercial iron(III) oxide gave no ketone from hexanoic acid.

Decomposition of the iron(II) carboxylates occurred in most instances at 250–300°; iron(II) ethanoate and propanoate were, however, amazingly stable up to 400–500°. To eliminate the possibility of loss of volatile carbonyl products during decarboxylation of iron(II) ethanoate and iron(II) propanoate, the evolved vapors were condensed in an ice water condenser and the gases were bubbled through a cold alcohol trap. The alcohol from this trap gave no precipitate with 2,4-dinitrophenylhydrazine reagent. The relatively poor yields of propanone and 3-pentanone cited in Table I may be explained by the fact that at the very high temperature required for the decomposition of iron(II) ethanoate and iron(II) propanoate, uncontrolled scission of other bonds of the molecule occurred. Reasonable explanation for the great stability of these salts as compared with those of longer chain acids is difficult. It is possible that longer chain acid moieties have a greater shielding effect toward iron(II) cation than do the smaller ethanoate and propanoate units, thus decreasing coulombic attraction between iron(II) cation and organic anion and resulting in a less ionic crystal lattice. This hypothesis was supported by two further observations: that the melting points of the iron salts decreased with increasing carbon chain length, and that the vapor pressures of the salts of acids of four carbon atoms or more were higher than either the iron(II) ethanoate or iron(II) propanoate. The vapor pressures of the iron salts of acids of four or five carbon atoms were found to be greater than all others of the series. Indeed, the iron salts of 2-methylpropanoic, 2-methylbutanoic, and 2,2-dimethylpropanoic acids sublimed extensively during attempts at destructive distillation. Those acids whose reflux temperatures were above the decomposition temperatures of the iron salts formed produced salts which decomposed during initial refluxing. The ferrous oxide thus formed reacted with more acid to give more iron(II) carboxylate for decomposition.

$$2\ \mathrm{RCOOH} + \mathrm{Fe} \longrightarrow (\mathrm{RCO\bar{O}})_2\mathrm{Fe}^{++} + \mathrm{H}_2$$

$$(\mathrm{RCO\bar{O}})_2\mathrm{Fe}^{++} \longrightarrow \mathrm{RCOR} + \mathrm{FeO} + \mathrm{CO}_2$$

$$2\ \mathrm{RCOOH} + \mathrm{FeO} \longrightarrow (\mathrm{RCO\bar{O}})_2\mathrm{Fe} + \mathrm{H}_2\mathrm{O}$$

Although all data reported in Table I were obtained by reaction of an equivalent of acid with an equivalent plus 10% of iron, the potential utility of the use of a catalytic amount of iron in certain cases was demonstrated. Butanoic acid, b.p. 162–164°, gave a 70% yield of ketone from an equivalent of iron, and only a 35% yield of ketone from one-half of an equivalent of iron powder; undecanoic

(5) L. Ruzicka, M. Stoll, W. Sherrer, H. Schinz, and C. Seidel, *Helv. Chim. Acta*, **15**, 1465 (1932).

TABLE I

DECARBOXYLATION PRODUCTS FROM IRON(II) CARBOXYLATES

Acid	Products	%
Ethanoic	Propanone	25
Phenylethanoic	1,3-Diphenylpropanone	71
Methoxyethanoic	Methanol	1
Phenoxyethanoic	Phenol	60
Propanoic	3-Pentanone	48
2-Methylpropanoic	2,4-Dimethylpentanone-3	53
2,2-Dimethylpropanoic	None	—
3-Phenylpropanoic	1,5-Diphenylpentanone-3	43
Butanoic	4-Heptanone	70
trans-2-Butenoic	None	—
2-Methylbutanoic	None	—
3-Methylbutanoic	2,6-Dimethylheptanone-4	46
4-Phenylbutanoic	1,7-Diphenylheptanone-4	35
Pentanoic	5-Nonanone	69
Hexanoic	6-Undecanoic	70
Heptanoic	7-Tridecanone	74
Octanoic	8-Pentadecanone	80
Nonanoic	9-Heptadecanone	91
Decanoic	10-Nonadecanone	96
Undecanoic	11-Henicosanone	91

acid, b.p. *ca.* 280°, on the other hand, gave 91% of ketone with either set of reaction conditions!

The mechanism of ketonic, thermal decarboxylation reactions is still not completely elaborated; however, three significant and consistent papers on this mechanism have been published.[6-8] These papers propose an aldol-type condensation mechanism which requires that a carboxylic acid possess at least one alpha hydrogen atom in order to undergo the ketonic decarboxylation reaction. The completely negative results observed from the attempted ketonic decarboxylation of 2,2-dimethylpropanoic acid are consistent with the current views on the mechanism of the ketonic decarboxylation reaction.

The drop in yield observed as a phenyl group is substituted onto the terminal carbon atom of ethanoic, propanoic, and butanoic acids respectively, may indicate increasing intramolecular interaction between the unsaturation pi electrons of the benzene ring and iron of the carboxylate salt. As the number of atoms between benzene ring and carboxylate group increases from one to three carbon atoms, the benzene ring may be shown to have the possibility of lying closer to the carboxylate group.

All the products listed in Table I are known compounds and were characterized by boiling points, melting points, densities, and, where appropriate, by the melting points of 2,4-dinitrophenylhydrazone and/or oxime derivatives.

EXPERIMENTAL[9]

Materials. With the exception of the five acids listed below, the carboxylic acids were purchased and purified prior to use either by redistillation and/or recrystallization. The iron was H reduced iron powder, produced by Fisher Scientific Co.

Pentanoic acid. Due to the wide boiling ranges of commercial pentanoic acids obtained from a variety of sources, pentanoic acid was prepared both by hydrolysis of butanonitrile and by carbonation of the Grignard reagent of 1-bromobutane, according to the procedures of Vogel.[10]

Undecanoic acid. Eighty-seven grams (0.47 mole) of redistilled (b.p. 273–275°) 10-undecenoic acid was dissolved in 200 ml. of 95% ethanol in a Parr pressure flask and reduced over 3 g. of Raney nickel catalyst[11] at 25° and 60 psi.

In 1.5 hr., 97% of the theoretical amount of hydrogen was absorbed. Following removal of catalyst and solvent, 65.3 g. (74%) of undecanoic acid, b.p. 166–168° at 11 mm., m.p. 24.0–24.5°, was obtained by distillation *in vacuo*. (Reported[12] m.p. 28.5°; reported[13] b.p. 168° at 11 mm.)

3-Phenylpropanoic acid. This material was prepared in 93% yield by the reduction of 3-phenyl-2-propenoic acid in a manner similar to that reported above for the preparation of undecanoic acid; m.p. 47–48° (reported[14], m.p. 47–48°).

4-Phenylbutanoic acid. This substance was prepared from 3-benzoylpropanoic acid[14] by use of a somewhat altered Huang-Minlon[16] modification of the Wolff-Kischner reduction. A solution of 5 g. (0.028 mole) of 3-benzoylpropanoic acid, 5 g. of potassium hydroxide, 7.5 ml. of 85% hydrazine hydrate, and 20 ml. of diethylene glycol was refluxed 1 hr., then 8.5 ml. of liquid was distilled from the reaction solution to raise the boiling point of the solution to 200°; the solution was refluxed for 3 hr. more. To the cool solution were added 24 ml. of water and 12 ml. of hydrochloric acid (sp. gr. 1.18); the solution was extracted with three 5-ml. portions of carbon tetrachloride. After treatment of the carbon tetrachloride solution with charcoal and Filter-aid, the solution was filtered and evaporated to yield 4.6 g. (100%) of colorless crystals, m.p. 49–50°. (Reported[17] m.p. 46–48°).

Phenoxyethanoic acid. This substance was prepared according to the procedure of Koelsch.[18]

General decarboxylation procedure. A quantity of the appropriate carboxylic acid from 0.1 mole to 1.0 mole, was mixed with an equivalent plus 10% (0.055 to 0.55 mole) of H reduced iron powder in a round bottom flask. A thermometer was suspended in the mixture through a condenser attached to the flask. A gas delivery tube led from the top of the condenser through an Ascarite tube (to absorb carbon dioxide) and thence to a test tube containing water to serve as a bubble counter. In some experiments the volume of hydrogen evolved was determined by collecting the hydrogen by water displacement from inverted glass cylinders placed in a reservoir of water. The volume of hydrogen collected in all instances was within 5% of the theoretical, regardless of the yield of ketone finally obtained.

The mixture of iron and acid was refluxed until hydrogen evolution ceased; 1 to 3 hr. were required for complete reaction of iron and acid. In those instances where the boiling point of the acid and ketone were below the decompostion temperature of the salt, the mixture was cooled and protected from air by dry nitrogen while the flask was set for

(6) O. Neunhöfer and P. Pascke, *Ber.*, **72**, 919 (1939).
(7) R. Curtis, A. Dobson, and H. Hatt, *J. Soc. Chem. Ind.*, **66**, 402 (1947).
(8) A. Miller, N. Cook, F. Whitmore, *J. Am. Chem. Soc.*, 72, 2732 (1954).
(9) All temperatures are uncorrected.
(10) A. Vogel, *A Textbook of Practical Organic Chemistry*, Green, New York, 1954, p. 353; p. 355.
(11) R. Mozingo, *Org. Syntheses*, Coll. Vol. III, 181 (1955).
(12) F. Krafft, *Ber.*, 11, 2219 (1878).
(13) P. Bagard, *Bull. soc. chim. France*, (4)1, 353 (1907).
(14) V. Grignard, *Compt. rend.*, 138, 1049 (1904).
(15) L. Somerville and C. Allen, *Org. Syntheses*, Coll. Vol. II, 81 (1943).
(16) Huang-Minlon, *J. Am. Chem. Soc.*, 68, 2487 (1946).
(17) E. Martin, *Org. Syntheses*, Coll. Vol. II, 500 (1943).
(18) C. Koelsch, *J. Am. Chem. Soc.*, 53, 304 (1931).

downward distillation. Distillation was continued until no further volatile material evolved.

For those acids and ketones of boiling point above the decomposition temperature of the iron(II) carboxylates, the reflux apparatus was retained following cessation of the evolution of the hydrogen. The Ascarite tube was removed from the gas delivery train and refluxing was continued until evolution of carbon dioxide ceased. Usually 1 hr. sufficed for complete decarboxylation of the iron(II) carboxylate. At this point the flask was set for downward distillation and the crude ketone distilled from the reaction mixture.

The crude ketone was shaken with a saturated solution of sodium hydrogen carbonate to remove traces of unreacted acid, then dried with silica gel and redistilled, or recrystallized from ethanol, or ethanol and water, depending upon the properties of the product.

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF BOSTON UNIVERSITY]

Erythrophleum Alkaloids. Synthesis of 1,2,8,10-Tetramethylphenanthrene[1]

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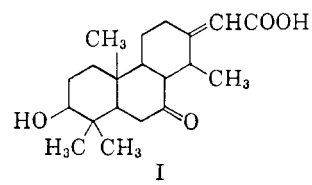
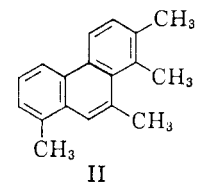
1,2,8,10-Tetramethylphenanthrene, the degradation product from cassaic acid that served to fix the location of the carbonyl group in the latter compound, has been synthesized. 7-Methyl-1-oxo-1,2,3,4-tetrahydronaphthalene, by reaction with methyl Grignard reagent followed by dehydration and hydrogenation, gave 1,7-dimethyl-1,2,3,4-tetrahydronaphthalene. Friedel-Crafts acetylation, Reformatsky condensation with ethyl 2-bromopropanoate, dehydration, and catalytic reduction afforded 2-methyl-3-(3′,5′-dimethyl-5′,6′,7′,8′-tetrahydro-2′-naphthyl)butanoic acid. After dehydrogenation to the corresponding naphthalene derivative, the side chain was extended by application of the Arndt-Eistert process. Cyclization of the resulting homolog gave 4-oxo-1,2,8,10-tetramethyl-1,2,3,4-tetrahydrophenanthrene, which on reduction followed by aromatization furnished the desired 1,2,8,10-tetramethylphenanthrene. The availability of this authentic synthetic material permitted direct comparisons to be made with, and so proved the structure of, the tetramethylphenanthrene obtained from cassaic acid.

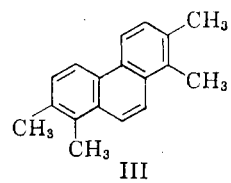
One of the hydrolysis products from cassaine, the major alkaloid from *Erythrophleum guinneense*, is cassaic acid (I). The tricyclic irregular diterpenoid skeleton of cassaic acid was inferred from degradation experiments[4,5] and was later firmly established by relating the material to vouacapenic acid.[6] The hydroxyl and carbonyl groups were at first placed provisionally as shown in formulation I.[5] Subsequently, confirmation of this assignment was obtained on the one hand by attaching a methyl group to the carbon atom originally part of the carbonyl group of cassaic acid (I) and aromatizing to produce 1,2,8,10-tetramethylphenanthrene (II) and, on the other hand, by attaching a methyl group to the carbon originally carrying the hydroxyl group and aromatizing to produce 1,2,7,8-tetramethylphenanthrene (III). As aromatization of cassaic acid derivatives



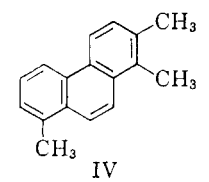
I



II



III



IV

to which no extra methyl group had been added gave 1,2,8-trimethylphenanthrene (IV),[4] the tetramethyl derivatives served to fix the locations of the two oxygen functions.[7] Although authentic 1,2,7,8-tetramethylphenanthrene (III) had been reported before[8] and fortunately was available for direct comparisons, the 1,2,8,10-tetramethyl derivative was unknown. Synthesis of the latter compound accordingly was necessary; and it is with this synthesis that the present paper is concerned.

The starting point was the tetralone V, which was prepared in three steps from toluene and succinic anhydride.[9,10] Methyl Grignard reagent

(1) Abstracted from the Dissertation submitted by Subodh C. Chakravarti to the Graduate School of Boston University in partial fulfillment of the requirements for the Degree of Doctor of Philosophy, 1960.

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(4) *Cf.* G. Dalma in Chapter 36 of *The Alkaloids*, by R. H. F. Manske and H. L. Holmes, Vol. IV, Academic Press, New York, 1954; T. A. Henry, *The Plant Alkaloids*, 4th edition, Blakiston Company, Philadelphia, Pa., 1949, p. 725.

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(6) F. E. King, T. J. King, and J. M. Uprichard, *J. Chem. Soc.*, 3428 (1958).

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