Derivatives of the Magnesium Compound (IX).—The magnesium derivative IX (2 g.) was heated with methanol (20 cc.) and methyl sulfate (5 g.). The hot solution was filtered and the dark yellow filtrate, on cooling, deposited fine yellow needles. Crystallized from acetic acid, the product (X) weighed 0.9 g. and melted at 240–241°.

Anal. Calcd. for $C_{13}H_{13}O_6Br$: C, 45.22; H, 3.80; OCH_3, 9.0. Found: C, 45.75; H, 3.90; OCH_3, 9.7.

The substance X was unchanged after refluxing for three hours with acetone–hydrochloric acid, but when refluxed with acetic acid (15 cc.) and hydrobromic acid (5 cc., 40%), X gave the coumarin acid IV, melting point and mixed melting point 250°. Acetylation of X by warming it with acetic anhydride and a drop of sulfuric acid gave a white substance (XII) which melted at 187–188° after crystallization first from dilute acetic acid and then from methanol. The substance was analyzed but the analysis did not correspond to that required for any simple acetyl derivative of IX.

The yellow acetyl derivative XI resulted when the magnesium compound IX (1 g.) was warmed with pure acetyl chloride (freshly distilled from dimethylaniline). Crystallized from acetic acid, the product formed yellow needles which melted at 231–232°.

Anal. Calcd. for $C_{14}H_{13}O_7Br$: C, 45.04; H, 3.50. Found: C, 45.08; H, 3.87.

When the yellow acetyl derivative XI was methylated by methyl sulfate and methyl alcoholic potassium hydroxide, the product was the methyl derivative VII, melting point and mixed melting point 210°.

Summary

1. Sodium and magnesium ethoxides have been used as condensing agents for the addition of malonic ester to bromopseudocumoquinone leading to the formation of a sodium and a magnesium derivative, respectively.

2. Both metallic derivatives were converted by acids to the same substance, 3-carbethoxy-6-hydroxy-5,7-dimethyl-8-bromocoumarin (III), the structure of which was proved by conversion to the bromine-free coumarin acid (XX) and synthesis of the latter from *m*-xyloquinone.

3. The chemical properties of the coumarin ester III and many of its derivatives have been described.

4. In the reaction with the enolates of malonic ester, the bromine atom of the bromoquinone was unaffected. The quinone behaved as a pentad-enol system, the methyl group meta to the bromine atom reacting.

5. The magnesium compound gave rise to two series of derivatives: one identical with the series of derivatives obtained from the sodium compound and the other closely related to, but different from, this series.

6. Starting with *p*-xyloquinone, 3-carboxy-6-methoxy-5,8-dimethylcoumarin (XVII) was synthesized.

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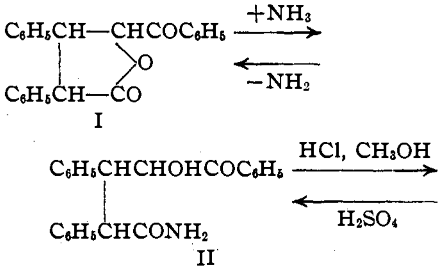
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF MCGILL UNIVERSITY]

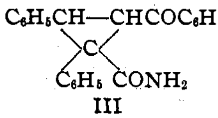
The Action of Alkaline Reagents on Diphenylbenzoylbutyrolactone

BY C. F. H. ALLEN, E. E. MASSEY[1] AND R. V. V. NICHOLLS

The γ-lactone ring is usually opened by alkaline reagents with the consequent formation of a salt of a γ-hydroxy acid; upon acidification an equilibrium mixture is formed, which is usually preponderantly in the lactone form. This behavior is exhibited by α,β-diphenyl-γ-benzoylbutyrolactone I, but if the alkaline solution is not acidified immediately it becomes yellow and deposits a mixture of solids and oil when treated with acids. The new substances are obviously secondary products resulting from the action of alkalies on the highly substituted salt obtained on ring opening. The nature of these products varies to some extent with the reagent used, and hence it is convenient to describe separately the action of each basic substance.

The lactone is insoluble in ammonium hydroxide but gradually dissolves in alcoholic ammonia to give a substance, the properties of which are in best agreement with the open chain hydroxy amide structure II. Thus, analysis shows that





III

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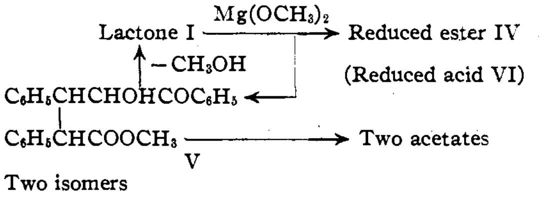
[1] Acknowledgment is hereby made of a bursary granted for one year by the National Research Council of Canada.

one ammonia has added; recrystallization from glacial acetic acid removes this and re-forms the lactone, while treatment with hydrogen chloride in methanol dehydrates it to the known cyclopropane amide III.[2] The direction of the latter reaction is reversed by concentrated sulfuric acid.

When alcoholic magnesium methylate was allowed to react with the lactone a mixture of oil and solids resulted; this was separated into unchanged lactone, the high melting open chain ester IV and two isomeric hydroxy esters V formed by addition of methanol. Evidence for the structure of the hydroxy esters is as follows: they contain one methoxyl group but are not acidic, they form isomeric acetates, on heating they lose methanol to re-form the lactone and the low melting form is isomerized to the high melting form by magnesium methylate. From the oily portion of the reaction mixture the acid VI was isolated after a sodium hydroxide treatment; since it is presumably a secondary product its formation will be considered later. However, it may be said that the formation of it and its ester involves a reduction reaction, which is presumably the same as that described with magnesium chloroethylate.[3,4]



The action of sodium methylate, alcoholic potash or sodium hydroxide on the lactone was very drastic, and only products of secondary reactions could be identified. These were a cyclopentadienone VII, one isomeric form of the acid VI, diphenylmaleic anhydride, diphenylsuccinic acid, the lactone VIII, benzaldehyde, stilbene and acetophenone. With the exception of the diketone, these substances are the ones that would be expected, taking into account the known action of alkaline reagents on α-hydroxy ketones[5] and hydrolysis. Opening of the lactone ring gives the salt of a hydroxy acid IX; part of this is reduced to the sodium salt of acid VI, and a part isomerized to a δ-hydroxy-γ-ketone X. Hydrolysis of the latter and oxidation would account for the diphenylsuccinic acid. Dehydrogenation of X either before or after reduction would give the salt of the unsaturated acid XI; one of the hydrolysis products of the latter is diphenylmaleic acid. The unsaturated acid XI (not isolated), as will become evident, is the intermediate in a series of reactions between the unsaturated lactone and the diketone. The ease of formation of benzaldehyde by hydrolysis of the several members of this series renders its detection of no significance.

On acidification, the free acids would be expected, though anhydride or lactol formation may occur when the configuration is favorable. Thus, the unsaturated acid XI at once gives the lactol XII, which loses water to form the lactone VIII actually isolated.

When the lactone VIII is dissolved in sodium hydroxide and carefully acidified and manipulated, the lactol XII is separated easily, in spite of the ease with which it loses water.

Both the lactone and lactol were known previously though obtained in another way.[6] By heating in a sealed tube with ammonia the lactone was reported to give a hydroxy amide XIII and lactam XIV and this was confirmed, as was the reduction by hydrogen iodide to give the 1,2-diphenyl-3-benzylcrotolactone XVI. The latter was also obtained in this paper by the action of zinc and acetic acid. The action of alkalies on the lactone is intimately connected with the diketone VII and is considered below.

The principal product (35%), resulting from the action of sodium methylate on lactone I is the bright yellow unsaturated 1,3-diketone VII. Its deep purple alkaline solutions are hydrolyzed very slowly and the products, after acidification, are the lactone VIII, diphenylmaleic anhydride and benzaldehyde; the last two are formed from the lactone VIII on similar treatment. Further evidence that the lactone and diketone are easily intraconvertible in alkaline solution is given by the fact that the same hydroxy amide XIII and lactam XIV are obtained from both by use of ammonia in a sealed tube. Hence the carbon chain and location of phenyl groups must be unchanged. Reduction of the diketone by zinc dust or hydriodic acid gives α,β-diphenyl-γ-benzal-

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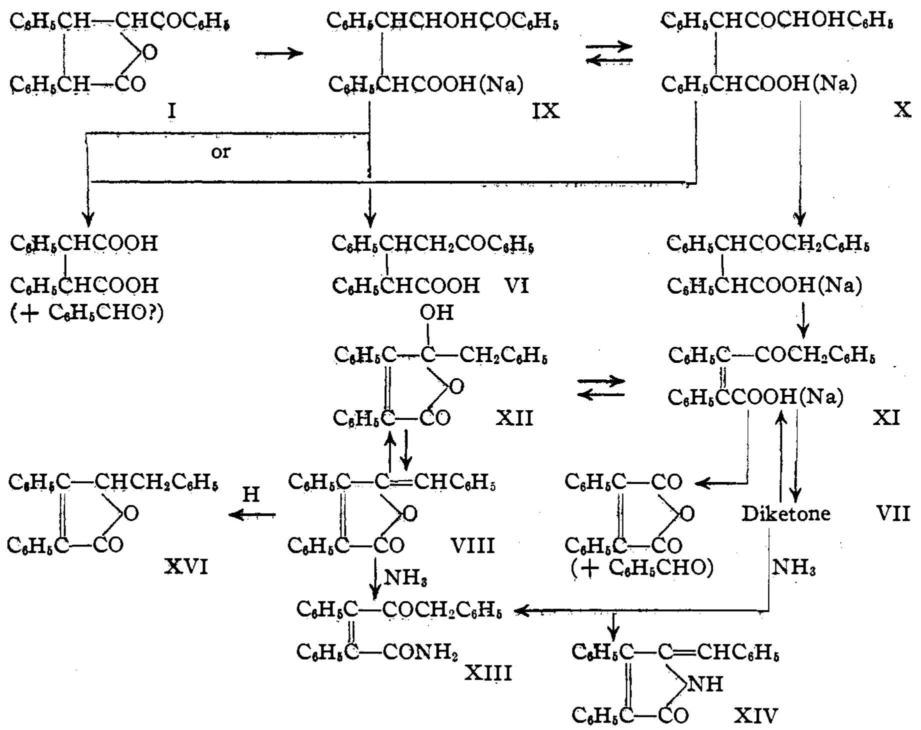
[2] Allen and Boyer, *Can. J. Research*, **9**, 159 (1933).

[3] Meerwein and Schmidt, *Ann.*, **444**, 221 (1935).

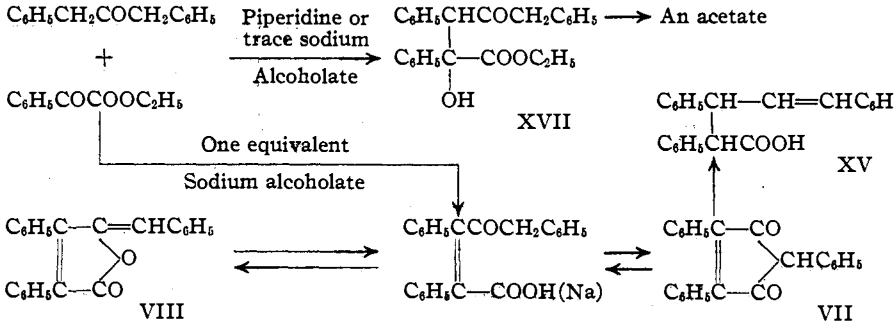
[4] It was important to know with certainty the structure of the hydroxy esters, since a single instance is recorded where a saturated lactone ring has been opened in the opposite way; butyrolactone and sodium ethylate give γ-ethoxybutyric acid and a dilactone. It may be a coincidence, but the b. p. of both γ-ethoxy- and γ-hydroxybutyric acids are the same, 231° [Fittig and Strom, *Ann.*, **267**, 191 (1892)].

[5] Kohler and Kimball, THIS JOURNAL, **56**, 729 (1934); Kohler and Leers, *ibid.*, p. 981.

[6] Cohn, *Ber.*, **24**, 3961 (1891).



butyric acid XV, confirming the chain. It gives a mono-2,4-dinitrophenylhydrazone but does not form a quinoxaline. In the Grignard machine it shows one active hydrogen and gives slowly two additions. These reactions suggest the structure of a 1,3-diketone, and this was confirmed by a synthesis that also gave the unsaturated lactone VIII.



Dibenzyl ketone readily adds to benzoylformic ester in the presence of piperidine or a trace of sodium alcoholate at room temperature, but if the mixture is heated in the presence of an equivalent of alcoholate, water is eliminated and the product isolated depends on operating conditions; the use of sodium methylate favors the diketone, whereas with sodium ethylate the lactone or lactol XII (as sodium salt) separates during the heating, owing to insolubility. It cannot be said with certainty that the ester XVII is an intermediate product, because it is not converted into the other substances by sodium alcoholates.

The diketone is oxidized by permanganate to benzaldehyde, benzoic acid and carbon dioxide; chromic acid gives benzoic acid and a bimolecular product, while selenium dioxide forms the latter quantitatively. Though the diketone can be sublimed and is stable in air for a short time at the melting point, it is readily oxidized by atmospheric oxygen at this temperature to the bimolecular product. Mineral acids are without action at room temperature but destroy it at 100°. Hydrogen peroxide adds an atom of oxygen. The structure of the new derivative was not determined; it is altered by acetyl chloride, but the result is neither dehydration nor esterification. Other properties are recorded in the experimental part.

A comparison of the highly phenylated keto-hydroxy acid described in this paper with those previously known shows that the introduction of an additional phenyl has greatly increased the reactivity of the various groups. The most conspicuous differences are the facilitation of cleavage, the occurrence of dehydrogenation products and the tendency for the unsaturated lactone obtained to isomerize to a cyclic diketone. It is believed that the latter is the first representative of a new series.

Experimental

The bromination of a variety of δ-ketonic esters and the properties of the products has been well described[7] and there was no difficulty in adapting the procedure to the synthesis of methyl α,β-diphenyl-γ-benzoylbutyrate IV. The mixture of stereoisomers obtained by the addition of methyl phenylacetate to benzalacetophenone was used without separation, since all the bromo esters gave the lactone I as the principal product. The position of the bromine atom was thus made evident, the four monobromo substitution products being γ-bromo esters XVIII; their interrelation was shown by treatment with hydrogen bromide in acetic acid. Pyrolysis of the bromo esters gave the expected variety of substances. Thus, when methyl bromide was evolved[7a,c,8] the lactone resulted, but loss of hydrogen bromide[7,9] gave the reduced ester IV, the stereoisomeric acids VI, and a trace of what may be diketo acid.[10]

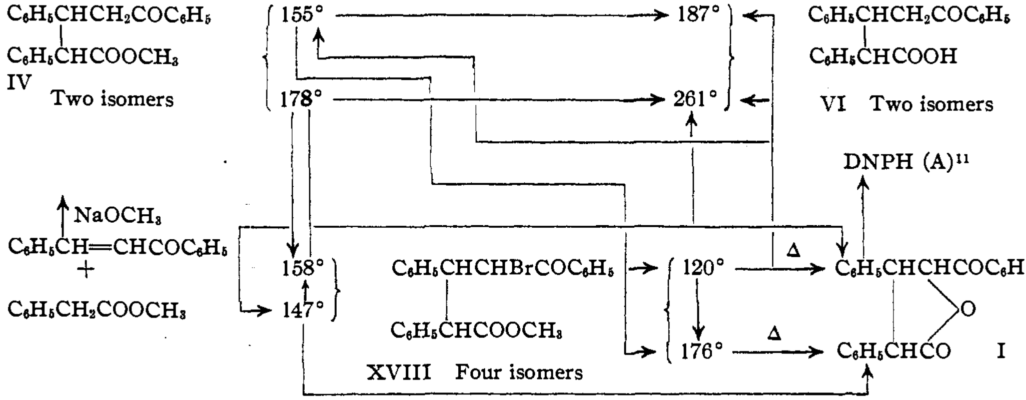
A. Preparation and Properties of the Lactone I.—1. Methyl α,β-diphenyl-γ-benzoylbutyrate IV was obtained by the addition of methyl phenylacetate[12] to benzalacetophenone in the presence of slightly over one equivalent of sodium methylate.[10] Since it was found unnecessary to use the separated bromo esters in a subsequent step, the mixture of esters, after recrystallization from benzene to remove some insoluble acid, was brominated directly. This gave four monobromo substitution products, m. p. 120, 147, 158 and 176°.

Seventy grams of the mixed keto ester was suspended in 400 cc. of carbon tetrachloride or glacial acetic acid, a few cc. of bromine added and the whole warmed in sunlight until the reaction commenced. Then the remainder of the bromine (total = 32 g.) was added slowly, during which time the suspended ester gradually dissolved. The thick, pasty solid that separated on cooling was filtered, washed and dried. The separation into the stereoisomeric forms involved a tedious fractionation, using ethyl acetate and methanol. The 176° isomer is isolated easily owing to its insolubility but the 158° isomer is the principal product; a constant melting (125°) mixture of the 158 and 147° isomers complicated the fractionation. When pure high melting ester (178°) was used, the yield of the 158° isomer was 60% if the bromination was done in acetic acid, but only 40% in carbon tetrachloride; this ester does not give the 176 or 120° forms.

The 176° form is sparingly soluble in all solvents; it separated in prisms from ethyl acetate. The other forms are moderately to very soluble in all solvents except petroleum ether. The 158° isomer separated from ethyl acetate in rods, and the other two from methanol as fine needles.

Anal. Calcd. for $C_{24}H_{21}O_3Br$: Br, 18.3. Found: (176°, 120°) 18.5; (158°) 18.2; (147°) 18.9.

One gram of each isomer in acetic acid was saturated with hydrogen bromide and worked up after three days. The 158 and 176° isomers were unchanged, but the 147° had completely isomerized to the 158° form and the 120°



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[7] (a) Kohler, *Am. Chem. J.*, **46**, 217, 474 (1911); (b) THIS JOURNAL, **39**, 1404, 1699, 2405 (1917); **41**, 683, 992 (1919); **44**, 840, 2536 (1922); (c) Hill, *ibid.*, **49**, 566 (1927).

[8] Kohler and his students, THIS JOURNAL, **41**, 683, 992, 1093 (1919); Hahn and Albee, *Am. Chem. J.*, **49**, 171 (1913). In the present instance, the loss of methyl bromide seems to take place even in boiling acetic acid; indeed, the best preparative method involved a short period of refluxing with potassium acetate.

[9] Haerdi and Thorpe, *J. Chem. Soc.*, **127**, 1237 (1925).

[10] The relation between the acids and esters is known from Avery's work, THIS JOURNAL, **52**, 3628 (1930).

[11] DNPH = 2,4-dinitrophenylhydrazone.

[12] We are grateful to Compagnie Parento Limited for the gift of a quantity of this ester.

to the 176° form. This is in agreement with the fact that only the 158 and 176° isomers are readily obtained.

The lactone I was most conveniently prepared from the mixed bromo esters by refluxing for two hours a mixture of 20 g. of the latter, an equal weight of potassium acetate and 100 cc. of glacial acetic acid; potassium bromide separated fairly rapidly. After pouring into water, the lactone was isolated by appropriate manipulations; the average yield of once recrystallized product was 65%. The filtrate contained considerable amounts of reddish oils and gums, with traces of lactone. The use of pyridine and dimethylaniline for an hour gave the same product but isolation was more laborious.

α,β-Diphenyl-γ-benzoylbutyrolactone is very soluble in benzene and chloroform, slightly soluble in the alcohols and ether, insoluble in petroleum ether, but moderately soluble in the other usual solvents. It is conveniently recrystallized from *n*-butanol or a chloroform–methanol mixture, from which it separates as rods, m. p. 157°.

Anal. Calcd. for $C_{24}H_{18}O_3$: C, 80.7; H, 5.0. Found: C, 80.8; H, 5.2.

A Zeisel determination was negative. In the Grignard machine it showed no active hydrogen, but gave two additions.

Pyrolysis of the pure bromo esters gave mixtures of products consisting of the reduced keto esters, the corresponding keto acids, the lactone and traces of what is probably a diketo acid. The 176° isomer gave the lactone nearly quantitatively; the methyl bromide (80% yield) evolved was collected in a freezing mixture. The diketo acid separated from methanol in long rods, m. p. 160°.

Anal. Calcd. for $C_{23}H_{18}O_4$: C, 77.1; H, 5.0. Found: C, 76.6, 76.7, 77.1; H, 4.4, 4.5, 4.3.

The phenylhydrazone (C; pale yellow cubes from ethanol m. p. 180°) and 2,4-dinitrophenylhydrazone (A; yellow prisms from methanol m. p. 210°) were prepared in the usual manner.

Anal. Calcd. for (A); $C_{29}H_{22}O_6N_4$: N, 10.7; for (C) $C_{29}H_{24}O_2N_2$: N, 6.5. Found: N; (A) 10.5; (C) 6.6.

2. **Reduction.**—The lactone was reduced by zinc and acetic acid to the low melting open-chain acid VI, but by hydrogen bromide to the high melting isomer. In the latter case the γ-bromoketo acid corresponding to the ester XVIII was presumably formed as an intermediate product; the reduction of α-bromo ketones by hydrogen bromide is well known.[13]

A mixture of 10 g. of the lactone, 20 g. of zinc dust and 100 cc. of glacial acetic acid was boiled for two hours, poured into water, and the precipitated solid filtered and recrystallized from acetone. It was identified as the low melting form (187°) of the acid VI by a mixed melting point, and conversion into the corresponding ester (155°). The same acid resulted if methanol was used as a solvent.

The lactone was unchanged after twenty-four hours of standing at room temperature in methanol, or after a week in chloroform or acetic acid, each saturated with hydrogen bromide, as well as after refluxing for two hours in acetic acid solution through which hydrogen bromide was passed. However, when 1 g. in 25 cc. of acetic acid, saturated with hydrogen bromide at room temperature, was heated in a sealed tube at 100° for eight hours it gave as the single product the high melting form (261°) of the acid VI, identified by mixed melting point and conversion into the ester (178°).

3. **Action of Ammonia: α,β-Diphenyl-γ-hydroxy-γ-benzoylbutyramide II.**—A suspension of 10 g. of the lactone in 125 cc. of absolute ethanol was saturated with dry ammonia; most of the solid dissolved. The supernatant liquid was decanted and left in a closed flask overnight; fine needles separated in a nearly quantitative amount. The amide melts with decomposition at about 202°, and after a few minutes at 205° all the ammonia has been evolved and the lactone re-formed. Recrystallization from glacial acetic acid, or heating with phosphorus pentoxide in xylene, also removes the ammonia.

Anal. Calcd. for $C_{23}H_{21}O_3N$: C, 76.8; H, 5.8; N, 3.9. Found: C, 76.0, 76.1; H, 5.5, 5.5; N, 3.7.

The cyclopropane III resulted when an absolute alcoholic solution of the amide, saturated with hydrogen chloride, was allowed to stand for a day. On recrystallization from a methanol–chloroform mixture it formed rods, m. p. 179°; a mixed melting point with an authentic specimen[2] was not depressed, and on dehydration it gave the cyclic nitrile, m. p. 166°. When dissolved in acetic anhydride containing a trace of sulfuric acid, and poured upon ice and sodium carbonate, the cyclic amide gave an oil, which, on long standing, became solid and proved to be the hydroxyamide.[14]

4. **Action of Magnesium Methylate; Methyl α,β-Diphenyl-γ-hydroxy-γ-benzoylbutyrate V.**—The magnesium methylate from 5 g. of magnesium and 80 cc. of methanol, and 25 g. of the lactone were shaken mechanically for an hour at room temperature and decomposed by pouring upon 400 g. of ice and 25 cc. of concd. hydrochloric acid. The pale yellow, oily solid was separated by the usual manipulations into a yellow oil and 6 g. of the 178° keto ester. After standing for several days, 1 g. of the hydroxy ester (180°) had separated and after several more days, 8 g. of the 118° isomer was collected. When the time of contact with the magnesium methylate was short, the quantity of the latter ester was higher, but if prolonged, more of the high melting isomer was found. The low melting form was isomerized to the other by fifteen minutes of shaking with cold magnesium methylate but the 180° variety was unchanged by this reagent. From the residual oils were isolated high melting ketoacid, unchanged lactone, and benzaldehyde. Sodium methylate brought about removal of alcohol and reformation of the lactone.

The esters were recrystallized from methanol, from which they separated as fine rods, melting at 180 and 118°.

Anal. Calcd. for $C_{24}H_{22}O_4$: C, 77.0; H, 7.9; OCH_3, 8.3. Found: (180°) C, 76.8, 76.8; H, 7.8, 7.8; OCH_3, 8.6; (118°) C, 76.6, 76.5; H, 7.6, 7.7; OCH_3, 8.4, 8.5.

Reactions.—(a) The esters were heated in an apparatus arranged to sweep out and condense any gas formed. At 190°, each ester evolved methanol (identified as the 3,5-dinitrobenzoate) and left the lactone as a residue. (b) On treatment of the high melting form in boiling methanol

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(13) Kröhnke and Timmler, *Ber.*, **69**, 614 (1936).

(14) The "stereoisomeric amide"[2] (p. 161) is really this hydroxyamide; thus there is a little ring opening of the cyclopropane by sulfuric acid.

with 2,4-dinitrophenylhydrazine and a little hydrochloric acid, and allowing to stand, bright red rods of a dinitrophenylhydrazone (B) separated and were filtered; the filtrate then deposited yellow leaflets, the dinitrophenylhydrazine (A) of the lactone. Under the same conditions, the 118° ester gave only derivative A. When a chloroform solution of B containing a little hydrogen chloride was refluxed, the substance was converted into A, whereas in methanol A was partially converted into B. The derivative B crystallized from methanol in red rods, m. p. 224°.

Anal. Calcd. for $C_{30}H_{26}O_7N_4$: N, 10.1. Found: N, 10.0, 9.9.

(c) The acetate of the 180° ester was obtained by allowing an acetyl chloride solution of the ester to evaporate spontaneously after standing for sixteen hours, but it was necessary to reflux the 118° form for four hours to get the derivative. Both were recrystallized from methanol. The acetate of the 180° ester formed rods, m. p. 145°, while its isomer separated in rosets of rods, m. p. 132°.

Anal. Calcd. for $C_{26}H_{24}O_5$: C, 75.0; H, 5.8; OCH_3, 7.4. Found: C, 74.8, 74.7; H, 5.8, 5.9; OCH_3, 7.5.

5. **Action of Sodium Methylate. (a) 2,4,5-Triphenyl-1,3-diketocyclopentene-4, VII.**—A suspension of 20 g. of the lactone in 300 cc. of methanol, containing the methylate from 4 g. of sodium, was shaken for ten hours when all had dissolved. The dark brown solution was decomposed by adding to dilute acetic acid and the semi-solid mass that separated was filtered. After trituration with methanol the bright yellow solid that remained undissolved was filtered, and recrystallized from a 2:1 methanol–chloroform mixture. It formed fine, yellow rods, m. p. 166°; the yield was 6.5 g. or 32%. It was not found when sodium or potassium hydroxide was used instead of sodium methylate. A Zeisel determination was negative.

Anal. Calcd. for $C_{23}H_{16}O_2$: C, 85.2; H, 4.9. Found: C, 85.3, 85.4; H, 5.1, 5.3.

(b) **Other Products.**—After several months of standing, the only other solid that had separated was unchanged lactone, so a chloroform solution of the oil was submitted to a systematic extraction with sodium bicarbonate, potassium carbonate, copper acetate and sodium hydroxide, and then given a water wash. Nothing was obtained from the potassium carbonate or copper acetate, but the substances listed were found as indicated: (1) from the bicarbonate, the high melting acid VI and diphenylmaleic anhydride; (2) from the sodium hydroxide, high melting form of diphenylsuccinic acid; (3) from the final water wash, the lactone VIII; (4) by steam distillation of the residual oil, benzaldehyde. The oil gave no phenylhydrazone or phenacyl ester. It decomposed badly on attempted vacuum distillation; from the distillate were isolated benzoic acid, acetophenone and stilbene, obviously decomposition products. An unexplained phenomenon was the production of a green color in the chloroform during the sodium hydroxide wash, while the latter became orange. When the green solution was washed with water, the latter became green and the chloroform turned yellow. On greatly diluting the wash water, the unsaturated lactone VIII separated. On acidifying this basic solution, a thick yellow oil was obtained, but beyond noting its lactonic nature (insoluble in carbonates, soluble in hydroxides) nothing definite was learned.

The identification of each substance was assured by comparison with authentic specimens at hand or prepared by directions in the literature; *e. g.*, diphenylmaleic anhydride, m. p. 154°,[15] the unsaturated lactone VIII, m. p. 175°,[6] and diphenylsuccinic acid, m. p. 229°.[15b]

B. **Reactions of the Unsaturated Lactone VIII.**—For further identification, and for purposes of obtaining reference samples, the action of ammonia to form a hydroxy amide XIII, m. p. 199–201° dec., and a lactam XIV, m. p. 241°, reduction by hydrogen iodide to give α,β-diphenyl-γ-benzylcrotolactone XVI, m. p. 127–128°,[6] and alkaline fusion to give the lactol XII, m. p. 181°, were repeated and confirmed. The drastic procedure in the latter reaction is unnecessary; one only needs to acidify the solution of the sodium salt at room temperature with dilute acetic acid and recrystallize from this reagent, to obtain the lactol at will. To dehydrate, it may be recrystallized from anhydrous solvents—the phosphorus oxychloride treatment is unnecessary.

The new reactions determined were reduction by zinc and acetic acid (one hour) which gave the dihydro derivative XVI, hydration and dehydration, just described, and the action of alkaline solutions.

(1) A solution of 2 g. of the lactone in 30 cc. of absolute alcohol containing 0.4 g. of potassium hydroxide was refluxed for twenty-four hours and the mixture distilled with steam. The distillate contained benzaldehyde, which was identified as the phenylhydrazone (0.05 g., m. p. 156°). After acidification to remove the reagent, the distillate was shaken with ether, to remove toluene, if present, but nothing was found in the extract. From the residual solution in the steam distillation flask, 0.8 g. of unchanged lactone was recovered, and, on adding acetic acid, 0.6 g. of diphenylmaleic anhydride was obtained.

(2) A similar solution containing an equivalent of sodium ethylate turned purple on an hour's boiling and the diketone VII was isolated after acidification. On shaking 1 g. of the lactone with 15 cc. of absolute methanol containing 9.2 g. of sodium for ten hours, the solution became purple, but 0.65 g. of lactone was still undissolved. From the colored solution, 0.25 g. of the diketone was isolated on acidification.

C. **Reactions of the Diketone VII.**—In the Grignard machine, the diketone evolved one equivalent of methane and slowly consumed three moles of reagent.

(1) **The 2,4-dinitrophenylhydrazone** was prepared in the usual manner; it separated from a methanol–chloroform mixture in fine, orange needles, m. p. 235°.

Anal. Calcd. for $C_{29}H_{20}O_6N_4$: N, 11.1. Found: N, 11.1, 11.1.

(2) **Alkaline Reagents.**—The diketone dissolves in alcoholic sodium or potassium hydroxide and in alcoholates, producing a deep purple color, and is recovered on acidification. After prolonged refluxing (twenty-four hours) as in (1) above, it gave the same products.

(3) **Alcoholic Ammonia.**—A mixture of 1 g. of the diketone and 15 cc. of alcohol was saturated with ammonia at 0° and heated at 100° in a sealed tube for six hours. The initially formed deep purple color changed to brown. On

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[15] Reimer, (a) *Ber.*, **13**, 742 (1880); (b) *ibid.*, **14**, 1802 (1881).

opening, crystals of the lactam XIV were filtered, and on concentrating the solution and decoloring by Nuchar, a mixture of the hydroxy amide XIII and lactam separated; they were identical with the specimens prepared above. Meyer[16] has made an extensive study of the action of ammonia on a variety of lactones and in no case was an amino acid obtained, but only hydroxy amides or lactams.

(4) **Reduction; α,β-Diphenyl-γ-benzalbutyric Acid XV.**—(a) A mixture of 10 g. of the diketone, 200 cc. of acetic acid and 20 g. of zinc dust was refluxed for a half hour; the yellow color had disappeared after ten minutes. It was filtered into 400 cc. of water and the precipitated acid collected; 9 g. was obtained after one recrystallization from methanol. It forms white needles, m. p. 204–205°.

Anal. Calcd. for $C_{23}H_{20}O_2$: C, 84.1; H, 6.0; mol. wt., 328. Found: C, 83.9; H, 5.8; mol. wt., 345.

(b) A mixture of 2 g. of the diketone, 1 g. of red phosphorus and 10 cc. of constant boiling hydriodic acid was refluxed for two hours and decanted from the resinous deposit. The latter was treated by sodium bisulfite several times and then the organic material extracted with hot methanol and worked up as above; the same acid resulted. It was soluble in aqueous carbonate and recovered unchanged on acidification. An acetone solution instantly decolorized permanganate, and a chloroform solution instantly added bromine. It did not give a carbonyl derivative.

(c) The chromic acid oxidation was performed in acetic acid in the usual manner; the isolation of diphenylsuccinic acid was difficult, owing to the unfavorable nature of the material. It was eventually purified and shown to be the high melting isomeric form of diphenylsuccinic acid by melting and mixed melting point (229°). A permanganate oxidation was carried out in such a way that the benzaldehyde could be distilled as formed; identification was made through the phenylhydrazone. From the residual solution the same diphenylsuccinic acid was isolated.

(5) **Oxidation.** (a) **The Bimolecular Product.**—To a solution of 0.4 g. of selenium dioxide in 15 cc. of boiling dioxane was added 1 g. of the diketone and the whole refluxed with stirring for one and one-half hours. After filtering, the solution was poured into water, ammonium chloride added to hasten coagulation and the solid filtered. It was recrystallized from chloroform–methanol, and formed microscopic yellow prisms, m. p. 247°; the yield was nearly quantitative.

Anal. Calcd. for $C_{46}H_{30}O_4$: C, 85.6; H, 5.3; mol. wt., 646. Found: C, 85.0; H, 5.1; mol. wt., 716.

The same substance was obtained, along with benzoic acid, by the action of chromic acid, with benzaldehyde and unreacted lactone from dilute sulfuric acid at water-bath temperature, and from the mixture resulting on ozonization in ethyl bromide. Permanganate, however, destroyed the molecule completely, giving benzaldehyde, benzoic acid and carbon dioxide. Dilute nitric acid gave oils and a little *p*-nitrobenzoic acid. Potassium hypobromite was without action.

(b) **Hydrogen Peroxide Product.**—To a solution of 0.5 g. of the diketone in 15 cc. of acetone, 10 cc. of 30% hydrogen peroxide was added; this precipitated the diketone. A 10% solution of potassium hydroxide was then added, dropwise from a buret, each drop being admitted only after the deep purple coloration was discharged by shaking; this took 0.3 cc. and a period of an hour. A yellow precipitate (0.3 g.) was filtered and recrystallized from methanol; it formed yellow prisms, m. p. 185°.

Anal. Calcd. for $C_{23}H_{16}O_3$: C, 81.2; H, 4.7; mol. wt., 340. Found: C, 81.0, 81.2; H, 4.5, 4.5; mol. wt., 372.

The new substance is soluble in warm, aqueous sodium hydroxide, does not decolorize bromine and is unaffected by hydrogen chloride in acetic acid. It did not give a dinitrophenylhydrazone.

A solution in acetyl chloride gave a new yellow solid on evaporation, which separated from methanol–chloroform in rods, m. p. 155°.

Anal. Found: C, 80.0, 79.8; H, 4.9, 4.8.

A Zeisel determination was negative; it did not contain halogen. The composition shows fair agreement with $C_{50}H_{34}O_7$, a diacetate of a dehydrated bimolecular product.

D. Synthesis.—To a warm solution of 6.1 g. of dibenzyl ketone and 5 g. of ethyl benzoylformate in 15 cc. of absolute alcohol was added the freshly prepared sodium ethylate from 0.6 g. of sodium and 15 cc. of alcohol (absence of water is essential) and the solution refluxed. It at once became deep yellow and after fifteen minutes a solid began to separate.[17] After an hour it was acidified with acetic acid and the pale yellow lactone filtered; the average yield of several runs was 3 g. or 27%. It was best recrystallized from *n*-propanol. By acidifying with diluted acid, the lactol could be isolated. When the same amounts of reactants were taken but in methanol, using enough of the latter to keep everything in solution, a deep purple color was noted and after two hours of acidification gave the diketone in a 40% yield. With larger quantities an excess of sodium methylate is advisable.

With the same amounts but 0.5 g. of piperidine or a trace of sodium ethylate as a catalyst, white needles of the ester XVII shortly separated. The first crop weighed 3.5 g., and on standing and evaporation, successive amounts were obtained. It recrystallized from ethanol in fine needles, m. p. 128°.

Anal. Calcd. for $C_{25}H_{24}O_4$: C, 77.3; H, 6.2; OC_2H_5, 11.6. Found: C, 77.0, 69.9; H, 6.0, 5.1; OC_2H_5, 11.4, 11.7.

This ester gave only oils with alcoholates.

After refluxing for four hours with acetyl chloride, an acetate resulted; this was very soluble in the usual solvents. It separated from methanol in rods of m. p. 101°.

Anal. Calcd. for $C_{27}H_{26}O_5$: C, 75.3; H, 6.0. Found: C, 75.1, 75.1; H, 6.0, 6.1.

(6) **Other Reagents.**—The lactone was unaffected by ozone and only slightly attacked by chromic acid. Bromine was decolorized very slowly, with some evolution of hydrogen bromide; 40% of the lactone was recovered, while the remainder of the reaction product was a sticky gum.

This work has been assisted by a generous grant from the Cyrus M. Warren Fund of the American Academy of Arts and Sciences.

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[16] Meyer, *Monatsh.*, **20**, 717 (1899).

[17] The white sodium salt sometimes separated if the amount of solvent was less.

Summary

1. When dissolved in alkaline solutions, α,β-diphenyl-γ-butyrolactone undergoes a diversified series of reactions, involving oxidation and reduction, cleavage and hydrolysis.

2. Among new products are a pair of stereoisomeric ketohydroxyesters and a highly phenylated cyclopentadienone.

3. The latter is capable of a great variety of reactions; in general, it shows a marked resemblance to 2-phenylindandione-1,3.

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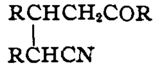
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF McGILL UNIVERSITY]

Gamma-Benzoylbutyronitrile

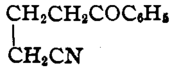
BY C. F. H. ALLEN AND W. L. BALL

Up to the present time all δ-ketonic nitriles (I) investigated have been highly substituted[1]



$$\begin{matrix}\mathrm{RCHCH_2COR}\\ |\\ \mathrm{RCHCN}\end{matrix}$$

I

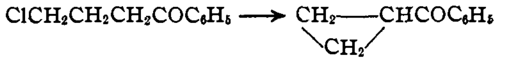


$$\begin{matrix}\mathrm{CH_2CH_2COC_6H_5}\\ |\\ \mathrm{CH_2CN}\end{matrix}$$

II

Therefore it was of interest to prepare the simplest member of the series, γ-benzoylbutyronitrile (II), and compare its properties with those of the more complex homologs.

There are several series of reactions that might be expected to yield the desired nitrile, but those that seemed to involve the fewest steps and utilize readily available materials gave other products. Thus, the action of potassium or cuprous cyanide on γ-chlorobutyrophenone was to remove hydrogen chloride, giving an excellent yield of benzoylcyclopropane.[2]



$$\mathrm{ClCH_2CH_2CH_2COC_6H_5} \longrightarrow \mathrm{CH_2{-}CHCOC_6H_5},\ \text{ring closed by } \mathrm{CH_2}$$

The nitrile was finally obtained by dehydration of the corresponding amide (III) in a particular manner; the amide was secured from γ-benzoylbutyric acid by the following series of reactions

$$\mathrm{C_6H_5COCH_2CH_2CH_2COOH} \longrightarrow \mathrm{C_6H_5COCH_2CH_2CH_2COOCH_3} \xrightarrow{\mathrm{NH_3}} \mathrm{C_6H_5COCH_2CH_2CH_2CONH_2{\cdot}NH_3} \longrightarrow \mathrm{C_6H_5COCH_2CH_2CH_2CONH_2}$$

Kugel[3] prepared the lower homolog, β-benzoylpropionamide, in a similar manner, though Biedermann[4] had obtained cyclic compounds by a like procedure. Our results resembled those of Kugel and will be described in the experimental part.

The nitrile forms carbonyl derivatives and is very easily hydrolyzed to γ-benzoylbutyric acid; it is possible to arrest the hydrolysis at the intermediate amide stage. It reacts with bromine with immediate evolution of hydrogen bromide; most of the reaction product is an untractable oil, but a small amount of 2-phenyl-α-pyridone (VI) can be isolated.

The two characteristic properties of δ-ketonic nitriles are isomerization to a tetrahydropyridine (through the amide) on treatment with mineral acids in indifferent media, and the formation of 2-bromopyridines on bromination in acetic acid.[1a] As mentioned above, it was not possible to determine completely the course of bromination of γ-benzoylbutyronitrile. The formation of the 2-phenylpyridone is probably best explained as follows: the nitrile is isomerized to the cyclic isomer by some of the hydrogen bromide evolved, the hydropyridine then being dehydrogenated to the pyridone by bromine in the usual manner.[1a] This mechanism could not be confirmed, since no pyridone resulted when the pure cyclic substance was brominated in a similar manner.

All attempts at isomerization gave either the amide or the acid; this is not a real difference because it has been shown that the hydropyridine formation proceeds through the amide.[1b] The reactions are thus essentially the same as with the substituted homologs, but owing to less favorable physical properties, all the products cannot be determined.

The isomeric tetrahydropyridine (V) can be obtained in a variety of ways; in fact, it is usually obtained by reactions that might be expected to yield the nitrile, *e. g.*, dehydration of the amide

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[1] (a) Kohler, Graustein and Merrill, THIS JOURNAL, **44**, 2536 (1922); Kohler and Souther, *ibid.*, p. 2903; Kohler and Allen, *ibid.*, **46**, 1522 (1924); (b) Allen, *ibid.*, **47**, 1733 (1925); **49**, 1112 (1927); Allen and Bell, *Can. J. Research*, **11**, 40 (1934); Allen and Scarrow, *ibid.*, p. 395. (c) Corson, Dissertation, Harvard University, 1924; Lowry, *ibid.*, 1924.

[2] Allen and Boyer, *Can. J. Research*, **9**, 159 (1933).

[3] Kugel, *Ann.*, **299**, 50 (1897).

[4] Biedermann, *Ber.*, **24**, 4074 (1891).