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.

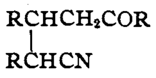
Montreal, Canada Received January 11, 1937

[Contribution from the Chemical Laboratory of McGill University]

Gamma-Benzoylbutyronitrile

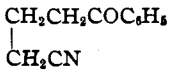
By C. F. H. Allen and W. L. Ball

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



$RCHCH_2COR$ / $RCHCN$

I

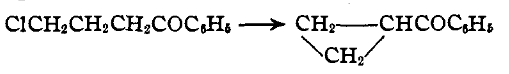


$CH_2CH_2COC_6H_5$ / CH_2CN

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]



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

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

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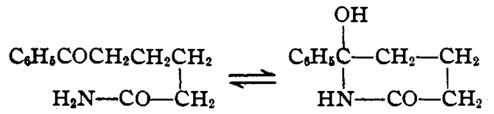
[1] (a) Kohler, Graustein and Merrill, This Journal, **44**, 2536 (1922); Kohler and Souther, *ibid.*, p. 2903; Kohler and Allen, *ibid.*, **46**, 1522 (1924); (b) Allen, *ibid.*, **47**, 1733 (1925); **49**, 1112 (1927); Allen and Bell, *Can. J. Research*, **11**, 40 (1934); Allen and Scarrow, *ibid.*,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

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

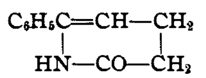
[3] Kugel, *Ann.*, **299**, 50 (1897).

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

by the use of acetyl chloride or by heating alone, or from the reaction between phenylmagnesium bromide and glutaronitrile. The relative ease of formation may indicate that the amide exists as one component of a tautomeric mixture (III ⇄ IV)



III IV

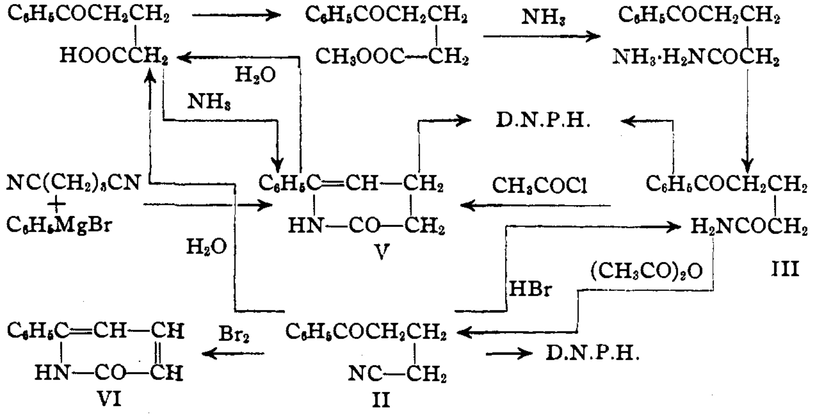


V

In the case of other delta ketonic amides, the available evidence points to their existence only in the cyclic form.[1b,5]

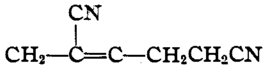
The reactions of the cyclic form (V) are in accordance with the structure written. Thus, acid hydrolysis leads to γ-benzoylbutyric acid. It decolorizes bromine instantly; after about two-thirds of the calculated amount of bromine has been added, hydrogen bromide begins to be evolved. A bromide–bromate titration shows one double bond. When treated with 2,4-dinitrophenylhydrazine in the usual manner (acid solution) the ring is opened with addition of a molecule of water, and the dinitrophenylhydrazone of the amide is obtained.

These reactions are conveniently summarized in the flow-sheet.



D.N.P.H. = 2,4-Dinitrophenylhydrazone.

Bruylants[6] has examined the action of several Grignard reagents on glutaronitrile and, among the numerous products, found substances which he believed to be open chain δ-ketonic nitriles; thus, he wrote structure (II) for the substance obtained when phenylmagnesium bromide was used. We have repeated the reaction following Bruylants' directions and isolated the product having the properties[7] as described, and found it to be identical with (V), the cyclic isomer of (II). It is easy to understand the confusion, for both give the same hydrolysis product and react with bromine, the tests employed by Bruylants; the differences on bromination would hardly be noticed unless one were expecting them. Aliphatic Grignard reagents brought about condensation, and gave, as the principal product, a substance $C_{10}H_{11}ON_3$, for which he wrote an open chain keto-trinitrile structure; from the available data, supplemented by the results just mentioned, it probably should have the ring formula (VII).



VII

Experimental

A. Action of Ammonia on Methyl γ-Benzoylbutyrate; γ-Benzoylbutyramide, III.—Cyclopentanone was oxidized to glutaric acid by 50% nitric acid;[8] the latter was dehydrated by acetic anhydride[9] and converted into γ-benzoylbutyric acid by the Friedel–Crafts reaction.[10] A mixture of 5 g. of the methyl ester,[11] 10 cc. of alcohol and 50 cc. of concd. ammonium hydroxide were shaken mechanically for four hours, and the solvent allowed to evaporate; a solid of m. p. 110–125° separated. A similar product resulted after spontaneous evaporation of a solution of 25 g. of the ester in 75 cc. of alcohol that had been saturated with ammonia. This solid was dissolved in a slight excess of a warm 1:1 mixture of chloroform and ether; on cooling, white needles, m. p. 118–120°, separated from a purple solution. Two recrystallizations from benzene raised the melting point to 120–121°. By continued reworking of all filtrates, additional amounts of solid of varying degrees of homogeneity resulted.

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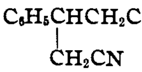
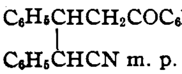
(5) Barat, *J. Ind. Chem. Soc.*, **7**, 321 (1930).

(6) Bruylants, (a) *Bull. soc. chim. Belg.*, **32**, 307 (1923); (b) *Bull. sci. acad. roy. Belg.*, [5] **7**, 252 (1921); (c) Bruylants and Dewail, *ibid.*, [5] **12**, 464 (1926).

(7) Bruylants gave the melting point as 158°. This seemed to us surprisingly high for an unsubstituted nitrile, when compared with the melting points of the phenylated homologs,[1a,c] but in accord with a cyclic structure. We



$\underset{\displaystyle CH_2CN}{C_6H_5CHCH_2COC_6H_5}$ m. p. 76°



$\underset{\displaystyle C_6H_5CHCN}{C_6H_5CHCH_2COC_6H_5}$ m. p. 103, 118°

have found that the melting point of γ-benzoylbutyronitrile is 38°.

(8) *Organic Syntheses*, **14**, 90 (1934).

(9) Sircar, *J. Chem. Soc.*, 898 (1928).

(10) *Organic Syntheses*, **13**, 12 (1933).

(11) Allen and Cressman, This Journal, **55**, 2953 (1933).

This substance was unstable; after standing overnight the melting point became much less sharp. It evolved ammonia on being heated; it decolorized bromine and permanganate on warming with the reagents in appropriate solvents. It dissolved in warm chloroform, carbon tetrachloride, and benzene to give a reddish solution; if not cooled at once, a colorless solid, m. p. 140–142°, separated; treatment with boiling water gave this same substance. This was the amide III, which, when pure, formed flat rods, m. p. 144°. The amide was also obtained from the purple melt of the 120° solid, and from the various oily by-products by repeating the ammonia treatment, dissolving the dark oil in benzene and decolorizing with charcoal. The total yield was thus raised to 70%.

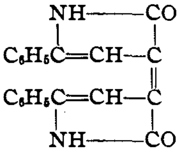
Anal. Calcd. for the ammonia addition product: (a), $C_{11}H_{16}O_2N_2$: C, 63.5; H, 7.7; N, 13.5; for the amide III, $C_{11}H_{13}O_2N$: C, 69.1; H, 6.8; N, 7.3. Found: (A), C, 63.9; H, 7.6; N, 13.8; (III) C, 69.4; H, 6.8; N, 7.3.

The amide was hydrolyzed easily to γ-benzoylbutyric acid. The 2,4-nitrophenylhydrazone of the amide was prepared in the usual manner; it separated from a methanol–ethyl acetate mixture in clusters of orange rods having square ends, m. p. 195–196°.

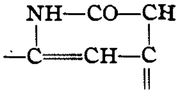
Anal. Calcd. for $C_{17}H_{17}O_6N_5$: N, 18.8. Found: N, 18.6.

A mixed melting point with the reagent (m. p. 198°) was depressed 20°.

With a view to securing a higher yield in the alcohol–ammonia method, the saturated solution was allowed to stand for three weeks; it became a deep red, then purple. A small amount of a black, crystalline solid was removed; from the solution a poor yield of amide and ammonia addition product were separated. The black solid did not melt below 320°, but sublimed in brown fumes when heated on porcelain. It gave a blue solution in concd. sulfuric acid, being precipitated unchanged on dilution, but dissolved to a colorless solution in sodium hydroxide. In all its properties it resembles Kugel's product obtained from ammonia and ethyl β-benzoylpropionate[3] for which he wrote the structure VIII.



VIII



IX

By analogy, our substance would be the homolog IX; it was not investigated further.

B. **γ-Benzoylbutyronitrile, II.**—A solution of 5 g. of the amide in 25 cc. of acetic anhydride was unchanged after being allowed to stand overnight, but on refluxing an hour and distilling *in vacuo*, an oil, b. p. 135–140°, at 10 mm., was obtained; this solidified on standing, only if a pure amide had been used. The yield was 3.5 to 4.9 g. (82–94%); it is very soluble in the usual solvents. It formed plates, m. p. 38°.

Anal. Calcd. for $C_{11}H_{11}ON$: C, 76.3; H, 6.4. Found: C, 76.2, 76.0; H, 6.4, 6.5.

The 2,4-dinitrophenylhydrazone separated as red-brown plates from (1:2) alcohol–ethyl acetate, m. p. 173–175°.

Anal. Calcd. for $C_{17}H_{15}O_4N_5$: N, 19.9. Found: N, 19.5.

The semicarbazone, prepared in the usual way, separated from chloroform as plates, m. p. 176–177°. It is only sparingly soluble in alcohol.

Anal. Calcd. for $C_{12}H_{14}ON_4$: N, 24.3. Found: N, 24.1.

The nitrile was easily hydrolyzed to γ-benzoylbutyric acid in moist solvents in the presence of acid. When a solution in chloroform (that had been dried with calcium chloride) was saturated with hydrogen bromide and allowed to stand overnight, a brownish paste remained as the green solution evaporated. When this was washed with dry ether, a white solid (m. p. 205–210°—a red liquid) that could not be purified, remained; treatment with alcohol or acetic acid gave γ-benzoylbutyric acid. If the white residue was dissolved in absolute alcohol containing freshly fused potassium acetate, and evaporated to dryness, the benzene extract deposited the amide III. The properties of the white substance agree with those of an "imide bromide."

Bromination is described in section D.

C. **2 - Keto - 6 - phenyl - 1,2,3,4 - tetrahydropyridine, V.**—This substance was obtained in several ways. The purest product resulted on refluxing an acetyl chloride solution of the amide for a half hour, filtering the solid, and washing it with dry ether. On vacuum distillation, the oily residue gave a further quantity. The properties agreed with those given by Bruylants[6] but repeated recrystallization of crude material was necessary to get a pure substance; dry benzene or carbon tetrachloride was found preferable to alcohol.

The cyclic compound was also obtained in the following ways, the identification in each case being by mixed melting point and comparable behavior in solvents: (a) when the amide was heated alone, the melt changed colors, blue, red, brown; the residue was taken up in alcohol and decolorized by charcoal; (b) dry ammonia was passed through molten γ-benzoylbutyric acid at 160–170° for nine hours;[12] (c) by repetition of Bruylants' directions, through the action of phenylmagnesium bromide on glutaronitrile.

The tetrahydropyridine was shown to have one double bond by titration; 0.200 g. used 0.195 g. of bromine (calcd., 0.185 g.). Hydrolysis gave γ-benzoylbutyric acid. The action of nitrous acid was indeterminate. On treatment with 2,4-dinitrophenylhydrazone in the usual manner (acid solution) the derivative of the amide III resulted. Bromine gave oils.

D. **2-Phenyl-α-pyridone, VI.**—An excess (3 g.) of bromine was added to 3 g. of γ-benzoylbutyronitrile in 50 cc. of chloroform; the solution turned black and hydrogen bromide was evolved. The solvent was removed on the steam-bath and the residue distilled *in vacuo*, since preliminary attempts had shown the futility of any other kind of manipulation. At 20 mm. a preliminary, nondescript fraction came over up to 180°, but from the second (mostly at 190°) a solid separated; the latter was very soluble in benzene, carbon tetrachloride, and chloroform, soluble in hot water but insoluble in cold, and recrystal-

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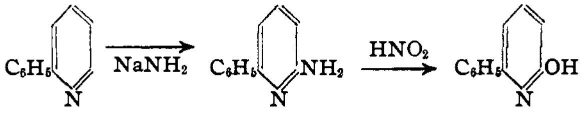
(12) Work of Mr. L. F. Somerville.

lized best from methanol in flat rods with square ends, m. p. 195°; although it appeared to crystallize well from petroleum ether the melting point was lower by 10°. A hydrochloride of m. p. 101–103° was prepared as directed in the literature, which gave the melting point 104°. All the properties agree with those described by Leben.[13] In order to establish the identity with certainty, a specimen was prepared as directed in the literature,[14,15] the melting point was not depressed on admixture.

Owing to the roundabout method of synthesis, several attempts were made to obtain it by a simpler procedure, but without success. It was relatively easy to prepare 2-aminopyridine and 2-phenylpyridine but impossible to introduce both groups into the same molecule. The action of sodium amide on 2-phenylpyridine led to a high melting, bimolecular product.



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

Summary

γ-Benzoylbutyronitrile has been prepared by the dehydration of the corresponding amide with acetic anhydride. Other dehydrating agents gave a cyclic, isomeric derivative of tetrahydropyridine. The characteristic properties of each have been determined.

MONTREAL, CANADA RECEIVED FEBRUARY 8, 1937

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[13] Leben, *Ber.*, **29**, 1673 (1896).

[14] Kalff, *Rec. trav. chim.*, **46**, 594 (1927).

[15] In this work we were assisted by Mr. J. C. W. Evans. Some of the preliminary steps were first carried out by Dr. A. C. Bell. Their aid is gratefully acknowledged.

[CONTRIBUTION FROM THE ORGANIC RESEARCH LABORATORY, CHEMISTRY DEPARTMENT, UNIVERSITY OF THE PHILIPPINES]

On the Naturally Occurring Linolic Acid in Cottonseed and Soya Bean Oils and the Regenerated Linolic Acid from Alpha Linolic Acid Tetrabromide of These Oils

BY D. M. BIROSEL

In a previous paper,[1] it was reported that only two isomeric linolic acid tetrabromides were isolated from the products of direct bromination of the free fatty acids of lumbang or candle nut (*Aleurites moluccana*) oil and of the regenerated linolic acid; that only two tetrahydroxystearic acids were isolated from the products of oxidation with alkaline permanganate solution of the free fatty acids of lumbang oil and of the regenerated linolic acid; and that the β- and δ-linolic acid tetrabromides which have been reported by other workers as obtainable from the bromination product of the free fatty acids of lumbang oil are ethyl ester mixed with varying amount of free solid acid tetrabromide.

Considerable work[2] has been done on linolic acid but the literature presents conflicting observations and conclusions. The present work is primarily intended to supplement the observations previously recorded by the writer. It is desired to report in this paper the observations made on linolic acid naturally present in soya bean and in cottonseed oils and on the regenerated linolic acid from α-linolic acid tetrabromide prepared by direct bromination of the free fatty acids of these oils.

From the direct bromination of the dried free fatty acids of soya bean and cottonseed oils, using ether as reaction medium and low boiling point petroleum ether[3] as vehicle of crystallization, α-linolic acid tetrabromide (m. p. 114°) was the only

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[1] Birosel, *Natural and Applied Science Bulletin of the University of the Philippines*, **2**, 103 (1932).

[2] Meyer and Beer [*Monatsh.*, **33**, 325 (1912)] obtained β-sativic acid of m. p. 174° and α-sativic acid of m. p. 163° from the oxidation with cold alkaline permanganate solution of the free fatty acids of "Jimson weed" *Datura Stramonium*. Nicolet and Cox [THIS JOURNAL, **44**, 144 (1922)] doubted the existence of these sativic acids on the ground that the fatty acids of Jimson weed seeds yield α-linolic acid tetrabromide, m. p. 117°, whereas the highest melting point recorded in the literature is 114°. A. P. West and co-workers [*Philippine J. Sci.*, **32**, 41 (1927); *cf. C. A.*, **21**, 1720 (1927); *ibid.*, **32**, 297 (1927); *cf. C. A.*, **21**, 2250 (1927); *ibid.*, **42**, 251 (1930)] reported having isolated three solid linolic acid tetrabromides from the free fatty acids of lumbang oil. They claimed that their β-linolic acid tetrabromide corresponds to the compound which was reported by Takahashi [*J. Tokyo Chem. Sci.*, **4**, 233 (1919); *C. A.*, **13**, 1583 (1919)] but regarded their α-linolic acid tetrabromide of lumbang oil as different from a similar compound from soya bean oil on the ground that their regenerated linolic acid did not yield the β-linolic acid tetrabromide of Takahashi. Birosel[1] has shown that the β- and δ-linolic acid tetrabromides of West are ethyl ester of the acid mixed with varying amount of free α-linolic acid tetrabromide.

[3] Birosel[1] reported that with ethyl alcohol as vehicle of crystallization for the crude solid acid tetrabromide, the β- and δ-acids of West[2] were obtained whereas if low boiling petroleum ether was used none was obtained. West's[2] compounds were also obtained when pure α-linolic acid tetrabromide, m. p. 114°, was refluxed with ethyl alcohol until oil separated upon cooling the solution. The supposedly β- and δ-acids did not give neutralization value but their alcoholic solutions to which a few drops of phenolphthalein solution were added turned red upon addition of the first drop of standard alkali.