at first but later disappeared with the formation of a clear, light red solution. The solution was cooled, decomposed with iced ammonium chloride and steam distilled. Recrystallization of the residue from alcohol yielded colorless needles, m. p. 238–239°. From the mother liquors was isolated a small amount of the glycol (III), identified by m. p. and conversion into VII.

Anal. Calcd. for $C_{27}H_{22}O_2$: C, 85.7; H, 5.9; active H, 1; carbonyl, 1. Found: C, 85.5; H, 6.1; active H, 0.96; carbonyl (addition), 1.05.

The compound gives a red-violet color in concd. sulfuric acid. It does not react with bromine in acetic acid or carbon tetrachloride nor with cold potassium permanganate solution in acetone. It is reduced by hydriodic acid (in boiling acetic acid) with the formation of a compound, m. p. 157°, which was obtained in small amounts only and was not further characterized.

1,7-Diphenyl-7-methoxy-8,8-dimethylperinaphthindanone-9 (VIII).—The ether was formed when a solution of IV in boiling methanol was treated with a trace of hydrochloric acid and allowed to cool. It formed colorless crystals, m. p. 224°.

Anal. Calcd. for $C_{28}H_{24}O_2$: C, 85.7; H, 6.2; OCH_3, 7.8. Found: C, 85.4; H, 6.3; OCH_3, 7.9.

1,7-Diphenyl-7-chloro-8,8-dimethylperinaphthindanone-9 (IX).—Anhydrous hydrogen chloride was passed into a solution of 0.2 g. of IV in warm, anhydrous benzene, containing a few granules of calcium chloride. Evaporation of the benzene left a colorless oil which crystallized slowly when dissolved in benzene–petroleum ether and allowed to stand. The chloro compound melted at 158–162°, dec.

Anal. Calcd. for $C_{27}H_{23}OCl$: C, 81.3; H, 5.8; Cl, 8.9. Found: C, 81.1; H, 5.7; Cl, 9.4.

Summary

A study has been made of the reaction between phenylmagnesium bromide and 8,8-dimethylperinaphthindandione-7,9. The diketonic function was not cleaved under any of the conditions used. Three products were obtained, two of which were the result of normal addition to either one or both of the carbonyl groups, the other being the result of 1,2-addition to one of the carbonyl groups and 1,4-addition to the other.

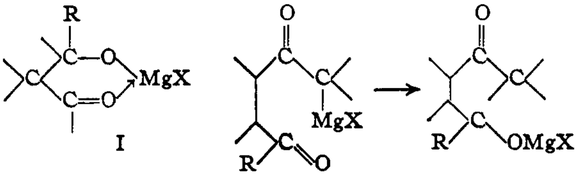
LOS ANGELES, CALIFORNIA RECEIVED JANUARY 6, 1944

[CONTRIBUTION FROM DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA, LOS ANGELES]

The Reaction between Cyclic β-Diketones and Grignard Reagents. III. 2-Methyl-2-benzoylhydrindone

BY T. A. GEISSMAN AND VSEVOLOD TULAGIN

It has been shown in a number of instances that β-diketones in which the two carbonyl groups are members of a four-,[1] five-,[2] or six-membered[3] ring undergo normal addition when treated with Grignard reagents. This behavior is in contrast to that of many open-chain β-diketones, which are readily cleaved by alkyl- and arylmagnesium halides.[4] Among the possible explanations for this difference in behavior are[2] (1) that for cleavage to occur it must be necessary for a coördination complex such as I to form after the first mole of reagent adds, and (2) that the cleavage product (II) which would be expected in the case of a cyclic β-diketone is incapable of existence because of its readiness, for steric reasons, to reform the monoaddition product (III).

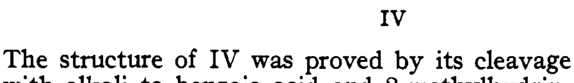


I II III

Implicit in the second explanation is the assumption that there is no bar to the initiation of cleavage, but only that it cannot proceed to such an extent as to allow a second mole of reagent to add to the resulting carbonyl group to yield an enolate-carbinolate. It is to be remarked that the conditions under which a β-diketone is allowed to react with a Grignard reagent will have an effect upon the nature of the reaction, and that a discussion of the presence or absence of cleavage in any case must take into account whether or not the reaction was carried out under conditions which would be expected to favor cleavage.

In the present paper are described the results of a study of the reaction between phenylmagnesium bromide and a β-diketone in which the carbonyl groups are disposed in such a way that chelation in the monoaddition product can occur, but in which the spatial arrangement of the groups is such that the sequence indicated by II→III could also occur.

2-Methyl-2-benzoylhydrindone (IV) was prepared by the treatment of methylbenzylmalonyl chloride with aluminum chloride in benzene solution. Simultaneous ring closure and condensation occurred smoothly to form IV in good yield.



IV

The structure of IV was proved by its cleavage with alkali to benzoic acid and 2-methylhydrindone, and by the nature of the products formed when it reacted with phenylmagnesium bromide.

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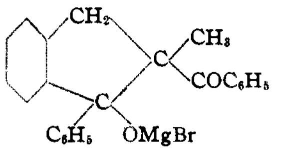
[1] Wedekind and Miller, *Ber.*, **44**, 3285 (1911).

[2] Geissman and Tulagin, THIS JOURNAL, **63**, 3352 (1941).

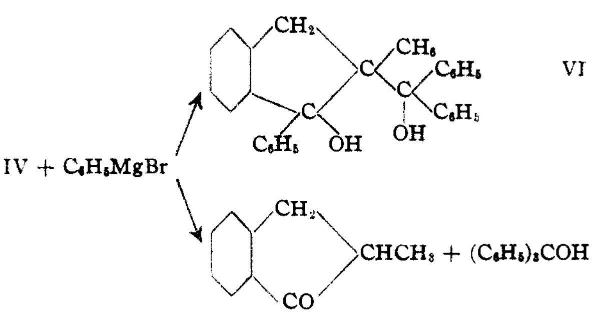
[3] Geissman and Morris, *ibid.*, **66**, 716 (1944).

[4] Kohler and Erickson, *ibid.*, **53**, 230 (1931).

It was anticipated that the cyclic carbonyl group of IV would be the more reactive, and that the monoaddition compound V would arise as the first product of the reaction of IV with phenylmagnesium bromide.

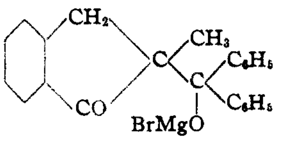

V

This compound (V) fulfils the conditions which should lead to cleavage if a chelated intermediate is a sufficient condition for cleavage. The reaction actually went in two ways, resulting in diaddition to form the glycol (VI), and cleavage into products which could only have arisen as the result of an initial attack of the reagent at the *benzoyl* group.


VI

The relative amounts of the products isolated indicated that about one-fifth of the total amount of reaction followed the route leading to cleavage, the remainder leading to VI.

The initial products formed by the attack of phenylmagnesium bromide on IV would be the monoaddition compounds V and VII

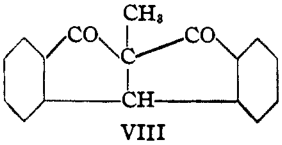

VII

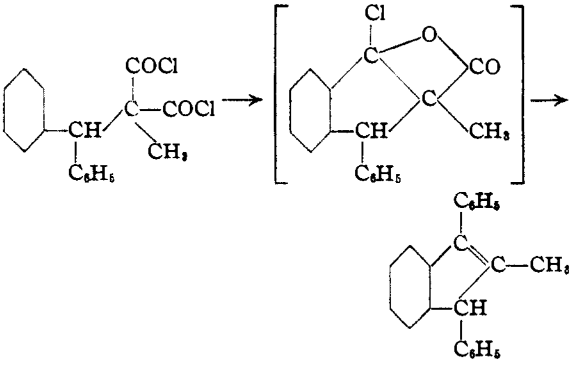
It is clear from the products isolated that the subsequent reaction of V involved the addition of a second mole of the reagent to yield VI (after hydrolysis). The further reaction of VII may have led in part to the formation of an additional amount of VI, but the formation of 2-methylhydrindone and triphenyl carbinol is evidence that VII underwent the cleavage reaction typical of open-chain diketones.

The cleavage of IV, through VII, cannot be considered evidence that the formation of a chelated intermediate is a necessary condition for cleavage, since this case parallels that of a simple open-chain β-diketone. The lack of cleavage through the intermediate V does prove, however, that the formation, or possibility of formation, of a chelated intermediate is not a sufficient condition for cleavage. The question of the necessity for such an intermediate in the cleavage reaction must be examined in a different way, but it can be said that in no case so far examined in which such an intermediate cannot form has cleavage been observed.

Preliminary to the preparation and study of IV attempts were made to prepare two other diketones in which the carbonyl groups are disposed in such a way that it appeared (from models) that a coördinated complex such as I could form, but in which the conditions for the reaction II→III were also present. These experiments were unsuccessful, but will be described briefly because of certain features of interest in the synthetic work done.

The preparation of the diketone VIII was attempted by the sequence: diethyl benzalmalonate + phenylmagnesium bromide→diethyl benzhydrylmalonate[5]→diethyl methylbenzhydrylmalonate→methylbenzhydryl malonic acid→chloride, and ring-closure of this to yield VIII. The only product isolated in attempts to bring about this ring closure resulted when the reaction was carried out in benzene solution. It was a crystalline substance the analysis of which corresponded to the formula $C_{22}H_{18}$. This compound is assumed to have arisen as follows, and to have the structure IX


VIII


IX

This observation is to be compared with that of Leuchs and Wutke, who reported that dibenzylmalonyl chloride, when treated with aluminum chloride, yielded 1-chloro-2-benzylindene.[6] Thomas[7] has reported other, analogous cases.

The preparation of the diketone X was attempted in the following way: dibenzylacetic

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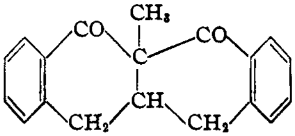
[5] Kohler, *Am. Chem. J.*, **34**, 134 (1904).

[6] Leuchs and Wutke, *Ber.*, **46**, 2428 (1913).

[7] Thomas, "Anhydrous Aluminum Chloride in Organic Chemistry," Am. Chem. Soc. Monograph, Reinhold Publishing Co., New York, N. Y., 1941, pp. 237–239.



X

acid→β,β-dibenzylpropionic acid (by the Arndt–Eistert reaction)→3-benzyltetralone→ethyl 3-benzyltetralone-2-glyoxylate → ethyl 3-benzyltetralone-2-methyl-2-glyoxylate → ethyl 3-benzyltetralone-2-methyl-2-carboxylate → acid, followed by ring closure to yield XI. Difficulties were encountered in attempts to hydrolyze ethyl 3-benzyltetralone-2-methyl-2-carboxylate to the corresponding acid, and the synthesis was finally abandoned in favor of studies on the diketone IV.

Experimental

Methylbenzylmalonic Acid.—Absolute alcohol was added in small portions to a suspension of 8 g. of powdered sodium in 50 ml. of boiling, dry benzene, until a clear solution was obtained. The solvents were removed at 100° and 22 mm., and to the dry sodium ethoxide was added a solution of 90 g. of ethylbenzylmalonate in 150 ml. of dry benzene. The mixture was treated with 70 g. of methyl iodide and allowed to stand overnight. After the addition of water, the benzene layer was separated and the benzene removed under reduced pressure. The residue was dissolved in a solution of 40 g. of sodium hydroxide in 60 ml. of water and 300 ml. of alcohol and the solution refluxed for twenty-four hours. The resulting suspension was dissolved in 1 liter of water, the alcohol removed by distillation, the aqueous solution decolorized and acidified. The oily acid was taken up in ether and after the removal of the ether, crystallized from benzene. The product weighed 60 g. (80%); m. p. 139.5–140° (literature[8] 135°).

2-Methyl-2-benzoylhydrindone (IV).—A suspension of 20 g. of methylbenzylmalonic acid in a mixture of 50 ml. of dry benzene, 50 g. of thionyl chloride and 3 drops of pyridine was allowed to stand, with occasional agitation, until all of the solid had dissolved. The solution was evaporated and to the residual oil was added 12 g. of phosphorus pentachloride and a few ml. of benzene. After thirty minutes the volatile material was removed at 22 mm. and 100°, the residue taken up in 50 ml. of dry benzene, and 40 g. of aluminum chloride added in small portions. Hydrogen chloride was evolved and the solution changed through red to a deep violet. After standing overnight, the mixture was decomposed with ice and hydrochloric acid, the benzene layer separated and evaporated and the residue distilled at 3 mm. Most of the material distilled at 195–197° as a light yellow oil which crystallized when rubbed with a few drops of acetic acid. The material was crystallized from dilute methanol, from which it formed large clumps of colorless needles, m. p. 62.5–63.5°.

Anal. Calcd. for $C_{17}H_{14}O_2$: C, 81.6; H, 5.6. Found: C, 81.3; H, 5.7.

Alkaline Cleavage of 2-Methyl-2-benzoylhydrindone.—A mixture of 5 g. of the diketone, 5 g. of sodium hydroxide and 10 ml. of water was refluxed overnight and then steam-distilled. The residue was acidified; upon cooling it deposited crystals of benzoic acid: m. p. and mixed m. p., 120–121°; neutral equivalent found, 123; calculated, 122. The steam distillate contained 2-methylhydrindone as a light yellow, mobile oil from which were prepared an oxime, m. p. 103–104.5 (literature[9] 104–106°), a *p*-nitrophenylhydrazone, m. p. 171–172° (literature[9] 167–168°), and a 2,4-dinitrophenylhydrazone, m. p. 213–215°.

The Reaction of 2-Methyl-2-benzoylhydrindone with Phenylmagnesium Bromide.—A solution of phenylmagnesium bromide in equal parts of ether and benzene was added dropwise to a refluxing solution of 4 g. of the diketone in 50 ml. of dry benzene. The first mole of the reagent caused the formation of a gummy, orange-yellow precipitate which dissolved as a second mole was slowly added, a clear yellow solution resulting. The addition of the first two moles of reagent took an hour; a third mole was then added all at once to insure the completion of the reaction. The resulting solution was refluxed for two hours, cooled and decomposed with ice and hydrochloric acid. The solvents were removed by steam distillation. The semi-crystalline residue remaining was crystallized from toluene, yielding 3.9 g. of colorless crystals, m. p. 214–215°. This material (VI) is readily soluble in hot acetone, acetic acid, benzene and toluene, but only slightly soluble in these solvents in the cold.

Anal. Calcd. for $C_{29}H_{26}O_2$: C, 85.9; H, 5.9. Found: C, 85.8; H, 6.2.

The mother liquor from which VI had crystallized was evaporated and the residue taken up in hot acetone. An additional amount of VI separated; this was removed and the solution cooled to 0°. On standing, the solution deposited 1.3 g. of triphenylcarbinol, m. p. (after recrystallization) and mixed m. p. 159–162°. In order to isolate 2-methylhydrindone, another sample of 8 g. of the diketone was treated as above; the benzene layer, separated after decomposition with ice and ammonium chloride, was cooled to remove VI and then distilled through a small helix-packed column. The last traces of benzene were removed at 100° and 22 mm. and the residue steam-distilled. The light yellow oil present in the steam distillate was converted into a 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 214–215°.

Oxidation of the Diol (VI).—A suspension of 2 g. of VI in a solution of 20 ml. of concentrated nitric acid in 60 ml. of water was refluxed for one hour. The resulting dark red oil was taken up in ether, the ether solution washed with water and with sodium bicarbonate solution, dried and evaporated. The residue was distilled at 3 mm., yielding an oily distillate which crystallized when seeded with benzophenone. The material melted, alone or mixed with benzophenone, at 48–49°. It formed a 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. with an authentic sample of benzophenone 2,4-dinitrophenylhydrazone, 235–237°. The yield was 48%, based upon unrecovered diol.

The sodium bicarbonate extract of the original ether solution was acidified and extracted with ether. From the ether solution was isolated 210 mg. of *o*-benzoylbenzoic acid: neutral equivalent found, 227; calculated, 228. It melted at 126–128° and did not depress the m. p. of an authentic sample of *o*-benzoylbenzoic acid. It formed a hydrate, m. p. 93–94°, identical with an authentic sample. There was no neutral fraction other than that represented by benzophenone and no ether-soluble acid other than *o*-benzoylbenzoic acid.

Methylbenzhydrylmalonic Acid.—A solution of 58 g. of ethyl benzhydrylmalonate in 600 ml. of dry ether was stirred with 4 g. of sodium wire until all of the metal had disappeared. A solution of 55 g. of methyl iodide in 50 ml. of ether was then added dropwise during thirty minutes and the mixture allowed to stand overnight. Water was added and the layers separated. The crude ester weighed 60 g.; it was not purified before saponification.

A solution of 53 g. of the ester, 100 g. of sodium hydroxide, 200 ml. of water and 300 ml. of alcohol was heated on the steam-bath for one hour. The thick crystalline magma was dissolved by the addition of 150 ml. of water and the resulting solution refluxed for twenty hours. After dilution with water the solution was acidified; the dark brown oil which separated crystallized on standing at 0°. The crude acid was recrystallized from dilute acetic acid. It formed nearly colorless prisms, m. p. 143–145° with gas evolution. The yield was 26.5 g.

Anal. Calcd. for $C_{17}H_{16}O_4$: C, 71.8; H, 5.7; neut. eq., 142. Found: C, 71.9; H, 6.0; neut. eq., 140.

Attempted Ring Closure of Methylbenzhydrylmalonyl Chloride.—(A) In benzene solution: to a solution of 5 g.

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[8] Conrad and Bischoff, *Ann.*, **204**, 177 (1880).

[9] Auwers and Auffenberg, *Ber.*, **52**, 107 (1919).

of the acid in benzene was added 5 g. of phosphorus pentachloride. After thirty minutes the benzene and phosphorus compounds were removed on the water-bath at 20 mm. and to the residue, dissolved in 50 ml. of benzene, was added 6 g. of aluminum chloride in small portions. The initial yellow color slowly changed to red in the course of several hours. After twenty-four hours the mixture was decomposed with ice and hydrochloric acid, the benzene layer separated, dried and evaporated. The residue was distilled at 2 mm., yielding a light yellow distillate which crystallized from dilute acetic acid. There was obtained 0.81 g. of colorless crystals, m. p. 91–92°. The compound was not soluble in cold, concentrated sulfuric acid, very soluble in ligroin and slightly soluble in acetone.

Anal. Calcd. for $C_{22}H_{18}$: C, 93.6; H, 6.4. Found: C, 93.2; H, 6.6.

When stannic chloride was used in place of aluminum chloride the same compound was formed.

(B) In carbon bisulfide: No crystalline material could be isolated when carbon bisulfide was used as the solvent in place of benzene.

β,β-Dibenzylpropionic Acid.—A solution of 15 g. of dibenzylacetic acid, 18 g. of thionyl chloride, 3 drops of pyridine and 60 ml. of dry benzene was allowed to stand for an hour at room temperature. The solution was evaporated at 22 mm. and 100°, the residue taken up in 50 ml. of dry benzene and treated with a dried solution of diazomethane, prepared from 30 g. of nitrosomethylurea, in ether. After an hour the solution was filtered and the solvents removed under reduced pressure. The residue crystallized as orange needles. Recrystallized from 90% methanol, the diazoketone formed pale yellow needles, m. p. 72–74°; yield, 15 g. (90%).

Anal. Calcd. for $C_{17}H_{16}ON_2$: C, 77.3; H, 6.1. Found: C, 76.9; H, 6.2.

The recrystallized diazoketone was dissolved in 100 ml. of anhydrous ethanol and treated with 3 g. of dry silver oxide. On warming to 50° a vigorous evolution of nitrogen occurred and the solution was cooled. The solution was then warmed at 60° for an hour and filtered. Five grams of potassium hydroxide was added and after three hours at room temperature the silver oxide which had precipitated was removed and the solution refluxed for thirty minutes. Water was added, the alcohol removed by distillation and the solution acidified. The precipitated acid was extracted with ether and, after removal of the ether, crystallized from dilute acetic acid. The product melted at 85–86°; the yield was 13.1 g. (91%, based on the diazoketone).

Anal. Calcd. for $C_{17}H_{18}O_2$: C, 80.3; H, 7.1; neut. eq., 254. Found: C, 80.0; H, 7.1; neut. eq., 255.

The acid was also prepared through the Reformatsky reaction starting with ethyl bromoacetate and dibenzyl ketone, the hydroxy ester being dehydrated to the unsaturated ester, the latter saponified and the acid reduced with Raney nickel at 150° and 1700 lb. The over all yield was 15% of a product identical with that prepared as described above.

3-Benzyltetralone.—Five grams of β,β-dibenzylpropionic acid was converted into its chloride with thionyl chloride and cyclized by treating it with 8 g. of stannic chloride in benzene solution. The crude product, isolated in the usual way, was distilled at 2 mm., then crystallized from ligroin (b. p. 90–100°) and petroleum ether (b. p. 30–60°). The yield was 4 g. of material melting at 54–56°.

Anal. Calcd. for $C_{17}H_{16}O$: C, 86.4; H, 6.8. Found: C, 86.6; H, 7.1.

Methyl 3-Benzyltetralone-2-glyoxalate.—Dry sodium methoxide was prepared from 1.5 g. of sodium and absolute methanol, and to it was added 15 g. of dimethyl oxalate and 50 ml. of dry benzene. A solution of 15.5 g. of 3-benzyltetralone in 15 ml. of benzene was added dropwise, and the mixture allowed to stand overnight. Water was added, the benzene layer separated and evaporated, and the residue crystallized from methanol. There was obtained 14 g. of colorless needles, m. p. 85–87°.

Anal. Calcd. for $C_{20}H_{18}O_4$: C, 74.6; H, 5.6. Found: C, 74.4; H, 5.7.

Methyl 3-Benzyltetralone-2-carboxylate.—The glyoxylic ester was mixed with 20 g. of powdered soft glass (previously treated with aqua regia, water, alkali and then thoroughly washed) and the mixture heated for twenty minutes at 175°. The product was extracted with acetone, the acetone removed, and the residue recrystallized from methanol. Large colorless needles, m. p. 77–78°, were obtained. The yield was quantitative.

Anal. Calcd. for $C_{19}H_{18}O_3$: C, 77.6; H, 6.1. Found: C, 77.3; H, 6.3.

Methyl 2-Methyl-3-benzyltetralone-2-carboxylate.—To the dry sodium methoxide prepared from 0.46 g. of sodium was added a solution of 5.9 g. of methyl 3-benzyltetralone-2-carboxylate in 25 ml. of dry benzene. When the solid had dissolved, 6 g. of methyl iodide was added and the solution allowed to stand overnight. After the addition of water and ether, the ether layer was separated, dried and evaporated. The residue crystallized from methanol, yielding a first crop of 4.4 g. of material, m. p. 114–115°, and a second crop of 0.7 g. of slightly less pure material. The total yield was 5.1 g. (84%).

Anal. Calcd. for $C_{20}H_{20}O_3$: C, 77.9; H, 6.5. Found: C, 77.5; H, 6.7.

Summary

The reaction between phenylmagnesium bromide and 2-methyl-2-benzoylhydrindone follows two courses, leading to products derived from (a) diaddition to the carbonyl groups and (b) cleavage. Cleavage occurs only when the initial attack by the reagent is on the extracyclic carbonyl group.

It is postulated that the ability of the monoaddition product to form an intramolecular coordination complex is not a sufficient condition for cleavage.

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