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

# THE BEHAVIOR OF CERTAIN 1,3-INDANDIONES IN ATTEMPTED HYDANTOIN FORMATION<sup>1</sup>

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Aldehydes and ketones may be converted into the corresponding 5-monosubstituted or 5,5-disubstituted hydantoins by the action of ammonium carbonate and a soluble cyanide under suitable conditions. This procedure, developed by Bucherer, *et al.* (1), has been used repeatedly to produce hydantoins from a variety of carbonyl compounds but chiefly from ketones. Since, in many instances, this reaction proceeds readily to yield products of high purity and sharp melting points, hydantoin formation has been suggested as a means of characterization of carbonyl compounds (2).

While a total of only seventeen hydantoins possessing a spiro structure has been made from cyclic ketones (1a, 2-7), apparently but few diketones have been studied in attempted hydantoin formation. The results of such studies do not warrant generalization. Thus, for example, a 1,2-diketone was found to undergo cleavage to yield a monosubstituted hydantoin (4), while a 1,3-diketone gave little or no hydantoin derivative in experiments from which reproducible results were difficult to obtain (8). Further, a 1,4-diketone, under the conditions of attempted hydantoin synthesis, reacted solely with ammonia to yield a pyrrole derivative (4).

The uniform success in conversion of open chain ketones into 5,5-disubstituted hydantoins is thus in rather sharp contrast to the variable results encountered in attempts to convert diketones of the type  $\text{RCO}(\text{CH}_2)_n\text{COR'}$  where n = 0 or an integer. And the relative paucity of knowledge concerning the formation of spirohydantoins from cyclic ketones has made it seem to be of considerable interest to study the possibility of obtaining bis-spirohydantoins from cyclic diketones.

Since the spirohydantoins derived from fluorenone (5), 1-tetralone (2), and 1-indanone (2) had been shown to possess considerable activity in controlling electrically-induced seizures in experimental animals (9), the ready availability of 1,3-indandione and of its 2,2-dimethyl and 2-methyl-2-phenyl derivatives, suggested that attempts be made to convert these cyclic 1,3-diketones into spirohydantoins. It should be noted that indanones and indandiones represent poorly studied families of compounds. In fact, although their enolization has been the subject of several investigations (10, 11, 12), relatively little attention has been directed to the stability of the ring or the activity of their carbonyl groups. It is clearly evident that these compounds, possessing the -COCH<sub>2</sub>COgrouping in their structures, exhibit tautomerism and might be expected to undergo ring cleavage on exposure to alkali.

Attempts to convert 1,3-indandione into a hydantoin derivative failed under

<sup>&</sup>lt;sup>1</sup> From the M. A. thesis of William Joseph Leanza, June, 1950.

the conditions of the Bucherer procedure (1); this failure so to react under these conditions may be attributed to the ease with which this compound dimerizes in alkaline solution (13). The 2-methyl derivative likewise did not react; however, this substance was for the most part recovered unchanged. It was observed that when potassium cyanide or an alcoholic solution of ammonium cyanide was added to a neutral, alcoholic solution of 2-methyl-1,3-indandione, hydrogen cyanide was evolved and the solution turned the dark red color of, supposedly, the enol form of the 1,3-diketone. From 2,2-dimethyl-1,3-indandione there was obtained a mixture of the mono- and bis-spirohydantoins, separation of which was not effected readily by use of the more common organic solvents. However, the separation was achieved using acetophenone as a solvent, from which the pure bis-spirohydantoin crystallized in solvated form. However, when hydantoin formation was attempted using fused acetamide (8), instead of diluted alcohol, as solvent, an excellent yield of the bis-spirohydantoin resulted.

In sharp contrast to these results, 2-methyl-2-phenyl-1,3-indandione was recovered unchanged from exposure to the cyanide and ammonium carbonate in diluted alcohol solution. But using fused acetamide as the solvent, the 1,3diketone yielded two, different, neutral nitrogenous compounds (I) and (II); however, neither of these products was a hydantoin derivative.

$$C_{16}H_{12}O_2 + KCN + (NH_4)_2CO_3 + H_2O \rightarrow C_{16}H_{13}NO \text{ and } C_{17}H_{16}N_2O$$
  
I II

The product  $C_{16}H_{13}NO$  (I) was shown to result from interaction of 2-methyl-2phenyl-1,3-indandione and ammonium carbonate. In order to establish the presence in I of the unaltered cyclopentene ring of the indan nucleus, a simultaneous hydrolysis and reduction was attempted. The Clemmensen reduction procedure, which gave good yields of 2-methyl-2-phenylindan from its related 1,3-dione, was utilized; however, none of the sought-for hydrocarbon was obtained. Compound (I) contained one "active hydrogen", and did not react with carbonyl reagents nor form a picrate or hydrochloride.

Although a small amount of I was obtainable from the interaction of the 1,3diketone and ammonium carbonate in alcoholic solution, the main product was an unidentifiable gum. Recovery of some acetophenone from the reaction in acetamide solution indicated that hydrolytic cleavage of the cyclopentene ring had occurred. The first product of such fission might be o-(hydratropoyl)benzoic acid; the latter,<sup>2</sup> presumably, is in part converted into acetophenone.

<sup>2</sup> Benzalphthalide, under suitable conditions, is acted upon by ammonia to form the amide of *o*-phenylacetylbenzoic acid; the latter, as a result of ring closure, subsequently yields benzalphthalimidine [see Gabriel and Michael, *Ber.*, **11**, 1628, 1682 (1878); Natelson and Gottfried, *J. Am. Chem. Soc.*, **63**, 487 (1941)].





The existence of unsaturation in I was indicated by its ability to decolorize solutions of bromine and potassium permanganate. The position of this unsaturation was demonstrated through ozonolysis, which yielded acetophenone and phthalimide. These data indicate that the structure of I is that of  $\alpha$ -methylbenzalphthalimidine;<sup>3</sup>



The other reaction product (II) was insoluble in dilute acids, but by heating with stronger acid hydrolysis occurred and led to the recovery of a carboxylic acid (III). Decarboxylation of III yielded IV, which differed in molecular formula from that of I by only two hydrogen atoms. In fact, some of IV could be recovered from the attempted hydrogenation of I by the Clemmensen procedure.<sup>4</sup>

The initial experiment which led to the preparation of II was repeated several times, but with the period for reaction varied from one to twenty-one days; however, there was no perceptible change in the ratio of II to I formed. Compound II was not obtained when I was exposed in solution to the action of additional ammonium carbonate and potassium cyanide. Therefore, I does not seem to be the precursor of II, and the latter, probably the result of the simultaneous action of ammonia and hydrogen cyanide upon 2-methyl-2-phenyl-1,3-indandione, is  $1-(\alpha-methybenzyl)-3-\inftyo-1-isoindolinecarboxamide (or, synonymously, <math>1-(\alpha-methylbenzyl)-1-phthalimidinecarboxamide).$ 

<sup>3</sup> The question may be raised whether acetophenone might not be formed, during the attempted ozonolysis in acid solution, through some other oxidative hydrolysis, for example, of a 2,2-disubstituted-1,3-diketone derivative. However, the stability of I to acid hydrolysis has been established, and the conditions of ozonolysis and recovery of products certainly were not favorable to the formation of phthalimide from a phthalamic acid.

<sup>4</sup>Subsequently, an attempt was made to convert I into IV through catalytic hydrogenation. In one experiment, essentially one mole-equivalent of hydrogen was absorbed by I, yet, the product formed was not IV. A plausible sequence of reaction leading to II follows:<sup>5</sup>



#### EXPERIMENTAL

Preparation of 1,3-indandiones. Ethyl sodio-diketohydrindenecarboxylate was prepared in 80% yield by the method of Wislicenus (13) by condensing ethyl acetate with diethyl phthalate, and was decarboxylated by heating with 10% sulfuric acid (14) to yield 1,3indandione.

In a similar manner, utilization of ethyl propionate led to the production of 2-methyl-1,3-indandione. The sodio salt of the latter reacted with methyl iodide to form 2,2-dimethyl-1,3-indandione (13).

Benzalphthalide was prepared by Gabriel's modification (15) of the Perkin synthesis, and was converted to the sodio salt of 2-phenyl-1,3-indandione (16); subsequent methylation resulted in the formation of 2-methyl-2-phenyl-1,3-indandione.

Reduction of 2-methyl-2-phenyl-1,3-indandione. This 1,3-diketone was reduced to the hydrocarbon by the method of Clemmensen (17). Five grams of 2-methyl-2-phenyl-1,3-indandione was mixed with 50 g. of zinc amalgam and treated from a dropping-funnel with

<sup>&</sup>lt;sup>5</sup> It is recognized that this sequence may not be the only one possible. However, whether the first step in this reaction is hydrolysis, ammonolysis, or addition at the carbonyl group to form a cyanohydrin or aminonitrile, seems relatively immaterial, since subsequent hydrolysis and ring closure, in whatever sequence, seemingly should lead to II, namely 1-(amethylbenzyl)-3-oxo-1-isoindolinecarboxamide.

a mixture of 125 ml. of conc'd hydrochloric acid, 20 ml. of acetic acid, and 20 ml. of water. As heat was applied, hydrogen was evolved and within 20 minutes all of the solid organic material had become liquid. The temperature was raised and the mixture steam-distilled for one hour. The distillate was extracted with ether; the ether extract was neutralized, dried over sodium sulfate, and distilled, yielding about 3 g. of an oil at 110–120° (1–2 mm.). This material was redistilled at 172–175° (18 mm.): Fraction I,  $n_D^{25}$  1.5816; Fraction II,  $n_D^{25}$  1.5847; Fraction III,  $n_D^{25}$  1.5910;  $d_4^{23}$  1.0374.

When allowed to stand over anhydrous calcium chloride, Fraction I began to crystallize. One of these crystals was removed and used to seed Fraction II. After standing at room temperature, the resulting crystals were removed and pressed dry on filter paper; m.p. 40-42°.

Anal. Calc'd for C<sub>16</sub>H<sub>16</sub>: C, 92.25; H, 7.74.

Found: C, 92.05; H, 7.84.

These crystals of 2-methyl-2-phenylhydrindene were carefully melted on a dust-free watch glass and could be supercooled to room temperature without solidifying;  $n_D^{20}$  1.5836;  $n_D^{25}$  1.5812;  $d_1^{22}$  1.0406;  $\Sigma$ MR 66.69; MR calc'd 66.74. This hydrocarbon has not previously been reported in the literature.

Attempted conversion of 1,8-indandione to the spirohydantoin. A mixture of 1,3-indandione, potassium cyanide,<sup>6</sup> and ammonium carbonate in 70% alcohol was heated at 58-60° for two hours. Since the color of the mixture now was a deep red, a small amount of sodium bisulfite was added and the mixture was heated four hours longer. After acidification and attempts to isolate an hydantoin derivative, the only product recovered was impure biindone (18); m.p. 206-208°.

In a second attempt, a sample of 1,3-indandione was converted into its sodium bisulfiteaddition product and the latter was warmed with ammonium carbonate and potassium cyanide in diluted alcohol over the temperature range 45–75°. The only material isolated was a green, nitrogen-free powder which did not melt or decompose below 360°. This product probably was a salt of isobiindone. From the mother liquor could be isolated trace amounts of nitrogenous products.<sup>7</sup>

Attempted conversion of 2-methyl-1,3-indandione into a spirohydantoin. Treatment of a sample of 2-methyl-1,3-indandione in 70% alcohol with an aqueous solution of potassium cyanide caused the development of a straw yellow color which soon darkened to a deep red; the odor of hydrogen cyanide was quite evident. Ammonium carbonate was added and the mixture was warmed for several hours. No isolable product could be found.

In another attempt, a solution of sodium bisulfite was added to an alcohol solution of 2-methyl-1,3-indandione causing formation of a precipitate which dissolved in more solvent. An aqueous solution of potassium cyanide and solid ammonium carbonate was added and the mixture was heated at 70°; two layers formed but became homogeneous upon further addition of water. Much of the indandione was recovered unaltered.

Following the method of Henze and Long (8), the intermediates were dissolved in fused acetamide and heated in a closed container at 120°. Only a resinous semi-solid material, sintering over a range of 100°, could be isolated.

A final attempt involved treating 2-methyl-1,3-indandione with potassium cyanide and ammonium sulfate in 70% alcohol (with hope to form a cyanohydrin). The mixture turned red and inorganic salt separated. More potassium cyanide was added and the mixture was allowed to stand for three days. Most of the diketone was recovered unaltered; the only other organic product identified was urea.

Conversion of 2,2-dimethyl-1,3-indandione into two spirohydantoins. A mixture of 25 g. (0.15 mole) of this ketone, 37 g. (0.6 mole) of potassium cyanide, and 136.8 g. (1.2 moles) of ammonium carbonate cubes in 70% alcoholic solution was heated at 60° for 12 hours. At

<sup>6</sup> The alcohol solution of the 1,3-diketone became dark red in color.

<sup>7</sup> Elsevier's Encyclopedia of Organic Chemistry. Elsevier's Publishing Company, New York-Amsterdam, 1948, Vol. 12A, p. 394 lists a number of polymers of indandione.

this temperature, two liquid layers were present; raising the temperature to  $75^{\circ}$  caused the mixture to become homogeneous. After three hours, the warm solution was filtered from inorganic material. Chilling the filtrate caused separation of 8 g. of unreacted dione. The mother liquor was extracted repeatedly with ether, concentrated, and acidified. About 20 g. of a tan solid was obtained; after recrystallization from 30% alcohol, the product melted with decomposition over the range 240-264°.

Anal. Calc'd for  $C_{13}H_{12}N_2O_3$ : N, 11.47;

Calc'd for C<sub>15</sub>H<sub>14</sub>N<sub>4</sub>O<sub>4</sub>: N, 17.83.

Found: N, 13.75.

This percentage indicates an approximate ratio of two-thirds mono-spirohydantoin to one-third bis-spirohydantoin.

Separation was attempted by crystallization from water, alcohols, acetone, and some higher ketones, and by fractional acidification of an alkaline solution, but without significant success. A partial separation was affected by dissolving the mixture of spirohydantoins in hot isobutyl alcohol and, at intervals, filtering off each successive precipitate as the solution evaporated at room temperature. It was found that the crystals which separated during the first two hours melted sharply at 265°, whereas those which appeared between the twenty-fourth and forty-eighth hours decomposed over the range 290–325°; intermediate fractions and the residue from final evaporation of the mother liquor melted between 252° and 262°. The fractions of lowest melting point were found to contain 12.10%, 12.38%, and 11.78% of nitrogen, indicating their chief component to be the monospirohydantoin.

Acetophenone permitted a sharp separation of the two spirohydantoins; the mixture was dissolved in boiling acetophenone, and crystallization began almost immediately. After removal by filtration, the crystals were dried at 120° for 12 hours; m.p. 325–330°.

Anal. Calc'd for C23H22N4O5: C, 63.44; H, 5.14; N, 12.90.

Found: C, 63.38; H, 5.35; N, 12.56.

When this product was heated with an alcoholic solution of semicarbazide hydrochloride and sodium acetate, there was obtained the semicarbazone of acetophenone mixed with the bis-spirohydantoin. The latter could also be isolated by heating the solvated compound  $[C_{15}H_{14}N_4O_4 \cdot C_8H_8O]$  at 190-210° for six hours at 5 mm.; acetophenone was collected in a cold trap and there remained dispiro-[2,5-dioxoimidazole-4,1'-(2',2'-dimethylindan)-3',4"-(2",5"-dioxoimidazole)]; m.p. 325-330°.

Anal. Calc'd for C<sub>15</sub>H<sub>14</sub>N<sub>4</sub>O<sub>4</sub>: Mol. wt. 314; C, 57.32; H, 4.49; N, 17.83.

Found: Mol. wt.  $320 \pm 20$ ; C, 57.39; H, 4.80; N, 17.81.

The filtrate of the acetophenone solution was evaporated to dryness and the residue was crystallized repeatedly from isobutyl alcohol to give fine, white crystals of *spiro*-[*imidazolidine-4,3'*-(2',2'-dimethyl-1'-oxindan)]-2,5-dione, of m.p. 265-266°.

Anal. Calc'd for C<sub>13</sub>H<sub>12</sub>N<sub>2</sub>O<sub>3</sub>: C, 63.92; H, 4.95.

Found: C, 63.51; H, 5.12.

The preparation of a spirohydantoin from 2,2-dimethyl-1,3- indandione was repeated using acetamide as solvent. The diketone (14 g.) was allowed to react with excess potassium cyanide and ammonium carbonate in acetamide solution for 18 hours at 110°. The reaction mixture was diluted with water and acidified to obtain 20 g. (80% yield) of a solid consisting entirely of the bis-spirohydantoin. By dissolving this material in dilute alkali and reprecipitating through addition of solid carbon dioxide, crystals were obtained which, by their m.p. behavior, gave evidence of hydration. They were dired in a desiccator for several days; m.p. 265-266°.

Anal. Calc'd for C15H14N4O4 · H2O: N, 16.86.

Found: N, 16.88.

Attempted conversion of 2-methyl-2-phenyl-1,3-indandione to an hydantoin derivative. A mixture of 40 g. of this diketone and 26 g. of potassium cyanide dissolved in 800 ml. of hot 80% alcohol was treated with 90 g. of ammonium carbonate causing considerable precipitation of both organic and inorganic material. The mixture could not be made homogeneous by addition of diluted alcohol, so it was heated at 70° for 12 hours. After concentration, and acidification of the reaction mixture, about 30 g. of the unreacted diketone was recovered.

In another experiment, 20 g. (0.084 mole) of this diketone was dissolved in 200 g. of fused acetamide in the glass liner of a Monel metal bomb; after addition of 13.5 g. (0.2 mole) of potassium cyanide and 35 g. (0.3 mole) of ammonium carbonate, the closed container was heated at 125° for eight days. After cooling, the reaction mixture was diluted with water, acidified, and boiled for 30 minutes. The resulting tan, amorphous material was removed and dissolved in alcohol. Upon cooling, the first crop of crystals (I) was removed and examined; 4 g. (20% yield); m.p. 242-245°.

Anal. Calc'd for C16H13NO: Mol. wt., 235; C, 81.64; H, 5.53; N, 5.95.

Found: Mol. wt.,  $250 \pm 20$ ; C, 80.92; H, 5.70; N, 5.98.

The alcoholic filtrate from I was evaporated to leave a brown residue; m.p. 220-280°; no organic material was obtained by extraction of this residue with either acid or alkaline solutions. The residue was boiled with benzene, filtered, and recrystallized from alcohol to obtain a white solid (II); 5 g. (20% yield); m.p. 294-306°.

Anal. Calc'd for C17H16N2O2: Mol. wt., 280; C, 72.84; H, 5.75; N, 10.00.

Found: Mol. wt.,  $283 \pm 10$ ; C, 72.71; H, 5.87; N, 9.95.

Evaporation of the benzene extract yielded additional I. Further investigation showed that higher yields of I and II could be obtained following removal of most of the acetamide through vacuum evaporation of the reaction mixture at 100°. The residue from such concentration was shaken with water and filtered before treatment with alcohol and benzene as before. Thus, yields of 35-40% of each of I and II resulted.

One gram of I was boiled with an excess of potassium cyanide and ammonium carbonate in fused acetamide solution at  $135^{\circ}$  for 12 hours; no conversion of I into II was observed.

Chemical behavior of compound I,  $C_{16}H_{13}NO$ . In a manner analogous to that used with 2-methyl-2-phenyl-1,3-indandione, 2.2 g. of I was boiled with 20 g. of amalgamated zinc and a hydrochloric-acetic acid mixture. The organic material, however, did not go readily into solution nor appear to change. Neither was any product recovered from an attempted steam-distillation. The acid mixture was neutralized and extracted with ether, and about 2 g. of a dark gum was obtained. By vacuum distillation, and after several recrystallizations there remained about 0.5 g. of a finely divided purple powder, which in alcohol solution showed orange fluorescence, turned blue when acidified, brown when made alkaline, and could not be decolorized by sulfur dioxide treatment.

One gram of I was dissolved in 100 ml. of hot 50% sulfuric acid and boiled at  $135-140^{\circ}$  for three hours; the compound was recovered unchanged upon cooling, neutralizing, and filtering.

Attempts to form a picrate of I were unsuccessful, and no tendency towards such reaction was observed.

Two grams of I was dissolved in 20 g. of dry pyridine, treated with 1 g. of hydroxylamine hydrochloride, and the resulting solution was heated on a steam-bath for four hours; when cooled in an ice-bath, unchanged I was deposited.

Compound I does not dissolve in dilute or concentrated aqueous sodium hydroxide solution, and is recovered unchanged when heated for several hours with alcoholic potassium hydroxide solution. A small amount of I was heated overnight in a propylene glycol solution of potassium hydroxide; a slight evolution of ammonia could be detected through use of Nessler's reagent.

A solution of I in acetone decolorized a dilute potassium permanganate solution. Likewise, a benzene solution of bromine was decolorized upon addition of I.

When 0.3044 g. of I was allowed to react with a solution of methylmagnesium iodide in *n*-butyl ether, there was collected 30.6 ml. of methane (equivalent to 0.95 "active hydrogen").

Reaction of 2-methyl-2-phenyl-1,3-indandione with ammonium carbonate. This diketone (3 g.) and 5 g. of sodium bicarbonate were heated with excess of ammonium carbonate in

50% alcohol at  $60-70^{\circ}$  for three days. The solution was diluted with water and cooled to cause precipitation of unaltered diketone. The filtrate was evaporated to dryness and the residue was extracted with hot methanol. Evaporation of this solvent yielded a gum, which was recrystallized from acetone-water; 0.05 g.; m.p.  $241^{\circ}$ ; m.p. of a mixture with I,  $240^{\circ}$ .

The 1,3-diketone (10 g.) was heated with excess ammonium carbonate in a fused acetamide solution in a closed container at 135° for 16 hours. After cooling, the reaction mixture was diluted with water and neutralized to produce a black, amorphous mass. The latter was dissolved in alcohol, boiled with Norit for one hour, and filtered. The filtrate yielded about 5 g. of yellow crystals, m.p. 240-243°, which were shown to be identical with I by mixture melting point. A small amount of acetophenone was recovered by steam-distillation of the aqueous acetamide solution.

Ozonolysis of I. A solution of 0.21 g. of I in 20 ml. of glacial acetic acid was treated with a 2.1 excess of 5% ozone in oxygen during a period of 30 minutes. A slight yellowing of color in the solution was noticed within a few minutes. The reaction mixture was hydrolyzed and dilute sodium hydroxide solution was added until the solution became cloudy; the odor of acetophenone was apparent. The solution (still acidic) was extracted with ether, and the extract in turn was washed with a very dilute alkaline solution. Evaporation of the ether left an oily residue which gave color reactions with sodium nitroprusside solution identical with those of an authentic sample of acetophenone.

This residue was dissolved in a small amount of alcohol and warmed with semicarbazide hydrochloride and sodium acetate. Upon diluting with water and cooling, a white precipitate formed, was filtered off, and dried; m.p. 198°; m.p. of acetophenone semicarbazone is 199° (19).

The sodium hydroxide washings of the ether extract were neutralized and cooled to obtain a white precipitate; 0.05 g.; m.p. 234°. This m.p. remained unchanged as a result of solution of the product in alkali with subsequent reprecipitation by acid. Some technical grade phthalimide was purified through base and acid treatment and recrystallization from alcohol to m.p. 234° (20); a mixture m.p. was unchanged.

Compound I was reduced using a very active platinum catalyst (21); to the reduced catalyst suspended in 15 ml. of acetic acid was added 0.296 g. of I dissolved in 15 ml. of acetic acid to which a few drops of water had been added, and the mixture was exposed to hydrogen under atmospheric pressure. Initially, hydrogen was absorbed very rapidly but the rate fell sharply after about 30 minutes. Exposure was terminated when very slightly more than the calculated amount for one mole-equivalent of hydrogen had been utilized. After removal of the catalyst, the acetic acid filtrate was diluted with 100 ml. of water and chilled to produce fine white crystals (V); 0.22 g. (75% yield); m.p. 167-170°. Recrystallization of V from ether and acetone raised the m.p. to 169-173°. A mixture of V with IV, subsequently produced from II, melted at 139-155°. Compound V did not decolorize solutions of potassium permanganate or of bromine.

Hydrogenation of I was repeated using truly anhydrous solvents; now, the rate of hydrogenation did not fall off until after three mole-equivalents had been utilized. The reduction was stopped after 12 hours, when approximately five mole-equivalents of hydrogen appeared to have been absorbed. The product very largely consisted of V, but contained a small amount of another white, semi-solid material. No acid-soluble products were recovered.

Chemical behavior of compound II. Compound II (4 g.) of m.p.  $294-296^{\circ}$ , 75 ml. of water, and 75 ml. of conc'd sulfuric acid were heated to  $140^{\circ}$  before the formation of bubbles throughout the solution was noted. A slow stream of purified air was passed through the heated solution and into a solution of sodium hydroxide; after a while, the latter was shown not to contain cyanide ion. The stream of effluent gas was then passed into a solution of barium hydroxide causing precipitation of barium carbonate. The residual reaction mixture, which gave a strong positive test for ammonium ion, was neutralized and chilled to produce a white precipitate. The latter was removed, washed and dried; 2 g.; m.p.  $140-155^{\circ}$ ; this material was later found to consist mainly of a decarboxylation product (IV). The filtrate from IV was neutralized with dilute acid to produce another white precipitate (III) which, after being dried, weighed 2 g.; m.p. 131–132° with effervescence.

Anal. Calc'd for (III) C<sub>17</sub>H<sub>15</sub>NO<sub>3</sub>: Neut. equiv., 281.3; C, 72.58; H, 5.38; N, 4.98.

Found: Neut. equiv., 289; C, 72.59; H, 5.45; N, 5.05.

In another experiment it was found that the acid (III) could be obtained quantitatively, and without any of the decarboxylation product (IV), by heating II at 110-120°, rather than at 140°, for one hour. This acid (III) did not exhibit amphoteric properties, nor did it give a coloration with ninhydrin.

Decarboxylation of compound III. A 0.66-g. sample of III was heated gently; at about  $132^{\circ}$  the acid slowly melted and evolved carbon dioxide; the loss in weight of the sample was 0.10 g. (15.2%); the loss of carbon dioxide from the monocarboxylic acid (C<sub>17</sub>H<sub>15</sub>NO<sub>3</sub>) is calculated as 15.6%. The melt solidified to a hard, vitreous mass which was suspended in acetone, treated with 10 ml. of 0.1 N sodium hydroxide, and filtered. The residue (IV) was recrystallized from diluted alcohol and dried to constant weight in a vacuum oven at 75-80° for three hours; wt. 0.45 g. (80% yield); m.p. 141-142°.

Anal. Calc'd for C<sub>16</sub>H<sub>15</sub>NO: C, 80.98; H 6.37; N, 5.91.

Found: C, 80.76; H, 6.48; N, 5.90.

Compound IV was soluble in alcohol, acetone, conc'd sulfuric acid, and glacial acetic acid; insoluble in dilute acids and bases; and slightly soluble in conc'd hydrochloric acid. It did not form a picrate.

Ozonolysis of compound II ( $C_{17}H_{16}N_2O_2$ ). This material was exposed to ozone under the same conditions as was compound I. From 0.23 g. of II there was recovered 0.13 g. of starting material. No odor of acetophenone was noted. The effluent gases produced a color in potassium iodide solution within 30 seconds after exposure of II to ozone began.

### SUMMARY

Neither 1,3-indandione nor 2-methyl-1,3-indandione yields a spirohydantoin derivative through interaction with potassium cyanide and ammonium carbonate in solution.

From 2,2-dimethyl-1,3-indandione there was obtained both the mono- and bis-spirohydantoins.

Under identical conditions, 2-methyl-2-phenyl-1,3-indandione forms two different derivatives. Through interaction with ammonium carbonate solution, the 1,3-diketone was converted into  $\alpha$ -methylbenzalphthalimidine. The other product, resulting from interaction with ammonium cyanide and subsequent hydrolysis, is 1-( $\alpha$ -methylbenzyl)-3-oxo-1-isoindolinecarboxamide. The latter could be hydrolyzed to the corresponding acid, and the acid decarboxylated to yield 1-( $\alpha$ -methylbenzyl)-3-oxo-1-isoindoline [or  $\alpha$ -methylbenzylphthalimidine].

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