[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

THE REACTIONS AND ENOLIZATION OF CYCLIC DIKETONES. V. (1) SOME CARBONYL REACTIONS

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α-Diketones derived from cyclopentane have two features of special interest: their enolizability and the reactivity of their carbonyl groups. During previous investigations of the factors most noticeably affecting enolizability (1), isolated observations of the heightened reactivity of one of the carbonyl groups have been made; but these observations have not been correlated and interpreted. The present paper is a report on a study of this reactivity, undertaken in order to answer the questions: which of the carbonyl groups in a cyclic α-diketone of given structure is more prone to undergo additive reactions, and how does the activity of this carbonyl group compare with that of a carbonyl group in an acyclic diketone?

The activation of a carbonyl group by an adjacent negative (electron attracting) group appears to be quite general. Only brief reference to a few of the numerous examples of this activation in acyclic carbonyl compounds need be made. Chloral, glyoxalic acid (2), mesoxalic ester (3), mesityl glyoxal (4), 2,3,4-triketopentane (5) all show peculiarities in behavior, especially a tendency to add alcohols or water, which can be ascribed to the activation under discussion. Acyclic α-diketones apparently are not quite active enough to add alcohols or water, but this type of reactivity is pronounced with α-keto aldehydes and with triketones.

The same effects are found among the cyclic dicarbonyl compounds. While cyclopentanedione-1,2 (6) and diosphenols (7), perhaps because of their existence in enolic forms, do not add hydroxylated substances, some cyclic α-diketones have this property in a marked degree. The first case of this sort was noted by Perkin, Roberts, and Robinson (8), who found that while indandione-1,2 in keeping with its α-diketone structure formed yellow solutions in non-polar solvents, it gave colorless solutions in alcohols. Attempts to isolate acetals or hemiacetals from such solutions, however, were entirely unsuccessful. When the colorless alcoholic solutions were evaporated or chilled, the original yellow diketone separated (9).

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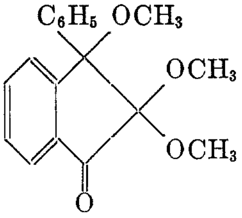
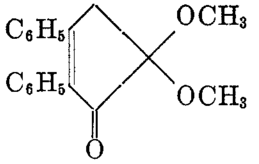
[1] Abstracted from a Thesis by C. D. LeClaire, presented to the Graduate Faculty of the University of Minnesota in partial fulfilment of the requirements for the Ph.D. degree, March 1939.



I



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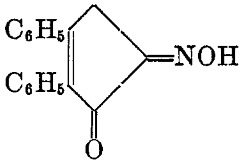

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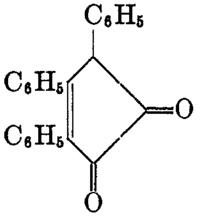

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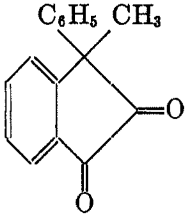


V

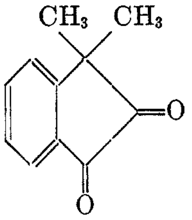
A still more pronounced activity has been observed in 3-bromo-3-phenylindandione-1,2 and in 3-methoxy-3-phenylindandione-1,2 (10). These substances are both deeply colored, but their solutions in alcohol are nearly colorless. From these solutions were isolated colorless crystalline acetals of the probable structure I. The parent substance from which these derivatives were obtained, 3-phenylindandione-1,2 did not form acetals; but since this diketone exists entirely in the enolic state, the lack of this type of reactivity is not surprising.

4,5-Diphenylcyclopentane-4-dione-1,2, a compound which exists wholly in the ketonic state, readily formed a methyl acetal (II), and it has been shown that the reaction involves the carbonyl group adjacent to the methylene carbon (9). This same diketone reacted with two equivalents of phenylmagnesium bromide under all conditions, but it was converted into a monoxime (III), reaction again involving the carbonyl group adjacent to the methylene carbon.

3,4,5-Triphenylcyclopentene-3-dione-1,2 (IV) (1), like the diketone discussed in the preceding paragraph, does not enolize; but it formed no acetal when treated with alcohols. It reacted with two equivalents of phenylmagnesium bromide, but unfortunately its behavior towards hydroxylamine was not studied.

Still another diketone, 3-methyl-3-phenylindandione-1,2 (V) (11) which would be expected to show heightened reactivity of one of its carbonyl groups has been prepared. Contrary to expectation, however, this diketone did not react with alcohols; its behavior towards hydroxylamine was not studied.

Three diketones were studied in the present research: 3,3-dimethylindandione-1,2 (VI), 3,3-dimethyl-6-nitroindandione-1,2 (VII), and 3,3-diphenylindandione-1,2 (VIII). Diketones in which carbon-3 was quaternary were selected so that complications due to possible enolization could not arise.



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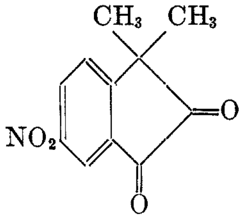
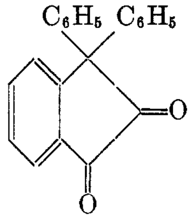
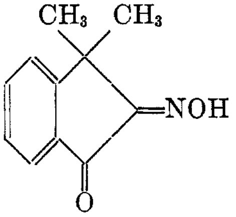


VII

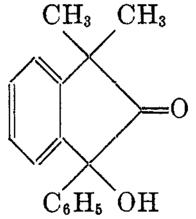


VIII

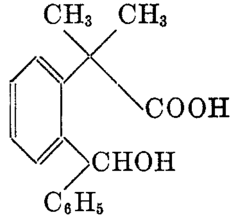
3,3-Dimethylindandione-1,2 (VI) showed many properties characteristic of reactive carbonyl compounds, such as an ability to add sodium bisulfite or potassium cyanide. When treated with an excess of hydroxylamine, the diketone formed a dioxime, but if only one equivalent of hydroxylamine was used a mono-oxime was formed, identical with the compound (IX) obtained by the nitrosation of 3,3-dimethylindanone-1.



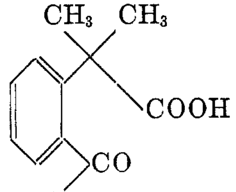
IX



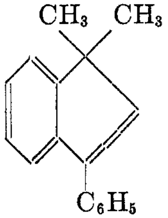
X



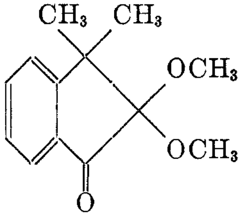
XI



XII



XIII



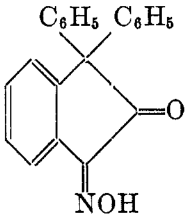
XIV

The formation of this mono-oxime indicated that the 2-carbonyl of the diketone was more reactive than the 1-carbonyl. It was therefore at first surprising to find that the 1-carbonyl was attacked preferentially by phenylmagnesium bromide. Treated with one mole of this reagent, the diketone yielded 1-phenyl-3,3-dimethylindanol-1-one-3 (X) a compound whose structure was proved by cleavage with sodium hydroxide to the acid (XI) and oxidation of this in the form of its lactone to *o*-benzoylphenyldimethylacetic acid (XII). The structure of this degradation product was established by an independent synthesis. Treatment of 3,3-dimethylindanone-1 with phenylmagnesium bromide followed by dehydration of the resulting carbinol yielded 1,1-dimethyl-3-phenylindene (XIII) and this on oxidation gave *o*-benzoylphenyldimethylacetic acid (XII) identical with the acid obtained from the indanolone.

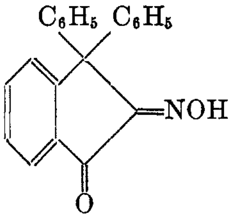
3,3-Dimethylindandione-1,2 dissolved in alcohols to give solutions whose yellow color was markedly different from the orange of solutions of the diketone in non-polar solvents; but cooling the alcoholic solutions caused the separation of the unchanged diketone. When hydrogen chloride was added to a methanol solution of the diketone and the mixture was allowed to stand, a colorless acetal (XIV) was formed. That the acetal formation involved the 2-carbonyl was shown by treatment of the acetal with an excess of phenylmagnesium bromide and hydrolysis of the oily product. This procedure led to the keto alcohol (X) which had been obtained previously by the action of one mole of phenylmagnesium bromide on the diketone itself.

6-Nitro-3,3-dimethylindandione-1,2 (VII) behaved in much the same way as the un-nitrated diketone, although its reactions were not investigated fully. It yielded pink solutions in non-polar solvents, yellow solutions in alcohols; it reacted with sodium bisulfite and with potassium cyanide.

3,3-Diphenylindandione-1,2 (VIII) did not show properties of a very reactive carbonyl compound: it did not add sodium bisulfite, nor did it form an acetal with acidified methanol. Treated with hydroxylamine, the diketone yielded a monoxime (XV) which, since it was different from the product (XVI) obtained by the nitrosation of 3,3-diphenylindanone-1, had the oxime group on carbon-1.



XV



XVI

The data concerning the additive reactions involving one carbonyl group of the cyclic diketones pertinent to the present discussion are

TABLE I

MONO-ADDITION REACTIONS OF CYCLIC α-DIKETONES

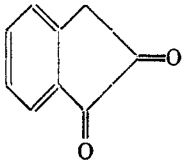
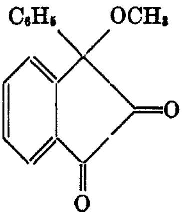
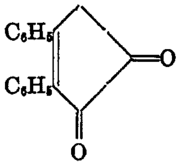
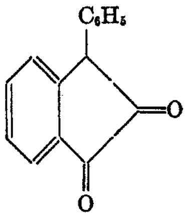
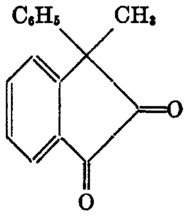
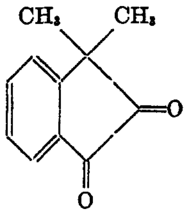
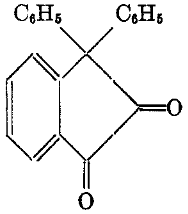
	ROH	1 EQ. NH_2OH	1 EQ. C_6H_5MgBr
	Unstable hemi-acetal formed (?)	Carbonyl-2 oximated	—
	Carbonyl-2 gives acetal	—	—
	Carbonyl-2 gives acetal	Carbonyl-2 oximated	Both carbonyls react
	No reaction	—	Both carbonyls react, carbonyl -2 as enol
	No reaction	—	—
	Carbonyl-2 gives acetal	Carbonyl-2 oximated	Carbonyl-1 reacts

TABLE 1—*Concluded*

	ROH	1 EQ. NH_2OH	1 EQ. C_6H_5MgBr
	No reaction	Carbonyl-1 oximated	—

summarized in Table I. It is apparent here that in compounds bearing no phenyl group on carbon-3, carbonyl-2 shows an additive tendency greater than that of a carbonyl group in an acyclic α-diketone. When carbon-3 bears a phenyl group, this additive tendency is diminished, and two phenyl groups on carbon-3 remove it completely. In the case of 3-phenyl-3-methoxyindandione-1,2, it may be assumed that the deactivating effect of the phenyl group is overcome by the methoxyl also present.

That the 2-carbonyl usually shows a greater tendency than the 1-carbonyl to be involved in reactions with hydroxylamine or alcohols may be explained by considering that the double bond conjugated with the 1-carbonyl tends to lessen the polarization of the latter. Hence in the reversible reactions of oxime or hemiacetal formation, any reagent attacking the 1-carbonyl even if this is the major original point of attack, is subsequently given up to the 2-carbonyl.[2]

The exceptional formation of the 1-oxime and not the 2-oxime from 3,3-diphenylindandione-1,2 is probably due in small part to steric hindrance of the 2-carbonyl by the adjacent phenyl groups, mainly, however, to the ability of the phenyl groups to deactivate the 2-carbonyl through electron donation. Steric hindrance could diminish only the rate of oximation, while the other process, also acting in preventing acetal formation from *e.g.* 3-methyl-3-phenylindandione-1,2, would detract from the stability[3] of the 2-oxime.

Phenylmagnesium bromide, like hydroxylamine, attacks the more exposed rather than the more polar carbonyl group of 3,3-dimethylindandione-1,2. But unlike hydroxylamine, the Grignard reagent adds

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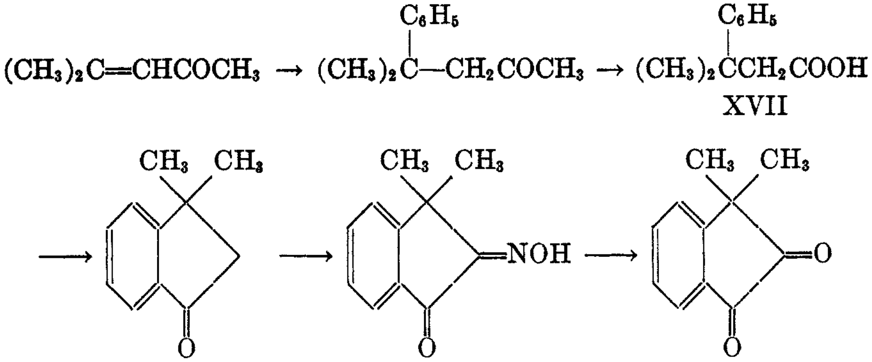
[2] It must be acknowledged that if this explanation is true, little weight can be attached to the method used for determining the structures of the mono-oximes. The structure determination used is thus offered only for lack of an alternative.

[3] This stability would be described by the hydrolysis constant of the oxime or acetal. See CONANT AND BARTLETT, *J. Am. Chem. Soc.*, **54**, 2896 (1932).

irreversibly, so that the 2-carbonyl is involved only if a second mole of phenylmagnesium bromide is available.

A number of points in connection with the preparations and incidental reactions of the diketones used in this study should be mentioned. 3,3-Dimethylindandione-1,2 was prepared through the following series of reactions:



$$(CH_3)_2C{=}CHCOCH_3 \rightarrow (CH_3)_2\overset{\overset{C_6H_5}{|}}{C}{-}CH_2COCH_3 \rightarrow (CH_3)_2\overset{\overset{C_6H_5}{|}}{C}CH_2COOH$$

XVII

XVIII IX VI

β-Phenylisovaleric acid (XVII) has been prepared previously by the aluminum chloride catalyzed addition of benzene to β,β-dimethylacrylic acid (12). It was found much more convenient in the present work to carry out the reactions in the order shown (13), since β-phenylisovaleric acid was more easily extracted than was β,β-dimethylacrylic acid from the large volume of water required in the hypochlorite oxidations of the corresponding ketones. It was also found that cyclization of the acid to 3,3-dimethylindanone-1 (XVIII) did not require the isolation and purification of the acid chloride (12).

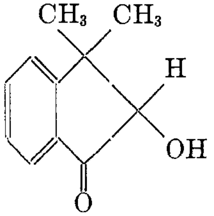
Nitrosation of 3,3-dimethylindanone-1 was carried out both by the action of butyl nitrite and hydrochloric acid and by the action of butyl nitrite and sodium methoxide on the ketone. Although less convenient, the latter procedure is to be recommended, since the acid method sometimes led to the oxime, and sometimes under apparently identical conditions to dimethylhomophthalimide (14).

Acid hydrolysis of the oxime to the diketone proceeded smoothly when formaldehyde was used as a hydroxylamine acceptor in the procedure originated by Perkin (8).

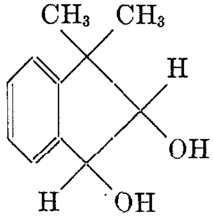
In addition to the reactions already described, 3,3-dimethylindandione-1,2 showed the usual characteristic reactions of α-diketones. It reacted with excess hydroxylamine to give a dioxime (also obtained from the nitroso compound IX and hydroxylamine), it formed a quinoxaline with *o*-phenylenediamine, and it yielded dimethylhomophthalic anhydride on treatment with alkaline hydrogen peroxide.

In addition to its property of forming acetals, 3,3-dimethylindanedione-1,2 showed another interesting behavior. When an acid-free alcoholic solution of the diketone was illuminated it lost its deep yellow color, the alcohol was oxidized (formaldehyde was isolated from a methanol solution), and the diketone was converted into a colorless dihydro compound. This reaction is analogous to the photochemical reduction of quinone by alcohols discovered by Ciamician and Silber (15).

The dihydro compound from 3,3-dimethylindandione was very unstable towards many reagents, and no crystalline product other than the original diketone could be obtained from it when it was treated with aqueous alkali, with benzoyl chloride, acetyl chloride, or acetic anhydride, alone or in aqueous alkali or in pyridine. With phenylmagnesium bromide the dihydro compound yielded an oil and 1,2-diphenyl-3,3-dimethylindandiol-1,2 (XXI), a glycol also obtainable by the action of phenylmagnesium bromide on the original diketone. The dihydro compound could be titrated with aqueous permanganate, yielding thus the diketone almost quantitatively. On melting, the dihydro compound became orange, but no gas was evolved; from the melt was isolated 3,3-dimethylindandione-1,2 in a yield of 50%, and a faintly yellow oil which benzoyl chloride converted into a solid that analyzed for 1,2-dibenzoyloxy-3,3-dimethylindene. The most likely explanation for these data is that the dihydro compound was 3,3-dimethylindanol-2-one-1 (XIX), and that it readily underwent disproportionation to 3,3-dimethylindandione-1,2 and 3,3-dimethylindandiol-1,2 (XX).



XIX



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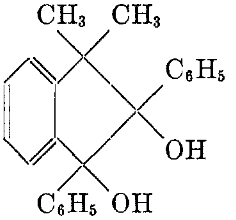
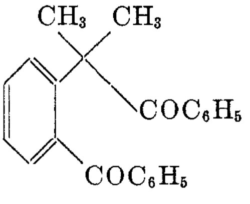
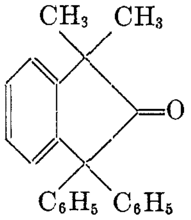


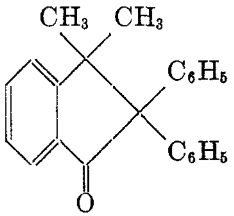
XXI



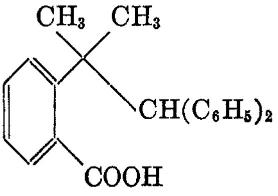
XXII

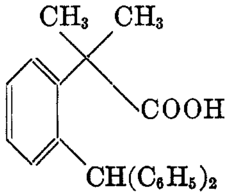


XXIII



XXIV


XXV


XXVI

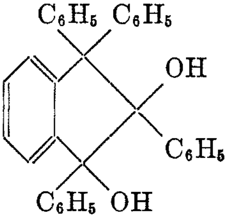
When 3,3-dimethylindandione was treated with an excess of phenylmagnesium bromide, both of its carbonyl groups were attacked and a glycol (XXI) was formed. This glycol was characterized by its behavior towards lead tetraacetate, whereby it was converted into *o*-α-dibenzoylcumene (XXII), and by its behavior towards sulfuric acid in acetic acid. The latter reagent brought about a pinacol rearrangement, but whether the resulting ketone was XXIII or XXIV could not be ascertained definitely. Fusion of the ketone with sodium hydroxide converted it into an acid (XXV) or (XXVI), but when the sodium salt of this acid was distilled with soda-lime it lost sodium hydroxide instead of sodium carbonate and gave back the ketone (XXIII or XXIV). Such a ring closure would involve the intermediate formation of a C–Na derivative, and this type of compound would be more likely to be formed from the Ar_3CH group in XXVI than from the Ar_2RCH group in XXV. Thus formula XXIII is the preferred one for the pinacolone.

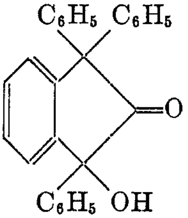
3,3-Dimethylindanone-1 was readily converted into a mononitro derivative by the action of fuming nitric acid. The structure of the product could not be proved definitely, since oxidation led either to a nitrodimethylhomophthalic acid of unknown orientation or to complete destruction. There is little doubt, however, that the nitro ketone was the 6-nitro compound, since it has been shown that while nitration of hydrindone leads to the formation of one part of 4-nitrohydrindone to five parts of 6-nitrohydrindone (16), the nitration of 3-methylhydrindone yields only 3-methyl-6-nitrohydrindone (17).

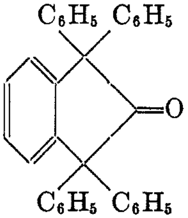
3,3-Dimethyl-6-nitrohydrindone-1 was nitrosated by treatment with butyl nitrite and acetyl chloride, and the oximino compound so produced was hydrolyzed using hydrochloric acid and formaldehyde. The resulting orange-yellow α-diketone was characterized through its ability to form a quinoxaline with *o*-phenylenediamine, and through its reaction with alkaline hydrogen peroxide, which led to 6-nitrodimethylhomophthalic anhydride.

An unsuccessful attempt to hydrolyze 2-isonitroso-3,3-diphenylindanone-1 has been reported (18), but it was found in the present work that with formaldehyde and hydrochloric acid this hydrolysis could be carried out easily. As noted previously in this paper the resulting 3,3-diphenylindandione-1,2 did not react with potassium cyanide or with sodium bisulfite. In some other reactions characteristic of α-diketones, however, it took part readily. Thus with *o*-phenylenediamine it formed a quinoxaline, and with alkaline hydrogen peroxide it yielded diphenylhomophthalic anhydride.

When 3,3-diphenylindandione-1,2 was treated with an excess of phenylmagnesium bromide and the addition-product was hydrolyzed, a non-crystalline product was obtained. Since this product, on dehydration with sulfuric acid in acetic acid yielded a substance $C_{33}H_{24}O$ (XXX), together with a small amount of oil, it was probably a mixture of the two forms of 1,2,3,3-tetraphenylindandiol-1,2 (XXVII). In support of this conclusion a separate synthesis of the substance $C_{33}H_{24}O$ was carried out. 1,3,3-Triphenylindanol-1-one-2 (XXVIII) (19) with phenylmagnesium bromide yielded only one form of 1,2,3,3-tetraphenylindandiol-1,2 (XXVII), obtained here as a crystalline substance. When this crystalline glycol was dehydrated, it yielded a mixture of compounds, both $C_{33}H_{24}O$. One of these, comprising about 25% of the mixture, melted at 218–219°; the other, comprising some 75% of the mixture, melted at 185–186° and was identical with the dehydration product of the non-crystalline glycol mixture. The higher-melting dehydration product was probably the symmetrical ketone (XXIX), while the lower-melting dehydration product probably had the unsymmetrical structure (XXX). An attempt to cleave the lower-melting substance by fusion with sodium hydroxide led only to a resin, a result which might be expected in view of the known instability of pentaphenylethanes in air (20).


XXVII


XXVIII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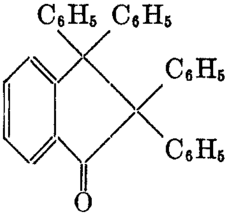
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EXPERIMENTAL

Preparation and Reactions of 3,3-Dimethylindandione-12

Addition of benzene to mesityl oxide. Mesityl oxide (350 g.) was added slowly to a well-stirred suspension of aluminum chloride (630 g.) in benzene (1400 ml.) at 10°. After the mixture had stood for three hours it was decomposed with iced hydrochloric acid; the 4-phenyl-4-methylpentanone-2 obtained (541 g.) boiled at 115° at 11 mm. [literature (13), 134° at 22 mm.].

Hypochlorite oxidation. 4-Phenyl-2-methylpentanone-2 (350 g.) was added to a stirred sodium hypochlorite solution (4 liters of 3.3 *N*) while the whole was heated on a steam-bath. The chloroform produced was allowed to distil during the initial exothermic reaction, and stirring was continued as long as any hypochlorite remained (18–25 hours). The unused ketone was then separated, the aqueous layer was acidified, and the solid β-phenylisovaleric acid was removed. It was purified by distillation (b.p. 155° at 10 mm.) and crystallization from petroleum ether; it melted at 58–59° [literature (13) 58–58.5°]. Yields from such runs averaged 163 g. or 73% calculated on the basis of the ketone not recovered.

Ring closure to 3,3-dimethylindanone-1. To a solution of β-phenylisovaleric acid (237 g.) in 750 ml. of benzene was added 320 g. (1.15 eq.) of phosphorus pentachloride, and the mixture was heated until no more hydrogen chloride was evolved (20 minutes). Then 180 g. of aluminum chloride was added with stirring, and heating was continued for an additional twenty minutes. The mixture was decomposed by pouring onto ice, and the benzene layer was washed with dilute hydrochloric acid and then with dilute sodium carbonate to remove unchanged acid. The 3,3-dimethylindanone-1 (180 g. = 84%) distilled at 110° at 8 mm. [literature (12), 119° at 13 mm.].

Nitrosation of 3,3-dimethylindanone-1. A mixture of butyl nitrite (50 g.) and 3,3-dimethylindanone-1 (50 g.) was added to 250 g. of methanol in which had been dissolved 11.2 g. of sodium. The mixture was allowed to stand in the ice-box for two days, then water and dilute acid were added and the butyl alcohol and unchanged ketone were removed by steam distillation. The remaining pale yellow oil (54 g.) solidified on cooling and was used directly for the preparation of the diketone. Recrystallized from water, the nitroso compound was obtained in the form of white scales that melted at 138–141°, while when it was crystallized from ethanol it formed white hexagonal plates that melted at 145–147°. The higher-melting modification was analyzed.

Anal. Calc'd for $C_{11}H_{11}NO_2$: C, 69.8; H, 5.9.
Found: C, 70.0; H, 5.7.

The nitroso compound was soluble in aqueous sodium carbonate; with benzoyl chloride in ether it gave a benzoate that melted at 169–171° after crystallization from acetic acid.

Hydrolysis of the nitroso compound. The crude oxime described above (50 g.) was boiled for three hours in a mixture consisting of 150 ml. of acetic acid, 50 ml. of 40% formaldehyde, and 30 ml. of concentrated hydrochloric acid. The solution became deep red, and on cooling the diketone precipitated; water was added to complete the precipitation, giving an almost pure product in nearly quantitative yield. After distillation under reduced pressure and crystallization from acetic acid, the 3,3-dimethylindandione-1,2 formed orange crystals that melted at 106–107°.

Anal. Calc'd for $C_{11}H_{10}O_2$: C, 75.9; H, 5.8.
Found: C, 75.4; H, 5.9.

The diketone gave a colorless crystalline addition-product when it was added to a concentrated aqueous solution of sodium bisulfite. This addition-product was quite soluble in water and was useful in experiments where the diketone had to be removed from other substances inert towards bisulfite, since the diketone could be regenerated from it by warming with dilute hydrochloric acid.

Anal. Calc'd for $C_{11}H_{11}NaO_5S$: Na, 8.3.
Found: Na, 8.7.

The diketone also gave a colorless crystalline addition-product with concentrated aqueous potassium cyanide. This substance was easily soluble in water; it gave oily products when its aqueous solution was acidified or when its solution in alcoholic hydrogen chloride was boiled for some time.

Anal. Calc'd for $C_{11}H_{10}O_2 \cdot KCN \cdot H_2O$: K, 15.2.
Found: K, 15.0.

Oximation of 3,3-dimethylindandione-1,2. (*Monoxime*). To a solution of hydroxylamine hydrochloride (0.2 g.) and hydrated sodium acetate (0.43 g.) in 5 ml. of water and 2 ml. of ethanol was added 0.5 g. of the diketone. The solid gradually dissolved and an oil separated which later became partly crystalline. The product was recrystallized from water (charcoal), and shown to be identical with the previously described nitroso compound of m.p. 138–141° by a mixed melting point determination.

(*Dioxime*). One gram of the diketone was added to a solution of hydroxylamine hydrochloride (2.5 g.) in a mixture of 10 ml. of ethanol and 10 ml. of 10% sodium hydroxide. The diketone rapidly disappeared when the mixture was warmed and the dioxime (1.07 g.) separated. After recrystallization from dilute ethanol it melted at 191–193° with decomposition. The dioxime gave a yellow solution in aqueous sodium hydroxide, but it was not soluble in sodium carbonate.

Anal. Calc'd for $C_{11}H_{12}N_2O_2$: C, 64.7; H, 5.9.
Found: C, 64.8; H, 5.9.

The same dioxime (0.88 g.) was obtained from the nitroso compound (1.0 g.), but the reaction was much slower than that between hydroxylamine and the diketone, requiring four days for practical completion.

Anal. Found: C, 64.8; H, 6.0.

The dioxime gave a dibenzoyl derivative that melted at 192–193°.

Anal. Calc'd for $C_{25}H_{20}N_2O_4$: C, 72.8; H, 4.9.
Found: C, 72.9; H, 4.9.

Quinoxaline from 3,3-dimethylindandione-1,2. Mixed with *o*-phenylenediamine in hot alcohol, the diketone was converted rapidly into its quinoxaline (11,11-dimethyl-11-indeno[1,2-b]quinoxaline, Ring Index 2517) which was sparingly soluble in hot alcohol. Crystallized from acetic acid, it melted at 146°.

Anal. Calc'd for $C_{17}H_{14}N_2$: C, 82.9; H, 5.7.
Found: C, 83.0; H, 5.7.

Cleavage of 3,3-dimethylindandione-1,2 by hydrogen peroxide. To a solution of the diketone (2 g.) in ethanol (25 ml.) was added 25 ml. of 3% hydrogen peroxide in which had been dissolved 0.5 g. of sodium hydroxide. When the slightly exothermic reaction was over and the diketone color had faded, the solution was acidified. Since no satisfactory analysis could be obtained on the resulting dimethylhomophthalic acid (2.4 g.), the compound was converted into its anhydride by heating. Crystalized from acetic acid, the anhydride melted at 81–82° [literature (21) 82–83°].

Anal. Calc'd for $C_{11}H_{10}O_3$: C, 69.4; H, 5.3.
Found: C, 69.4; H, 5.5.

Acetal formation by 3,3-dimethylindandione-1,2. The diketone was dissolved in methanol which had been nearly saturated with hydrogen chloride. After the solution had been allowed to stand for ten hours, it was poured into water and ether. The ether layer was removed, washed with aqueous sodium bisulfite to remove unchanged diketone (about 50% of this substance was recovered), and dried with sodium sulfate. The acetal was precipitated with ligroin (30–60°), and was recrystallized from ether-ligroin. The 2,2-dimethoxy-3,3-dimethylindanone-1 so obtained formed colorless prisms that melted at 75–76°.

Anal. Calc'd for $C_{13}H_{16}O_3$: C, 70.8; H, 7.3.
Found: C, 70.2; H, 7.3.

On warming with dilute hydrochloric acid the acetal was converted into the diketone.

Reaction of the acetal with phenylmagnesium bromide. To a solution of the acetal (1.03 g.) in ether was added with stirring 5 ml. of 2.65 *M* phenylmagnesium bromide (1.8 ml. required). The mixture was allowed to stand for fifteen minutes at 35° and then was decomposed with iced ammonium chloride. The biphenyl and bromobenzene from the Grignard solution were steam distilled, but no crystalline product could be isolated from the non-volatile oil. The oil was boiled with hydrochloric acid in water and methanol, but this treatment failed to yield a solid product. The oil was then boiled for eight hours with methyl alcoholic sodium hydroxide. This procedure resulted in the formation of two substances, an acid and a neutral compound, the former probably benzohydrol-*o*-dimethylacetic acid since it gave the lactone of this substance (see below) on crystallization, and the latter certainly 3,2-dimethyl-1-phenylindanol-1-one-2, since it melted at 126–128° alone or mixed with an authentic sample (see below) of this hydroxy ketone. The neutral and acid fractions were separately oxidized with chromic acid in acetic acid. The acid fraction was not completely oxidized, and yielded 0.34 g. of unoxidized lactone as well as some *o*-benzoylphenyldimethylacetic acid. The neutral fraction gave 0.21 g. of *o*-benzoylphenyldimethylacetic acid which sintered at 188° and melted at 196–198° alone or mixed with a sample of the acid obtained by the oxidation of 1,1-dimethyl-3-phenylindene.

Reaction of 3,3-dimethylindandione-1,2 with one equivalent of phenylmagnesium bromide. To an ether-toluene solution of 6 g. of the diketone at −18° was added with stirring 1.3 equivalents of phenylmagnesium bromide in a concentration of 2.65 *M*. The yellow product which formed was decomposed by the addition of aqueous ammonium chloride, and the mixture was steam distilled. The residue was dried in ether, and the 3,3-dimethyl-1-phenylindanol-1-one-2 (4.2 g.) was precipitated by the addition of ligroin. Recrystallized from dilute ethanol, the hydroxy ketone formed white plates that melted at 128–129°.

Anal. Calc'd for $C_{17}H_{16}O_2$: C, 80.9; H, 6.4.
Found: C, 80.6; H, 6.3.

When it was boiled for six hours with 25% aqueous-alcoholic potassium hydroxide the hydroxy ketone (1 g.) was partly recovered unchanged (0.67 g.) and partly converted into benzohydrol-*o*-dimethylacetic acid. The latter precipitated as its lactone (0.33 g.) when the alkaline solution was acidified. The lactone was insoluble in aqueous sodium carbonate, slowly soluble in aqueous sodium hydroxide, and rapidly soluble in alcoholic sodium hydroxide. Acidification of its alkaline solutions precipitated it unchanged in the form of needles that melted at 126–127°.

Anal. Calc'd for $C_{17}H_{16}O_2$: C, 80.9; H, 6.4.
Found: C, 80.9; H, 6.2.

The lactone of benzohydrol-*o*-dimethylacetic acid (0.12 g.) in acetic acid was oxidized by adding twice the required amount of chromic acid in acetic acid and warming the solution on a steam-bath. Water was added, whereupon the *o*-benzoylphenyldimethylacetic acid (0.11 g.) separated in compact crystals. Recrystallized from acetic acid, it sintered at 188° and melted at 196–198° alone or mixed with a sample prepared as described below.

o-*Benzoylphenyldimethylacetic acid from 1,1-dimethyl-3-phenylindene.* 1,1-Dimethyl-3-phenylindene was prepared by the addition of an excess of phenylmagnesium bromide to 3,3-dimethylindanone-1 in ether and dehydration of the resulting carbinol by boiling it with acetic acid containing a drop of sulfuric acid. After crystallization from methanol the hydrocarbon melted at 49–51° [literature (12) 50–51°]. The indene (0.8 g.) was oxidized by boiling it with twice the calculated amount of chromic acid in acetic acid, giving *o*-benzoylphenyldimethylacetic acid (0.63 g.) which sintered at 188° and melted at 196–198°.

Anal. Calc'd for $C_{17}H_{16}O_3$: C, 76.1; H, 6.0; Neut. equiv., 268.
Found: C, 76.1; H, 6.0; Neut. equiv., 265.

Reaction of 3,3-dimethylindandione-1,2 with two equivalents of phenylmagnesium bromide. Four times the calculated quantity of phenylmagnesium bromide in standardized solution was added to the diketone (8 g.) in ether (200 ml.). The reaction-mixture was allowed to stand for a short time at room temperature and was then worked up in the same way as has been described for the reaction with one equivalent of Grignard reagent. The resulting 3,3-dimethyl-1,2-diphenylindandiol-1,2 (10.1 g.) melted at 125–126° after crystallization from ether-ligroin.

Anal. Calc'd for $C_{23}H_{22}O_2$: C, 83.6; H, 6.7.
Found: C, 83.7; H, 6.8.

Treated with an excess of lead tetraacetate in benzene, the glycol gave *o*-α-dibenzoylcumene in good yield. Recrystallized from acetic acid this diketone formed colorless needles or prisms that melted at 115–116°.

Anal. Calc'd for $C_{23}H_{20}O_2$: C, 84.1; H, 6.1.
Found: C, 83.7; H, 6.2.

Pinacol rearrangement of 3,3-dimethyl-1,2-diphenylindandione-1,2. When the glycol was warmed in acetic acid containing a few drops of sulfuric acid, an exothermic reaction took place and a new compound separated in nearly quantitative yield. This substance melted at 125–126° (a mixture with the original glycol of the same melting point melted below 100°), and analyzed for 3,3-dimethyl-1,1- (or 2,2-)diphenylindanone-2 (or -1).

Anal. Calc'd for $C_{23}H_{20}O$: C, 88.4; H, 6.5.
Found: C, 88.5; H, 6.6.

The ketone was not attacked by alcoholic alkali, but when it was stirred with a eutectic mixture of sodium and potassium hydroxides at 300° it melted and then solidified. The excess alkali was dissolved by adding water in small amounts, the alkali salt being insoluble in the strongly basic solution. The salt was then dissolved in a large amount of hot water (1 g. was soluble in about 500 ml. at 100°), filtered, and acidified with hydrochloric acid. The acid crystallized from acetic acid in fine needles that melted at 185–186°.

Anal. Calc'd for $C_{23}H_{22}O_2$: C, 83.6; H, 6.7.
Found: C, 83.6; H, 6.5.

The acid was recovered unchanged after it had been boiled with copper acetate in quinoline. When it was mixed with a large excess of soda-lime and strongly heated a solid distillate was obtained in poor yield. Crystallized from methanol this substance (Found: C, 88.6; H, 6.2) melted at 121–123°; a mixture with dimethyldiphenylindanone melted at 124–126°.

Photochemical reduction of 3,3-dimethylindandione-1,2. A solution of the diketone (0.2 g.) in isopropyl alcohol (12 ml.) retained its deep yellow color indefinitely when kept in the dark, but it was completely decolorized after it had been exposed to direct sunlight for twenty-five minutes. A colorless product was then precipitated by water.

A more concentrated solution of the diketone (9.4 g. in 150 ml.) became pale yellow on illumination for three and one-half hours, and a slightly pink product was precipitated by water. Crystallization from ether-ligroin gave 3,3-dimethylindanol-2-one-1 in the form of colorless prisms (8.25 g.) that melted to an orange liquid at 111–115°.

Anal. Calc'd for $C_{11}H_{12}O_2$: C, 74.9; H, 6.9.
Found: C, 74.9; H, 6.6.

The preparation of the hydroxy ketone succeeded equally well in methanol or ethanol. After illumination of 1 g. of the diketone in methanol, the hydroxy ketone was precipitated and the solution was shaken out with ether. The addition of dimedon to the aqueous solution gave a precipitate (0.08 g.) that melted at 189° and was identical with the dimedon derivative of formaldehyde. A similar treatment of methanol in the absence of the diketone gave no precipitate.

Titrated in acetone solution at room temperature, the hydroxy ketone (1 g.) decolorized 7.35–7.40 ml. of 0.52 *M* potassium permanganate in acetone (calc'd 7.27 ml.). The resulting solution yielded 3,3-dimethylindandione-1,2 in nearly the theoretical amount together with a trace of dimethylhomophthalic acid.

Disproportionation of 3,3-dimethylindanol-2-one-1. The hydroxy ketone (1.5 g.) was melted and boiled for a few minutes. The melt was treated with ether, giving a part (0.62 g.) of the resulting 3,3-dimethylindandione-1,2 directly; the rest of this compound (0.13 g.) was obtained by extracting the ether solution with sodium bisulfite. Remaining in the ether was a faintly yellow oil which could not be crystallized. It was treated in ether with benzoyl chloride, and the resulting benzoyl derivative was crystallized from ligroin. This derivative, 3,3-dimethyl-1,2-dibenzoyloxyindane, formed white needles that melted at 86–87°.

Anal. Calc'd for $C_{25}H_{22}O_4$: C, 77.7; H, 5.7.
Found: C, 77.3; H, 6.0.

Preparation and Reactions of 3,3-Dimethyl-6-nitroindandione-1,2

Nitration of 3,3-dimethylindanone-1. Five grams of the ketone was cooled to −10° and added to 25 g. of nitric acid (*d.* 1.5) at the same temperature. A small amount of urea was added and the mixture was allowed to warm to 15° and to stand at this temperature for thirty minutes. It was then poured on ice; the separated solid was filtered and washed with ligroin (30-60°) to remove un-nitrated ketone (used in a subsequent nitration). If the mixture became red during the nitration through the formation of nitrous acid, the nitro ketone was accompanied by a brown alkali-soluble oil, but in satisfactory experiments this was not formed, the yield of pure 3,3-dimethyl-6-nitroindanone-1 being 2.5–4.0 g. Crystallized from methanol the compound formed colorless prisms that melted at 133–134°.

Anal. Calc'd for $C_{11}H_{11}NO_3$: C, 64.4; H, 5.4.
Found: C, 64.2; H, 5.4.

When it was boiled for one hour with aqueous potassium permanganate, the nitro ketone gave nitrodimethylhomophthalic acid in good yield, but no other compound could be isolated when the time of boiling was greatly increased.

Nitrosation of 3,3-dimethyl-6-nitroindanone-1. To a solution of the nitro ketone (1 g.) in ether was added butyl nitrite (1 g.) and acetyl chloride (0.4 g.). The reaction was slow at the start, but soon became vigorous. The product was crystallized from acetic acid, giving faintly yellow prisms (1.05 g.) that melted at 210–222°.

Anal. Calc'd for $C_{11}H_{10}N_2O_4$: C, 56.4; H, 4.3.
Found: C, 56.3; H, 4.5.

Hydrolysis of the nitroso compound. A mixture of the above nitroso compound

(1 g.), acetic acid (10 ml.), formalin (2 ml.), and conc'd hydrochloric acid (2 ml.) was boiled for three to five hours and then cooled. The resulting 3,3-dimethyl-6-nitroindandione-1,2 crystallized in almost the calculated amount. Recrystallized from acetic acid, it formed bright orange prisms that melted at 172–174°. It gave yellow solutions in alcohols and pink solutions in non-polar solvents.

Anal. Calc'd for $C_{11}H_9NO_4$: C, 60.3; H, 4.1.
Found: C, 60.1; H, 4.3.

With an excess of hydroxylamine, the nitro diketone gave a substance that crystallized in white needles melting at 171–180°. Analysis indicated that it was an impure dioxime.

Anal. Calc'd for $C_{11}H_{11}N_3O_4$: C, 53.0; H, 4.0.
Found: C, 53.9, 54.7; H, 4.8, 4.8.

Treated in alcohol with a slight excess of 3% hydrogen peroxide to which had been added a little sodium hydroxide, the nitro diketone gave α,α-dimethyl-5-nitrohomophthalic acid. The acid was recrystallized from acetic acid containing a small amount of sulfuric acid, which converted it into the corresponding anhydride; small white prisms that melted at 163–165°.

Anal. Calc'd for $C_{11}H_9NO_4$: C, 56.1; H, 3.9.
Found: C, 55.7; H, 4.0.

When the nitro diketone (70 mg.) was warmed in ethanol (5 ml.) with *o*-phenylenediamine (50 mg.), the corresponding quinoxaline separated in long white needles (91 mg.). This compound, 3-nitro-11,11-dimethyl-11-indeno[1,2-b]quinoxaline (R.I. 2517), melted at 269–271° after crystallization from acetic acid.

Anal. Calc'd for $C_{17}H_{13}O_2N_3$: C, 70.1; H, 4.5.
Found: C, 70.1; H, 4.7.

Preparation and Reactions of 3,3-Diphenylindandione-1,2

3,3-Diphenylindanone-1. Phosphorus pentachloride (18 g.) was added to β,β,β-triphenylpropionic acid (25 g.) [prepared in 56% yield by the method of Gagnon (22)] in 100 ml. of dry benzene, and the mixture was warmed until no more hydrogen chloride was evolved. Then aluminum chloride (11 g.) was added and the mixture was boiled for thirty minutes longer. The product, worked up in the usual way, melted at 130–131° [literature (22) 131–132°] and weighed 22.5 g.

Nitrosation of 3,3-diphenylindanone-1. To a solution of sodium (2 g.) in absolute ethanol (200 ml.) was added a mixture of diphenylindanone (8 g.) and butyl nitrite (8 g.). After it had stood at room temperature for three days, the solution deposited the sodium salt of the isonitroso compound in orange-red crystals. This was filtered and acidified, giving 4.5 g. of the isonitroso compound. The remainder of the product (4 g.) was obtained by adding dilute hydrochloric acid to the filtrate from the sodium salt, and steam distilling the butyl alcohol. The product crystallized from acetic acid in the form of yellow prisms that melted at 206–209° [literature (18), 220°].

Hydrolysis of the isonitroso compound. A mixture of 3,3-diphenyl-2-oximinoindanone-1 (7.8 g.), 60 ml. of acetic acid, 30 ml. of 40% formaldehyde, and 15 ml. of conc'd hydrochloric acid was boiled for sixteen hours. On cooling, the solution deposited 3,3-diphenylindandione-1,2 in orange prisms that melted at 150–151°.

Anal. Calc'd for $C_{21}H_{14}O_2$: C, 84.6; H, 4.7.
Found: C, 84.3; H, 5.0.

Treated in alcohol with a slight excess of 3% hydrogen peroxide containing a little sodium hydroxide, the diketone (1 g.) was rapidly decolorized, and then diphenylhomophthalic acid was precipitated on acidification. The acid was recrystallized from acetic acid containing a small amount of sulfuric acid, which converted it into diphenylhomophthalic anhydride (0.9 g.), small white prisms that melted at 227–228°.

Anal. Calc'd for $C_{21}H_{14}O_3$: C, 80.0; H, 4.6.
Found: C, 80.2; H, 4.6.

Warmed in alcohol with a slight excess of *o*-phenylenediamine, the diketone was converted quantitatively into its nearly insoluble quinoxaline. This compound, 11,11-diphenyl-11-indeno[1,2-b]quinoxaline (R.I. 2517), crystallized from ethyl acetate in faintly tan prisms that melted at 244–245°.

Anal. Calc'd for $C_{27}H_{18}N_2$: C, 87.6; H, 4.9.
Found: C, 87.5; H, 4.8.

Treated with one equivalent of hydroxylamine, the diketone was transformed into 3,3-diphenyl-1-oximinoindanone-2. This substance formed pale yellow prisms that melted at 215–217° and showed a great lowering in melting point when mixed with 3,3-diphenyl-2-oximinoindanone-1.

Anal. Calc'd for $C_{21}H_{15}NO_2$: C, 80.5; H, 4.8.
Found: C, 80.1; H, 4.9.

Reaction of 3,3-diphenylindandione-1,2 with phenylmagnesium bromide. To a benzene solution of the diketone was added a large excess of phenylmagnesium bromide in ether. The mixture was boiled for thirty minutes and then decomposed with iced ammonium chloride. Volatile substances were removed by steam distillation, leaving an oil which became glassy on cooling, but which could not be crystallized. This substance was boiled with acetic acid containing a few drops of sulfuric acid, when it was converted into 2,2,3,3-tetraphenylindanone-1. This ketone crystallized from acetic acid in the form of small white prisms that melted at 185–186°.

Anal. Calc'd for $C_{33}H_{24}O$: C, 90.8; H, 5.5.
Found: C, 90.8; H. 5.6.

Reaction of 1,3,3-triphenylindanol-1-one-2 with phenylmagnesium bromide. To a solution of the hydroxy ketone (19) (0.5 g.) in xylene was added an excess (5 ml. of 2.65 *M* phenylmagnesium bromide. The mixture was distilled to 100° and kept at this temperature for fifteen minutes, and then decomposed with iced ammonium chloride. The volatile substances were removed by steam distillation, and the residue was crystallized from ether-ligroin. 1,2,3,3-Tetraphenylindandiol-1,2 obtained in this way in good yield, melted at 177–178°.

Anal. Calc'd for $C_{33}H_{26}O_2$: C, 87.2; H, 5.8.
Found: C, 87.3; H, 6.2.

The crystalline glycol was boiled for a few minutes with acetic acid containing a few drops of sulfuric acid. The product was separated by crystallization from ether into two substances, 2,2,3,3-tetraphenylindanone-1 (75%) which melted at 185–186° and 1,1,3,3-tetraphenylindanone-2 (25%) which melted at 218–219°. The lower-melting substance was identified by direct comparison with a sample of the ketone obtained by the dehydration of the glassy glycol; the higher-melting compound was analyzed.

Anal. Calc'd for $C_{33}H_{24}O$: C, 90.8; H, 5.5.
Found: C, 89.3, 89.8; H, 5.4, 5.9.

SUMMARY

The mutual activating effect of the carbonyl groups in some derivatives of indandione-1,2 is greater than that in acyclic α-diketones. Although

carbonyl-1 of the indandiones is more available for reaction, carbonyl-2 is more polar. The polarization of carbonyl-2 is cut down when aromatic nuclei are substituted on carbon-3. These conclusions are reached through a consideration of data already published and through a study of the reactions of 3,3-diphenyl-, 3,3-dimethyl-, and 3,3-dimethyl-6-nitroindanione-1,2 towards a number of carbonyl reagents.

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