B. With Hydrogen.—Raney nickel was used as the catalyst. The product had a melting point of 52–53° which was not depressed by the addition of 1,4-dipivalylbutane.

Reaction of the Butadiene with Phenylmagnesium Bromide.—This reaction was carried out in the usual manner. A solid was isolated melting at 206–207° which is the melting point given for 2,3-diphenyl-1,4-dipivalylbutane.[4]

1,4-Dicyano-1,4-dipivalylbutane.—A mixture of 8 g. of 1,4-dibromo-1,4-dipivalylbutane, 4 g. of powdered sodium cyanide, 120 cc. of absolute alcohol and 120 cc. of dry ethyl acetate was refluxed for forty hours. Removal of the solvents left a dark brown residue to which was added 150 cc. of water. The aqueous solution was extracted with four 50-cc. portions of ether. The resulting solution was evaporated to dryness and the residue crystallized from alcohol. The dinitrile was obtained in yields of 1.4 to 1.7 g., m. p. 92–93°.

Anal. Calcd. for $C_{16}H_{24}N_2O_2$: C, 69.53; H, 8.75; N, 10.13. Found: C, 69.75; H, 8.72; N, 10.17.

Reaction of the Dinitrile with Hydrochloric Acid.—A mixture of 0.5 g. of the dinitrile and 10 cc. of concentrated hydrochloric acid was heated in a closed tube (capacity about 30 cc.) for two hours at 140–150°. A solid was obtained which after recrystallization from benzene melted at 198–200°. The yield was 0.33 g.

Anal. Calcd. for $C_{16}H_{26}Cl_2N_2O_2$: C, 55.02; H, 7.50; N, 8.02; Cl, 20.30; mol. wt., 349. Found: C, 55.18; H, 7.43; N, 7.46; Cl, 20.70; mol. wt., 330.

The alcoholic filtrate left after the separation of the dicyano compound was found to contain a neutral oil boiling at 163–168° (6 mm.); $n^{20}D$ 1.4722.

The 2,4-dinitrophenylhydrazone was crystallized from alcohol, m. p. 225–227°.

Anal. Calcd. for $C_{21}H_{27}N_5O_6$: C, 58.76; H, 6.34; N, 16.30. Found: C, 58.30; H, 6.49; N, 16.45.

An **oxime** was formed by heating a mixture of 1 g. of the oil, 1.5 g. of hydroxylamine hydrochloride, 3 g. of potassium acetate and 10 cc. of water. It was crystallized from alcohol, m. p. 183–185°.

Anal. Calcd. for $C_{15}H_{24}N_2O_2$: C, 68.15; H, 9.15. Found: C, 68.28; H, 8.96.

Repetition of the foregoing test using sodium hydroxide in place of potassium acetate gave an **isomeric** oxime melting at 146–148°.

Anal. Calcd. for $C_{16}H_{24}N_2O_2$: C, 68.15; H, 9.15; N, 10.59. Found: C, 68.23; H, 9.14; N, 10.47.

Summary

1,4-Dipivalylbutane (II) has been prepared by the action of *t*-butylmagnesium chloride on adipyl chloride.

1,4-Dibromo-1,4-dipivalylbutane (V) has been converted to the corresponding dicyano compound (VI) and to 1,4-dipivalyl-1,3-butadiene (VIII).

URBANA, ILLINOIS RECEIVED DECEMBER 4, 1939

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(4) Hill and Susselman, THIS JOURNAL, **53**, 4424 (1931).

[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA]

The 1,2,4-Trimesityl 1,4-Diketones and Related Compounds, Including the Stereoisomeric Mono and Dienols[1]

BY ROBERT E. LUTZ AND CHARLES J. KIBLER

The preparation of this series of compounds was undertaken in order to extend the study of the hindering effect of mesityl groups. It was expected that here the damping of the keto–enol shift and the consequent increase in the persistence of enolic forms would make it possible to prepare some of the stereoisomeric mono and dienols or, at least, to obtain evidence of their existence. Furthermore, it was hoped that new information might be obtained concerning the properties of highly hindered enolic groups and the mechanism of certain reactions which supposedly proceed through enolic intermediates, particularly furan ring closure.[2] This report deals with a preliminary investigation in which these objectives were in a degree accomplished.

The Saturated 1,4-Diketone (III).—The starting point in the synthesis of these compounds was di-(trimethylbenzoyl)-ethylene (I). Addition of mesitylmagnesium bromide at 20° gave the monoenolate II by 1,4-addition, the reaction proceeding quickly but stopping at this point. When the reaction mixture was hydrolyzed by means of dilute hydrochloric or acetic acid, the saturated diketone III was produced in good yield; the free monoenol could not be isolated and was quite mobile, ketonizing quickly to the saturated diketone even when dilute acetic acid under mild conditions was used.

That the reaction between mesitylmagnesium bromide and di-(trimethylbenzoyl)-ethylene actually stopped at the stage of the monoenolate, II, was demonstrated (a) by conversion of the product with alcoholic iodine or bromine into the

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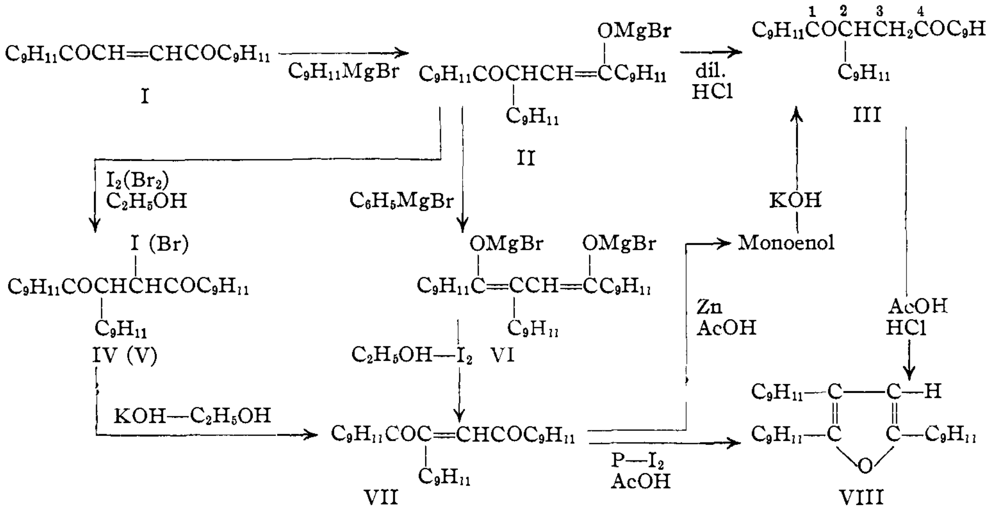
(1) This paper was presented at the Boston meeting of the American Chemical Society, September 14, 1939.

(2) Lutz and Reveley, THIS JOURNAL, **61**, 1854 (1939).



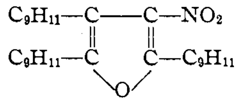
monohalogeno saturated diketones IV and V, (b) by the failure of the product to undergo oxidation to the unsaturated diketone VII when hydrolyzed in the presence of iodine or quinone, a reaction characteristic[2] of dienolates of the type of VI, and (c) by actual enolization upon more drastic treatment with the Grignard reagent to the true dienolate VI which was readily oxidizable to the unsaturated diketone when treated in the usual way with alcoholic iodine.

From these results it appears that the newly introduced mesityl group in the 1,4-addition product II definitely hinders enolization at the adjacent carbonyl. This effect is to be contrasted with the absence of any such marked hindrance in the case of the reactions between phenyl[2,3] and mesityl[4] magnesium bromides and dibenzoylethylene, and between phenylmagnesium bromide and di-(trimethylbenzoyl)-ethylene,[3] where even under mild conditions dienolates corresponding to VI are obtained.

The Unsaturated 1,4-Diketone (VII).—The trimesityl unsaturated 1,4-diketone of this series can be made in either of two ways: (a) through elimination of halogen acid from the halogeno saturated diketones IV and V by means of alcoholic potassium hydroxide, or (b) by hydrolysis under oxidizing conditions with alcoholic iodine, of the dienolates obtained by the action of a Grignard reagent on suitable compounds in this series such as the monoenolate II, the halogeno saturated diketones IV and V, or the saturated diketone III.

The unsaturated diketone VII is distinctly less reactive than the other compounds of this type which have been studied, as would be expected in view of the extreme hindrance offered by the three mesityl groups. It is reduced by zinc and boiling acetic acid through a 1,6-mechanism to a monoenol (to be described later) which is easily ketonized to the saturated diketone III; and the phosphorus–iodine–acetic acid reagent converts it directly into trimesitylfuran, VIII. Attempts to convert it into trimesitylacetoxyfuran by means of acetic anhydride and sulfuric acid failed.

2,3,5-Trimesitylfuran (VIII).—Trimesitylfuran (VIII) was obtained from the saturated diketone III in excellent yield by the prolonged action of boiling acetic acid saturated with dry hydrogen chloride. Furanization was effected also, although less efficiently, by the action of hydriodic acid at 170° and by the phosphorus–iodine–acetic acid reagent.



IX

The action of nitric–acetic acid mixtures on the furan produces a mononitro derivative without disrupting the furan nucleus. The nitro group presumably is located in the β-position as formulated in IX.[5] The resistance of the furan nucleus here toward oxidative ring fission constitutes another illustration of the striking stabilizing influence of two mesityl groups in the 2,5-positions, an effect which is presumably due to the hindrance of the mesityl groups toward addition of the reagents at the ends of the diene system.

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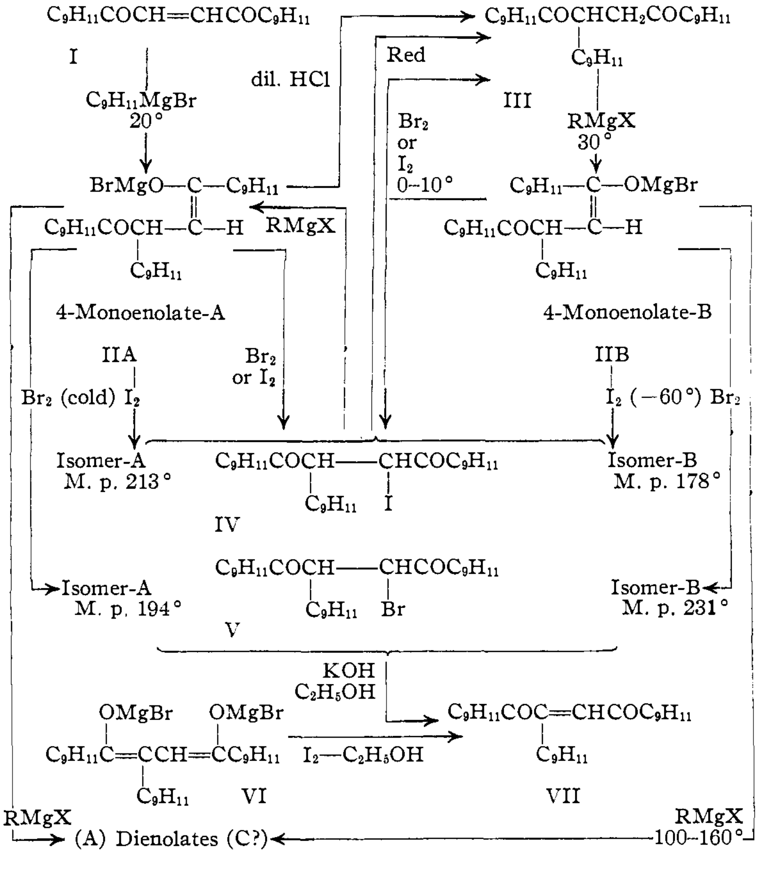
(3) Lutz and Tyson, This Journal, **56**, 1341 (1934).

(4) Lutz and Kibler, *ibid.*, **61**, 3007 (1939).

(5) The β-position is the reactive one in all of the analogous compounds studied. (Lutz and Kibler, a study of 2,5-dimesitylfurans to be published shortly.)

The Halogeno Saturated 1,4-Diketones, IV and V.—The halogeno trimesityl 1,4-diketones IV and V are of special interest because of their ready conversion into one of the two possible stereoisomeric 4-monoenolates (II) by the action of Grignard reagents, and also because of the various stereochemical relationships involved. The bromo and the iodo compounds exist each in two stable diastereoisomeric forms. These are prepared by the action of the appropriate halogen on one or the other of the isomeric (*cis-trans*) 4-monoenolates IIA and B which will be described separately below. The reactions are illustrated in the second diagram where the configurations and stereochemical relationships have been indicated as far as they have been determined. In order to simplify the naming of these various compounds, particularly the different types of enolates, the chain has consistently been numbered as in formula III.

The structures of the halides, given as IV and V, follow from the formation of both pairs of isomers in the same reaction, namely, the halogenation of the 4-monoenolate-A (IIA) in which the position of the enolic group is known from the mode of preparation through 1,4-addition of mesitylmagnesium bromide to di-(trimethylbenzoyl)-ethylene (I). The stereoisomeric halides of the type A are best obtained in quantity by the action of the appropriate halogen on this 4-monoenolate-A and are obtained almost exclusively under controlled conditions. The B-isomers are obtained almost exclusively by halogenation at −60° of the stereoisomeric 4-monoenolate-B which is obtained by direct partial enolization of the saturated diketone III (to be described below).



The existence of these stereoisomeric halides is somewhat surprising in view of the instability of di-(trimethylbenzoyl)-bromo[5] and chloro[6]-ethanes, $C_9H_{11}COCH_2CH(Br\ or\ Cl)COC_9H_{11}$, which lose hydrogen halide even during crystallization under relatively mild conditions. The halides in this series withstand the prolonged action of sodium acetate in boiling alcohol. Hydrogen halide is eliminated only by the action of the more powerful reagent, potassium hydroxide, with the formation of the unsaturated diketone VII.

On the other hand, the halogens are very easily eliminated from these compounds by reduction with zinc and acetic acid and also with sodium bisulfite or potassium iodide in acetic acid. The latter two reductions are of a type characteristic for α-halogeno ketones, and particularly halogen derivatives of β-diketones. The iodides, of course, are much more easily reduced than the bromides, and liberate iodine from potassium iodide in acetic acid at room temperature, whereas the bromides react thus only at elevated temperature. The product of reduction in all cases is the saturated diketone III.

The 4-Monoenolate-A (IIA).—The monoenolate obtained by the 1,4-addition of mesitylmagnesium bromide to di-(trimethylbenzoyl)-ethylene is designated as the 4-monoenolate-A. It is obtained also by the action of a Grignard reagent on any one of the halogeno satu-

(6) Lutz and Wood, This Journal, **60**, 229 (1938).

rated diketones IV or V. It is characterized by the reactions with bromine and iodine. When it is brominated a mixture of two stereoisomeric halides A and B results with the isomer-A in the larger proportion; at lower temperatures the bromide of type A is obtained as the chief product. In iodination chiefly the iodo diketone-A is obtained even at room temperature, and only very small amounts of the isomer-B can be detected; at low temperature the iodide-A appears to be formed exclusively.

The direction of enolization in the 4-monoenolate-A indicated in formula IIA is certain from the mode of formation by the addition of mesitylmagnesium bromide to di-(trimethylbenzoyl)-ethylene (I).

The 4-Monoenolate-B (IIB).—The existence of the stereoisomeric 4-monoenolate, designated as isomer-B, was discovered in studying the direct enolization of the saturated diketone III by means of different Grignard reagents. Methylmagnesium iodide reacts rapidly with evolution of *one* molecule of methane, but the secondary reaction involving enolization of the other carbonyl group, with evolution of the second molecule of methane and the formation of a dienol, takes place very slowly and only at elevated temperatures. In respect to this secondary enolization the 4-monoenolate-B is distinctly different from the 4-monoenolate-A which undergoes this reaction easily at a moderate temperature and gives the dienolate-A quickly and in good yield. The rigorous proof of the existence of the 4-monoenolate-B and its stereoisomerism with the isomer-A is the halogenation with iodine or bromine at a lowered temperature with the formation of the iodo and bromo diketones-B consistently and almost exclusively in good yield.

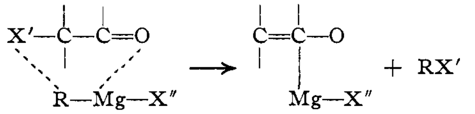
In some of the first experiments in which the reaction between iodine and the 4-monoenolate-B was carried out at room temperature or at 10°, largely the saturated diketone III was obtained and the full extent of the presence of the 4-monoenolate-B was overlooked; this result was found to be due to the high rate of ketonization of the 4-monoenolate-B at ordinary temperatures, which apparently is greater than in the case of the 4-monoenolate-A, and which under the conditions of this experiment enables ketonization to compete on favorable terms with iodination. When the halogenation was carried out at $-60°$ the ketonization was relatively slow and became negligible, and at the same time the stereochemical mode of reaction was much more sharply defined.

The Configurations at the 4-Enolic Group.—There exists a basis for assignment of configurations at the 4-enol group in the striking fact that the configuration greatly influences the ease of the secondary enolization at the hindered 1-carbonyl. It seems reasonable to assume that the configuration offering the greater resistance to this secondary enolization will be that with the 4-mesityl group in the *cis* position with respect to the rest of the chain since this arrangement should involve the greater degree of steric hindrance. Thus the 4-monoenolate-B which undergoes the secondary enolization with great difficulty should have the configuration indicated in formula IIB, and the 4-monoenolate-A which is very easily converted into a dienolate should have the structure IIA. This argument is strengthened by the fact that the relative rates of ketonization at the 4-enolic group are consistent with the conclusion. Assuming that the ketonization of a free 4-enolic group would be hindered to the greater degree when the enolic hydroxyl group is *cis* with respect to the residue of the chain, and to the lesser degree when *cis* with respect to the hydrogen atom, then again, the 4-monoenolate-A must have the configuration indicated in IIA and the 4-monoenolate-B the structure IIB.

Stereochemical Relationships and Mechanism of Reaction.—It is clear from the foregoing discussion that the *cis* and *trans* isomeric 4-monoenolates IIA and B actually exist and are stable, and that halogenation of these isomers occurs in a consistent stereochemical manner. Whether the reaction is *cis* or *trans*, however, is not known because no information is available concerning the actual configurations of the halides produced.

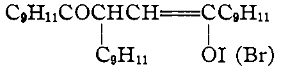
The halides IV and V, both the A and B-isomers, react readily with the Grignard reagent, the first stage of the reaction proceeding very rapidly in the cold with the formation of one and the same 4-monoenolate, isomer-A. Since the two 4-monoenolates, A and B, appear to be stable once formed, it may safely be assumed that the reaction is not guided or influenced by the configuration of the starting material as is the addition of halogen to the two monoenolates. This result would be expected because it is not easy to conceive of a marked stereochemical guiding influence emanating from the kind of configurational difference (diastereoisomerism) involved in the two types of halides.

In the formation of the 4-monoenolate by the two different methods, namely, the direct enolization of the saturated diketone III and the interaction of a Grignard reagent and the halogeno diketones A or B (IV or V), opposite stereochemical results are obtained. This is not surprising because the two reactions differ sharply in that α-hydrogen is involved in the one case and α-halogens in the other, with the elimination, respectively, of hydrocarbon and alkyl halide. This does not necessarily indicate different mechanisms in the two reactions, however. Probably, the mechanism of the reaction in the case of the halides is a simple 1,4-reaction between alkyl-magnesium halide and the conjugated system of carbonyl group and carbon–halogen linkage, as follows:



The enolizing action of the Grignard reagent on the saturated diketone may possibly follow a similar path but with opposite stereochemical results.

Alternative Formulations.—The hypohalite structures for the halogeno diketones IV and V (namely, X and XI), although perhaps not excluded, are highly improbable. On the basis of these formulations, which involve *cis–trans* rather than diastereoisomerism, each type of isomer should react with the Grignard reagent to give a different stereoisomeric 4-monoenolate since the 4-monoenolates-A and B are known to be stable under these conditions; actually, however, this is not the case.

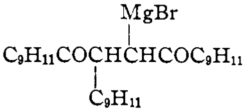


$$C_9H_{11}CO\underset{C_9H_{11}}{C}HCH{=\!=}\underset{OI\ (Br)}{C}C_9H_{11}$$

X (XI)

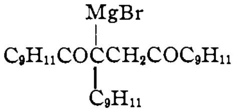
cis and *trans*

The various mono and dienolates described in this paper may of course be formulated as true Grignard reagents, namely, XII, XIII and XIV[7]; no stereoisomerism is possible with XIII, but XII and XIV would involve diastereoisomerism instead of *cis–trans* isomerism. In view of the possibility that the whole conjugated system of the enolate group, namely, C═C—O or C═C—O—Mg, may function in reaction as a unit, and that conversely the system O═C—C—Mg might also react as a unit with one addend going to oxygen, it may not be possible from the reactions of the various compounds to decide conclusively as to which type of structure is correct. However, the true enolate formulations have been assumed here because they seem best to account for all of the reactions studied so far, particularly hydrolysis which leads to definite mono and dienols, and the existence of two isomeric 1-monoenols (described below) which would be impossible on the basis of formula XIII alone.



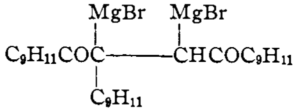
$$C_9H_{11}CO\underset{C_9H_{11}}{C}H\overset{MgBr}{C}HCOC_9H_{11}$$

XII



$$C_9H_{11}CO\underset{C_9H_{11}}{\overset{MgBr}{C}}CH_2COC_9H_{11}$$

XIII



$$C_9H_{11}CO\underset{C_9H_{11}}{\overset{MgBr}{C}}\text{———}\overset{MgBr}{C}HCOC_9H_{11}$$

XIV

The Stereoisomeric 1-Monoenolates and the Dienolates.—In the foregoing discussion the question of enolization exclusively at the end of the molecule carrying the 2-mesityl group has not entered. Just as with the 4-monoenolates, the 1-monoenolates should exist in *cis* and *trans* forms, but due to the hindrance of the extra mesityl group these monoenolates should be harder to form, and the free 1-monoenols, once formed, should be extraordinarily persistent. Since the saturated diketone III enolizes first at the 4-carbonyl, it was necessary to go to the dienolates and then, avoiding oxidation to the unsaturated diketone, to allow the dienol to ketonize partially, the mobile 4-enol group ketonizing first and leaving the more persistent 1-enol. One of the two possible 1-monoenols has thus been obtained and in this case it was isolated as a metastable crystalline solid; also, there is definite evidence for the existence of the stereoisomer. These two 1-monoenols are best considered along with the stereoisomeric dienolates of which four are possible; of the latter, the existence of at least two has been demonstrated; furthermore, one free dienol has been isolated crystalline. The study of these dienolates, of course, is handicapped by the sensitivity of the free dienols toward oxygen, and the mobility of the free 4-enol group.

The Dienolate-A (VIA).—The dienolate VIA, arbitrarily named isomer-A, has been obtained from the 4-monoenolate-A by the enolizing action of mesitylmagnesium bromide. The preparation of this dienolate is most conveniently carried out by allowing an excess of mesitylmagnesium bromide to react either with di-(trimethylbenzoyl)-ethylene (I) or the halides IV or V, followed by

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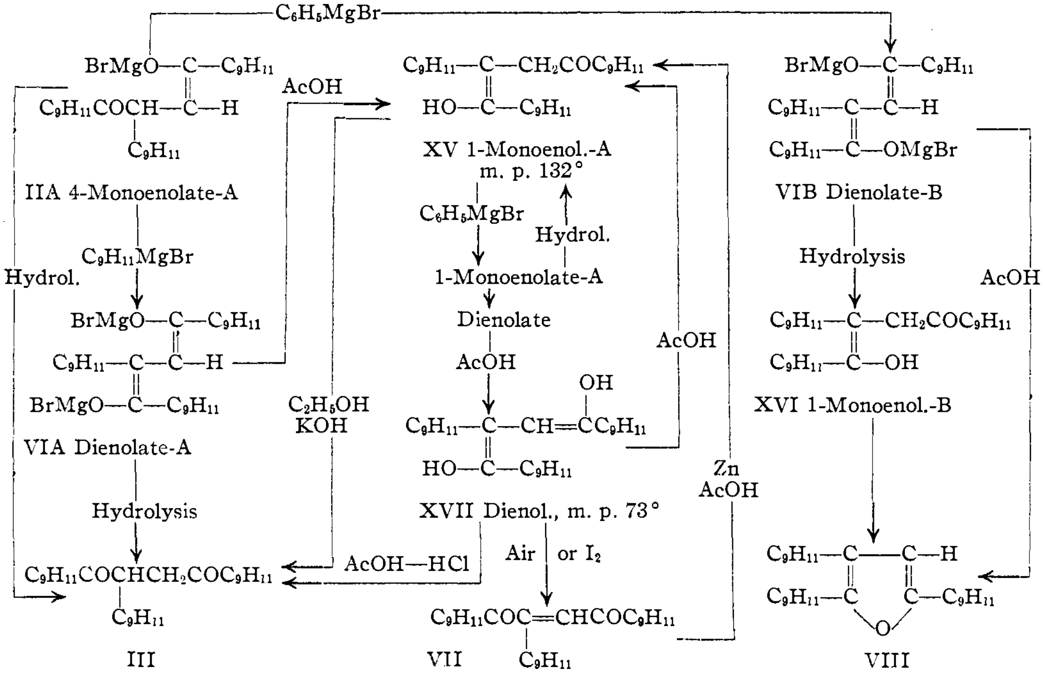
(7) *Cf.* Fuson, Fugate and Fisher, THIS JOURNAL, **61**, 2362 (1939).

heating for a short time to enolize the remaining and hindered 1-carbonyl group. That a dienolate was actually present was shown by hydrolysis in alcoholic iodine solution with resulting oxidation to the unsaturated diketone VII.

The configuration at the 4-enol group is undoubtedly the same as that in the 4-monoenolate-A because this group was already formed and possessed the configuration indicated before enolization at the 1-carbonyl took place (inversion appears to be unlikely under the conditions).



The dienolate-A was characterized by its behavior upon hydrolysis; treatment with acetic acid gave the 1-monoenol-A and the use of the stronger acid, dilute hydrochloric acid, produced the saturated diketone III. The end result is in sharp contrast with that obtained on hydrolysis of the 1-monoenolate-B and the dienolate-B (described below) where trimesitylfuran (VIII) is formed exclusively under comparable conditions. The inability of the dienolate-A to go to the furan has been used as the basis for assignment of the configuration at the 1-enol group. The complete configuration is given in formula VIA.

The 1-Monoenolate-A (XV).—When the hydrolysis of the dienolate-A was carried out cautiously using acetic acid, the 1-monoenol-A was produced. It was isolated in crystalline form and characterized. It was obtained also by the zinc and acetic acid reduction of the unsaturated diketone VII. The structure XV follows for this monoenol since it is distinctly different from the two 4-monoenols-A and B and since the partial ketonization of the dienol would be expected to occur far more rapidly at the more mobile 4-enol group. The configuration is obviously similar to that of the corresponding 1-enol group in the dienolate-A, with the 1 and 2-mesityl groups *trans* to each other as indicated in formula XV. This configuration is assigned on the basis of the ready ketonization exclusively to the saturated diketone III and the absence of furanization which is the sole result when the isomeric 1-monoenolate-B XVI and the dienolate-B (VIB) are hydrolyzed under comparable conditions.

The 1-monoenol-A is rearranged readily to the saturated diketone III; however, it does not react with ferric chloride, bromine or diazomethane although it reacts instantly with methylmagnesium iodide with evolution of one molecule of methane. The failure of these typical enol tests must be attributed to the combined hindering effects of the two mesityl groups. The failure of the ferric chloride test might be expected, however, since it is known that another mesityl ketone,[8] $(C_6H_5)_2CHCH=C(OH)C_9H_{11}$, does not give the color test although it reacts normally with bromine. It is

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(8) Kohler and Thompson, THIS JOURNAL, **59**, 888 (1937).

evident then that the dimesityl enol group, $C_9H_{11}\overset{|}{C}{=}C(OH)C_9H_{11}$, has none of the usual enol properties except some of those due to the active hydrogen.

Because of the inability of the enolic group of the 1-monoenol-A to react normally, the proof that it is really an enol should be examined. The evidence is as follows: the compound is isomeric with the saturated diketone and must be the enol by difference; it has an active hydrogen atom, is metastable and is convertible into the saturated diketone by the catalytic action of acids or bases.

In this connection, because of the difficulty of distinguishing between the keto and the 1-monoenol forms in this series, it was necessary to consider the saturated diketone III and the evidence that it is not itself an enol form. The saturated diketone does not react with bromine or iodine and is stable toward alkali or acid as catalysts for ketonization. It is enolized rapidly by methylmagnesium iodide with evolution of only *one* molecule of methane, and the resulting 4-monoenolate-B is shown to be the monoenolate by its reaction with one molecule of halogen to give the B-halides IV and V. From these facts then there can be no question that the saturated diketone is correctly formulated.

Reduction of the unsaturated diketone VII with zinc and boiling acetic acid, as mentioned above, proceeds slowly with the formation of the 1-monoenol-A. Reduction undoubtedly is 1,6, with the 4-enol group of the resulting dienol quickly ketonizing under these conditions.

A Crystalline Dienol.—The crystalline dienol XVII was isolated in one of the reactions studied. The 1-monoenol-A XV was treated with an excess of phenylmagnesium bromide and the resulting dienolate (probably A) was decomposed cautiously in dilute alcohol acidified with acetic acid, the free dienol separating in crystalline form. A purified sample absorbed oxygen from the air and was completely oxidized in the solid state within one week in contact with air, and reacted immediately with one equivalent of iodine; it gave in both cases the unsaturated diketone VII in approximately quantitative yields. It reacted instantly with methylmagnesium iodide with evolution quantitatively of two molecules of methane. Treatment with acetic acid caused partial ketonization to the 1-monoenol-A. Thus the configuration at the 1-enol group must correspond to that of the 1-monoenol-A as indicated in formula XVII. The configuration at the 4-enol group has not yet been ascertained.

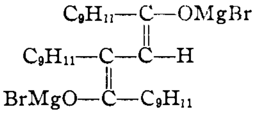
The Dienolate-B (VIB).—As described above, the 4-monoenolate-A (IIA) reacts further with mesitylmagnesium bromide to give the dienolate-A (VIA). However, if *phenyl*magnesium bromide is used instead to bring about enolization of the hindered carbonyl group, a dienolate of distinctly different properties is obtained. The new dienolate is designated as the isomer-B (formula VIB). That this new product is actually a dienolate is shown by hydrolysis and oxidation by means of alcoholic iodine to the unsaturated diketone VII.

The new dienolate-B is characterized by hydrolysis. Under the usual conditions trimesitylfuran is produced exclusively, a result entirely different from that in the case of the dienolate-A where only the saturated 1,4-diketone is obtained under similar conditions. On the basis of this fact and the mode of preparation, the formula VIB has been assigned.

The 1-Monoenol-B (XVI).—Decomposition of the dienolate-B in acetic acid gave an oil which evidently was not the dienol since it did not undergo oxidation to the unsaturated diketone VII. The oil was distillable in the vacuum oven but resisted attempts at crystallization. On standing it slowly and spontaneously changed to the furan VIII which was not immediately isolable at the beginning. Under no conditions could it be converted into the saturated diketone III. It is evident that this oil contains the fourth monoenol which is therefore designated as the 1-monoenol-B XVI. In view of the ease of furan ring closure here, coupled with the fact that the 1-monoenol-A does not undergo furanization except under drastic conditions capable of dehydrating any of the compounds in the series, it is possible with reasonable assurance to assign a definite configuration at the 1-enol group both in the dienolate-B and in the 1-monoenol-B, with the 1- and the 2-mesityl groups *cis* to each other, as indicated in formulas XVI and VIB.

In the formation of the dienolate-B from the 4-monoenol-A, it is probable that the 4-enolate group remains unchanged in configuration, and in consequence it seems likely that both the dienolates-A and -B and the 4-monoenolate-A are identical in respect to the 4-enolic group, as formulated in the diagram. The new dienolate-B, then, presumably differs from the dienolate-A only in the configuration at the 1-enol group. Whether or not this be true, it is noteworthy that the enolization at the 1-carbonyl of the 4-monoenolate-A goes in different ways with mesityl and phenylmagnesium bromides to produce configurationally opposite arrangements at the 1-enolic grouping.

The Possible Existence of a Third Dienolate (C).—The saturated diketone III when enolized by the action of the Grignard reagent gives first the 4-monoenolate-B, as described above. When the secondary enolization is forced under drastic conditions a second molecule of methane is evolved, but some decomposition occurs and the result is not of quantitative significance. The formation of some dienolate was demonstrated by oxidation with iodine to the unsaturated diketone, but the yield was poor. If no rearrangement at the 4-enol group took place, then this must be a third dienolate, C (formula XVIII), with the 4-enol group corresponding in configuration to that of the 4-monoenolate-B, and differing in this respect from the dienolates-A and -B; and since no furan was obtained from the reactions the configuration at the 1-enol must correspond to that of the 1-monoenol-A (as indicated). However, in view of the poor yields, the production of a mixture of products, and the possibility of rearrangement at the 4-enol group under the drastic conditions involved, and in the absence of any definite characterizing reaction, this question must be regarded as unsettled. It is conceivable that the configuration of the 4-monoenolate-B may actually inhibit enolization at the 1-carbonyl with rearrangement necessarily preceding the secondary enolization, and in such a case the dienolate formed here would be either A or B (VIA or B). Unfortunately, attempts to test these points were not successful.



$$\begin{array}{lll} & C_9H_{11}\text{—}C\text{—}OMgBr & \\ & \qquad\quad \| & \\ C_9H_{11}\text{—} & C\text{—}C\text{—}H & \\ & \| & \\ BrMgO\text{—} & C\text{—}C_9H_{11} & \end{array}$$

XVIII

Dienolate—C (?)

The Bearing of the Results on the Mechanism of Furan Ring Closure.—The foregoing results are entirely consistent with the probable mechanism of furan formation[2] involving addition of an enolic hydroxyl to a γ-carbonyl followed by loss of a molecule of water. According to this theory the dienols should not be capable of giving the furan directly. The two stereoisomeric dienols which are known with certainty (IVA and B) do not do so (one of them gives the furan but only after partial ketonization and consequent destruction of the dienol system). It is hoped that the two remaining theoretically possible dienols can be isolated and tested in this connection since it is conceivable that one of them might undergo direct furanization, even though the dienol form has now been shown to be unnecessary to this reaction in at least one instance.[9]

If the suggested mechanism of furanization is correct, then in cases of unsymmetrical compounds where the enol groups, as here, can exist in four forms (two *cis–trans* pairs), two of the isomers with the enolic hydroxyl and chain in the *cis* relationship could theoretically give the furan.[10] However, if one of the two γ-carbonyl groups is unreactive due to great steric hindrance (as in the case of the 1-carbonyl group in this series), then only one of these two isomers of favorable configuration would be at all likely to undergo furanization. In the trimesityl series under discussion, neither of the two stereoisomeric 4-monoenols IIA and B gives the furan. One of these, of course, would have a favorable configuration but in this case furanization would not be expected because of the enormous and undoubtedly prohibitive steric hindrance at the γ-carbonyl coupled with the mobility and speed of ketonization of the 4-enolic group. Of the two 1-monoenols the A-isomer XV cannot be furanized under ordinary conditions and undergoes ketonization exclusively, but the B-isomer XVI gives the furan directly and spontaneously and is the only compound in the series to do so. Here then is a definite case of spontaneous furanization through a monoenol where the dienol certainly cannot be involved, and where there evidently exists the only possible combination of factors which would be favorable to this reaction, namely, the *cis* configuration with respect to the enolic hydroxyl and the chain bearing the γ-carbonyl, a marked persistence of the

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[9] *Cf.* also the supposed monoenol of 1,4-diphenyl-2-mesitylbutanedione-1,4 (Ref. 4).

[10] Kleinfeller and Trommsdorff [*Ber.*, **72**, 257 (1939)] have made the suggestion that the failure of their substituted saturated 1,4-diketone to undergo dehydration to the furan was not because of any difficulty of enolization but rather because of enolization in one-half of the molecule to an enolic group of unfavorable configuration. Presumably, these authors in referring to the "enolform" involved in dehydration mean the dienol since they state that only one of the four possible stereoisomers would have a configuration favorable for ring closure. If the monoenols were meant, then of the four possible isomers (two *cis–trans* pairs), two would have configurations favorable to ring closure, assuming, of course, a mechanism of reaction such as has been suggested in Ref. 2 According to this theory of the mechanism, however, there is no obvious explanation of the failure of this saturated 1,4-diketone to undergo dehydration (perhaps it will do so if suitable conditions are found).

enol group due to hindrance by the substituted mesityl groups, and a γ-carbonyl with a minimum of hindrance and capable of reaction, given time to do so.

The inconsistency in the ease of furanization of various saturated 1,4-dimesityl 1,4-diketones is understandable in terms of some resultant of the various factors which have been discussed.[11]

Continuation of the work on this series of compounds with extension to tetraaryl types is in progress.

Experimental Part

1,2,4-Trimesitylbutanedione-1,4, III.—In a typical experiment 5.7 g. of finely powdered di (trimethylbenzoyl)-ethylene was added in half-gram portions to a thoroughly stirred solution of four equivalents of mesitylmagnesium bromide in 45 cc. of absolute ether. The temperature was held at 20° as the immediate and vigorous reaction proceeded. The resulting clear brown solution was stirred for fifteen minutes, cooled to 0° and poured into ice water acidified with dilute hydrochloric acid. The product was extracted by means of ether, the solution on concentration depositing 5.3 g. of triphenylbutanedione. After repeated crystallization from acetone it was obtained as slender needles melting at 147–147.5°.[12] It is very soluble in acetone, butanone, ethyl acetate and ligroin but difficultly soluble in methanol and ethanol.

Anal. Calcd. for $C_{31}H_{36}O_2$: C, 84.5; H, 8.2. Found: C, 84.5; H, 8.2.

Bromination in chloroform solution did not give a crystalline product.

Reaction with methylmagnesium iodide at room temperature according to the Zerewitinoff method in isoamyl ether gave a precipitate and showed evolution quantitatively of one molecule of methane; further evolution of methane did not occur even on long standing. At 100°, fifteen hours were required for a half of a molecule more of methane to form. On hydrolysis of the products in alcoholic iodine and working up in the usual way, some unsaturated as well as saturated diketone was isolated. A yield of 20% of unsaturated diketone was isolated upon hydrolysis in alcoholic iodine.

2,3,5-Trimesitylfuran, VIII.—Dehydration of the saturated 1,4-diketone (III) with acetic anhydride and sulfuric acid in the usual way failed. The effective procedures developed are described below, the best one being (a).

(a) A solution of 0.5 g. of III in 15 cc. of concd. acetic acid containing 0.6 cc. of water was refluxed gently for thirty hours with a continuous stream of dry hydrogen chloride passing through at the rate of about 20 bubbles per minute. The solution on cooling deposited 0.41 g. of nearly pure furan and 0.13 g. more was recovered from the filtrate. On repeated crystallization from concd. acetic acid or ethanol, it melted at 106.5°. It crystallizes slowly.

Anal. Calcd. for $C_{31}H_{34}O$: C, 88.1; H, 8.1. Found: C, 87.84; H, 7.9.

(b) A mixture of 0.2 g. of III and 1 cc. of hydriodic acid (sp. gr. 1.7, protected with hypophosphorous acid) was heated in a sealed tube at 160–170° for one hour. The product upon standing for several days in ethanol deposited the furan in 50% yield.

(c) A mixture of 0.2 g. of III, 8 cc. of concd. acetic acid, 6 drops of hydriodic acid (sp. gr. 1.7) and 0.1 g. each of red phosphorus and of iodine, was refluxed for one hour (the peculiar conditions here used were chosen for a control experiment). When the mixture was poured into water and worked up in the usual way, 0.13 g. of the furan was isolated.

Bromination of the furan with phosphorus pentabromide at 90° for half an hour gave an amorphous solid melting at 120–150°. Analysis indicated it to be a tetrabromide.

Anal. Calcd. for $C_{31}H_{30}OBr_4$: Br, 43.4. Found: Br, 41.7.

4(?)-Nitro-2,3,5-trimesitylfuran, IX.—A suspension of 0.2 g. of VIII in 2 cc. of concd. acetic acid at 15° was treated with 0.4 cc. of a 1–3 mixture of concd. nitric and acetic acids. On standing for thirty minutes the suspended solid dissolved, and scratching and seeding caused deposition of 0.12 g. of the mononitro derivative which on repeated crystallization from isopropanol was obtained as rhombic prisms melting at 206.5–207°.

Anal. Calcd. for $C_{31}H_{33}O_3N$: C, 79.6; H, 7.1; N, 3.0. Found: C, 79.9; H, 7.1; N, 3.2.

3-Iodo-1,2,4-trimesitylbutanedione-1,4-A, IV.—The solution of magnesium 4-monoenolate-A, prepared from 20 g. of di-(trimethylbenzoyl)-ethylene and 90 cc. of an ether solution of two equivalents of mesitylmagnesium bromide, was decomposed by adding it slowly to a vigorously stirred solution of 20 g. of iodine in 400 cc. of ethanol cooled in an ice-bath, the temperature varying between 0 and 10°. The product crystallized directly from the ethanol solution. After standing for half an hour at 0° with stirring to ensure complete precipitation, enough concd. hydrochloric acid was added to dissolve the magnesium hydroxide, and the product was filtered off; yield 26.5 g. of practically pure material. The yields in different runs varied from 74–79%. After repeated crystallization from concd. acetic acid and from ethyl acetate it was obtained as colorless rectangular plates melting at 213° with decomposition and liberation of iodine.

Anal. Calcd. for $C_{31}H_{35}O_2I$: C, 65.7; H, 6.2. Found: C, 65.8; H, 6.2.

Small amounts of the isomeric iodo compound B were obtainable by fractional crystallization of the residues from this experiment.

Reduction was brought about in four ways as follows:

(a) A sample of the iodo compound reacted with potassium iodide in concd. acetic acid at room temperature with liberation of approximately one equivalent of iodine (titrated) and formation of trimesitylbutanedione III in quantitative yield.

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[11] 1,4-Dimesitylbutanedione-1,4, $C_9H_{11}COCH_2CH_2COC_9H_{11}$ [Lutz, Johnson and Wood, THIS JOURNAL, **60**, 716 (1938)] and the saturated diketone of this series, III, for example, are dehydrated only with considerable difficulty, whereas 2,3-dimethyl-1,4-dimesitylbutanedione-1,4, $C_9H_{11}COCH(CH_3)CH(CH_3)COC_9H_{11}$ [Lutz and Taylor, *ibid.*, **55**, 1593 (1933)] is converted into the corresponding furan with extraordinary ease.

[12] Melting points of all analytical samples are corrected.

(b) The action of zinc dust in boiling concd. acetic acid (three min.) gave III.

(c) Refluxing for one hour in 60% ethanol with an excess of sodium bisulfite gave III.

(d) Hydrogenation in ethyl acetate using platinum oxide catalyst liberated iodine and gave III in good yield.

Alcoholic potassium hydroxide, refluxed for one hour, converted the iodo compound into the unsaturated diketone VII. Refluxing with an excess of anhydrous sodium acetate in ethanol for eight hours was without effect.

3-Iodo-1,2,4-trimesitylbutanedione-1,4-B, IV.—Solutions of the magnesium 4-monoenolate-B from the action of an excess of phenyl, ethyl or methylmagnesium halide at room temperature on trimesitylbutanedione, III, were poured into excess of cooled alcoholic iodine. From 0.4 g. of III, upon decomposition in alcoholic iodine at −10 to −15°, 0.25 g. of IVB was obtained, and from the mother liquors 0.15 g. of unchanged material (III). The iodide was not pure, however, and contained a little of the higher melting isomer-A. When the decomposition in alcoholic iodine was carried out at −60° the yield of the iodo compound-B was about the same but it was practically pure. Exhaustive crystallization from ethyl acetate and from concd. acetic acid gave a product of constant melting point of 178° (elongated hexagonal plates). It did not give a mixture melting point depression with the higher melting isomer-A but did with the bromo compound, isomer-A.

Anal. Calcd. for $C_{31}H_{35}O_2I$: C, 65.7; H, 6.2. Found: C, 65.5; H, 6.1.

Examination of the mother liquors of the above experiment failed to reveal the presence of even small amounts of the unsaturated diketone VII which would be expected as a result of oxidation of small amounts of dienolate by the iodine.

Reaction with the Grignard Reagent.—A sample (0.1 g.) of IVB was added to 1 cc. of ether containing two equivalents of ethylmagnesium bromide at 20° and the resulting mixture immediately was poured into 15 cc. of boiling concd. acetic acid. On diluting with water and crystallizing from ethanol 0.05 g. of the saturated diketone III was obtained.

In a similar experiment in which the ether solution was heated for five minutes and then poured into boiling acetic acid, a mixture of about equal parts of the saturated and unsaturated diketones III and VII was obtained, indicating that part of the material had been enolized at both of the carbonyls. Phenylmagnesium bromide, used instead of ethylmagnesium bromide, caused complete enolization to the dienolate under these conditions.

Reduction with sodium bisulfite in boiling 60% ethanol (thirty minutes) gave a quantitative yield of III.

The action of potassium hydroxide in excess in boiling ethanol (one hour) converted the iodide in good yield into the unsaturated diketone VII.

3-Bromo-1,2,4-trimesitylbutanedione-1,4-A, V.—A solution of the 4-monoenolate-A (II) and 12 cc. of an ether solution of two equivalents of ethylmagnesium bromide at 20° was cooled immediately to 0° and added to 25 cc. of ethanol solution containing 1.5 g. of bromine also at 20°. The product crystallized and was filtered off (2.4 g.). Fractional crystallization from acetone and from isopropanol gave 1.35 g. of nearly pure bromo diketone VA and 0.1 g. of the stereoisomer (B). The isomer-A was purified by repeated crystallization from isopropanol and melted at 192.5–193.5°.

Anal. Calcd. for $C_{31}H_{35}O_2Br$: C, 71.7; H, 6.8. Found: C, 71.7, 71.9; H, 6.9, 6.8.

When the 4-monoenolate-A solution was decomposed in alcoholic bromine at higher temperatures (10°) a difficultly separable mixture of the bromodiketones A and B was obtained.

Ethylmagnesium bromide at 20° enolized the bromodiketone-A quickly and when the mixture was decomposed in alcoholic iodine at 10° the iododiketone-A (IV) was obtained exclusively and in good yield.

The bromodiketone-A was not affected by the prolonged action of boiling ethanolic sodium acetate (twelve hours), but when refluxed for thirty minutes with a 95% methanolic solution of an excess of potassium hydroxide, the unsaturated diketone VII was obtained.

Reduction with sodium bisulfite in 60% ethanol (refluxing for four hours) gave the saturated diketone III.

3-Bromo-1,2,4-trimesitylbutanedione-1,4-B, V.—A solution of the 4-monoenolate-B, prepared by the action of phenyl, methyl or ethylmagnesium halide on III, was decomposed in alcoholic bromine. In a typical experiment starting with 0.2 g. of III, decomposing in alcoholic bromine at −60°, 0.2 g. of nearly pure bromodiketone-B was obtained (80%). Repeated crystallization from acetone gave a pure product melting at 230–231°.

Anal. Calcd. for $C_{31}H_{35}O_2Br$: C, 71.7; H, 6.8; Br, 15.4. Found: C, 71.5; H, 7.1; Br, 15.5.

When in several different experiments the solution of the 4-monoenolate-A was decomposed in alcoholic bromine at temperatures ranging from 0 to −15°, a mixture of the isomers A and B was obtained.

Ethylmagnesium bromide at 20° reacted rapidly with the bromodiketone-B. On decomposition in alcoholic iodine at 10°, the iododiketone-A was obtained exclusively in good yield.

Reduction in the usual way with zinc dust and concd. acetic acid gave III.

Sodium acetate in boiling ethanol (two hours) was without effect, but refluxing for two hours in 95% ethanol containing an excess of potassium hydroxide gave the unsaturated diketone in nearly quantitative yield.

1,2,4-Trimesityl-2-butenedione-1,4, VII.—A suspension of 4 g. of the iododiketone IVA in 125 cc. of ethanol and 3 g. of potassium hydroxide was refluxed for one hour, giving a dark red solution which was diluted with water cautiously as it cooled, the product separating in 90% yield. On repeated crystallization from methanol, ethanol or ligroin it was obtained as colorless needles which melted at 142–144°, turning yellow as it melted. It became colorless on solidification. Its solutions in common solvents are yellow.

Anal. Calcd. for $C_{31}H_{34}O_2$: C, 84.9; H, 7.8. Found: C, 85.1; H, 7.6.

The unsaturated diketone VII is obtainable similarly as described from the other halides IVB and V (A and B). Methanol may be substituted for ethanol as the solvent but it is not as satisfactory due to the difficult solubility of the halides.

Various attempts to make the acetoxyfuran by means of acetic anhydride and concd. sulfuric acid failed, no reaction occurring even at boiling temperature.

The unsaturated diketone was not changed on exposure to sunlight in ethanol or in chloroform containing iodine.

Reduction.—Zinc dust and concd. acetic acid produced the 1-monoenol-A (see this compound). Sodium hydrosulfite in dilute ethanol as medium did not bring about reduction. The combination 8 cc. of concd. acetic acid, 4 drops of water, 0.1 g. of iodine and 0.1 g. of red phosphorus, refluxed for one hour, gave the furan VIII in good yield.

1,2,4-Trimesitylbutane-1,4-dione-4-enolate-A, IIA.—A solution of this enolate is obtained by the action of mesitylmagnesium bromide on the saturated 1,4-diketone III as already described. Since neither it nor the free enol could be isolated, this compound was characterized by its reactions as follows:

(a) The reaction with iodine and bromine leads to the iodo and bromodiketones IVA and VA.

(b) Decomposition in an alcoholic solution of quinone or ferricyanide produced only the saturated diketone III and no unsaturated diketone VII, showing that significant amounts of the dienolate were absent.

(c) When decomposed in dilute hydrochloric acid the saturated diketone III was formed exclusively.

(d) Decomposition by dropping the ether solution slowly into boiling concd. acetic acid in an apparatus arranged to collect the ether boiled off, gave the saturated diketone III exclusively and in good yield.

(e) Mesitylmagnesium bromide in isopropyl ether with refluxing for two hours under an atmosphere of nitrogen converts it into the dienolate-A (see this compound). When ethyl ether was used and the mixture refluxed for two hours and decomposed in alcoholic iodine in the usual way, only the iododiketone-A was obtained, showing that the higher temperature obtainable in boiling isopropyl ether is required to produce the dienolate.

(f) Phenylmagnesium bromide converted it readily into the dienolate-B (see this compound), the reaction proceeding upon five minutes of refluxing with ethyl ether as solvent.

Preparation of the 4-Monoenolate-A from the Iododiketone IVA.—This method is the most convenient and the product is obtainable thus free from tarry secondary products which are formed in the reaction between mesitylmagnesium bromide and di-(trimethylbenzoyl)-ethylene. The general procedure was to add the sample of iododiketone to 3–4 equivalents of phenylmagnesium bromide in ether, controlling the temperature by means of an ice-bath to 20°, and allowing the solution to stand not more than two to three minutes before use. The other three halogeno diketones can be used in the same experiment and ethyl or mesitylmagnesium bromides can be used with equal success.

The 4-monoenolate-A from the iododiketone-A was characterized by application of the tests (a), (d) and (f) listed under the first preparation described above. The products from the iododiketone-B and from the bromodiketones A and B were characterized by application of (a) with conversion into the iododiketone-A.

An attempt was made to isolate the 4-monoenolate-A under mild conditions by hydrolysis in ice water acidified with dilute acetic acid, extraction by ether, and evaporation at room temperature. An oil was obtained which crystallized promptly from ethanol as the saturated diketone III. Similarly a solution of the 4-monoenolate-A was decomposed in ice water and extracted with ether without acidification, separated, the ether layer dried over anhydrous sodium sulfate for a few minutes, and added to an ether solution of an excess of diazomethane. Only the saturated diketone was recovered.

1,2,4-Trimesitylbutane-1,4-dione-4-monoenolate-B, IIB.—The action of phenyl, ethyl or methylmagnesium halide in ether on trimesitylbutanedione III at room temperature gives the 4-monoenolate-B. The reaction was carried out under a variety of conditions, in some cases with refluxing, but heating proved to be unnecessary and introduced some dienolate. The enolization of the second and hindered carbonyl here is much more difficult to bring about than in the case of the 4-monoenolate-A. The solutions of the 4-monoenolate-B on decomposition in alcoholic bromine or iodine gave the B-halides IV and V when the temperature was lowered. At temperatures from 0–25° mixtures of the bromides (largely B) were obtained, but with iodine ketonization took place so rapidly that the saturated diketone III was obtained in large amounts (over 75% in one case) along with smaller amounts of the iododiketone IVB.

Characterization of the 4-monoenolate-B was best made by halogenation at lowered temperature (−60°). Hydrolysis of a sample in boiling concd. acetic acid gave only the saturated diketone III, and careful examination of the products failed to reveal the presence of trimesitylfuran. The 4-monoenolate-B was decomposed in a cooled (10°) solution of quinone in ethanol, but only the saturated diketone could be isolated, showing that there was little dienolate present in the sample. Unsuccessful attempts were made to isolate the free 4-monoenol-B by hydrolysis of the enolate in ice water acidified with acetic acid and extraction with ether. The oil obtained crystallized quickly at room temperature when triturated with isopropanol, giving the saturated diketone.

1,2,4-Trimesitylbutane-1,4-dione-1-monoenol-A, XV.—A mixture of 8 g. of the unsaturated diketone VII, 20 g. of zinc dust, and 125 cc. of concd. acetic acid was refluxed with mechanical stirring for one hour. On filtration and dilution with ice water the product coagulated and was filtered, dried and recrystallized from ligroin. The yields averaged 60%. On repeated crystallization from ligroin it was obtained as cubic prisms melting at 131–131.5°.

Anal. Calcd. for $C_{31}H_{36}O_2$: C, 84.5; H, 8.2. Found: C, 84.3; H, 8.2.

The 1-monoenol-A was obtained also from the hydrolysis of the dienolate-A (see that compound). It crystallized from ethanol with water of crystallization and melted with effervescence at 95–100°, solidified and remelted at 130°. On standing the hydrate loses its solvent of crystallization and reverts to the anhydrous form. It does not give a color reaction with alcoholic ferric chloride nor does it react at all readily with alcoholic bromine or with diazomethane (in ether for eighteen hours). In a quantitative test it reacted with methylmagnesium iodide at room temperature under nitrogen with evolution of 0.93

molecule of methane. Phenylmagnesium bromide at 20° gives the monoenolate also as was shown by decomposition in alcoholic iodine and recovery of the 1-monoenol-A unchanged, with little or no oxidation to the unsaturated 1,4-diketone. Under more drastic conditions the monoenol reacts with phenylmagnesium bromide to give the dienolate-A (see that compound).

The 1-monoenol-A, when heated with iodine, red phosphorus and concd. acetic acid for one hour, gave trimesitylfuran. The saturated diketone III is furanized under these conditions also.

The action of potassium hydroxide in 95% ethanol (refluxed for one hour) produced the saturated diketone.

1,2,4-Trimesitylbutanedione-1,4 Dienolate-A, VIA.—The dienolate-A was obtained as an ether insoluble powder by adding di-(trimethylbenzoyl)-ethylene to mesitylmagnesium bromide in isopropyl ether (giving first the 4-monoenolate-A) followed by refluxing for two hours under an atmosphere of nitrogen. A dienolate which was presumably the same was obtained by adding the 1-monoenol-A, XV, to an ether solution of an excess of phenylmagnesium bromide and refluxing for thirty minutes. These dienolates from the two sources appeared to be identical since they gave similar results when tested in the following experiments carried out independently on samples prepared in the two ways.

(a) The suspension of product was poured into an ethanol solution of an excess of iodine (10°), and the mixture was then diluted with water containing sodium bisulfite (acidified) to destroy the excess of iodine. The resulting oil was crystallized from ethanol and a good yield of the unsaturated diketone VII was obtained.

(b) Decomposition in boiling acetic acid andre fluxing for one hour after expulsion of all of the ether, gave an oil from which only the saturated diketone III could be isolated. No furan was detected. The presence of the magnesium salts evidently was responsible for ketonization of the 1-monoenol-A in this reaction.

(c) When the ether solution of the dienolate was poured into concd. acetic acid magnesium salts crystallized and were filtered off. The ether was then boiled off; the remaining solution in concd. acetic acid was then refluxed for one hour and diluted with water. Extraction with ether and concentration gave the 1-monoenol-A, XV, which was crystallized from ligroin or isopropanol and identified.

While the identity of the two samples with respect to configuration at the 1-enol group is certain, the identity of configurations at the 4-enol group is not rigorously proved because in one case (dienolate-A) the group was formed before and in the other case after enolization at the 1-enol group, and because the tests listed do not distinguish between the 4-monoenolate configurations. Attempts to prove the point by converting both samples of dienolate to the same crystalline dienol were unsuccessful. The dienol (described below) was isolated only in the second case when the dienolate was prepared from the 1-monoenol-A. The failure to isolate the dienol from the first preparation (dienolate-A) is of no significance in view of the experimental difficulties involved, particularly the difficulty of crystallizing, the presence of mesitylene from excess Grignard reagent, and the sensitivity of the dienol itself. It is hoped that in the further investigations under way derivatives may be obtained which will throw light on this question.

1,2,4-Trimesitylbutanedione-1,4 Dienol, XVII.—Two-tenths gram of the 1-monoenol-A (XV) was added to 4 cc. of phenylmagnesium bromide solution in ether (concn. 0.001 mole per g.) and the mixture was refluxed for thirty minutes, the dienolate precipitating. On cooling to 0° and adding 20 cc. of 80% ethanol containing 2 cc. of concd. acetic acid, followed quickly by 50 cc. of water, a white solid separated and was filtered quickly and crystallized from ethanol. The first crop of crystals melted low and successive crops of material were then obtained (rectangular plates) which melted sharply at 70–71°. In another run a sample melting at 72–73° was obtained. The yield was 0.1 g. The compound in the solid state was oxidized by air and after standing for a week was converted quantitatively into the unsaturated diketone VII. The change proceeded rapidly when the material was treated with iodine in ethanol, and in a quantitative experiment where the excess of iodine was estimated by titration with sodium thiosulfate, one molecule of iodine was used up with the formation of the unsaturated diketone in quantitative yield. In the Zerewitinoff apparatus with methylmagnesium iodide at room temperature 1.89 molecules of methane was liberated with the formation of a white precipitate.[13]

Rearrangement to the saturated diketone III was brought about by heating a solution of the dienol in concd. acetic acid containing a small amount of concd. hydrochloric acid for fifteen minutes. Rearrangement to the 1-monoenol-A (without isolating the dienol from the magnesium dienolate) was described under the preparation of this compound.

While the configuration at the 1-enol group is certain the configuration at the 4-enol group has not been established relative to the 4-monoenolates-A and B.

1,2,4-Trimesitylbutanedione-1,4 Dienolate-B, VIB.—The dienolate-B is obtained in two ways: (1) by the enolization of the 4-monoenolate-A in diethyl ether after its preparation from di-(trimethylbenzoyl)-ethylene and mesitylmagnesium bromide; this was done by adding *phenyl*-magnesium bromide to the mixture and refluxing for thirty minutes; and (2) by the action of phenylmagnesium bromide on the iododiketone IVA in ethyl ether, with refluxing for five minutes.

The dienolate-B differs from the A-isomer by its solubility in ether. The probable identity of the materials from the two sources was established by the following experiments carried out on each sample separately.

(a) Samples were decomposed in alcoholic iodine solution at 10° and worked up in the usual way, giving the unsaturated diketone VII and showing that they actually contained the dienolate.

(b) Solutions were decomposed by adding them slowly to boiling concd. acetic acid in an apparatus arranged to collect the ether which volatilized, the solution then being

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(13) Unfortunately before carbon and hydrogen analyses could be carried out on the above described sample, oxidation to VII had occurred. New samples prepared subsequently were not as good and analyses were unsatisfactory (carbon was low). It did not seem worth while to delay publication further, however, and the formulation of the dienol is therefore based on the quantitative data described.

refluxed for one hour, diluted with water and extracted with ether. Crystallization of the resulting oil from isopropanol gave trimesitylfuran VIII exclusively, no saturated diketone being detected.

In one experiment the dienolate-B was decomposed in cold dilute acetic acid and only traces of the furan were isolable from the oily product which could be distilled in the vacuum oven. This oil is very evidently the **1-monoenolate-B.**

From the fact that the two samples of the dienolate-B give the furan rather than the saturated diketone, it is certain that they both have the same configuration at the 1-enol group as indicated in formula VIB. Both samples, of course, must have the same configuration at the 4-enol group (corresponding to that of the 4-monoenolate-A) since this group was formed in both experiments before enolization occurred at the 1-carbonyl group.

Summary

1,2,4-Trimesitylbutanedione-1,4 was obtained as the result of 1,4-addition of mesitylmagnesium bromide to di-(trimethylbenzoyl)-ethylene. The 4-monoenolate-A was first formed (proved by halogenation) and was further enolized to the dienolate (proved by oxidation).

1,2,4-Trimesityl-2-butenedione-1,4 was obtained by oxidation of the dienols and by elimination of halogen acid from the 3-halogeno-1,2,4-trimesitylbutane-1,4-diones.

2,3,5-Trimesitylfuran and its mononitro derivative are described.

The 3-halogeno-1,2,4-trimesityl-1,4-butanediones have been obtained each in diastereoisomeric forms.

The existence of two 4-monoenolates, A and B, was demonstrated: A was formed by the addition of mesitylmagnesium bromide to di-(trimethylbenzoyl)-ethylene or by the action of any Grignard reagent on the 3-halogeno-1,2,4-trimesitylbutane-1,4-diones, and B by the enolization of the saturated 1,4-diketone. They were characterized by halogenation to the stereoisomeric halogeno diketones. A basis for assignment of configurations is discussed.

The 1-monoenol-A (m. p. 145°) was obtained by partial ketonization of the dienolate. It lacked most of the usual enolic properties. Ketonization gave the saturated diketone. Enolization gave a crystalline dienol which was metastable and easily oxidized to the unsaturated 1,4-diketone.

The existence of two dienolates, A and **B**, was demonstrated. A was obtained from the 4-monoenolate-A by enolization with mesitylmagnesium bromide, and was converted by hydrolysis and ketonization to the saturated diketone. B was obtained by the action of phenylmagnesium bromide on the 4-monoenolate-A and was characterized by hydrolysis with spontaneous formation of trimesitylfuran.

Configurations at the 1-enol group are assigned on the basis of the relative ease of furan formation and ketonization.

The mechanism of furan ring closure is discussed in the light of this work.

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[Contribution from the Research Laboratories of the Calco Chemical Division of the American Cyanamid Company]

Sulfanilamide Derivatives. V. Constitution and Properties of 2-Sulfanilamidopyridine[1]

By M. L. Crossley, E. H. Northey and Martin E. Hultquist

Although 2-sulfanilamidopyridine[2] (now named "sulfapyridine" by the American Medical Association) has received wide publicity as a result of its use in the treatment of pneumonia,[3] attention has been drawn to the fact that practically nothing has been published on its physical and chemical properties, and no evidence has been given in support of the assigned structure.[4]

We had independently synthesized this compound as part of our program on N^1-substituted sulfanilamides and had made a pharmacological study, but the announcements from England were made before we were prepared to publish our information. We offer the following evidence on constitution as well as data on the properties of the carefully purified compound.

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[1] Presented in part before the Division of Medicinal Chemistry, A. C. S. Meeting, Baltimore, Md., April, 1939.

[2] See Sulfanilamide Derivatives I, This Journal, **60**, 2217 (1938), for nomenclature.

[3] Whitby, *Lancet*, **1**, 1210 (1938); synthesized by J. A. Ewins and M. A. Phillips.

[4] Marshall, *J. Am. Med. Assoc.*, **112**, 352 (1939).