[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

STERIC HINDRANCE IN CERTAIN MESITYLENIC KETONES

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RECEIVED MAY 20, 1932 PUBLISHED OCTOBER 5, 1932

Many reactions of organic compounds are affected to a remarkable degree by the extent to which the reacting system is surrounded by other groups. Opinion is divided with respect to the manner in which these groups exercise their influence but whether the effect be regarded as spatial or chemical it is generally designated as "Steric Hindrance." In time this hindrance will, doubtless, yield to analysis by general methods, but in the meantime it is important to be able to predict in what form it is most likely to manifest itself and, in particular, whether addition and substitution reactions are affected in like manner. It was this latter question that interested us most in the present investigation.

Most of our work was done upon three ketones, namely, acetomesitylene, dimesityl ketone and dimesityl diketone.

$CH_3COC_6H_2(CH_3)_3$ $(CH_3)_3C_6H_2COC_6H_2(CH_3)_3$ $(CH_3)_3C_6H_2COCOC_6H_2(CH_3)_3$

The first, being a methyl ketone, can enolize when the hindrance to other reactions is prohibitive; the second contains a carbonyl group of which the reactions are subject to the greatest hindrance that can be exercised by methylated aromatic rings; and in the third, the additive power is increased by the interaction of carbonyl groups which are twinned.

One of these compounds, acetomesitylene, has been known and studied heretofore; it gives few of the characteristic reactions of ketones. Its oxime cannot be obtained by any of the ordinary methods,[1] but the ketone doubtless reacts slowly with hydroxylamine at high temperatures, because Feith and Davies[2] found that when it is heated at 160° with hydroxylamine hydrochloride it is converted into acetylmesidine, the product which would be formed by a Beckmann rearrangement of the oxime. Its behavior toward phosphoric acid and toward alkalies is the reverse of that of acetophenone, it being cleaved to mesitylene and acetic acid by the former and completely resistant to the latter,[3] and this resistance to alkalies persists even after all of the hydrogen of the methyl group has been replaced by halogens.[4]

In contrast with this behavior, which indicates a pronounced hindrance to reactions involving addition to carbonyl, acetomesitylene is easily reduced to the carbinol,[5] and according to Klages[6] it also readily combines

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[1] Baum, *Ber.*, **28**, 3207 (1895); V. Meyer, *ibid.*, **29**, 830 (1896).

[2] Feith and Davies, *ibid.*, **24**, 3546 (1891).

[3] Klages and Lickroth, *ibid.*, **32**, 1549 (1899).

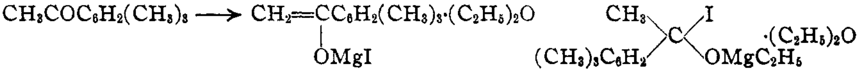
[4] Fuson and Walker, THIS JOURNAL, **52**, 3269 (1930).

[5] Klages and Allendorff, *Ber.*, **31**, 1003 (1898).

[6] Klages, *ibid.*, **35**, 2631 (1905).

with Grignard reagents. Its reduction by sodium and alcohol is not necessarily inconsistent with its general behavior because this mode of reduction may not involve the direct addition of two atoms of hydrogen to the carbonyl group; but the addition of organic magnesium compounds appears completely inexplicable.

In reality, acetomesitylene does not add Grignard reagents. Klages, on treating it with ethylmagnesium iodide in the usual manner, obtained a magnesium compound which he recognized as abnormal because it regenerated acetomesitylene when it was hydrolyzed, but he failed to observe that the reaction is accompanied by evolution of gas. He therefore represented the magnesium compound as an abnormal addition product (III). A quantitative examination of the reaction showed, however, that one mole of gas was evolved and that but one mole of reagent disappeared. The process therefore involves enolization and the product is the magnesium derivative represented by II.



$$CH_3COC_6H_2(CH_3)_3 \longrightarrow \underset{\displaystyle OMgI}{CH_2{=}C}C_6H_2(CH_3)_3\cdot(C_2H_5)_2O \qquad \begin{matrix}CH_3 \\ (CH_3)_3C_6H_2\end{matrix}\!\!>\!C\!<\!\!\begin{matrix}I \\ OMgC_2H_5\end{matrix}\cdot(C_2H_5)_2O$$

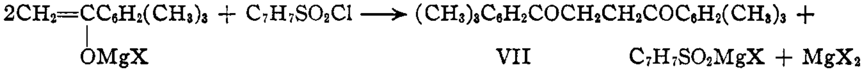
I II III

Many cases are known in which ketones are partially enolized by Grignard reagents but acetomesitylene alone of all ketones that have been examined forms no addition product at all and gives a quantitative yield of hydrocarbon. It appeared possible that this difference in the behavior of acetomesitylene and other ketones might be due to greater ease or rapidity of enolization, but this proved not to be the case. It does not contain enough of the enolic modification to be detectable by the Kurt Meyer method, and at the ordinary temperature it reacts with methylmagnesium iodide slowly, liberating gas for nearly an hour. Moreover, we prepared 2,4,6-trimethylbenzoylacetic ester and found that it does not differ materially from benzoylacetic ester with respect to the extent to which it is enolized. The mesitylene group, therefore, neither hinders nor promotes enolization and it is reasonable to conclude that acetomesitylene is completely enolized by organic magnesium compounds because the hindrance to addition is great enough to allow ample time for the process.

The non-volatile product of this reaction, the iodomagnesium salt of the enolic modification (II), was accurately described by Klages. Unlike many other enolates of ketones it neither combines with oxygen to form a peroxide nor undergoes autoxidative cleavage. It combines with carbon dioxide to form a carbonate which loses carbon dioxide and regenerates acetomesitylene when it is acidified. It also reacts very readily with acid chlorides. With the chlorides of carboxylic acids—acetyl chloride, benzoyl chloride and even chlorocarbonic ester—the products are invariably diacyl derivatives, regardless of the quantities of the reactants employed or the order in which they are brought together

$(CH_3CO)_2CHCOC_6H_2(CH_3)_3$ IV $(C_6H_5CO)_2CHCOC_6H_2(CH_3)_3$ V $(CH_3)_3C_6H_2COCH(CO_2C_2H_5)_2$ VI

p-Toluenesulfonyl chloride likewise reacts readily but as usual forms a halogen compound which subsequently couples with a second molecule of the enolate



$$2CH_2{=}\underset{\displaystyle OMgX}{\underset{|}{C}}C_6H_2(CH_3)_3 + C_7H_7SO_2Cl \longrightarrow \underset{\text{VII}}{(CH_3)_3C_6H_2COCH_2CH_2COC_6H_2(CH_3)_3} + C_7H_7SO_2MgX + MgX_2$$

From the foregoing summary it is clear that the behavior of the iodomagnesium derivative of acetomesitylene is essentially the same as that of the metallic derivatives of β-ketonic esters and β-diketones. It is, however, entirely different from that of a number of magnesium derivatives which have recently been obtained in a similar manner by Grignard and Blanchon.[7] By treating a series of ketones—cyclohexanone, thujone, carvone and mesityl oxide—with isopropylmagnesium bromide, these investigators obtained mixtures which contained considerable quantities of bromomagnesium derivatives of the ketones. These magnesium enolates likewise reacted readily with acetyl chloride but instead of forming diketones they formed acetates which could be hydrolyzed to the corresponding enolic modifications. We know of no satisfactory explanation for this difference in the behavior of such closely related magnesium derivatives, but we do not believe that it can be attributed to steric hindrance.

As a result of this stage of the investigation it seems established that while acetomesitylene has an effective hindrance to reactions involving addition to carbonyl, it can participate in a number of other reactions by reason of its ability to undergo enolization. We turned, therefore, to dimesityl ketone in which enolization is impossible. It was not to be expected that this substance would enter into any of the common reactions of ketones except those involving reduction. But it seemed barely possible that it might combine with Grignard reagents because it has been discovered that even though the hindrance to all other addition reactions may be prohibitive, these extremely effective agents can add to highly phenylated compounds by unlocking the aromatic nucleus.[8] In the case of dimesityl ketone, however, even this reaction failed, leaving reduction as the only possibility.

Weak reducing agents like zinc in acetic acid or in alcoholic alkali had no effect on dimesityl ketone. Aluminum amalgam in moist ether and ethyl magnesium bromide in boiling benzene appeared to attack it slowly but yielded no definite product. Sodium and pure sodium amalgam in alcohol, however, reduced it rapidly and quantitatively to the carbinol, its behavior in this respect being precisely like that of acetomesitylene.

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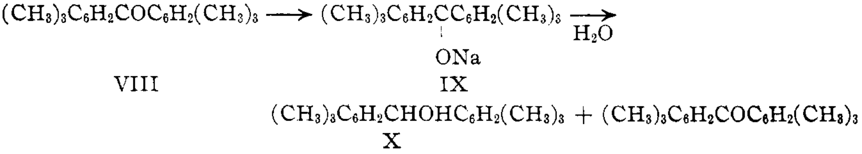
[7] Grignard and Blanchon, *Bull. soc. chim.*, [4] **49**, 23 (1931).

[8] Gilman, Kirby and Kinney, THIS JOURNAL, **51**, 2252 (1929); Kohler and Nygaard, *ibid.*, **52**, 4128 (1930).

Dimesityl carbinol was obtained from dimesityl ketone by other reactions which throw more light on the manner in which it is formed. In benzene the ketone readily combined with sodium to form a greenish blue ketyl which, on hydrolysis, gave the usual equimolar mixture of ketone and secondary alcohol



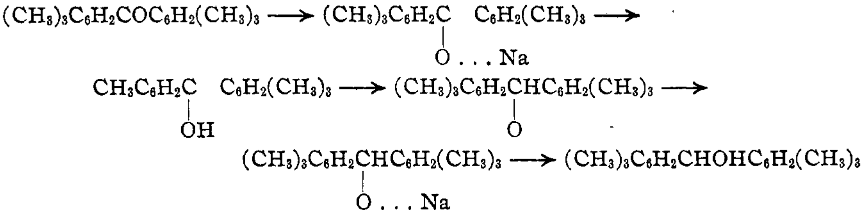
$$(CH_3)_3C_6H_2COC_6H_2(CH_3)_3 \longrightarrow (CH_3)_3C_6H_2\underset{ONa}{\underset{|}{C}}C_6H_2(CH_3)_3 \xrightarrow[H_2O]{}$$

VIII IX

$$(CH_3)_3C_6H_2CHOHC_6H_2(CH_3)_3 + (CH_3)_3C_6H_2COC_6H_2(CH_3)_3$$

X

The ketone also reacted with Gomberg and Bachmann's[9] binary combination of magnesium and magnesium iodide, forming a dark purple ketyl which was obtained in crystalline form and which, on hydrolysis, likewise yielded equivalent quantities of ketone and carbinol. These metal ketyls showed no tendency to associate to ethane derivatives and no pinacol could be detected in the product of hydrolysis. Experiments are under way to determine whether substituents in the ortho positions actually promote the formation of free radicals, but the foregoing facts show clearly that they have no effect on the formation of metal ketyls. In view of the ease with which these ketyls are formed and the difficulty of saturating the carbonyl group by direct addition, it seems probable that they are intermediates in the rapid reduction of the ketone by sodium or pure sodium amalgam. A train of addition, hydrolysis and rearrangement products that would be consistent both with the general behavior of the ketone and the action of pure sodium amalgam[10] is represented by the scheme

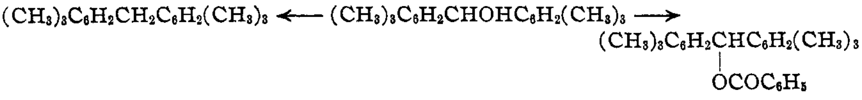


$$(CH_3)_3C_6H_2COC_6H_2(CH_3)_3 \longrightarrow (CH_3)_3C_6H_2\underset{O\,...\,Na}{\underset{|}{C}}\ C_6H_2(CH_3)_3 \longrightarrow$$

$$CH_3C_6H_2\underset{OH}{\underset{|}{C}}\ C_6H_2(CH_3)_3 \longrightarrow (CH_3)_3C_6H_2\underset{O}{\underset{|}{C}}HC_6H_2(CH_3)_3 \longrightarrow$$

$$(CH_3)_3C_6H_2\underset{O\,...\,Na}{\underset{|}{C}}HC_6H_2(CH_3)_3 \longrightarrow (CH_3)_3C_6H_2CHOHC_6H_2(CH_3)_3$$

The hindrance which is so conspicuous in the addition reactions of the ketone appears to be lacking completely in the metathetical reactions of the carbinol. The combination of hydrogen iodide and red phosphorus has no effect on the ketone at the boiling point of the acid but it readily reduces the



$$(CH_3)_3C_6H_2CH_2C_6H_2(CH_3)_3 \longleftarrow (CH_3)_3C_6H_2CHOHC_6H_2(CH_3)_3 \longrightarrow (CH_3)_3C_6H_2\underset{OCOC_6H_5}{\underset{|}{C}}HC_6H_2(CH_3)_3$$

XI X XII

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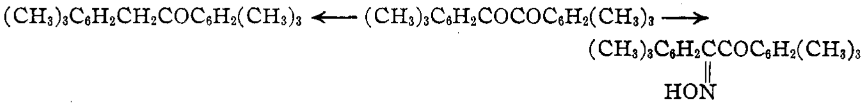
[9] Gomberg and Bachmann, THIS JOURNAL, **49**, 286 (1927).

[10] Willstätter, Seitz and Bumm, *Ber.*, **61**, 871 (1928).

carbinol to dimesitylmethane. And the carbinol is benzoylated as easily as it is reduced.

The last of our ketones—dimesityl diketone or hexamethyl benzil—was of special interest because it has long been known that mesityl glyoxylic acid forms hydrazones and that its esters form oximes. By many this behavior of the glyoxylic acid and its esters has been regarded as anomalous because they have compared these substances with mesitylenic ketones, ignoring the fact that the twinning of carbonyl groups greatly increases their additive power—as illustrated, for example, in the stability of the hydrates of glyoxylic aldehydes, mesoxalic acid and diphenyl triketone. In order to get a correct estimate of the hindrance due to the mesityl group it is necessary, therefore, to compare the glyoxylic ester with other glyoxylic esters and the diketone with other α-diketones.

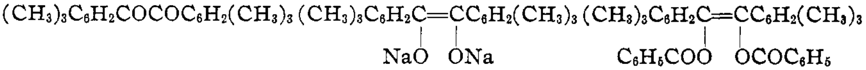
Dimesityl diketone can be reduced to the desoxy compound with zinc and alcoholic potassium hydroxide and it forms a monoxime when it is digested for a long time with excess of strongly alkaline hydroxylamine. These are the only reactions that we could find which presumably involve addition to carbonyl



$$(CH_3)_3C_6H_2CH_2COC_6H_2(CH_3)_3 \longleftarrow (CH_3)_3C_6H_2COCOC_6H_2(CH_3)_3 \longrightarrow (CH_3)_3C_6H_2\underset{\underset{HON}{\|}}{C}COC_6H_2(CH_3)_3$$

XIV XIII XV

The diketone neither combines with Grignard reagents nor forms a quinoxaline derivative with ortho phenylenediamine. It also does not undergo the benzilic acid rearrangement, confirming the view of those who hold that the first step in this rearrangement consists in the addition of an alkaline hydroxide to a carbonyl group. One of the most useful reactions of α-diketones is their cleavage to acids with sodium peroxide. Weitz and Scheffer,[11] the originators of the reaction, claimed that it is specific for α-diketones and wrote a mechanism which involves addition to the ends of the conjugated system. The behavior of dimesityl diketone brings support to this view because it is cleaved quantitatively to two molecules of trimethylbenzoic acid. The diketone also enters into another reaction that involves addition to the ends of the conjugated system, namely, addition of alkali metals; it combines with sodium forming a brown disodium compound which reacts with benzoyl chloride to form the corresponding dibenzoate-hexamethyl isobenzil



$$(CH_3)_3C_6H_2COCOC_6H_2(CH_3)_3 \quad (CH_3)_3C_6H_2\underset{NaO}{C}{=}\underset{ONa}{C}C_6H_2(CH_3)_3 \quad (CH_3)_3C_6H_2\underset{C_6H_5COO}{C}{=}\underset{OCOC_6H_5}{C}C_6H_2(CH_3)_3$$

XVI XVII

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[11] Weitz and Scheffer, *Ber.*, **54**, 2327 (1921).

In these three mesitylenic ketones the sole effect of the two methyl groups in the diortho positions is a hindrance to reactions that involve addition to the carbon atom which is in direct union with the mesityl group. The diortho substitution neither promotes nor hinders enolization of alkyl mesityl ketones and it does not affect the chemical properties of the enolates formed from these ketones. It also interferes neither with addition to the oxygen of the carbonyl group nor with 1,4-addition to the two oxygen atoms in α-diketones. In general the hindrance is adequate to prevent all reactions involving addition to the alpha carbon atom excepting, possibly, reduction; but it may be overcome, in part, by the action of a carbonyl group in the alpha position.

Experimental

I. Acetomesitylene

In the quantitative study of the reaction between acetomesitylene and organic magnesium compounds described in an earlier paper[12] the reagent as usual was methylmagnesium iodide. In the present work a standard quantity of the bromomagnesium enolate of acetomesitylene was made by adding an ethereal solution of 10 g. of acetomesitylene, drop by drop, to a solution of ethylmagnesium bromide which had been prepared from 2.2 g. of magnesium, and warming until gas was no longer evolved. The enolate began to crystallize by the time half of the ketone had been added and at the end most of it had separated as a fine white crystalline powder. The suspension obtained in this manner was employed in the subsequent operations.

Acetylation. Diacetyl-2,4,6-trimethylbenzoylmethane (IV).—An ethereal solution of 8 g. of acetyl chloride was added slowly to the suspension of the enolate. An olive-green color developed in the solution and a thick paste accumulated on the bottom of the flask. After heating for half an hour the magnesium derivatives were decomposed with iced acid and the organic products collected in ether in the usual manner. When the ethereal solution was shaken with excess of saturated aqueous copper acetate, it assumed the rich dark blue color of the copper derivative of the triketone, which is surprisingly soluble in ether, but which was precipitated as a blue-gray powder by addition of petroleum ether. The washed and dried powder was recrystallized from ether, from which it separated in dark blue crystals.

Anal. Calcd. for $(C_{15}H_{17}O_3)_2Cu$: C, 65.0; H, 6.2; Cu, 11.5. Found: C, 64.2; H, 6.5; Cu, 11.4.

For the purpose of isolating the triketone the copper derivative, which is insoluble in water, was warmed with moderately concentrated hydrochloric acid until it was completely disintegrated. The colorless ethereal extract of the resulting liquid was washed, dried, concentrated to small volume and finally diluted with petroleum ether. It deposited crystals which after recrystallization from ether and petroleum ether melted at 66–67°.

Anal. Calcd. for $C_{15}H_{18}O_3$: C, 73.2; H, 7.3. Found: 73.6; H, 7.2.

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[12] Kohler, Fuson and Stone, THIS JOURNAL, **49**, 3181 (1927).

In another experiment the suspension of the enolate was siphoned slowly into a large excess of acetyl chloride dissolved in ether. The product was collected in ether in the usual manner and, after removing the ether, distilled under diminished pressure. Acetomesitylene distilled first, then the temperature rose rapidly to the boiling point of the diacetyl derivative. The distillate solidified and the solid melted at 64–66°—sufficient evidence that no other products had been formed.

The triketone is insoluble in sodium bicarbonate solution, readily soluble in sodium carbonate. When it was examined quantitatively in the "machine"[13] it liberated one mole of methane and consumed three moles of methylmagnesium iodide.

Benzoylation. Dibenzoyl-2,4,6-trimethylbenzoylmethane (VI).—An ethereal solution of 13 g. of benzoyl chloride was added slowly to the usual suspension of the enolate. It precipitated a gray-green gummy magnesium derivative which on treatment with iced hydrochloric acid changed to a colorless crystalline solid. The weight of the solid was 9 g. and the mother liquor on distillation with steam gave 5 g. of acetomesitylene, making a total yield of about 85%. The solid was purified by recrystallization from acetone.

Anal. Calcd. for $C_{25}H_{22}O_3$: C, 81.1; H, 6.0. Found: C, 81.4; H, 6.0.

The dibenzoyl derivative is moderately soluble in benzene and in acetone, sparingly soluble in ether and in alcohol, insoluble in petroleum ether. It crystallizes in stout prisms and it melts at 192°. Its copper derivative was obtained by shaking a solution in benzene with saturated aqueous copper acetate. It is sparingly soluble in most organic solvents, forming solutions which are olive green in color except in the case of benzene where the solution is yellow or brown. It separates from benzene in minute olive-green prisms.

Anal. Calcd. for $C_{50}H_{47}O_6Cu$: C, 74.8; H, 5.3; Cu, 7.9. Found: C, 75.3; H, 5.0; Cu, 7.9.

Reaction with *p*-Toluene Sulfone Chloride: Di-2,4,6-trimethylbenzoylethane (VII).—An ethereal solution of 17.5 g. of *p*-toluene sulfone chloride was added to the usual suspension of the enolate. It reacted vigorously, the solution became pink in color and deposited a crimson solid. The organic products of the reaction were collected in ether in the usual manner. From the ethereal solution sodium carbonate extracted *p*-toluene sulfinic acid, which was identified by comparison with a sample on hand. The extracted solution, on concentration, yielded a solid which melted at 138–139°, the melting point of the ethane reported by Conant and Lutz.[14]

Anal. Calcd. for $C_{22}H_{26}O_2$: C, 82.0; H, 8.2. Found: C, 81.6; H, 8.6.

Reaction with Ethyl Chlorocarbonate: 2,4,6-Trimethylbenzoylmalonic Ester (VI).—An ethereal solution of 7 g. of the chloro compound was added to the usual suspension of the enolate. The reaction was vigorous but the solution remained clear. It was boiled for half an hour, then treated with ice water and a very small quantity of sodium carbonate. The resulting magnesium derivative was thoroughly washed with water and ether, then repeatedly recrystallized from aqueous alcohol, and finally recrystallized from benzene. It then melted at 147°.

Anal. Calcd. for $Mg(C_9H_{11}COC(CO_2C_2H_5)_2)_2$: C, 64.4; H, 6.6; Mg, 3.8. Found: C, 64.2; H, 6.5; Mg, 4.2.

The composition showed that this substance must be the magnesium derivative of trimethylbenzoylmalonic ester, and this conclusion was confirmed by an ethoxyl determination which gave a value of 25.9 instead of 28.4, calculated for two ethoxyl

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[13] Kohler and Richtmyer, THIS JOURNAL, **52**, 3736 (1930).

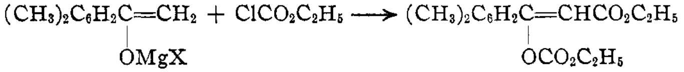
[14] Conant and Lutz, *ibid.*, **45**, 1303 (1923).

groups. All attempts to obtain the free ester were unsuccessful because all methods that we could devise for removing the magnesium led to the loss of one of the ester groups and resulted in the formation of 2,4,6-trimethylbenzoylacetic ester.

2,4,6-Trimethylbenzoylacetic Ester, $(CH_3)_3C_6H_2COCH_2CO_2C_2H_5$.—An attempt to prepare this ketonic ester by Claisen's general method,[15] namely, by the action of trimethylbenzoyl chloride on sodium acetoacetic ester, was unsuccessful, the only product being the ethyl ester of mesityl carbonic acid—a liquid which boiled at 139–141° (20 mm.).

Anal. Calcd. for $C_{12}H_{16}O_2$: C, 75.0; H, 8.4. Found: C, 74.8; H, 8.3.

Having failed to secure the ketonic ester by general methods, we proceeded to prepare it by means of the reaction between chlorocarbonic ester and the magnesium enolate of acetomesitylene. To this end we operated with sufficient quantities to enable us not only to isolate the magnesium derivative, but also to separate the liquid products by distillation. From 50 g. of acetomesitylene we obtained 25 g. of pure magnesium derivative, and a liquid which by distillation under diminished pressure was separated into 16.5 g. of acetomesitylene and 10 g. of 2,4,6-trimethylbenzoylacetic ester. The presence of this relatively large quantity of the ketonic acetic ester in the liquid suggests the possibility that in the case of chlorocarbonic ester a part of the product may be formed in accordance with the equation

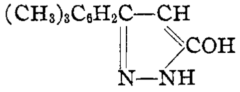


$$(CH_3)_2C_6H_2\underset{\displaystyle OMgX}{\underset{|}{C}}{=}CH_2 + ClCO_2C_2H_5 \longrightarrow (CH_3)_2C_6H_2\underset{\displaystyle OCO_2C_2H_5}{\underset{|}{C}}{=}CHCO_2C_2H_5$$

The ketonic ester, whether obtained from the liquid products or by the acidification of the pure magnesium derivative of 2,4,6-trimethylbenzoylmalonic ester, was a pale yellow liquid which boiled at 150° (11 mm.).

Anal. Calcd. for $C_{14}H_{18}O_2$: C, 71.8; H, 7.7. Found: C, 71.7; H, 7.8.

3-Mesityl-pyrazolone-5:



.—Diortho substitution evidently interferes in no way with the common condensation reactions of beta ketonic esters because trimethylbenzoylacetic ester reacted readily with an alcoholic solution of hydrazine. The product, which separated in very pale yellow plates, was purified by recrystallization from absolute alcohol. It decomposed, without melting, at 290–300°.

Anal. Calcd. for $C_{12}H_{14}ON_2$: C, 71.3; H, 7.0; N, 13.9. Found: C, 71.1; H, 7.2; N, 14.1.

The pyrazolone likewise gave no indication that its properties were in any way affected by the mesityl group. It was readily condensed with benzaldehyde, forming 3-mesityl-4-benzal-pyrazolone-5—yellow plates which decomposed at about 280°.

Anal. Calcd. for $C_{19}H_{18}N_2O$: C, 78.6; H, 6.2. Found: C, 78.2; H, 6.2.

Enolization of 2,4,6-Trimethylbenzoylacetic Ester.—The enol content was determined by the Kurt Meyer method both in the equilibrium ester and in alcoholic solutions which had been kept until they had attained equilibrium. In the case of the equilibrium ester six determinations, made with two different samples, gave a mean value of 24.5%, the maximum deviation from the mean being 0.7%. The alcoholic solutions gave a somewhat higher value—five determinations giving a mean value of 27.3% with a maximum deviation of 0.6%.

Behavior of the Enolate of Acetomesitylene toward Oxygen and Carbon Dioxide.—Oxygen free from moisture and carbon dioxide was passed through a suspension of the

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[15] Claisen, *Ann.*, **291**, 65 (1896).

enolate without producing any effect, subsequent hydrolysis yielding only unchanged acetomesitylene. Carbon dioxide on the other hand manifestly changed the appearance of the magnesium compound, and subsequent addition of acetyl chloride failed to effect acetylation. It was not possible, however, to isolate a carbonated product. When the curdy precipitate which was formed by passing the gas through the usual suspension of the enolate was decomposed with acid it evolved carbon dioxide; the ethereal solution contained nothing that could be extracted with bases, and when the residue, left after removing the ether, was distilled with steam it yielded 9.0 g. of acetomesitylene.

II. Dimesityl Ketone

Dimesityl ketone can be prepared without much difficulty both by the action of trimethylbenzoyl chloride on mesitylene in the presence of aluminum chloride and by the action of mesitylmagnesium bromide on the same acid chloride. We prefer the second method because it yields a product which can be purified without distillation. Inasmuch as the steps leading from mesitylene to mesitylmagnesium bromide have since been published it is unnecessary to describe them here. Mesitylene carbonic acid is most easily obtained by passing carbon dioxide into a solution of mesitylmagnesium bromide, and it is most easily converted into its chloride by means of thionyl chloride. Our yields were as follows.

After passing carbon dioxide through a solution of mesitylmagnesium bromide, prepared from 360 g. of the bromide, for twenty-five hours we isolated 211 g. of mesitylene carbonic acid and recovered 64 g. of mesitylene, the amount of acid corresponding almost exactly to the amount of active magnesium compound found by titration. The acid, on treatment with 250 g. of thionyl chloride, yielded 173 g. of acid chloride boiling at 102–104° (1 mm.). The acid chloride was added slowly to a solution of the magnesium compound prepared from 280 g. of mesityl bromide and 34 g. of magnesium. The reaction was vigorous and a red-purple color appeared in the solution. When the solution was decomposed with iced acid, most of the product separated as a solid, the ethereal layer containing, mainly, mesitylene, mesityl bromide and mesityl carboxylic acid which were recovered. The yield of solid ketone was 149 g. It was recrystallized from a benzene–alcohol mixture.

Anal. Calcd. for $C_{19}H_{22}O$: C, 85.6; H, 8.3. Found: C, 85.3; H, 8.5.

Dimesityl ketone crystallizes in stout needles or prisms. It melts at 136–137° and it boils at 200° (2 mm.). It is very soluble in benzene, moderately soluble in boiling alcohol and sparingly soluble in ether. It was recovered *in toto*, both after prolonged boiling with a strongly alkaline alcoholic solution of hydroxylamine, and after it had been heated for five hours to 150–170° in a sealed tube with alcoholic hydroxylamine hydrochloride.

Reduction with Sodium in Alcohol.—To a solution of 10 g. of the ketone in 100 cc. of boiling alcohol, 10 g. of sodium was added, piece by piece, the solution being heated toward the end when the reaction was no longer sufficiently vigorous to cause boiling. The solution was saturated with carbon dioxide, concentrated and gradually diluted with water. It yielded 9.6 g. of a crystalline solid melting at 149°.

Reduction with Sodium Amalgam.—Pure 0.5% sodium amalgam was prepared from distilled mercury and sodium. To 440 g. of this amalgam were added in succession 100 cc. of boiling alcohol and 10 g. of the ketone. The reaction was vigorous at the outset but there was no appreciable escape of hydrogen. The solution was boiled for four hours, then decanted and manipulated as in the preceding experiment. Here also the yield was quantitative and the product melted at 149–150°.

Dimesityl Carbinol (X).—The product obtained from the two preceding experiments was purified by recrystallization from alcohol and also from benzene and petroleum ether.

Anal. Calcd. for $C_{19}H_{24}O$: C, 85.1; H, 9.0. Found: C, 84.6; H, 9.2.

In freezing benzene the molecular weight was found to be 296 instead of 268 calcd.

The carbinol crystallizes in small prisms and it melts at 150°. At 60° it reduces a solution of chromic acid in glacial acetic acid and reverts to the ketone. In the "machine" it consumes one mole of gas and liberates one mole of methane.

The Benzoate (XII).—A suspension of two grams of the carbinol and 5 g. of benzoyl chloride in 40 cc. of 10% aqueous sodium hydroxide was warmed on a steam-bath and then left overnight. The resulting solid was collected on a filter, washed, dried and recrystallized from petroleum ether. It separated in needles and melted at 154°.

Anal. Calcd. for $C_{26}H_{28}O_2$: C, 81.5; H, 7.4. Found: C, 81.4; H, 7.6.

Reduction, Dimesitylmethane (XI).—A suspension of 5 g. of dimesityl carbinol and an equal weight of red phosphorus in 50 cc. of constant boiling hydriodic acid was boiled for twenty-five hours. Most of the acid was then removed by distillation. The residue was extracted with ether, the extract washed, dried and allowed to evaporate slowly. The resulting solid softened at 130°, then melted at 135°.

Anal. Calcd. for $C_{19}H_{24}$: mol. wt., 252; C, 90.4; H, 9.6. Found: mol. wt., 234; C, 90.6; H, 10.1.

The analytical values indicated dimesitylmethane and the product was completely identified by comparison with a sample that was synthesized by Baeyer's method.[16]

Action of the Combination, Magnesium + Magnesium Iodide on the Ketone.—In a 100-cc. globular flask 3 g. of powdered magnesium was mixed with 8 g. of iodine. A little benzene and some absolute ether were added and also, after the reaction between the metal and the halogen had subsided, 10 g. of dimesityl ketone in absolute ether. The air in the flask was displaced by boiling off a part of the ether and then the flask was securely stoppered. A royal-purple color developed rapidly and when the flask was cooled in a freezing mixture purple-black crystals separated from the solution.

As soon as the reaction appeared to be complete, the flask was warmed again, the stopper removed and the solution poured rapidly into ammonium chloride solution. The organic products were collected in ether, and the washed and dried ethereal solution was concentrated in a current of air. It left a solid from which 4.0 g. of pure dimesityl ketone and 3.5 g. of pure carbinol were separated, and an oil that could not be crystallized further.

Action of Sodium on the Ketone in Benzene.—A large excess of sodium in the form of wire was added to a solution of 10 g. of the ketone in 100 cc. of benzene. A blue-green color developed and rapidly became so dark as to make the liquid opaque. The mixture was shaken mechanically for about sixteen hours, and the solution was then decanted into water. The benzene layer was washed, dried and concentrated. It deposited 10 g. of a colorless crystalline product. This was partially separated into pure ketone and pure carbinol—further fractional crystallization being abandoned when it became evident that no other substances could be present in the mixture.

III. Dimesityl Diketone XIII

The diketone is extremely difficult to secure. After trying a great many methods which appeared feasible, but were not, we finally prepared it by the

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[16] Baeyer, *Ber.*, **5**, 1908 (1873).

action of mesitylmagnesium bromide on mesityl glyoxylic ester. The procedure was as follows.

To a solution of the magnesium compound prepared from 50 g. of mesityl bromide, 25 g. of mesityl glyoxylic ester was added drop by drop and then 100 cc. of benzene. The mixture was distilled until its boiling point rose to 75° and then heated at this temperature for three hours. The mixture was decomposed in the usual manner with iced acid. The benzene layer was first freed from mesityl glyoxylic acid by extraction with sodium carbonate, then washed, dried and distilled fractionally under diminished pressure. It was thus separated into mesitylene, mesityl glyoxylic ester, dimesityl, dimesityl diketone and some higher boiling yellow oil. The diketone fraction boiling at about 200° (6 mm.) partially solidified when it was diluted with methyl alcohol. The total yield of pure diketone obtained from this and higher fractions was 3 g. The substance was purified by recrystallization from methyl alcohol.

Anal. Calcd. for $C_{20}H_{22}O_2$: mol. wt., 294; C, 81.5; H, 7.5. Found: mol. wt., 289; C, 81.5; H, 7.7.

The diketone is much more highly colored than most other aromatic α-diketones, crystallizing in golden yellow plates that melt at 122°. It is moderately soluble in most organic solvents including petroleum ether.

Reduction. Mesityl-acetomesitylene (XIV).—The reduction of the diketone is much more difficult than is that of benzil. Zinc and acetic acid—Clemmensen combination of amalgamated zinc and concentrated hydrochloric acid—and catalytic hydrogenation were tried without success, the diketone being recovered in each case. The substance is, however, slowly attacked by zinc and alkali. A mixture composed of 0.5 g. of the diketone, 10 cc. of alcohol, 2 cc. of water, 1 g. of potassium hydroxide and 2.5 g. of zinc dust was boiled for thirty-six hours, at the end of which time it was light brown in color. It was then freed from alcohol and extracted with ether. The ethereal extract, on concentration, first deposited 0.3 g. of diketone, then a mixture from which 0.04 g. of a white crystalline compound was finally isolated by systematic fractional crystallization. The desoxy compound is moderately soluble in alcohol, sparingly soluble in ether. It melts at 141°.

Anal. Calcd. for $C_{20}H_{24}O$: C, 85.7; H, 8.6. Found: C, 85.8; H, 8.7.

Oxidation.—A solution of sodium hydrogen peroxide obtained by dissolving sodium peroxide in ice water was added to a solution of 0.02 g. of the diketone in methyl alcohol. The mixture was digested on a steam-bath for an hour, then cooled and extracted with ether. The ethereal extract contained some unchanged diketone, but the aqueous layer on acidification yielded 0.015 g. of mesitylene carboxylic acid.

Action of Alkali.—An aqueous alcoholic solution containing 0.25 g. of the diketone and 0.4 g. of water was heated for an hour, alcohol being added from time to time to maintain solution. Under these conditions benzil reacts rapidly but the diketone was not affected. Even fused potassium hydroxide failed to effect a benzilic acid rearrangement. Thus 1.3 g. of potassium hydroxide and 0.6 g. of water were heated in a porcelain crucible until most of the water had evaporated. After the addition of 0.2 g. of the diketone, the heating was continued but the molten substance failed to dissolve in the alkali and when the brown melt was cooled nearly all of the diketone was recovered by treatment with water and ether.

The Monoxime (XV).—All attempts to prepare a quinazine derivative by treating the diketone with ortho phenylenediamine were unsuccessful, as were also all attempts to prepare a dioxime. The monoxime, however, could be obtained without much difficulty. For this purpose a solution of 0.55 g. of potassium hydroxide and 0.45 g. of hydroxylamine hydrochloride in a little water was added to a solution of 0.3 g. of the diketone in 10 cc. of alcohol. The mixture was boiled for nine hours, then diluted and made feebly acidic. It deposited a colorless solid which, after crystallization from carbon bisulfide, and finally from ether–petroleum ether, melted at 209–210°. The yield of crude product was 0.23 g.

Anal. Calcd. for $C_{20}H_{25}O_2N$: C, 77.6; H, 7.5. Found: C, 77.9; H, 7.5.

Beckmann Rearrangement.—In order to determine whether the substance was really an oxime, 0.07 g. of the pure material was heated with formic acid for four hours, then diluted and extracted with ether. From the ethereal extract sodium bicarbonate removed 0.05 g. of mesitylene carbonic acid, and the ether, on evaporation, left 0.01 g. of unchanged oxime. In configuration, the substance, therefore, corresponds to the alpha oxime of benzil.

Reaction of the Diketone with Sodium.—A suspension of 0.1 g. of sodium in a solution of 0.65 g. of the diketone in 15 cc. of dry toluene was boiled in a current of pure nitrogen. The solution first turned brown in color, then deposited a brown solid. After two hours, 0.7 g. of benzoyl chloride was added. No reaction was apparent in the cold but when the mixture was heated the brown solid disappeared rapidly and the solution became yellow, the color being due to unchanged ketone which remained because the first reaction had not been carried to completion. The solution was decanted from the unused metal, freed from sodium chloride by filtration and evaporated.

The residue was a mixture of unchanged diketone and a colorless product. The mixture was separated by fractional crystallization from ether–petroleum ether.

Anal. Calcd. for $C_{34}H_{32}O_4$: C, 81.3; H, 6.4. Found: C, 81.4; H, 6.3.

Hexamethyl Isobenzil (XVII).—The dibenzoate obtained as described in the foregoing account is insoluble in petroleum ether, sparingly soluble in methyl and in ethyl alcohol, readily soluble in benzene and in ether. It crystallizes in needles and it melts at 190°. Like isobenzil it is readily hydrolyzed with alcoholic alkalies but the process is accompanied by oxidation and the products are benzoic acid and the diketone instead of benzoic acid and hexamethylbenzoin. Thus, using the method of Klinger and Standke,[17] 0.2 g. of powdered potassium hydroxide was added to a solution of 0.15 g. of the dibenzoate in 10 cc. of hot alcohol. The solution became yellow immediately. It was warmed for a few minutes, then cooled in a freezing mixture, whereupon it deposited the yellow plates of the diketone. The yield of diketone was practically quantitative and benzoic acid was isolated from the filtrates.

Summary

The results of a study of three mesitylenic ketones, acetomesitylene, dimesityl ketone and dimesityl diketone, show that the two methyl groups in the di-ortho positions affect only those reactions which involve addition to the carbon atom that is in direct union with the mesityl group. These methyl groups neither promote nor hinder the enolization of acetomesitylene, trimethylbenzoylacetic ester and similar substances. They also do not interfere with reactions which involve only addition to the oxygen of the carbonyl group.

In general the hindrance is adequate to prevent all addition reactions that involve the alpha carbon atom excepting reduction; but it may be overcome, in part, by another carbonyl group in the alpha position.

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[17] Klinger and Standke, *Ber.*, **24**, 1264 (1891).