

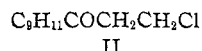
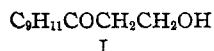
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

The Condensation of Paraformaldehyde with Aromatic Ketones. II.¹ Mesityl Ketones

BY REYNOLD C. FUSON, W. E. ROSS AND C. H. MCKEEVER²

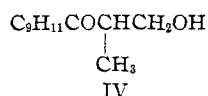
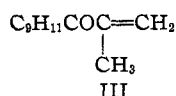
Acetophenone and propiophenone react with paraformaldehyde under suitable conditions to give simple derivatives.¹ To investigate the influence of steric hindrance on this type of condensation we have treated acetomesitylene, propiomesitylene and isobutyromesitylene with paraformaldehyde in excess. The reactions were carried out in methyl or ethyl alcohol solutions, potassium carbonate being used as the catalyst.

Acetomesitylene in contrast with acetophenone gave a monomethylol derivative, β -(2,4,6-trimethylbenzoyl)-ethyl alcohol (I). When the reaction was allowed to continue for four days at room temperature a 75% yield of the monomethylol derivative (I) was obtained along with small amounts of a solid melting at 107° whose structure will be discussed at a later point. The



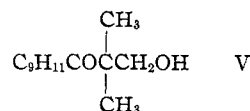
structure of I was established by oxidation which converted the substance into 2,4,6-trimethylbenzoylformic acid. Also, by the action of hydrogen chloride the keto alcohol was transformed into the corresponding chloro ketone (II). Treatment of the alcohol with benzoyl chloride or phenyl isocyanate failed to yield solid derivatives. Apparently dehydration occurred since the products were resinous.

Propiomesitylene reacted with paraformaldehyde much more sluggishly than did acetomesitylene. When the reaction mixture was refluxed for twenty-four hours there was obtained a 70% yield of a liquid whose composition and chemical behavior corresponded to those expected for isopropenyl mesityl ketone (III). In no case was any of the monomethylol derivative (IV) isolated; apparently as with propiophenone the monomethylol compound is formed but with the hindered ketone is less stable and undergoes dehydration. The structure of III was estab-



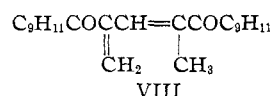
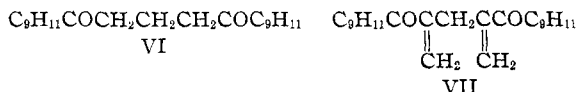
lished by reducing the compound to isobutyromesitylene which in turn was converted to the dinitro derivative. The latter was identified by means of a mixed melting point with an authentic specimen.

Isobutyromesitylene condensed with paraformaldehyde still more slowly than did acetomesitylene or propiomesitylene. After the reaction mixture had been refluxed for two days about 40% of the ketone was recovered unchanged. Under these conditions the monomethylol derivative, β -(2,4,6-trimethylbenzoyl)-isobutyl alcohol (V), was formed in yields of about 40%. It yielded a phenylurethan.



Interest in the solid by-product (m. p. 107°) formed in the reaction between acetomesitylene and paraformaldehyde was enhanced by the discovery that when formalin was used and sodium hydroxide employed as the catalyst the solid became a principal product of the reaction. Under these conditions it formed in yields of about 35% along with much resinous material.

The molecular weight of the solid proved to be approximately twice that of the simple monomethylol derivative and suggested that acetomesitylene had condensed with formaldehyde in the dimolecular manner characteristic of many active methylene compounds. This surmise was confirmed by the discovery that 1,3-di-(2,4,6-trimethylbenzoyl)-propane (VI) also reacted with paraformaldehyde to give the unknown solid. By analogy with propiomesitylene the diketone would be expected to yield 2,3-di-(2,4,6-trimethylbenzoyl)-1,4-pentadiene (VII) or 2,3-di-(2,4,6-trimethylbenzoyl)-1,3-pentadiene (VIII). The structure VIII having the higher degree of con-



(1) For the first paper of this series see Fuson, Ross and McKeever, *THIS JOURNAL*, **60**, 2935 (1938).

(2) Röhm and Haas Research Assistant.

jugation appeared to be the more probable of the two. In the presence of nickel the compound absorbed two moles of hydrogen, thus showing that it contains two olefinic bonds.

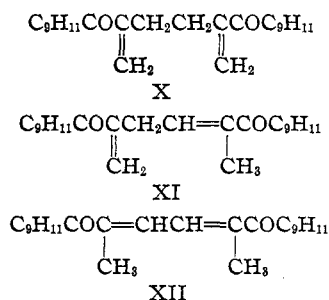
The most convincing evidence in favor of the unsymmetrical structure is that the substance yields a dibromo rather than a tetrabromo derivative when treated with bromine in a solution of carbon tetrachloride. This is the more striking in view of the observation that treatment of the dibromo derivative with sodium iodide reconverted it to the original unsaturated diketone. This shows that in the bromine derivative the bromine atoms are on adjacent carbon atoms, *i. e.*, that only one of the olefinic linkages was involved in the addition of bromine. The fact that one of the ethylenic linkages absorbed bromine while the other did not is best explained on the basis of the unsymmetrical structure (VIII).

When treated with acetyl chloride in the presence of zinc chloride the unsaturated compound reacted additively, taking up two moles of the acid chloride. Presumably these added to the olefinic linkages.

Nitration of the pentadiene gave a tetranitro derivative whose structure was not studied further.

Hydrogenation gave the expected saturated diketone, 2,4-di-(2,4,6-trimethylbenzoyl)-pentane. This compound was isolated as an unstable solid which changed spontaneously to an oil. The solid appears to be the enediol form of the ketone. It is being subjected to extended study.

1,4-Di-(2,4,6-trimethylbenzoyl)-butane (IX) was found to react with paraformaldehyde in a similar manner. In this instance the structure of the product may be X, XI or XII. The most



highly conjugated structure (XII) would seem to be the most probable; however, the structure of the compound has not been investigated.

Experimental

Treatment of Acetomesitylene with Paraformaldehyde.—A mixture of 81 g. of acetomesitylene, 45 g. of para-

formaldehyde, 200 cc. of methyl alcohol and 5 g. of potassium carbonate was shaken at room temperature for four days. It was then poured into 1 liter of water acidified with hydrochloric acid, and the mixture extracted with four 100-cc. portions of benzene. The combined benzene solutions were washed several times with water, the benzene distilled under reduced pressure and the residue fractionally distilled. A yield of 68 g. was obtained of a liquid boiling at 132–135° (4 mm.). The composition and properties of this compound corresponded with those expected for β -(2,4,6-trimethylbenzoyl)-ethyl alcohol (I).

Anal. Calcd. for $\text{C}_{12}\text{H}_{16}\text{O}_2$: C, 74.94; H, 8.39. Found: C, 74.59; H, 8.30.

The alcohol reduced boiling Benedict's solution and gave a silver mirror with Tollens' reagent. Treatment with phenyl isocyanate gave *sym*-diphenylurea but no urethan. Benzoyl chloride also caused dehydration and gave benzoic acid and a small amount of resin.

The residue remaining after the distillation of the alcohol deposited crystals when allowed to stand for several days. After recrystallization from ethyl alcohol these melted at 107°. This compound proved to be 2,4-di-(2,4,6-trimethylbenzoyl)-2,4-pentadiene (VIII) described more fully at a later point.

Oxidation of β -(2,4,6-Trimethylbenzoyl)-ethyl Alcohol.

—One gram of the alcohol was shaken with 100 cc. of a 1% potassium permanganate solution containing chipped ice. After five minutes ethyl alcohol was added to reduce any excess permanganate. The mixture was filtered the filtrate acidified with hydrochloric acid and extracted with three 10-cc. portions of benzene. Evaporation of the benzene left a solid which when recrystallized from carbon tetrachloride melted at 117–118°. A mixed melting point determination showed it to be 2,4,6-trimethylbenzoylformic acid.

β -(2,4,6-Trimethylbenzoyl)-ethyl Chloride.—Twenty grams of β -(2,4,6-trimethylbenzoyl)-ethyl alcohol was shaken for twenty-four hours with 200 cc. of concentrated hydrochloric acid. The mixture was extracted with three 50-cc. portions of benzene, the combined extracts washed twice with water and the solvent evaporated. Distillation of the residue under diminished pressure gave 16 g. of the chloride; b. p. 137–139° (3 mm.).

Anal. Calcd. for $\text{C}_{12}\text{H}_{15}\text{OCl}$: Cl, 16.83. Found: Cl, 16.61.

The chloride readily loses hydrogen chloride. If a small amount is heated with water, the water becomes acidic and gives a precipitate with silver nitrate.

The Action of Paraformaldehyde on Propiomesitylene.

—A mixture of 18 g. of propiomesitylene, 3.5 g. of paraformaldehyde, 1 g. of potassium carbonate and 50 cc. of ethyl alcohol was refluxed on a steam cone for thirty hours. It was then poured into 300 cc. of water, acidified with dilute hydrochloric acid and extracted with three portions of ether. The ether extracts were washed with several portions of water and dried over anhydrous sodium sulfate. The product, which distilled at 90–95° (3 mm.), weighed 14 g. This compound absorbed bromine very readily with no evolution of hydrogen bromide, and also decolorized a potassium permanganate solution.

Anal. Calcd. for $\text{C}_{13}\text{H}_{16}\text{O}$: C, 82.92; H, 8.6. Found: C, 83.26; H, 8.83.

Reduction of Isopropenyl Mesityl Ketone (III).—Five and two-tenths grams of the ketone was dissolved in 150 cc. of ethyl alcohol. A small amount of Raney nickel was added and the compound reduced at room temperature under a pressure of two atmospheres. The reduction period was thirty minutes. The mixture was filtered, the ethyl alcohol evaporated and the resulting oil distilled. There was obtained 4 g. of material boiling at 107–110° (5 mm.).

Nitration of the Reduction Product.—One cubic centimeter of the reduction product was added very slowly to 10 cc. of fuming nitric acid at 0°. The mixture was allowed to stand for five minutes, then poured on ice. A white precipitate formed immediately. It crystallized from ethyl alcohol in the form of large white plates; m. p. 138–139°. A mixed melting point with an authentic sample of dinitroisobutyromesitylene showed no depression.

Action of Paraformaldehyde with Isobutyromesitylene.—A mixture of 19 g. of isobutyromesitylene, 3.4 g. of paraformaldehyde, 1 g. of potassium carbonate and 60 cc. of ethyl alcohol was refluxed for fifty hours. It was worked up as indicated in the case of propiomesitylene. There was recovered 8 g. of isobutyromesitylene and 8.4 g. of β -(2,4,6-trimethylbenzoyl)-isobutyl alcohol (V) boiling at 153° (7 mm.).

Anal. Calcd. for $C_{14}H_{20}O_3$: C, 76.36; H, 9.09. Found: C, 76.21; H, 9.06.

Preparation of the Urethan.—One-half cubic centimeter of the oil (V) obtained from the above reaction was mixed with 0.3 cc. of phenyl isocyanate, and allowed to stand overnight. To the mixture was added 3 cc. of carbon tetrachloride. After the solution had remained at 0° for fifteen minutes crystals formed. They were recrystallized three times from ethyl alcohol; m. p. 116–116.5°.

Anal. Calcd. for $C_{21}H_{26}O_3N$: N, 4.13. Found: N, 4.35.

Preparation of 2,4-Di-(2,4,6-trimethylbenzoyl)-2,4-pentadiene (VIII).—A mixture of 32 g. of acetomesitylene, 10 g. of sodium hydroxide and 100 cc. of methyl alcohol was placed in a flask equipped with an efficient stirrer. Fifty grams of 40% formalin was added dropwise over a period of forty minutes. The solution became quite warm and after about an hour a light yellow precipitate started to form. After twenty hours stirring the mixture was poured into cold water and acidified with dilute hydrochloric acid. In a few minutes a white gummy material precipitated. It was separated, washed several times with water and dissolved in warm methyl alcohol. After three hours the pentadiene (VIII) started to precipitate as long hexagonal crystals. It was recrystallized from methyl alcohol; m. p. 107°. The yield was 13 g. The remaining material was a very viscous oil which would not distil or crystallize.

Anal. Calcd. for $C_{28}H_{38}O_2$: C, 83.3; H, 7.77; mol. wt., 360. Found: C, 83.21, 83.15; H, 7.83, 7.77; mol. wt., (Rast) 378, (in boiling chloroform) 370.

Preparation of 1,3-Di-(2,4,6-trimethylbenzoyl)-propane (VI).—A mixture of 22 g. of glutaric acid and 60 g. of thionyl chloride was allowed to stand at room temperature for ten hours. The excess thionyl chloride was removed at diminished pressure. The acid chloride was added

dropwise to a well-stirred mixture of 75 g. of mesitylene, 67 g. of aluminum chloride and 200 cc. of carbon disulfide. After the reaction mixture had been stirred for an additional three hours, it was decomposed with ice and hydrochloric acid. The carbon disulfide was evaporated and the excess mesitylene removed by steam distillation. The mixture was extracted with several portions of warm benzene, the benzene extracts washed with warm water and the benzene removed at reduced pressure. The light brown crystalline residue was recrystallized twice from methyl alcohol. The yield was 42.5 g. of white plates; m. p. 132–133°.

Anal. Calcd. for $C_{28}H_{38}O_2$: C, 82.09; H, 8.3. Found: C, 82.1; H, 8.46.

The Action of Paraformaldehyde on 1,3-Di-(2,4,6-trimethylbenzoyl)-propane.—A mixture of 10 g. of the diketone, 1.9 g. of paraformaldehyde, 0.1 g. of potassium carbonate and 60 cc. of ethyl alcohol was refluxed for ten hours, then poured into 100 cc. of ice water and acidified with dilute hydrochloric acid. In a few minutes a voluminous precipitate formed. The mixture was filtered and the solid crystallized from methyl alcohol. There was obtained 5 g. of long hexagonal crystals; m. p. 107°. A mixed melting point with the compound made from acetomesitylene showed no depression.

Reduction of 2,4-Di-(2,4,6-trimethylbenzoyl)-2,4-pentadiene (VIII).—Five grams of the pentadiene (VIII) was dissolved in 200 cc. of ethyl alcohol. A small amount of Raney nickel was added and the reduction allowed to proceed for two hours at room temperature at a pressure of two atmospheres. Two moles of hydrogen were absorbed. The reaction mixture was filtered and the ethyl alcohol removed at diminished pressure. The residue was a white solid. When this crude material was warmed to remove the last traces of alcohol it changed to a light yellow viscous oil. The oil was distilled at diminished pressure in a nitrogen atmosphere. There was obtained a small amount of material boiling at 180–190° (4 mm.) and 3 g. of a compound boiling at 225–230° (5 mm.). The latter on redistillation boiled at 228–230° (4 mm.).

Anal. Calcd. for $C_{28}H_{38}O_2$: C, 82.42; H, 8.79. Found: C, 82.16; H, 8.56.

In a subsequent reduction 5 g. was reduced as in the above procedure but the reaction mixture worked up differently. The alcoholic solution of the reduced compound was poured on ice and then extracted with two large portions of ice cold ether. The ether was evaporated at 0° as rapidly as possible. There remained 4 g. of a white solid which after washing with several portions of low-boiling petroleum ether melted at 100–105°. In attempts at recrystallization from methyl alcohol, ethyl alcohol, high-boiling petroleum ether or ether-petroleum ether mixture only an oil was obtained. The solid on standing twenty-four hours at room temperature changed completely to an oil. If the solid was kept at the temperature of dry ice it showed no tendency to change to the oil. After prolonged exposure to air the oil deposited crystals which when pure melted at 151°. A mixed melting point determination showed them to be 2,4,6-trimethylbenzoic acid.

Addition of Bromine to 2,4-Di-(2,4,6-trimethylbenzoyl)-2,4-pentadiene (VIII).—One-half gram of the pentadiene

(VIII) was dissolved in 10 cc. of carbon tetrachloride. A 20% solution of bromine in carbon tetrachloride was added very slowly at room temperature until there was no further absorption of bromine. The carbon tetrachloride was evaporated at room temperature and the light yellow residual oil was crystallized from methyl alcohol by scratching and cooling in a dry-ice-acetone bath. There was obtained after three crystallizations from methyl alcohol 0.5 g. of a compound; m. p. 108.5–109.5°.

Anal. Calcd. for $C_{25}H_{28}O_2Br_2$: C, 57.69; H, 5.38. Found: C, 57.87; H, 5.42.

The Reaction of Sodium Iodide with the Dibromo Derivative.—Three-tenths gram of the dibromo compound was dissolved in 4 cc. of acetone. To this solution was added 1 cc. of 0.6 molal sodium iodide solution. The reaction mixture turned yellow then red. After one and one-half hours a crystal of sodium thiosulfate was added. The solution was allowed to stand twelve hours at room temperature, then poured into water, extracted with ether, the ether extracts dried over anhydrous sodium sulfate and the ether evaporated. There remained a semi-crystalline material which was crystallized twice from methyl alcohol; m. p. 106–107°. A mixed melting point with the unsaturated compound (VIII) showed no depression.

Reaction of Acetyl Chloride on the Pentadiene (VIII) in the Presence of Zinc Chloride.—A mixture of 0.8 g. of the unsaturated compound (VIII), 3 cc. of acetyl chloride and 0.1 g. of powdered anhydrous zinc chloride was refluxed for one hour. The dark red solution was poured on ice. A light yellow precipitate formed immediately. The mixture was filtered and the solid crystallized from absolute ethyl alcohol. After three recrystallizations there was obtained 0.6 g. of a compound, m. p. 177–178°. This compound gave a positive iodoform test.

Anal. Calcd. for $C_{26}H_{34}O_4Cl_2$: C, 67.31; H, 6.58; Cl, 13.72; mol. wt., 517. Found: C, 67.70; H, 6.71; Cl, 13.59; mol. wt. (in boiling chloroform), 501.

Nitration of the Pentadiene (VIII).—One-half gram of the unsaturated compound was dissolved in 20 cc. of concentrated sulfuric acid at 5°. The orange solution was

cooled to 0° and 2 cc. of concentrated nitric acid added dropwise with stirring. The mixture was allowed to stand for ten minutes, then poured on ice. A white precipitate formed immediately. The solid was isolated and recrystallized twice from glacial acetic acid. There was obtained 0.2 g. of a solid melting at 258–259°.

Anal. Calcd. for $C_{25}H_{24}O_4N_4$: C, 55.55; H, 4.44; N, 10.37. Found: C, 55.56; H, 4.38; N, 10.31.

Action of Paraformaldehyde on 1,4-Di-(2,4,6-trimethylbenzoyl)-butane.—A mixture of 2.5 g. of the diketone, 0.5 g. of paraformaldehyde, 0.1 g. of potassium carbonate and 60 cc. of ethyl alcohol was refluxed for ten hours on a hot-plate. The mixture was poured into ice water and the solution acidified with dilute hydrochloric acid. It was allowed to stand for thirty minutes; the solid which precipitated was isolated and crystallized from methyl alcohol. There was obtained 0.7 g. of a compound melting at 122–123°.

Anal. Calcd. for $C_{26}H_{30}O_2$: C, 83.37; H, 8.07. Found: C, 83.65; H, 8.09.

Summary

Acetomesitylene reacts with paraformaldehyde to form a monomethylol derivative, $C_9H_{11}COCH_2CH_2OH$, and a dimolecular product, $C_9H_{11}COCCH=CH(CH_3)COC_9H_{11}$. The mode of

formation and structure of this unsaturated compound have been discussed.

Propiomesitylene gives a methylene derivative, $C_9H_{11}COC(CH_3)=CH_2$. Isobutyromesitylene gives a monomethylol derivative, $C_9H_{11}COC(CH_3)_2CH_2OH$.

The diketones, 1,3-di-(2,4,6-trimethylbenzoyl)-propane and 1,3-di-(2,4,6-trimethylbenzoyl)-butane, react in the normal fashion to yield unsaturated ketones.

URBANA, ILLINOIS

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

4-Alkyl Derivatives of 1,2-Naphthoquinone

BY LOUIS F. FIESER AND CHARLES K. BRADSHAW

In an investigation with Seligman¹ it was found that an alkyl substituent in the quinonoid ring of α -naphthoquinone inhibits the usual 1,4-additions to the conjugated system, whereas such additions occur readily with 3-alkyl-1,2-naphthoquinones. The unsaturated system (a) of the para quinones, however, like that (b) of the ortho quinones con-

(a) $—COCH=C(R)CO—$

(b) $—CH=C(R)COCO—$

(c) $—C(R)=CHCOCO—$

(1) Fieser and Seligman, *THIS JOURNAL*, **56**, 2690 (1934).

tains an ethylenic linkage sufficiently active for the addition of dienes.^{1–3} It seemed of interest to investigate for comparison the character of the system (c) of a 4-alkyl-1,2-naphthoquinone with respect to both 1,4-additions and the addition of dienes. For this purpose we first synthesized 4-methyl-1,2-naphthoquinone and, as the compound exhibited certain unusual properties but proved too sensitive for extensive study,

(2) Fieser and Seligman, *Ber.*, **68**, 1747 (1935).

(3) Fieser and Dunn, *THIS JOURNAL*, **59**, 1016 (1937).