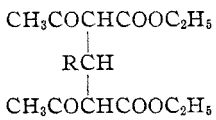
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF MICHIGAN]

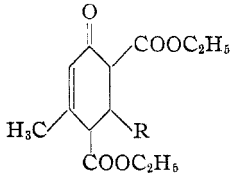
Preparation of 3-Methyl-5-aryl-2-cyclohexen-1-ones

BY E. C. HORNING[1] AND R. E. FIELD[2,3]

The Knoevenagel condensation of aliphatic or aromatic aldehydes with ethyl acetoacetate, in molar ratio of one to two, leads to bis-esters of the general structure I. From these bis-esters a series of cyclohexenones may be obtained through cyclization and removal of the carbethoxy groups.



I



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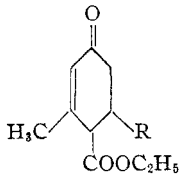

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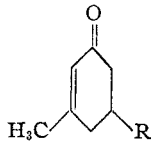
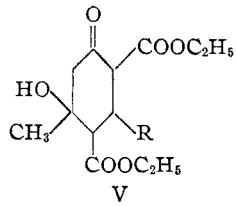


IV

Knoevenagel's procedures for preparing the ketones IV, where R is an alkyl or aryl group, involved prolonged heating of the bis-esters with strong (20–40%) sulfuric acid or with aqueous or alcoholic alkali. Under these conditions cyclization, saponification and decarboxylation are accomplished in a single operation. In using these methods to obtain the ketones (IV) from both aliphatic and aromatic aldehydes, it was found that the yields were frequently low and variable, and that purification of the ketones was often difficult. Through use of an ester-interchange method, improved general procedures were developed for the preparation of keto-esters (III) and ketones (IV) from bis-esters derived from aliphatic aldehydes.[4] These procedures have now been applied to derivatives of several aromatic aldehydes.

The Knoevenagel condensation of anisaldehyde, *o*-methoxybenzaldehyde and *m*-tolualdehyde with ethyl acetoacetate yielded in each case a bis-ester; the bis-esters from anisaldehyde and *o*-methoxybenzaldehyde corresponded to those reported previously.[5] 2,3-Dimethoxybenzaldehyde yielded a mixture from which two condensation products of identical analytical constitution were isolated. The structure and stereoisomerism of aldehyde–acetoacetic ester condensation products was studied by Rabe,[6,7,8] who concluded that the structure of these compounds was that of a cyclohexanolone V, and that 8 *dl*-isomers were possible. In the case of benzaldehyde it was



V

reported by Rabe[6] that three of these *dl* forms could be isolated from the crude condensation product through differences in alcohol solubility. Knoevenagel,[5,9] however, preferred the bis-ester structure for such condensation products. A single condensation product was reported by him in each case for a large number of aromatic aldehydes. So far as further reaction is concerned, it is evident that cyclohexenones could be obtained readily from either structure, and that the same (*dl*) ketone (IV) would be obtained from all stereoisomeric forms of either structure. These condensation products are referred to here as bis-esters, but no attempt was made to investigate their structure.

The preparation of a number of 3-methyl-5-aryl-4,6-dicarbethoxy-2-cyclohexen-1-ones (II, R = aryl) was described by Knoevenagel[5]; the method employed was a treatment of the initial condensation product with hydrogen chloride in alcohol. In the course of this investigation it was found that the same results could be obtained by heating bis-esters in acetic acid containing phosphoric acid. Using this procedure, keto-diesters (II) were obtained in which the aryl group was *p*-methoxyphenyl and *m*-methylphenyl. The two bis-esters from 2,3-dimethoxybenzaldehyde yielded two different keto-diesters. The bis-ester from *o*-methoxybenzaldehyde was not cyclized successfully by this method.

Ester-interchange studies of 3-methyl-5-(*p*-methoxyphenyl) - 4,6 - dicarbethoxy - 2 - cyclohexen-1-one, in acetic acid were carried out with sulfuric and phosphoric acids as catalysts. When phosphoric acid was used, no ester-interchange was observed. Heating with sulfuric acid in acetic acid resulted in ester-interchange with acetic acid, and removal (by decarboxylation after ester-interchange) of both carbethoxy groups. The effect of variations in conditions,

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(4) Horning, Denekas and Field, *J. Org. Chem.*, **9**, 547 (1944).
(5) Knoevenagel, *Ann.*, **303**, 223 (1898).
(6) Rabe, *ibid.*, **313**, 129 (1900).
(7) Rabe and Elze, *ibid.*, **323**, 83 (1902).
(8) Rabe and Billmann, *ibid.*, **332**, 22 (1904).
(9) Knoevenagel, *Ber.*, **36**, 2118 (1903).

involving variation in the amount of sulfuric acid, and the length of time of heating, were examined, but a mono-ester (III, R = *p*-methoxyphenyl) was not obtained. In the case of cyclohexenones derived from aliphatic aldehydes, heating with acetic acid–sulfuric acid resulted in the selective removal of the 6-carbethoxy group to give a mono-ester (III, R = alkyl), indicating a considerably different rate of ester-interchange for the 4- and 6-carbethoxy groups. Apparently, however, when an aromatic group is present in the 5 position the rate of ester-interchange is approximately the same for both carbethoxy groups. It is possible that a slight difference in rate of interchange exists, but that the difference is too small to be made the basis of a successful preparative procedure. When 3-methyl-5-(*m*-methylphenyl)-4,6-dicarbethoxy-2-cyclohexen-1-one and 3-methyl-5-(2′,3′-dimethoxyphenyl)-4,6-dicarbethoxy-2-cyclohexen-1-one were heated in acetic acid–sulfuric acid, both ester groups were removed. With 3-methyl-5-(*o*-methoxyphenyl)-4,6-dicarbethoxy-2-cyclohexen-1-one a small amount (3%) of a crystalline mono-ester was isolated, indicating that in this case there is a definite although slight, difference in reactivity of the two ester groups. This is probably also true for the *p*-nitrophenyl analog, since it has been reported[5] that prolonged refluxing of the bis-ester from *p*-nitrobenzaldehyde with 20% sulfuric acid (conditions which yield ketones (IV) in other cases) yielded a mono-ester. It is probable that the carbethoxy group which is retained in these two cases is in the 4 position.

Although the ketones (IV) may be obtained from keto-diesters (II) through removal of both carbethoxy groups in acetic acid–sulfuric acid, it was found that the most convenient method for preparing the ketones (IV) was a modification of the method previously used[4] for 5-alkyl-2-cyclohexen-1-ones. Bis-esters (I) were heated in acetic acid–sulfuric acid for thirty minutes; the crude products from this reaction were then heated for a short time in aqueous–alcoholic sodium hydroxide for complete hydrolysis of the ester groups. The yields of 3-methyl-5-(*p*-methoxyphenyl)-2-cyclohexen-1-one and 3-methyl-5-(2′,3′-dimethoxyphenyl)-2-cyclohexen-1-one from crude bis-esters were 78 and 66%, respectively (based on aldehyde); yields of the *m*-methylphenyl and *o*-methoxyphenyl analogs from recrystallized bis-esters were 73 and 56%, respectively (based on bis-ester).

Experimental

Ethyl α,α′-Diacetyl-β-arylglutarates.—The Knoevenagel condensation of anisaldehyde, *m*-tolualdehyde, *o*-methoxybenzaldehyde and 2,3-dimethoxybenzaldehyde with ethyl acetoacetate, in 1:2 molar ratio, was carried out according to the general method described for anisaldehyde.

To a mixture of 39.4 g. (0.30 mole) of ethyl acetoacetate and 20.4 g. (0.15 mole) of freshly distilled anisaldehyde was added a solution of 2 cc. of piperidine in 5 cc. of ethanol. After standing twenty-four hours at room temperature the addition of piperidine (2 cc.) in ethanol (5 cc.) was repeated, and the mixture was allowed to stand until solidification occurred. The time required for the condensation varied; under warm conditions (35–40°) the condensation was apparently completed within eight to ten hours after the addition of the catalyst. The mixture was allowed to stand for at least twenty-four hours after solidification. For the preparation of 3-methyl-5-(*p*-methoxyphenyl)-2-cyclohexen-1-one it was found advantageous to use this product in crude form. Crystallization from alcohol yielded 42.0 g. (74%) of ethyl α,α′-diacetyl-β-(*p*-methoxyphenyl)-glutarate, m. p. 141–142° (cor.), reported[5] m. p. 137°.

This bis-ester can be crystallized from aqueous acetic acid without undergoing cyclization to 3-methyl-5-(*p*-methoxyphenyl) - 4,6 - dicarbethoxy - 2 - cyclohexen - 1-one. The reaction product, obtained as described, was dissolved in boiling acetic acid. Addition of water to the cloud point, followed by cooling and chilling, yielded 40.0 g. (71%) of bis-ester.

Ethyl α,α′-Diacetyl-β-(*m*-methylphenyl)-glutarate was obtained from *m*-tolualdehyde; crystallization from alcohol yielded 58% of bis-ester, m. p. 118–120°. Further crystallization gave a product melting at 127–128.5° (cor.).

Anal. Calcd. for $C_{20}H_{26}O_6$: C, 66.28; H, 7.23. Found: C, 66.48; H, 7.27.

Ethyl α,α′-Diacetyl-β-(*o*-methoxyphenyl)-glutarate was obtained from *o*-methoxybenzaldehyde; crystallization from alcohol yielded 56% of bis-ester, m. p. 129–131°. Further crystallization gave a product melting at 131.5–132.5° (cor.) (reported[5] m. p. 125°).

Anal. Calcd. for $C_{20}H_{26}O_7$: C, 63.48; H, 6.93. Found: C, 63.40; H, 6.92.

Ethyl α,α′-Diacetyl-β-(2,3-dimethoxyphenyl)-glutarate was obtained in two isomeric forms from 2,3-dimethoxybenzaldehyde. When the reaction mixture was worked up after forty-eight hours, there was obtained 68% of material melting at 108–110°. Repeated crystallization from alcohol yielded a sample melting at 117–118° (cor.).

Anal. Calcd. for $C_{21}H_{28}O_8$: C, 61.75; H, 6.91. Found: C, 61.57; H, 6.87.

When the reaction mixture was allowed to stand without disturbance for two weeks a gradual deposition of crystals occurred. These were separated by filtration. An additional amount of material was obtained by treating the filtrate with a little alcohol; these combined products amounted to a 28% yield. Recrystallization from alcohol gave an analytical sample melting at 152.5–154° (cor.).

Anal. Calcd. for $C_{21}H_{28}O_8$: C, 61.75; H, 6.91. Found: C, 61.89; H, 6.93.

3-Methyl-5-aryl-4,6-dicarbethoxy-2-cyclohexen-1-ones

Phosphoric Acid Cyclization.—The general procedure followed in all cases was similar to that described for ethyl α,α′-diacetyl-β-(*p*-methoxyphenyl)-glutarate.

The crude bis-ester obtained from 39.4 g. (0.30 mole) of anisaldehyde was dissolved in 40 cc. of acetic acid containing 6 cc. of acetic anhydride and 5 cc. of phosphoric acid (85%). The solution was heated under reflux for one hour, cooled and poured with good stirring into 500 cc. of water. The crude crystalline product which separated was recrystallized from alcohol to yield 36 g. (67%) of **3-methyl-5-(*p*-methoxyphenyl)-4,6-dicarbethoxy-2-cyclohexen-1-one** as colorless needles, m. p. 98–99°. An additional crystallization from benzene–ligroin yielded a product of m. p. 103–104° (cor.); reported[5] m. p. 103°.

The bright yellow **2,4-dinitrophenylhydrazone** was obtained from alcohol; m. p. 156–157° (cor.).

Anal. Calcd. for $C_{26}H_{28}O_9N_4$: C, 57.77; H, 5.22. Found: C, 57.96; H, 5.36.

3-Methyl-5-(*m*-methylphenyl)-4,6-dicarbethoxy-2-cyclohexen-1-one obtained from crude ethyl α,α′-diacetyl-β-(*m*-methylphenyl)-glutarate did not crystallize on pour-

ing into water and was extracted with ether. The ether solution was stirred with sodium carbonate solution until neutral, and was then washed with 5% sodium hydroxide solution, with 5% aqueous acetic acid and with water. After evaporation of the ether, the residue was dissolved in a little hot alcohol and the product allowed to crystallize; yield 33%, m. p. 93–95°. Recrystallization from alcohol gave colorless needles, m. p. 105–106° (cor.).

Anal. Calcd. for $C_{20}H_{24}O_5$: C, 69.75; H, 7.02. Found: C, 69.79; H, 7.09.

The **2,4-dinitrophenylhydrazone** was obtained from alcohol as bright yellow needles, m. p. 167–168° (cor.).

Anal. Calcd. for $C_{26}H_{28}O_8N_4$: C, 59.53; H, 5.38. Found: C, 59.53; H, 5.47.

3-Methyl-5-(2′,3′-dimethoxyphenyl)-4,6-dicarbethoxy-2-cyclohexen-1-one was obtained in two stereoisomeric forms. Cyclization of the low-melting bis-ester gave a 38% yield of a keto-diester, crystallizing as colorless needles from alcohol; m. p. 92–94°. Recrystallization gave a sample of m. p. 94–96° (cor.).

Anal. Calcd. for $C_{21}H_{26}O_7$: C, 64.60; H, 6.71. Found: C, 64.45; H, 6.72.

The **2,4-dinitrophenylhydrazone** crystallized from alcohol as yellow-orange needles, m. p. 155–156° (cor.).

Anal. Calcd. for $C_{27}H_{30}O_{10}N_4$: C, 56.84; H, 5.30. Found: C, 56.81; H, 5.13.

Application of the same cyclization procedure to the high-melting bis-ester gave a keto-diester in 38% yield, crystallizing from alcohol as colorless needles, m. p. 83–85°. After recrystallization the melting point was 85–86° (cor.). A mixed melting point of this material with the keto-diester of m. p. 94–96° was 80–93°.

Anal. Calcd. for $C_{21}H_{26}O_7$: C, 64.60; H, 6.71. Found: C, 64.34; H, 6.86.

The **2,4-dinitrophenylhydrazone** crystallized from alcohol as light yellow needles, m. p. 194–195.5° (cor.).

Anal. Calcd. for $C_{27}H_{30}O_{10}N_4$: C, 56.84; H, 5.30. Found: C, 56.70; H, 5.36.

When the cyclization procedure was applied to ethyl α,α'-diacetyl-β-(*o*-methoxyphenyl)-glutarate (bis-ester from *o*-methoxybenzaldehyde) the product was a light yellow viscous oil, obtained in 89% yield (calculated as keto-diester) from which no crystalline product could be obtained. A cyclization product, m. p. 113°, was reported by Knoevenagel.[5]

Ester-interchange Studies

On 3-Methyl-5-(*p*-methoxyphenyl)-4,6-dicarbethoxy-2-cyclohexen-1-one.—Numerous experiments were carried out in an attempt to obtain 3-methyl-5-(*p*-methoxyphenyl)-4-carbethoxy-2-cyclohexen-1-one by analogy with procedures known to yield 3-methyl-5-alkyl-4-carbethoxy-2-cyclohexen-1-ones.[4] 3-Methyl-5-(*p*-methoxyphenyl)-4,6-dicarbethoxy-2-cyclohexen-1-one was heated in glacial acetic acid solution with varying amounts of mineral acids (phosphoric or sulfuric acid) as ester-interchange catalysts. When phosphoric acid was employed only unchanged starting material was recovered. When sulfuric acid was employed, unchanged starting material was recovered when the amount of sulfuric acid for a given weight of diester was low. When the amount of sulfuric acid was increased, conditions were found under which both carbethoxy groups were removed, yielding the ketone, 3-methyl-5-(*p*-methoxyphenyl)-2-cyclohexen-1-one.

The effect of time of reflux on the course of the reaction was also studied, employing the sulfuric acid concentration found suitable for ketone preparation. With a reflux time of ten minutes, only starting material was recovered. A reflux period of thirty minutes yielded the ketone. A reflux period of fifteen minutes yielded an oil from which no crystalline material was obtained and which presumably was a mixture containing ketone and unchanged diester.

Conditions leading to the removal of both carbethoxy groups by ester-interchange are illustrated by the following experiment. Thirty grams of 3-methyl-5-(*p*-methoxyphenyl)-4,6-dicarbethoxy-2-cyclohexen-1-one was added to 250 cc. of acetic acid containing 25 cc. of concentrated sulfuric acid. The mixture was heated under vigorous reflux for thirty minutes. After cooling, the solution was poured with good stirring into 800 cc. of water. The layers were separated with the aid of ether, and the ether solution was neutralized by stirring with water to which sodium carbonate was added slowly. The ether layer was separated, washed twice with 100 cc. of 5% sodium hydroxide solution and with 100 cc. of 5% aqueous acetic acid. After evaporation of the ether, the residue was crystallized from a little alcohol. There was obtained a total (three crops) of 7.3 g. (42%) of 3-methyl-5-(*p*-methoxyphenyl)-2-cyclohexen-1-one, m. p. 62–63.5° (cor.).

On 3-Methyl-5-(*m*-methylphenyl)-4,6-dicarbethoxy-2-cyclohexen-1-one.—An ester-interchange reaction, employing 17 g. of keto-diester, 90 cc. of acetic acid and 9 cc. of concentrated sulfuric acid, was carried out in the fashion described for the *p*-methoxyphenyl analog. The product, a viscous oil, was distilled *in vacuo*. There was obtained 9.0 g. (91%) of light yellow, viscous oil, b. p. 178–180° (2 mm.). This was identified as 3-methyl-5-(*m*-methylphenyl)-2-cyclohexen-1-one through preparation of the 2,4-dinitrophenylhydrazone.

On 3-Methyl-5-(2′,3′-dimethoxyphenyl)-4,6-dicarbethoxy-2-cyclohexen-1-one (m. p. 94–96°).—An ester-interchange reaction employing 17 g. of 3-methyl-5-(2′,3′ - dimethoxyphenyl) - 4,6 - dicarbethoxy - 2 - cyclohexen-1-one (m. p. 94–96°), 90 cc. of acetic acid and 9 cc. of concentrated sulfuric acid, yielded 7.2 g. (67%) of 3 - methyl - 5 - (2′,3′ - dimethoxyphenyl) - 2 - cyclohexen-1-one. The product, isolated by distillation *in vacuo*, was a light yellow viscous oil which solidified on standing; recrystallization from ethyl acetate–ligroin gave the colorless crystalline ketone, m. p. 74–75° (cor.).

On Reaction Product from Ethyl α,α'-Diacetyl-β-(*o*-methoxyphenyl)-glutarate.—The oil resulting from the phosphoric acid cyclization of ethyl α,α'-diacetyl-β-(*o*-methoxyphenyl)-glutarate was treated with acetic acid–sulfuric acid under the usual conditions. The product was a viscous oil, which on long standing deposited a small amount of colorless crystalline material. The latter was separated and recrystallized from alcohol, giving in low yield (3%) a product of m. p. 155–156° (cor.). The analytical data for this product corresponded to a ketone-monoester structure.

Anal. Calcd. for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 70.81; H, 6.80.

The **2,4-dinitrophenylhydrazone** crystallized from alcohol as orange needles, m. p. 190.5–191.5° (cor.).

Anal. Calcd. for $C_{23}H_{24}O_7N_4$: C, 58.96; H, 5.16. Found: C, 59.04; H, 5.27.

The remainder of the reaction product, after removal of the crystalline fraction, was distilled *in vacuo*. Treatment of a portion of the distillate with 2,4-dinitrophenylhydrazine gave a mixture of dinitrophenylhydrazones; the composition of the distillate was not investigated further.

3-Methyl-5-aryl-2-cyclohexen-1-ones

3-Methyl-5-(*p*-methoxyphenyl)-2-cyclohexen-1-one.—The crude bis-ester obtained from 68 g. (0.50 mole) of anisaldehyde and 130 g. (1.0 mole) of ethyl acetoacetate was added to 500 cc. of acetic acid containing 50 cc. of concentrated sulfuric acid. Several grams of clay boiling chips were added and the mixture was heated under reflux for thirty minutes. After cooling, the solution was poured into 2 liters of water, and the product was removed by extracting four times with 250-ml. portions of ether. The ether extracts were combined, and washed with 100-ml. portions of 5% sodium hydroxide solution until the wash was alkaline. The ether was boiled off and the residue was added to a solution of 30 g. of sodium hydroxide in 250 cc. of water and 150 cc. of alcohol. The mixture was heated under reflux for thirty minutes and then acidified carefully with 140 cc. of 1:1 hydrochloric acid. After

heating under reflux for fifteen minutes, the mixture was poured into 1.5 liters of water and the crude ketone extracted with three 250-cc. portions of ether. The ether solution was washed twice with 100 cc. of 5% sodium hydroxide solution, with 100 cc. of 3% aqueous acetic acid and with water. After drying over anhydrous magnesium sulfate, the ether was evaporated and the residue was distilled under reduced pressure through a short Vigreux column. There was obtained 84 g. (78%) of 3-methyl-5-(*p*-methoxyphenyl)-2-cyclohexen-1-one, distilling as a colorless viscous oil at 190–203° (3–5 mm.); the product solidified on cooling and then melted at 57–60°. Recrystallization from ethyl acetate–petroleum ether yielded colorless crystals, m. p. 62.5–64° (cor.), reported[5] m. p. 65°.

The yellow-orange **2,4-dinitrophenylhydrazone** was recrystallized from alcohol; m. p. 195.5–196.5° (cor.).

Anal. Calcd. for $C_{20}H_{20}O_5N_4$: C, 60.60; H, 5.09. Found: C, 60.56; H, 5.06.

3-Methyl-5-(*m*-methylphenyl)-2-cyclohexen-1-one was obtained from ethyl α,α'-diacetyl-β-(*m*-methylphenyl)-glutarate through the same procedure in 73% yield. The product was a colorless viscous oil, b. p. 131–135° (0.5 mm.).

Anal. Calcd. for $C_{14}H_{16}O$: C, 83.96; H, 8.06. Found: C, 84.23; H, 8.05.

The **2,4-dinitrophenylhydrazone** crystallized from alcohol as scarlet needles, m. p. 154–154.5° (cor.).

Anal. Calcd. for $C_{20}H_{20}O_4N_4$: C, 63.14; H, 5.30. Found: C, 63.22; H, 5.32.

3-Methyl-5-(*o*-methoxyphenyl)-2-cyclohexen-1-one was obtained from ethyl α,α'-diacetyl-β-(*o*-methoxyphenyl)-glutarate in 56% yield. The product was a colorless, viscous oil, b. p. 154–156° (1 mm.) and did not solidify on standing (reported[5] m. p. 51°).

The scarlet **2,4-dinitrophenylhydrazone** was recrystallized from ethanol–benzene; m. p. 175.5–176.5° (cor.).

Anal. Calcd. for $C_{20}H_{20}O_5N_4$: C, 60.60; H, 5.09. Found: C, 60.68; H, 5.09.

3-Methyl-5-(2',3'-dimethoxyphenyl)-2-cyclohexen-1-one was obtained from 2,3-dimethoxybenzaldehyde, following the procedure employed for anisaldehyde. A run in one mole quantity yielded 179 g. (73%) of crude ketone, isolated by distillation *in vacuo* as a viscous light yellow oil, b. p. 204–220° (4–7 mm.), which solidified on standing. The distillation was accompanied by slight decomposition; redistillation yielded 163 g. (66%) of an almost colorless, viscous oil, b. p. 176–181° (1 mm.). Recrystallization of a portion of the redistilled product from ethyl acetate–ligroin gave colorless prisms of the ketone, m. p. 75–76° (cor.).

Anal. Calcd. for $C_{15}H_{18}O_3$: C, 73.15; H, 7.36. Found: C, 72.94; H, 7.45.

The orange **2,4-dinitrophenylhydrazone** was recrystallized from alcohol; m. p. 204–205° (cor.).

Anal. Calcd. for $C_{21}H_{22}O_6N_4$: C, 59.15; H, 5.20. Found: C, 59.31; H, 5.19.

Summary

An improved preparative procedure for 3-methyl-5-aryl-2-cyclohexen-1-ones has been applied to cases in which the aryl group was *p*-methoxyphenyl, *o*-methoxyphenyl, *m*-methylphenyl and 2,3-dimethoxyphenyl. The Knoevenagel condensation of the corresponding aldehydes with ethyl acetoacetate, the cyclization of the condensation products with phosphoric acid in acetic acid to yield 3-methyl-5-aryl-4,6-dicarbethoxy-2-cyclohexen-1-ones, and ester-interchange studies on the cyclization products are also described.

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Synthesis of 3-Methyl-5-(*p*-methoxyphenyl)-4-carbethoxy-2-cyclohexen-1-one

BY E. C. HORNING[1] AND R. E. FIELD[2,3]

Attempts to prepare 3-methyl-5-(*p*-methoxyphenyl) - 4 - carbethoxy - 2 - cyclohexen - 1 - one (II) from the readily available 3-methyl-5-(*p*-methoxyphenyl) - 4,6 - dicarbethoxy - 2 - cyclohexen-1-one (V) have not been successful.[4,5] It has now been prepared by the cyclization of ethyl α,γ - diacetyl - β - (*p* - methoxyphenyl) - butyrate (I) with phosphoric acid in acetic acid.

The keto-ester (I) was obtained through the Michael addition of ethyl acetoacetate to anisalacetone, using piperidine as a catalyst. An analogous reaction, the addition of ethyl acetoacetate to benzalacetone, was attempted without success by Knoevenagel.[6] In the cyclization of this keto-ester (I), there is present the possibility of formation of two cyclohexenones, II and VI. The structure of the product, isolated in 22% yield, was shown to be II by reduction to the corresponding cyclohexanone, 3-methyl-5-(*p*-methoxyphenyl)-4-carbethoxycyclohexanone (III), and by independent synthesis of III.

3 - Methyl - 5 - (*p* - methoxyphenyl) - 4 - carbethoxycyclohexanone (III) was obtained in two steps from 3-methyl-5-(*p*-methoxyphenyl)-4,6-dicarbethoxy-2-cyclohexen-1-one (V). Catalytic reduction of V provided the cyclohexanone IV, and the 2-carbethoxy group of IV was removed by an ester-interchange reaction in acetic acid–sulfuric acid. The resulting cyclohexanone (III) was identical with that obtained from the catalytic reduction of the cyclohexenone II.

A related cyclohexanone, 3-methyl-5-(*p*-methoxyphenyl)-cyclohexanone, was also prepared through hydrogenation of 3-methyl-5-(*p*-methoxyphenyl)-2-cyclohexen-1-one.

Experimental

Ethyl α,γ-Diacetyl-β-(*p*-methoxyphenyl)-butyrate.—To a mixture of 106 g. (0.60 mole) of anisalacetone[7] and 79 g.

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(4) Knoevenagel, *Ann.*, **303**, 223 (1898).

(5) Horning and Field, THIS JOURNAL, **68**, 384 (1946).

(6) Knoevenagel and Speyer, *Ber.*, **35**, 395 (1902).

(7) "Organic Syntheses," Coll. Vol. 1, 77 (1941).