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.

ANN ARBOR, MICHIGAN RECEIVED NOVEMBER 17, 1945

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

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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(2) From the doctoral thesis of R. E. Field.

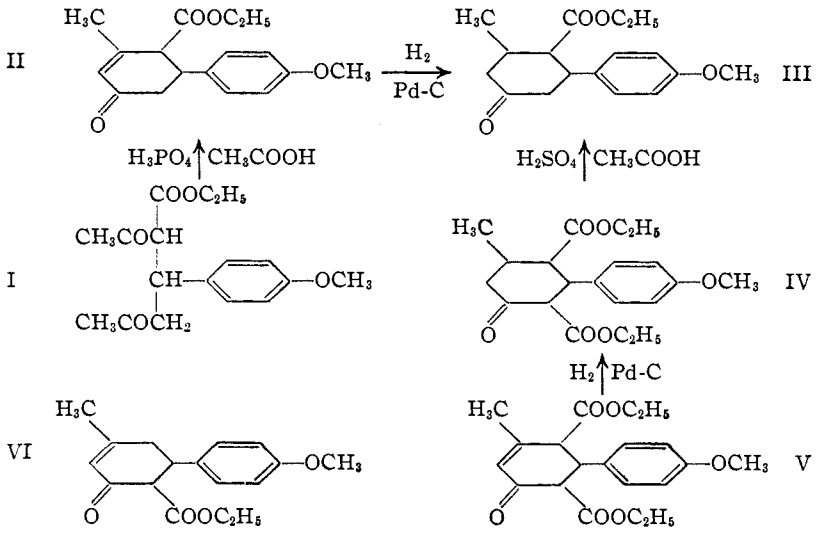
(3) Abbott Fellow, 1944–1945. Present address: General Aniline and Film Corp., Easton, Penna.

(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).



(0.60 mole) of ethyl acetoacetate was added a solution of 8 cc. of piperidine in 30 cc. of dry ethanol. The mixture was warmed gently on a steam cone until solution resulted and then was allowed to stand at room temperature. After six hours a second portion of 8 cc. of piperidine in 30 cc. of dry ethanol was added, and the mixture was again warmed until the anisalacetone, which had started to crystallize, was again in solution. Twenty-four hours later, a third portion of 4 cc. of piperidine in 15 cc. of dry ethanol was added, and the warming was repeated. After standing an additional twelve hours the mixture was seeded, resulting in almost complete crystallization of the mixture. Recrystallization from alcohol yielded (three crops) 100 g. (55%) of material melting at 145–148°. Recrystallization from alcohol gave colorless needles of ethyl α,γ-diacetyl-β-(*p*-methoxyphenyl)-butyrate, m. p. 156–157.5° (cor.).

Anal. Calcd. for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24. Found: C, 66.88; H, 7.22.

3-Methyl-5-(*p*-methoxyphenyl)-4-carbethoxy-2-cyclohexen-1-one.—A mixture of 41 g. of ethyl α,γ-diacetyl-β-(*p*-methoxyphenyl)-butyrate, 80 cc. of acetic acid, 10 cc. of phosphoric acid (85%) and 12 cc. of acetic anhydride was heated under reflux for one hour. After cooling, the solution was poured with good stirring into 800 cc. of water. The oil which separated was extracted with ether, and the ether solution was neutralized by stirring with sodium carbonate solution. The ether was evaporated with the aid of an air jet and the residue was dissolved in a small amount of alcohol. Crystallization occurred after chilling for some time, yielding 8.5 g. (three crops) (22%) of crude product; recrystallization from alcohol gave colorless needles of 3-methyl-5-(*p*-methoxyphenyl)-4-carbethoxy-2-cyclohexen-1-one, m. p. 71–73° (cor.).

Anal. Calcd. for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 70.63; H, 6.97.

The **2,4-dinitrophenylhydrazone** crystallized from alcohol in the form of red needles, m. p. 183–184° (cor.).

Anal. Calcd. for $C_{23}H_{24}O_7N_4$: C, 58.96; H, 5.16. Found: C, 58.87; H. 5.05.

3-Methyl-5-(*p*-methoxyphenyl)-4-carbethoxycyclohexan-1-one. (A).—To a solution of 5.8 g. of 3-methyl-5-(*p*-methoxyphenyl)-4-carbethoxy-2-cycohexen-1-one in 100 cc. of ethanol was added 1.0 g. of a 10% palladium–charcoal catalyst.[8] In a low-pressure hydrogenation apparatus, the absorption of one equivalent of hydrogen was completed in fifteen minutes. The catalyst was removed by filtration, and most of the solvent evaporated with the aid of an air stream; the residue was recrystallized from aqueous alcohol yielding 2.3 g. (40%) of crude product, m. p. 65–70°. Recrystallization from benzene–ligroin gave 1.8 g. of colorless needles of 3-methyl-5-(*p*-methoxyphenyl)-4-carbethoxycyclohexan-1-one, m. p. 78–79.5° (cor.).

Anal. Calcd. for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64. Found: C, 70.58; H, 7.95.

The **2,4-dinitrophenylhydrazone** crystallized from alcohol in orange leaflets; m. p. 184–185° (cor.).

Anal. Calcd. for $C_{23}H_{26}O_7N_4$: C, 58.71; H, 5.57. Found: C, 58.59; H, 5.60.

3-Methyl-5-(*p*-methoxyphenyl)-4,6-dicarbethoxycyclohexan-1-one.—Hydrogenation of 9.0 g. of 3-methyl-5-(*p*-methoxyphenyl)-4,6-dicarbethoxy-2-cyclohexen-1-one[4,5] in 100 cc. of ethanol, with 1.0 g. of a 10% palladium–charcoal catalyst[8] in a low-pressure apparatus was completed in twenty minutes and was followed by partial crystallization of the product. The catalyst was removed by filtration, and was washed with warm alcohol to remove all organic material. The alcohol filtrate was evaporated to a low volume and chilled to give (three crops) 5.5 g. (61%) of crude product, m. p. 132–134°. Recrystallization from alcohol raised the melting point to 139.5–140.5° (cor.).

Anal. Calcd. for $C_{20}H_{26}O_6$: C, 66.28; H, 7.23. Found: C, 66.27; H, 7.19.

The yellow **2,4-dinitrophenylhydrazone** was recrystallized from alcohol; m. p. 197–198° (cor.).

Anal. Calcd. for $C_{26}H_{30}O_9N_4$: C, 57.56; H, 5.57. Found: C, 57.51; H, 5.57.

3-Methyl-5-(*p*-methoxyphenyl)-4-carbethoxycyclohexan-1-one (B).—One gram of 3-methyl-5-(*p*-methoxyphenyl)-4,6-dicarbethoxycyclohexan-1-one in 5 cc. of acetic acid and 0.5 cc. of concentrated sulfuric acid was heated under reflux for thirty minutes. The solution was poured into an ice–water mixture and the precipitated solid was separated by filtration. Recrystallization of the crude product from aqueous alcohol gave 0.4 g. (51%) of colorless needles of 3-methyl-5-(*p*-methoxyphenyl)-4-carbethoxycyclohexan-1-one, m. p. 78.5–79.5° (cor.). A mixed melting point with the ketone, m. p. 78–79.5°, prepared by method (A) showed no depression. The identity of the product was also confirmed by preparation of the 2,4-dinitrophenylhydrazone.

3-Methyl-5-(*p*-methoxyphenyl)-cyclohexan-1-one.—Hydrogenation of 5.4 g. of 3-methyl-5-(*p*-methoxyphenyl)-2-cyclohexen-1-one in 100 cc. of ethanol with 1.0 g. of 10% palladium–charcoal catalyst[8] was carried out in a low-pressure apparatus. The time required for the reduction was fifteen minutes. After removal of the catalyst, the solvent was evaporated to a low volume. The solution deposited 2.5 g. (46%) of material melting at 67–68°. Recrystallization from benzene–ligroin gave colorless blocks of the ketone, m. p. 68.5–70° (cor.).

Anal. Calcd. for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 76.86; H, 8.30.

The yellow **2,4-dinitrophenylhydrazone** was recrystallized from alcohol; m. p. 181–182° (cor.).

Anal. Calcd. for $C_{20}H_{22}O_5N_4$: C, 60.29; H, 5.57. Found: C, 60.30; H, 5.53.

Summary

3-Methyl-5-(*p*-methoxyphenyl)-4-carbethoxy-2-

(8) Hartung, THIS JOURNAL, **50**, 3370 (1928); **66**, 888 (1944), ref. 7.

cyclohexen-1-one has been synthesized through cyclization of the Michael addition product of anisalacetone and ethyl acetoacetate.

ANN ARBOR, MICHIGAN RECEIVED NOVEMBER 17, 1945

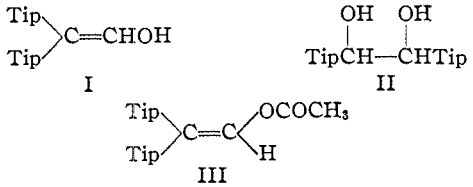
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Vinyl Alcohols. XVIII.[1] Increased Hindrance

BY REYNOLD C. FUSON, DAVID H. CHADWICK AND M. L. WARD[2]

The study of the influence of structure on the stability of trisubstituted vinyl alcohols, summarized in an earlier paper of this series,[3] consisted chiefly in a search for the minimum hindrance which would render a vinyl alcohol stable. In the present work an effort was made to bring the amount of hindrance to a maximum. As a result it has been possible to prepare an aldehyde enol with two 2,4,6-triisopropylphenyl[4] radicals and a ketone enol with three mesityl radicals.

Ditipylvinyl Alcohols.—2,2-Ditipylvinyl alcohol (I) was made by dehydration of 1,2-ditipylethylene glycol (II). Experiment showed that either the hydrobenzoin (II) or the isohydrobenzoin could be dehydrated successfully in a manner similar to that used with the mesityl and isoduryl analogs.[5] The rearrangement product formed an acetate (III), from which it could

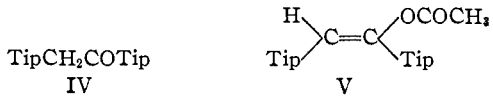


be regenerated by hydrolysis. By analogy with enols obtained in a similar manner, the compound was identified as 2,2-ditipylvinyl alcohol (I).

The study of the oxidation and reduction of 2,2-ditipylvinyl alcohol, though contributing little to the problem of structure determination, gave very interesting results. Thus, hydrogen peroxide, chromic anhydride and ozone converted the alcohol to ditipyl ketone, ditipyl diketone and the corresponding benzoin, respectively. Reduction with hydrogen iodide converted the vinyl alcohol to 1,2-ditipylethylene.

In unsuccessful efforts to prepare a ditipylvinyl chloride the 2,2-ditipylvinyl alcohol was treated with thionyl chloride and with phosphorus pentachloride. Another experiment which might have been expected to yield a ditipylvinyl chloride was the dehydrochlorination of 1,2-ditipyl-1,2-dichloroethane. The elimination of hydrogen chloride took place with unexpected ease. Simple heating converted the compound to a hydrocarbon which had approximately the composition of ditipylacetylene.

It appears probable that with very bulky substituents such as the tipyl radical 1,2-disubstituted vinyl alcohols might prove to be stable. An attempt was made to isolate an enol form of the hexaisopropyl desoxybenzoin (IV). The enol acetate (V) was made by treatment of the desoxy derivative with methylmagnesium iodide and then with acetyl chloride. Hydrolysis of the new acetate converted it to the original desoxy compound, showing that the corresponding enol was unstable.



In an attempted hydrogenation, 2,2-ditipylvinyl alcohol (I) was subjected to high pressure in the presence of hydrogen and Raney nickel; the result was not hydrogenation but merely isomerization. From the reaction mixture was isolated a new ditipylvinyl alcohol. It formed an acetate from which it could be regenerated by hydrolysis, and, in general, behaved like the original 2,2-ditipylvinyl alcohol. By the principle of exclusion it would be the missing stereoisomer of the unstable enol form of the desoxy compound—presumably the *trans* form (VI). It would follow

that in the *trans* configuration the two triisopropylphenyl groups afford enough hindrance to stabilize the enol whereas in the *cis* arrangement (VII) the crowding is less favorable to the existence of an enol.

Because of the great importance of this point, much effort has been expended in an attempt to confirm the structures assigned to the two stable ditipylvinyl alcohols. Degradation methods were found to be of little value. Reagents which attack the central ethylenic linkage often produce migration of a tipyl radical. Thus each of the isomers gave rise to both 1,2 and 2,2 derivatives. For example, reduction with hydrogen iodide converted both vinyl alcohols to 1,2-ditipylethylene.

(1) For the preceding communication in this series see Fuson, Maynert and Shenk, THIS JOURNAL, **67**, 1939 (1945).

(2) Abbott Fellow, 1941-1942.

(3) Fuson, Armstrong, Chadwick, Kneisley, Rowland, Shenk and Soper, THIS JOURNAL, **67**, 386 (1945).

(4) For convenience in presentation the 2,4,6-triisopropylphenyl radical will be called *tipyl* and will be represented by *Tip*.

(5) Fuson and Southwick and Rowland, THIS JOURNAL, **66**, 1109 (1944).