[CONTRIBUTION FROM THE DEPARTMENT OF ORGANIC CHEMISTRY, RESEARCH DIVISION, SHARP AND DOHME, INC.]

Synthesis of Substituted Cyclohexenones[1]

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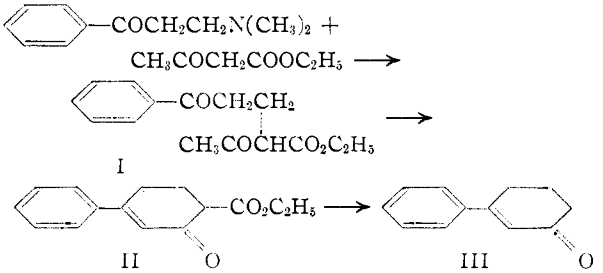
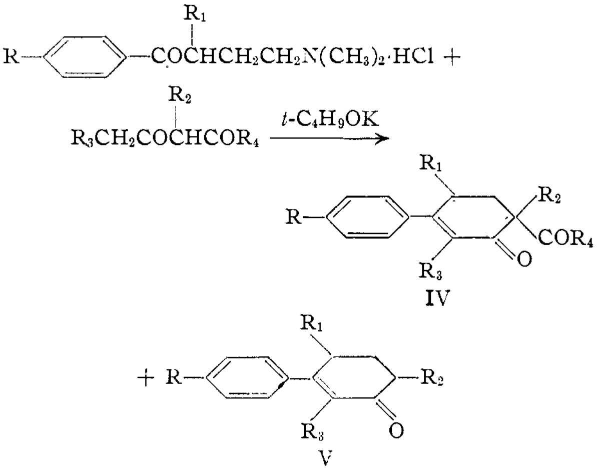
A number of 3-aryl-2-cyclohexenones have been prepared by a Michael-type reaction using the hydrochlorides of aryl β-dialkylaminoalkyl ketones and β-ketoesters or β-diketones. 4-Acetyl-4-carbomethoxydecalone has been prepared in a similar manner by an intramolecular Michael reaction of the product obtained from 1-(β-dimethylaminopropionyl)-cyclohexene hydrochloride and acetoacetic ester.

In 1935, Abdullah[2] reported that β-dimethylaminopropiophenone as well as phenyl vinyl ketone undergoes a Michael-type condensation with acetoacetic ester in the presence of sodium ethoxide to give a product (I), that by further reaction, leads to 3-phenyl-2-cyclohexenones (II, III). The formation of I occurs *via* a Michael condensation of the phenyl vinyl ketone that is employed as a reactant or is produced from the Mannich base during the course of the reaction. However, under the conditions of the reaction, I undergoes an aldol-type cyclization accompanied by loss of the carbethoxy group of either I or II and the final product is a mixture of I, II and III.

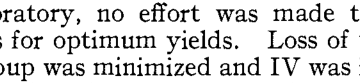


Although β-aminoalkyl ketones (and particularly their methiodides) have been utilized extensively as sources of vinyl ketones in syntheses of fused ring systems,[3] Abdullah's observations have been overlooked until recently.[4] Since this route offers an attractive approach to the synthesis of substituted cyclohexenones, provided that the course of the reaction can be controlled properly to give a homogeneous product, we investigated the application of Abdullah's method to a variety of reactants. Our results are presented in this paper.

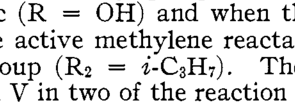
In our studies, aryl β-dimethylaminoalkyl ketones were employed as their hydrochlorides since these are stable crystalline compounds and are obtained readily by the Mannich reaction.[5] Other workers have employed the Mannich ketones as bases[2] or in the form of their quaternary salts.[2-4] Both of these reagents have their limitations; the former are unstable while the latter involve additional manipulation in their preparation and are frequently non-crystalline and difficult to purify. As active methylene components, β-ketoesters and β-diketones were investigated. Potassium *t*-butoxide was selected as the condensing agent since it gave higher yields of cyclized product and in some instances minimized loss of the carbethoxy group ($R_4 = OC_2H_5$) or the acetyl group ($R_4 = CH_3$) to afford IV ($R_4 = OC_2H_5, CH_3$).



In Table I are listed the various reactants employed and the products obtained. With β-ketoesters ($R_4 = OC_2H_5$), the product was generally a mixture of IV and V. In all instances, however, loss of the carboalkoxy group was extensive and V was the predominant product. Upon alkaline hydrolysis the mixture was converted to V in yields of 15–70%. However, since most of this work was exploratory, no effort was made to develop conditions for optimum yields. Loss of the carboalkoxy group was minimized and IV was isolated in 30% yield when the aryl group of the amino ketone was phenolic (R = OH) and when the methylene group of the active methylene reactant carried an isopropyl group ($R_2 = i\text{-}C_3H_7$). The presence of both IV and V in two of the reaction products was established by catalytic hydrogenation of the mixture followed by saponification and separation of the carboxylic acid and neutral fractions. In this manner, the product from the reaction of β-dimethylamino-*p*-methoxypropiophenone hydro-



VI



VII

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(1) Presented in part before the Third Meeting-in-Miniature of the Philadelphia Section of the American Chemical Society, January 18, 1951.

(2) S. M. Abdullah, *J. Ind. Chem. Soc.*, **12**, 62 (1935).

(3) C. Mannich, W. Koch and F. Borkowsky, *Ber.*, **70B**, 355 (1937); E. C. duFeu, F. J. McQuillin and R. Robinson, *J. Chem. Soc.*, 53 (1937); A. L. Wilds and S. H. Shunk, THIS JOURNAL, **65**, 469 (1943).

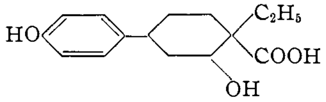
(4) (a) A. M. Downes, N. S. Gill and F. Lions, *Aust. J. Sci.*, **X**, 147 (1948); (b) THIS JOURNAL, **72**, 3464 (1950).

(5) F. F. Blicke in "Organic Reactions," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1947, p. 303.

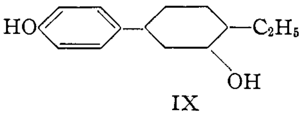
TABLE I

	Reactants R	R_1	R_2	R_3	R_4	Product -2-cyclohexen-1-one
1	H	H	H	H	OC_2H_5	3-Phenyl-
2	H	CH_3	H	H	OC_2H_5	3-Phenyl-4-methyl-
3	CH_3O	H	H	H	OC_2H_5	3-(*p*-Methoxyphenyl)-
4	HO	H	H	H	OC_2H_5	3-(*p*-Hydroxyphenyl)-
5	CH_3O	H	C_2H_5	H	OC_2H_5	3-(*p*-Methoxyphenyl)-6-ethyl-
6	HO	H	C_2H_5	H	OC_2H_5	3-(*p*-Hydroxyphenyl)-6-ethyl- 3-(*p*-Hydroxyphenyl)-6-ethyl-6-carbethoxy-
7	CH_3O	H	$CH(CH_3)_2$	H	OC_2H_5	(3-*p*-Methoxyphenyl)-6-isopropyl-
8	HO	H	$CH(CH_3)_2$	H	OC_2H_5	3-(*p*-Hydroxyphenyl)-6-isopropyl-6-carbethoxy-
9	HO	H	CH_3	CH_3	OC_2H_5	3-(*p*-Hydroxyphenyl)-2,6-dimethyl-
10	HO	H	C_6H_5	C_6H_5	OC_2H_5	3-(*p*-Hydroxyphenyl)-2,6-diphenyl-
11	CH_3O	H	H	H	CH_3	3-(*p*-Methoxyphenyl)-6-acetyl-
12	HO	H	H	H	CH_3	3-(*p*-Hydroxyphenyl)-6-acetyl-
13	CH_3O	H	CH_3	H	CH_3	3-(*p*-Methoxyphenyl)-6-methyl-

chloride with acetoacetic ester yielded 3-(*p*-methoxyphenyl)-6-carboxycyclohexanol (VI) and 3-(*p*-methoxyphenyl)-cyclohexanol (VII). Similarly, the product from β-dimethylamino-*p*-hydroxypropiophenone hydrochloride and ethyl α-ethylacetoacetate gave 3-(*p*-hydroxyphenyl)-6-carboxy-6-ethylcyclohexanol (VIII) and 3-(*p*-hydroxyphenyl)-6-ethylcyclohexanol (IX).

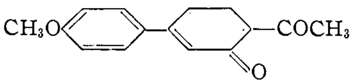


VIII

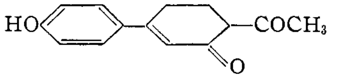


IX

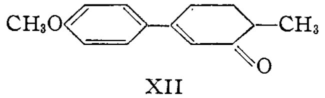
In reactions with acetylacetone, the acetyl group was retained to a greater extent than the carboalkoxy group of β-ketoesters and permitted the preparation of X and XI. The presence of the initial acyclic product was indicated in the preparation of X since a non-crystalline fraction was obtained which upon treatment with phosphoric acid or alcoholic hydrogen chloride afforded additional X. When the methylene group of acetylacetone was methylated, extensive cleavage occurred in the reaction with β-dimethylamino-*p*-methoxypropiophenone hydrochloride and the product was a mixture from which only XII was isolated. However, the anticipated XIII was prepared from X. Upon treatment with methyl iodide, the sodium derivative of X underwent methylation to give XIII together with its cleavage product XII.



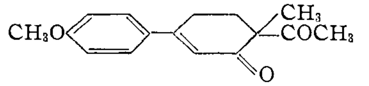
X



XI

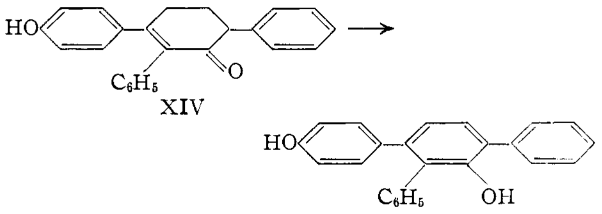


XII



XIII

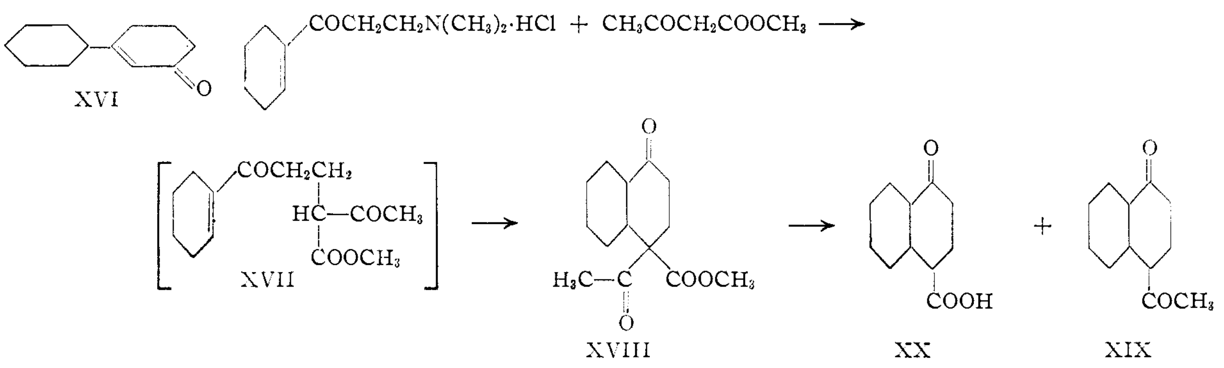
The structure of a few representative compounds prepared by these reactions was established by catalytic dehydrogenation to substituted biphenyls. Thus, 3-(*p*-methoxyphenyl)-2-cyclohexen-1-one gave 3-hydroxy-4′-methoxybiphenyl. Hydrogenation of 3-(*p*-methoxyphenyl)-2-cyclohexen-1-one to the cyclohexanol followed by dehydrogenation gave 4-methoxybiphenyl. Similarly, 3-(*p*-methoxyphenyl)-6-ethyl-2-cyclohexen-1-one was dehydrogenated through its reduction product, 3-(*p*-methoxyphenyl)-6-ethylcyclohexanol, to give 4-ethyl-4′-methoxybiphenyl. Dehydrogenation of 3-(*p* - hydroxyphenyl) - 2,6 - diphenyl - 2 cyclohexen-1-one (XIV) gave 3′,4-dihydroxy-2′-phenyl-*p*-terphenyl (XV).



XIV

XV

The application of this reaction was extended to the non-aromatic Mannich ketones, β-dimethylaminopropionylcyclohexane hydrochloride and 1-(β-dimethylaminopropionyl)-cyclohexene hydrochloride. The former upon reaction with methyl acetoacetate yielded 3-cyclohexyl-2-cyclohexen-1-one (XVI). 1-(β-Dimethylaminopropionyl)-cyclohexene hydrochloride when submitted to the same reaction behaved in a manner similar to the reaction between diethyl malonate and the methiodide of 1-(β-N-morpholinopropionyl)-cyclohexene reported by Downes, Gill and Lions[4b] and gave 4-acetyl-4-carbomethoxydecalone (XVIII). Although the formation of XVIII undoubtedly occurred as a result of two consecutive Michael reactions, the sequence of the two reactions is not known. However, it seems probable that the initial product was XVII which then underwent cyclization by an intramolecular Michael reaction to give the decalone, XVIII. Upon alkaline hydrolysis, XVIII yielded 4-acetyldecalone (XIX) and 4-carboxydecalone (XX). Catalytic dehydrogenation of XIX and XX was unsuccessful; similar behavior of



decalin compounds is known.[6] However, conversion of XIX to α-naphthol was accomplished in low yield. Bromination followed by dehydrobromination yielded an unsaturated product which was dehydrogenated with loss of the acetyl group to give α-naphthol.

Experimental[7]

The Michael condensation was generally conducted under the following conditions. A mixture of the aryl β-dialkylaminoalkyl ketone hydrochloride (0.05 mole), active methylene compound (0.05 mole) and potassium *t*-butoxide (0.0625 mole; 1.25 molar equiv.)[8] in 250 cc. of solvent[9] was refluxed for 24 hours, cooled, acidified with dilute acetic acid and concentrated to dryness *in vacuo*. The residual oil was taken up in ether and washed with 5% aqueous sodium hydroxide, water and dried over sodium sulfate. After filtration, the ethereal solution was evaporated to dryness. With β-diketones, the product was distilled and crystallized. With β-ketoesters, if the product did not crystallize at this stage, it was saponified with aqueous alkali for two hours and the resulting cyclohexenone purified by distillation *in vacuo* and crystallization.

3-Phenyl-2-cyclohexen-1-one (III) was prepared from β-dimethylaminopropiophenone hydrochloride and methyl acetoacetate in *t*-butyl alcohol; yield 60% of colorless plates from ether–petroleum ether, m.p. 63.8–64.6°(lit.[2] m.p. 64°).

3-Phenyl-4-methyl-2-cyclohexen-1-one was prepared from α-methyl-β-dimethylaminopropiophenone hydrochloride and ethyl acetoacetate in *t*-butyl alcohol; yield 40% of colorless prismatic needles from ether–petroleum ether, m.p. 63.5–65.2°.

Anal. Calcd. for $C_{13}H_{14}O$: C, 83.83; H, 7.58. Found[10]: C, 83.70, 83.84; H, 7.41, 7.67.

A semicarbazone was obtained as colorless needles from dilute ethanol, m.p. 207–207.9°.

Anal. Calcd. for $C_{14}H_{17}ON_3$: C, 69.11; H, 7.05. Found[10]: C, 69.50, 69.42; H, 7.33, 7.19.

3-(*p*-Methoxyphenyl)-2-cyclohexen-1-one was prepared from ethyl acetoacetate and β-dimethylamino-*p*-methoxypropiophenone hydrochloride with benzene as solvent; yield 40% of pale yellow plates, m.p. 86.2–87.2°.

Anal. Calcd. for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.00, 77.20; H, 6.91, 6.98.

An oxime was obtained as colorless plates from alcohol–water, m.p. 117–118.5°.

Anal. Calcd. for $C_{13}H_{14}O_2N$: C, 72.20; H, 6.53. Found: C, 71.85, 72.00; H, 6.81, 6.83.

3-(*p*-Methoxyphenyl)-6-carboxycyclohexanol (VI).—A 5.5-g. sample of distilled, unsaponified product (b.p. 184–202° (1 mm.)), from the reaction between β-dimethylamino-*p*-methoxypropiophenone hydrochloride and ethyl acetoacetate was hydrogenated in 25 cc. of ethanol with 500 mg. of Adams catalyst until reduction ceased. The colorless solution was filtered, refluxed for 1 hour with 10 cc. of 20% aqueous sodium hydroxide and the alcohol removed by distillation. After addition of water, the alkali-insoluble material was extracted with ether and the alkaline solution acidified. The resulting oil, VI, was taken up in ether, washed and dried and esterified with an ethereal solution of diazomethane (0.04 mole). The methyl ester of VI was obtained by distillation as a colorless liquid; yield 1.2 g., b.p. 155–160° (1 mm.).

Anal. Calcd. for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 67.92, 67.96; H, 7.84, 7.76.

The ethereal solution of alkali-insoluble material was washed with water and dried over sodium sulfate. **3-(*p*-Methoxyphenyl)-cyclohexanol** (VII) was obtained upon concentration and dilution with petroleum ether as colorless plates; yield 1.9 g., m.p. 75–78°. An analytical sample melted at 84.4–85.2°.

Anal. Calcd. for $C_{13}H_{18}O_2$: C, 75.69; H, 8.79. Found: C, 75.78, 75.85; H, 8.89, 8.86.

β-Dimethylamino-*p*-hydroxypropiophenone Hydrochloride.—A solution of 176 g. (1.3 moles) of *p*-hydroxyacetophenone, 42 g. (1.4 moles) of paraformaldehyde, 115 g. (1.4 moles) of dimethylamine hydrochloride in 750 cc. of alcohol containing 1 cc. of concentrated hydrochloric acid was refluxed for 2.5 hours. Upon cooling, the crystalline product was collected on the filter, washed with ether and dried *in vacuo*; yield 166 g. (56%) of colorless plates, m.p. 189–193°. A sample for analysis was recrystallized from ethanol, m.p. 195.6–196.9°.

Anal. Calcd. for $C_{11}H_{16}O_2NCl$: C, 57.51; H, 7.02. Found: C, 57.57, 57.45; H, 7.04, 6.84.

3-(*p*-Hydroxyphenyl)-2-cyclohexen-1-one was prepared from β-dimethylamino-*p*-hydroxypropiophenone hydrochloride and ethyl acetoacetate in dioxane; yield 30% of colorless plates from alcohol–benzene, m.p. 159–161.5°.

Anal. Calcd. for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.60, 76.64; H, 6.58, 6.67.

This compound was prepared also by brief refluxing (15 minutes) of 3-(*p*-methoxyphenyl)-2-cyclohexen-1-one in xylene with aluminum chloride[11]; yield 54%.

3-(*p*-Methoxyphenyl)-6-ethyl-2-cyclohexen-1-one.—A solution of 19.6 g. (0.124 mole) of ethyl α-ethylacetoacetate in 25 cc. of dry benzene was added dropwise to a cooled suspension of 4.84 g. (0.124 mole) of powdered potassium in 75 cc. of dry benzene. When all the potassium had reacted (15 minutes), 150 cc. of dry benzene was added followed by 15 g. (0.062 mole) of β-dimethylamino-*p*-methoxypropiophenone hydrochloride. After refluxing for 24 hours, the mixture was cooled, acidified with dilute acetic acid and extracted with benzene. The washed and dried benzene solution was concentrated to dryness *in vacuo*; yield 13.4 g. of viscous cloudy yellow oil. Crystallization from ether–petroleum ether gave 9.3 g. (64%) of yellow needles, m.p. 52–59°. A sample upon further recrystallizations was obtained either as colorless plates, m.p. 63.3–64.4°, or color-

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[6] R. P. Linstead, A. F. Millidge, S. L. S. Thomas and A. L. Walpole, *J. Chem. Soc.*, 1146 (1937).

[7] The authors are indebted to Mr. K. B. Streeter and his associates, Mrs. T. P. Buchanan, Mrs. R. L. Joyce and Miss J. L. Pyett for many of the microanalyses reported in this paper.

[8] With *p*-hydroxyphenyl-β-dialkylaminoalkyl ketone hydrochlorides, 2.25 molar equivalents of potassium *t*-butoxide were used.

[9] Benzene, *t*-butyl alcohol (Eastman Kodak white label) and dioxane were the solvents employed. Dioxane was purified according to the method described in L. F. Fieser, "Experiments in Organic Chemistry," 2nd Edition, D. C. Heath and Co., Boston, Mass., 1941, p. 368.

[10] Analysis by Dr. Carl Tiedcke, New York, N. Y.

[11] K. Fries and K. Schimmelschmidt, *Ber.*, **58**, 2835 (1925).

less dense rods, m.p. 66.5–67.5°. A mixture of plates and rods melted at 63.5–67.2°.

Anal. Calcd. for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: (plates) C, 78.34, 78.39; H, 7.91, 8.05; (rods) C, 78.26, 78.12; H, 7.91, 8.05.

A 2,4-dinitrophenylhydrazone was obtained as red needles from ethyl acetate, m.p. 198–203°.

Anal. Calcd. for $C_{21}H_{22}O_5N_4$: C, 61.45; H, 5.40. Found: C, 61.44, 61.34; H, 5.52, 5.58.

3-(*p*-Hydroxyphenyl)-6-ethyl-2-cyclohexen-1-one was prepared from β-dimethylamino-*p*-hydroxypropiophenone hydrochloride and ethyl α-ethylacetoacetate in dioxane; yield 71.4% of pale yellow needles from ether–petroleum ether, m.p. 121.4–122°.

Anal. Calcd. for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.86, 77.74; H, 7.71, 7.69.

A 2,4-dinitrophenylhydrazone was obtained from ethyl acetate as red needles, m.p. 196.1–197.2°.

Anal. Calcd. for $C_{20}H_{20}O_5N_4$: C, 60.60; H, 5.09. Found: C, 60.67, 60.63; H, 5.17, 5.21.

An acetate was prepared by the acetic anhydride–pyridine method and obtained as colorless needles from ether–petroleum ether, m.p. 86.8–87.8°.

Anal. Calcd. for $C_{16}H_{18}O_3$: C, 74.40; H, 7.02. Found: C, 74.50, 74.61; H, 7.22, 7.30.

Methylation with dimethyl sulfate and alkali gave 3-(*p*-methoxyphenyl)-6-ethyl-2-cyclohexen-1-one.

3-(*p*-Hydroxyphenyl)-6-carboxy-6-ethylcyclohexanol (VIII).—A solution of 8.2 g. of unsaponified product from the Michael reaction in 50 cc. of ethanol was hydrogenated in the presence of 1 g. of Adams catalyst until reduction ceased. The filtered solution was concentrated to dryness and the residue refluxed for 72 hours with 50 cc. of 20% aqueous sodium hydroxide. After acidification in the cold, the resulting oil was taken up in ether and the ethereal solution extracted with sodium bicarbonate solution. The bicarbonate extract was acidified and the product taken up in ether, dried and crystallized from ether–petroleum ether; yield 150 mg. of colorless rhombic prisms, m.p. 172.7–173.5°.

Anal. Calcd. for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.13, 68.24; H, 7.74, 7.75.

The neutral fraction upon distillation gave **3-(*p*-hydroxyphenyl)-6-ethylcyclohexanol (IX)**; yield 2 g. of viscous colorless oil, b.p. 183–185° (0.5 mm.).

Anal. Calcd. for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15. Found: C, 76.36, 76.29; H, 9.19, 9.26.

3-(*p*-Hydroxyphenyl)-6-ethyl-6-carbethoxy-2-cyclohexen-1-one.—A suspension of the potassium salt of ethyl α-ethylacetoacetate (0.13 mole) in 100 cc. of dry benzene and 150 cc. of purified dioxane was cooled in an ice-bath and treated with 15 g. (0.065 mole) of β-dimethylamino-*p*-hydroxypropiophenone hydrochloride. The mixture was stirred at room temperature for three hours and heated on the steam-bath for three hours. After standing at room temperature overnight, the cooled mixture was treated with dry hydrogen chloride for 0.5 hour, diluted with water and extracted with ether. The washed and dried ethereal extract was concentrated to dryness and the residue distilled *in vacuo*; yield 9.4 g. of cloudy viscous yellow oil, b.p. 230–235° (0.5 mm.). By prolonged cooling in a Dry Ice–methanol-bath, partial crystallization was accomplished; yield 1.55 g. of pale yellow crystals, m.p. 115–121°. Crystallization from acetone–petroleum ether afforded pale yellow prisms, m.p. 124–124.7°.

Anal. Calcd. for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 70.94, 70.94; H, 7.07, 7.16.

Further processing of the non-crystalline fraction yielded 0.65 g. of 3-(*p*-hydroxyphenyl)-6-ethyl-2-cyclohexen-1-one.

3-(*p*-Hydroxyphenyl)-6-carbethoxy-6-isopropyl-2-cyclohexen-1-one was prepared from ethyl α-isopropylacetoacetate, β-dimethylamino-*p*-hydroxypropiophenone hydrochloride in dioxane; yield 30% of pale yellow prisms from ether–petroleum ether, m.p. 140.4–141.8°.

Anal. Calcd. for $C_{18}H_{22}O_4$: C, 71.50; H, 7.34. Found: C, 71.69, 71.58; H, 7.51, 7.53.

Upon methylation in the cold with dimethyl sulfate and 5% aqueous sodium hydroxide, **3-(*p*-methoxyphenyl)-6-carbethoxy-6-isopropyl-2-cyclohexen-1-one** was obtained in 50% yield; pale yellow needles from ether–petroleum ether, m.p. 64.4–65°.

Anal. Calcd. for $C_{19}H_{24}O_4$: C, 72.12, H, 7.65. Found: C, 72.27, 72.22; H, 7.78, 7.68.

3-(*p*-Methoxyphenyl)-6-isopropyl-2-cyclohexen-1-one was prepared from β-dimethylamino-*p*-methoxypropiophenone hydrochloride and ethyl α-isopropylacetoacetate in dioxane; yield 30% of colorless plates from ether–petroleum ether, m.p. 63–64.8°.

Anal. Calcd. for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25. Found: C, 78.76, 78.73; H, 8.34, 8.37.

3-(*p*-Hydroxyphenyl)-2,6-dimethyl-2-cyclohexen-1-one was prepared from β-dimethylamino-*p*-hydroxypropiophenone hydrochloride and ethyl α-propionylpropionate[12] in dioxane; pale yellow rhombic prisms from ether–petroleum ether, m.p. 131.2–133.4°. Further processing of the residual non-crystalline fraction by treatment in the cold with alcoholic hydrogen chloride for 15 minutes afforded additional product; total yield 56%.

Anal. Calcd. for $C_{14}H_{16}O_2$: C, 77.74; H, 7.45. Found: C, 77.61, 77.50; H, 7.65, 7.63.

3-(*p*-Hydroxyphenyl)-2,6-diphenyl-2-cyclohexen-1-one (XIV) was prepared from β-dimethylamino-*p*-hydroxypropiophenone hydrochloride and ethyl α,γ-diphenylacetoacetate[13] in dioxane; yield 15% of pale yellow prismatic needles, m.p. 219.2–224.5°, bath preheated to 195°.

Anal. Calcd. for $C_{24}H_{20}O_2$: C, 84.68; H, 5.92. Found: C, 84.34, 84.37; H, 6.16, 6.09.

A benzoate was obtained as colorless plates from alcohol, m.p. 154–155.2°.

Anal. Calcd. for $C_{31}H_{24}O_3$: C, 83.76; H, 5.44. Found: C, 83.69, 83.77; H, 5.55, 5.54.

A bicarbonate soluble by-product was obtained as colorless prisms from acetone–petroleum ether, m.p. 207.1–208°.

3-(*p*-Methoxyphenyl)-6-acetyl-2-cyclohexen-1-one (X) was prepared from β-dimethylamino-*p*-methoxypropiophenone hydrochloride and acetylacetone in dioxane. The product was obtained from benzene–hexane as bright yellow needles, m.p. 103.5–106.5°. A sample produced an intense green color with alcoholic ferric chloride. The residual non-crystalline fraction on treatment with either phosphoric acid at room temperature or alcoholic hydrogen chloride in the cold afforded additional crystalline product; total yield 36%.

Anal. Calcd. for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60; OCH_3, 12.70. Found: C, 73.79, 73.94; H, 6.77, 6.84; OCH_3, 12.74, 12.86.

3-(*p*-Methoxyphenyl)-6-acetyl-6-methyl-2-cyclohexen-1-one (XIII).—A solution of 2.2 g. (0.009 mole) of 3-(*p*-methoxyphenyl)-6-acetyl-2-cyclohexen-1-one in 15 cc. of dry benzene was added to a solution of 1 g. of sodium in 25 cc. of absolute methanol, refluxed for 30 minutes, cooled and treated with 3.15 cc. of methyl iodide. After 45 minutes at room temperature, an additional 3 cc. (0.1 mole total) of methyl iodide was added. After 18 hours at room temperature, the mixture was cooled, acidified with acetic acid and concentrated to dryness *in vacuo*. The residue was taken up in ether, washed and dried. Upon crystallization from ether–petroleum ether, 0.25 g. of **3-(*p*-methoxyphenyl)-6-methyl-2-cyclohexen-1-one (XII)** was obtained as yellow needles; sublimation and crystallization afforded colorless glistening plates, m.p. 77.5–78.5°.

Anal. Calcd. for $C_{14}H_{16}O_2$: C, 77.74; H, 7.46. Found: C, 77.88, 77.87; H, 7.57, 7.52.

The residual non-crystalline fraction was distilled at 1 mm. and the product crystallized from ether–petroleum ether; yield 1.05 g. (45%) of pale yellow needles, m.p. 48–50°. Repeated crystallizations afforded **3-(*p*-methoxyphenyl)-6-acetyl-6-methyl-2-cyclohexen-1-one** as clusters of colorless needles, m.p. 55.8–56.8°.

Anal. Calcd. for $C_{16}H_{18}O_3$: C, 74.40; H, 7.02. Found: C, 74.96, 74.87; H, 7.30, 7.24.

3-(*p*-Hydroxyphenyl)-6-acetyl-2-cyclohexen-1-one (XI) was prepared from β-dimethylamino-*p*-hydroxypropiophe-

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(12) C. R. Hauser and B. E. Hudson, Jr., "Organic Reactions," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 280.

(13) H. Scheibler and A. Z. Mahbaub, *Ber.*, **60**, 564 (1927).

none hydrochloride and acetylacetone in dioxane; yield 12% of yellow plates from benzene–hexane, m.p. 139–141°. A sample gave an intense green color with alcoholic ferric chloride.

Anal. Calcd. for $C_{14}H_{14}O_3$: C, 73.02; H, 6.13. Found: C, 73.14, 73.14; H, 6.31, 6.34.

A by-product was isolated as yellow needles from alcohol–hexane, m.p. 213.5–216.5°. No coloration with alcoholic ferric chloride.

Dehydrogenation of 3-(*p*-methoxyphenyl)-2-cyclohexen-1-one with 10% palladium-on-charcoal at 300–315° for 2 hours gave 3-hydroxy-4′-methoxybiphenyl; colorless flakes from dilute methanol, m.p. 117–118°.

Anal. Calcd. for $C_{13}H_{12}O_2$: C, 77.98; H, 6.04. Found: C, 78.17, 78.03; H, 6.10, 6.11.

Dehydrogenation of 3-(*p*-methoxyphenyl)-cyclohexanol with 10% palladium–charcoal at 310–315° for 1.5 hours gave 4-methoxybiphenyl, m.p. 86.5–87.5°. A mixed m.p. with a known sample showed no depression.

4-Ethyl-4′-methoxybiphenyl.—3-(*p*-Methoxyphenyl)-6-ethyl-2-cyclohexen-1-one was hydrogenated to the saturated carbinol with Adams catalyst. Dehydrogenation of this product at 300–320° for 2 hours with 10% palladium–charcoal gave colorless plates from dilute methanol, m.p. 88.5–89.5°. No depression in m.p. was observed on admixture with a specimen prepared by Wolff–Kishner reduction[14] of 4-acetyl-4′-methoxybiphenyl.[15]

Anal. Calcd. for $C_{15}H_{16}O$: C, 84.86; H, 7.60. Found: C, 85.14, 84.81; H, 7.55, 7.45.

3,4′-Dihydroxy-2′-phenyl-*p*-terphenyl (XV) was obtained by dehydrogenation of XIV with 10% palladium-on-charcoal at 300° for 1 hour; colorless needles from methanol, m.p. 195–196°.

Anal. Calcd. for $C_{24}H_{18}O_2$: C, 85.18; H, 5.36. Found: C, 85.42, 85.22; H, 5.35, 5.36.

β-Dimethylaminopropionylcyclohexane Hydrochloride.—A mixture of 17 g. (0.14 mole) of methyl cyclohexyl ketone, 11.8 g. (0.145 mole) of dimethylamine hydrochloride and 8.1 g. (0.27 mole) of paraformaldehyde in 50 cc. of ethanol containing 1 cc. of concentrated hydrochloric acid was refluxed for 37 hours and concentrated to dryness at the water-pump. The crystalline residue was washed with ether and recrystallized from acetone; yield 13.5 g. (44%) of colorless plates, m.p. 151–154°. An analytical sample melted at 160.4–161.2°.

Anal. Calcd. for $C_{11}H_{22}ONCl$: C, 60.12; H, 10.09; N, 6.37. Found: C, 59.72, 59.75; H, 10.13, 9.97; N, 6.34, 6.34.

3-Cyclohexyl-2-cyclohexen-1-one (XVI) was prepared from β-dimethylaminopropionylcyclohexane hydrochloride and methyl acetoacetate in benzene. The product was obtained by distillation as a mobile colorless oil, yield 30%, b.p. 93° (0.3 mm.), $n^{25°}_D$ 1.5169.

Anal.[16] Calcd. for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.53, 80.67; H, 10.09, 10.02.

A 2,4-dinitrophenylhydrazone was obtained from alcohol as glistening red needles, m.p. 174.3–175.5°.

Anal.[16] Calcd. for $C_{18}H_{22}O_4N_4$: C, 60.32; H, 6.19; N, 15.63. Found: C, 60.30, 60.35; H, 6.26, 6.26; N, 15.75, 15.65.

1-(β-Dimethylaminopropionyl)-cyclohexene Hydrochloride.—1-Acetylcyclohexene prepared by the Friedel–Crafts reaction[17] between cyclohexene and acetyl chloride with aluminum chloride as catalyst proved highly unsatisfactory for the Mannich reaction. A more suitable product was obtained when stannic chloride was employed as catalyst for the Friedel–Crafts reaction. Our procedure was essentially the same as that described by Royals and Hendry.[18]

A mixture of 45.5 g. (0.37 mole) of 1-acetylcyclohexene, 22.0 g. (0.73 mole) of paraformaldehyde and 32.6 g. (0.4 mole) of dimethylamine hydrochloride in 150 cc. of alcohol containing 6 drops of concentrated hydrochloric acid was refluxed for 24 hours and concentrated *in vacuo*. The crystalline residue was washed in the cold with ether and recrystallized from acetone; yield 36 g. (45%) of colorless plates, m.p. 162–163°.

Anal. Calcd. for $C_{11}H_{20}ONCl$: C, 60.66; H, 9.28; N, 6.43. Found: C, 60.61, 60.62; H, 9.11, 9.09; N, 6.45, 6.44.

4-Acetyl-4-carbomethoxy-1-decalone (XVIII).—A mixture of 10.9 g. (0.05 mole) of 1-(β-dimethylaminopropionyl)-cyclohexene hydrochloride, 6.0 g. (0.052 mole) of methyl acetoacetate and potassium *t*-butoxide (0.0625 mole) in 250 cc. of dry benzene was refluxed for 24 hours, cooled and acidified with 100 cc. of dilute acetic acid. The aqueous layer was separated and extracted with ether and the combined benzene–ether fraction washed and dried and concentrated to dryness *in vacuo*. The solid residue was collected on the filter and washed with a small volume of ether; yield 6.0 g. (47%), m. p. 112-119°. A test sample gave no coloration with alcoholic ferric chloride and did not decolorize a solution of bromine in carbon tetrachloride. An analytical sample was obtained from acetone–petroleum ether as glistening, colorless rods, m.p. 122.7–123.8°.

Anal. Calcd. for $C_{14}H_{20}O_4$: C, 66.64; H, 7.99. Found: C, 66.42, 66.85; H, 7.78, 7.85.

4-Acetyl-1-decalone (XIX); 4-Carboxy-1-decalone (XX).—A solution of 4.2 g. (0.017 mole) of XVIII in 10 cc. of methanol was refluxed for six hours with a solution of 6 g. of potassium hydroxide in 25 cc. of methanol and 10 cc. of water. After cooling and dilution with water, the alkali-insoluble oil was taken up in ether, washed and dried. Upon distillation, XIX was obtained as a colorless, mobile oil; yield 1.6 g. (50%), b.p. 124° (0.5 mm.), n^{25}_D 1.4951.

Anal. Calcd. for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 73.95, 74.11; H, 9.12, 9.16.

A di-2,4-dinitrophenylhydrazone was obtained from ethyl acetate as glistening orange needles, m.p. 239–240° dec.

Anal. Calcd. for $C_{24}H_{26}O_8N_8$: C, 51.98; H, 4.73. Found: C, 51.99, 51.93; H, 4.85, 4.78.

The alkaline solution from the saponification reaction was acidified in the cold and the product taken up in ether, washed and dried. Upon evaporation to dryness, XX was obtained as a viscous yellow oil which solidified on standing at room temperature; yield 1.0 g. (30%). Recrystallization from alcohol–hexane afforded colorless prisms, m.p. 153.2–154.7°.

Anal.[16] Calcd. for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.46, 67.47; H, 8.27, 8.16.

A 2,4-dinitrophenylhydrazone was obtained from alcohol as orange needles, m.p. 210.5–213° dec. (lit.[4b] m.p. 200° dec.).

Anal. Calcd. for $C_{17}H_{20}O_6N_4$: C, 54.25; H, 5.36. Found[16]: C, 54.00, 54.05; H, 5.40, 5.52.

A methyl ester, prepared from methanol and dry hydrogen chloride, was obtained as a colorless mobile oil.

Anal. Calcd. for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63. Found: C, 68.70, 68.48; H, 8.38, 8.49.

Dehydrogenation of 4-Acetyl-1-decalone.—A solution of 1.0 g. (0.005 mole) of XIX in 5 cc. of carbon tetrachloride was treated in the presence of 2 g. of anhydrous potassium carbonate with a solution of 825 mg. (0.005 mole) of bromine in 5 cc. of carbon tetrachloride at room temperature. The product was refluxed for 4 hours with 10 cc. of mixed collidines, cooled, filtered and the filtrate poured onto ice and hydrochloric acid. The mixture was extracted with ether and the ethereal solution, washed, dried and evaporated to dryness. The residual red oil was heated at 340–360° for 3.5 hours with 750 mg. of 10% palladium-on-charcoal and afforded 15 mg. of α-naphthol, m.p. 94.1–95.3°. No depression in m.p. was observed on admixture with an authentic sample.

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