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Aromatization Studies. VIII. Catalytic Dehydrogenation of Di- and Trialkylcyclohexenones to Phenols

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An investigation² of the catalytic (palladium-carbon) dehydrogenation of 3-methyl-5-aryl-2-cyclohexen-1-ones indicated that aromatization of the alicyclic system to a phenolic system could be accomplished in good yield (*ca.* 70–85%) in a variety of boiling solvents. In contrast to most previous observations, it was found that the dehydrogenation process occurred rapidly under ordinary conditions of boiling, with the major part of the reaction taking place within the first fifteen minutes.

In order to study the effect of substituent groups on dehydrogenations leading to phenols, an investigation has now been carried out with several di- and trialkyl-2-cyclohexen-1-ones. 3-Methyl-5-alkyl-2-cyclohexen-1-ones, in which the alkyl group was methyl, ethyl, *n*-propyl, isopropyl and *n*-hexyl, were treated with a 5% palladium-carbon catalyst in a boiling solvent (usually trimethylbenzene) under the same general conditions employed previously.² The effects of variations in time and solvents on the yield of phenol are given in Table I. The effect of variations in the 5-alkyl group on the yield, for a two-hour reaction period at 168°, is shown in Table II. The 3-methyl-2,5-dialkyl-2-cyclohexen-1-ones listed in Table III were also aromatized, under the same conditions, to the corresponding phenols whose properties are in Table IV. The observed yields were generally in the range 40–50% (Tables I, II and IV) for a two-hour reaction period. This range is considerably below that found for 3-methyl-5-aryl-2-cyclohexenones, and the explanation is evidently to be found in a greater tendency of alkylcyclohexenones to undergo disproportionation. In the case of 3,5-dimethyl-2-cyclohexen-1-one, the expected 3,5-dimethylcyclohexanone was isolated as the semicarbazone (in about 25% of the total, or 50% of the expected yield) from the reaction mixture. The yields of phenols obtained here are not high, but the method described provides a convenient and useful means for obtaining alkyl phenols which are not available through ordinary aromatic reaction methods.

The 3-methyl-5-alkyl-2-cyclohexen-1-ones were obtained through the Knoevenagel condensation.³ The fact that 3-methyl-5-alkyl-4-carbomethoxy-2-cyclohexen-1-ones may be alkylated in the 2-position is well established, but when the reaction is carried out in ethanol with sodium ethoxide, the predominant reaction is loss of the 4-carbomethoxy group by alcoholysis. Sodamide alkylation affords a better means of obtaining alkylated esters,⁴

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TABLE I

DEHYDROGENATION OF 3,5-DIMETHYL-2-CYCLOHEXEN-1-ONE

Solvent	B. p., °C.	Time, hr.	Yield of phenol, %
Trimethylbenzene	168	0.5	37
Trimethylbenzene	168	2	38
Trimethylbenzene	168	4	39
Trimethylbenzene	168	6	44
Cymene	177	2	50
Triethylbenzene	214	2	46
Phenyl ether	252	2	48

TABLE II

DEHYDROGENATION TO 3-METHYL-5-ALKYLPHENOLS

5-Alkyl	Yield, %	M. p. or b. p., °C.
Methyl	38	62–63°
Ethyl	42	52–54° ^a
<i>n</i> -Propyl ^{b,c}	49	152–154° (40 mm.)
Isopropyl	49	49–51° ^d
<i>n</i> -Hexyl ^{e,f}	54	190–192° (35 mm.)

^a Reported m. p. 55° (Kruber and Schmitt, *Ber.*, **64**, 2270 (1931)). ^b *Anal.* Calcd. for C₁₀H₁₄O: C, 79.95; H, 9.39. Found: C, 79.99; H, 9.27. ^c Phenylurethan, m. p. 90–91° from cyclohexane–hexane. *Anal.* Calcd. for C₁₇H₁₈O₂N: C, 75.81; H, 7.11. Found: C, 75.83; H, 7.28. ^d Reported m. p. 48–49° and 54° (Horning, *THIS JOURNAL*, **67**, 142 (1945); Knoevenagel, *Ber.*, **27**, 2347 (1894)). ^e *Anal.* Calcd. for C₁₅H₂₀O: C, 81.19; H, 10.48. Found: C, 81.33; H, 10.49. ^f Aryloxyacetic acid, m. p. 76–77.5° from cyclohexane–hexane. *Anal.* Calcd. for C₁₅H₂₂O₃: C, 71.95; H, 8.86. Found: C, 71.99; H, 8.70.

although the low degree of reactivity and the tendency of the sodium salts to form gums may make it difficult to carry out this reaction. After careful fractionation of the alkylated esters, the 4-carbomethoxy group was removed by alkaline hydrolysis and decarboxylation. The resulting cyclohexenones are listed in Table III.

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Experimental

All melting points are corrected.

Palladium Catalyst.—A 5% palladium-carbon catalyst was prepared according to Hartung's method.⁵

Solvents.—All solvents were distilled before use. The trimethylbenzene solvent was the technical grade (mixed isomers) of the Eastman Kodak Co., b. p. 168–172°. This solvent was found to give particularly clean products.

Dehydrogenation.—The general procedure is illustrated by the following example. To 5.00 g. of 3,5-dimethyl-2-cyclohexen-1-one in 15 ml. of trimethylbenzene was added 1.50 g. of 5% palladium-carbon catalyst. The mixture was maintained under vigorous reflux for

(5) "Organic Syntheses," **26**, 77 (1946).

TABLE III
 3-METHYL-2,5-DIALKYL-2-CYCLOHEXEN-1-ONES

2-Alkyl	5-Alkyl	Yield, %	B. p., °C.	Analyses, %			
				Calcd.		Found	
				C	H	C	H
Ethyl	Methyl	52	97-106 (11 mm.)	78.89	10.59	78.87	10.43
Ethyl	Isopropyl	40	257-268 (atm.)	79.94	11.18	78.82 ^a	10.60 ^a
<i>n</i> -Butyl	Methyl	61	134-141 (18 mm.)	79.94	11.18	79.76	11.27

^a Not improved on further fractionation.

2,4-DINITROPHENYLHYDRAZONES OF 3-METHYL-2,5-DIALKYL-2-CYCLOHEXEN-1-ONES

2-Alkyl	5-Alkyl	M. p., °C.	Color	Analyses, %			
				Calcd.		Found	
				C	H	C	H
Ethyl	Methyl	215-217	Red	57.81	6.06	57.75	5.98
Ethyl	Isopropyl	116.5-118.5	Red	59.98	6.71	60.00	6.53
<i>n</i> -Butyl	Methyl	121.5-123.5	Red	59.98	6.71	59.66	6.60

 TABLE IV
 DEHYDROGENATION TO 3-METHYL-2,5-DIALKYLPHENOLS

2-Alkyl	5-Alkyl	Yield, %	M. p. or b. p., °C.	Analyses, %			
				Calcd.		Found	
				C	H	C	H
Ethyl	Methyl	45	78-80 ^a	79.96	9.39	79.95	9.31
Ethyl	Isopropyl	35	150-153 (26 mm.)	80.85	10.17	80.90	10.33
<i>n</i> -Butyl	Methyl	41	64-65.5 ^b 152-155 (20 mm.)	80.85	10.17	80.91	10.33

^a Recrystallized from hexane. ^b Recrystallized from pentane.

DERIVATIVES OF 3-METHYL-2,5-DIALKYLPHENOLS

2-Alkyl	5-Alkyl	Derivative	M. p., °C.	Analyses, %			
				Calcd.		Found	
				C	H	C	H
Ethyl	Methyl	4,6-Dibromo	51-53.5 ^a	38.99	3.93	38.86	3.81
Ethyl	Isopropyl	Phenylurethan	131.5-133.5 ^b	76.73	7.79	76.60	7.90
<i>n</i> -Butyl	Methyl	4,6-Dibromo	72.5-74 ^a	42.89	4.80	43.04	4.86

^a Recrystallized from pentane. ^b Recrystallized from cyclohexane.

two hours. After cooling to about 50°, the catalyst was removed by filtration, and washed with four 5-ml. portions of hot ethyl acetate. The solution was extracted with three 40-ml. portions of 10% sodium hydroxide solution. The combined alkaline extracts were washed with 40 ml. of pentane, and diluted with 100 ml. of water. Five milliliters of concentrated hydrochloric acid was added; the solution was chilled in an ice-bath and acidified with dilute hydrochloric acid. The phenol crystallized immediately. After chilling for several hours, the product was removed by filtration, washed well with water and air-dried. The yield was 1.89 g. (38%) of slightly discolored flakes, m. p. 62-63°.

Further extraction of the organic solution with Claisen solution and acidification of the alkaline extract did not yield additional 3,5-dimethylphenol.

The effect of variations in temperature of the boiling solvent and reaction time on the yield is shown in Table I. The yields given are for crude, dry product; all melting points were in the range 62-64°.

This general procedure, using trimethylbenzene as a solvent, with a two hour reaction time, was applied to 3-methyl-5-alkyl-2-cyclohexen-1-ones to provide the results shown in Table II. The dehydrogenation of the 3-methyl-2,5-dialkyl-2-cyclohexen-1-ones listed in Table III gave the corresponding phenols in the yield indicated in Table IV. In the case of trialkylphenols, the isolation procedure was modified in the following way. After removal of the catalyst, the organic solution was extracted with 5% sodium hydroxide solution; this alkaline wash was discarded. (In preliminary experiments, there were indications that small amounts of unchanged 4-carbomethoxycyclohexenones were occasionally present in the alkylated products, and this in turn would perhaps result in small amounts of 3,5-dialkylphenols along with the desired 2,3,5-trialkylphenols. In later experiments, the alkylated esters and ketones were fractionated care-

fully, but at the same time this step was retained. 3,5-Dialkylphenols may be extracted from organic solvents with aqueous alkali, while 2,3,5-trialkylphenols require Claisen alkali for extraction.) The phenolic product was then extracted with Claisen solution, and the extract was washed with pentane. The alkaline solution was diluted and acidified with hydrochloric acid, with cooling. Liquid phenols were isolated by extraction with ether, and the crude products were distilled under reduced pressure through a small Vigreux column.

Disproportionation to 3,5-Dimethylcyclohexanone.—The dehydrogenation of 5.00 g. of 3,5-dimethyl-2-cyclohexen-1-one was carried out under the usual conditions in 15 ml. of phenyl ether. After extraction of the phenolic fraction with 10% sodium hydroxide solution, the organic solution was steam distilled to provide a distillate which included ethyl acetate, a ketonic fraction, and traces of phenyl ether. The organic layer was separated, and the aqueous layer extracted with 30 ml. of ether. The combined organic solutions were dried with magnesium sulfate, and the ether was evaporated by warming. The residue was added to 15 ml. of ethanol containing 2.7 g. of semicarbazide hydrochloride, and 5.0 ml. of pyridine. After a reflux period of four hours, 30 ml. of ethanol was added, and approximately 30 ml. of solvents (ethanol-ethyl acetate) was removed by distillation. The residue was poured into 100 ml. of ice-water, and the colorless crystalline product was removed by filtration, washed well with water, and air dried. The dry product was triturated with pentane to remove traces of phenyl ether; the residue was 1.58 g. of colorless material, m. p. 192-194° (dec.). A mixed m. p. with a sample of 3,5-dimethylcyclohexanone semicarbazone, prepared separately, was not depressed.

In a separate experiment, it was found that the semicarbazone of 3,5-dimethylcyclohexanone could be obtained in 88% yield, using the alcohol-pyridine method

with the quantities indicated above, with 2.50 g. of ketone. This indicated that the isolation methods used in the experiment described accounted for approximately 25% of the starting material as 3,5-dimethylcyclohexanone, and about 50% as 3,5-dimethylphenol.

3,5-Dimethylcyclohexanone.—3,5-Dimethyl-2-cyclohexen-1-one was hydrogenated in a low-pressure apparatus, using a 5% palladium-carbon catalyst without added solvent. The boiling point of the product was 62–66° (9 mm.). The semicarbazone, prepared by the alcohol-pyridine method, was a colorless solid, m. p. 194–195° (dec.) after crystallization from methanol (crude m. p. 194–196° (dec.)).

This ketone was described by Knoevenagel⁶ as a mixture of *cis* and *trans* forms, giving a semicarbazone melting at 190–196°. The configuration of the methyl groups of the product obtained here is not known, but the materials obtained by catalytic reduction and by disproportionation were evidently identical.

3-Methyl-2,5-dialkyl-2-cyclohexen-1-ones.—These ketones were prepared through the sodamide alkylation of 3-methyl-5-alkyl-4-carbethoxy-2-cyclohexen-1-ones³ with the appropriate alkyl iodide, as illustrated by the following example.

A. Alkylation: Sodamide was prepared in the usual way from 12.0 g. (0.52 mole) of sodium and about 500 ml. of liquid ammonia, using ferric nitrate nonohydrate as a catalyst. There was added 98.6 g. (0.50 mole) of 3,5-dimethyl-4-carbethoxy-2-cyclohexen-1-one over ten minutes; a yellow amorphous salt formed immediately. About 350 ml. of dry ether was added, and the ammonia was allowed to evaporate. The precipitated salt became increasingly viscous, but stirring was continued as much as possible. A total of 125 g. (0.8 mole) of ethyl iodide was added in small portions as the mixture was brought to reflux temperature, and finally 100 ml. of dry ether and 100 ml. of dry toluene was added. The mixture was heated under reflux with stirring in a nitrogen atmosphere for nine hours. After addition of water, the organic solution was separated, washed with 5% aqueous acetic acid and water, and dried over magnesium sulfate. The ether and toluene were removed by distillation at atmospheric pressure, and the residue was fractionated through a 12-inch Vigreux column. The yield was 78.7 g. (70%) of 2-ethyl-3,5-dimethyl-4-carbethoxy-2-cyclohexen-1-one as a light yellow oil, b. p. 128–135° (4 mm.).

Anal. Calcd. for C₁₃H₂₀O₃: C, 69.61; H, 8.98. Found: C, 69.80; H, 9.09.

The red-orange 2,4-dinitrophenylhydrazone melted at 107.5–109°.

Anal. Calcd. for C₁₉H₂₄O₈N₄: C, 56.43; H, 5.98. Found: C, 56.53; H, 5.89.

Alkylation of the same ketoester with *n*-butyl iodide

(with a thirty-six-hour reflux period) gave a 43% yield of 2-*n*-butyl-3,5-dimethyl-4-carbethoxy-2-cyclohexen-1-one, b. p. 150–151° (4–5 mm.).

Anal. Calcd. for C₁₅H₂₄O₃: C, 71.39; H, 9.59. Found: C, 71.37; H, 9.77.

An alkylation of 3-methyl-5-isopropyl-4-carbethoxy-2-cyclohexen-1-one with ethyl iodide gave a 61% yield of 2-ethyl-3-methyl-5-isopropyl-4-carbethoxy-2-cyclohexen-1-one, b. p. 137–150° (4 mm.). The boiling range indicated that this material was not homogeneous, and it was hydrolyzed directly to the desired ketone without additional fractionation.

These two alkylated esters gave 2,4-dinitrophenylhydrazones which could be obtained only as red, non-crystalline gums. In the course of alkylation it is necessary for the double bond to shift to the 3,4-position, and this unusual behavior of the dinitrophenylhydrazones may indicate that the esters are mixtures of 2,3- and 3,4-double bond isomers.

B. Hydrolysis and decarboxylation: A solution of 71.2 g. (0.32 mole) of 2-ethyl-3,5-dimethyl-4-carbethoxy-2-cyclohexen-1-one, 40 g. (1.0 mole) of sodium hydroxide, 160 ml. of water and 75 ml. of ethanol (95%) was heated under reflux for three and one-half hours. The warm solution was acidified by the slow addition of 150 ml. of 1:1 sulfuric acid; a vigorous evolution of carbon dioxide resulted. The acidified mixture was boiled under reflux one and one-half hours, cooled and extracted with ether. The ether solution was washed well with 5% sodium hydroxide solution, with 2% aqueous acetic acid, with water, and dried over magnesium sulfate. The ether was removed, and the residue distilled under reduced pressure through a 12-inch Vigreux column to yield 25.1 g. (52%) of 2-ethyl-3,5-dimethyl-2-cyclohexen-1-one.

The yields, boiling points and derivatives of these trialkylcyclohexenones are listed in Table III.

Summary

A series of di- and trialkylcyclohexenones have been dehydrogenated with a palladium-carbon catalyst to the corresponding di- and trialkylphenols. The yields were usually 40–50%; in the case of arylcyclohexenones the yield is usually 70–85%, and the lowered yield observed here is apparently due to a greater tendency for the alkylcyclohexenones to undergo disproportionation.

The procedures described here provide a route to certain types of alkyl-substituted phenols which are not available by ordinary aromatic substitution methods.

(6) Knoevenagel, *Ann.*, **297**, 183 (1897).