rings of any of the derivatives of the hydrocoumarin or of the hydrocarbostyril.

4. The formation of the hydrocoumarin V by nitration of the ester II is paralleled by a similar reaction in connection with the tocopherols and compounds related to them. Here also the action of nitric acid is equivalent to hydroxylation of a ring at one of the stages of the reaction.

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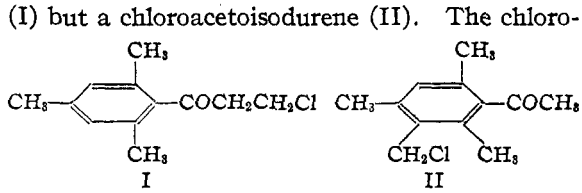
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Chloromethylation of Aryl Ketones

BY REYNOLD C. FUSON AND C. H. MCKEEVER[1]

The chloromethylation of methyl aryl ketones was undertaken in the hope of obtaining a useful synthesis of β-chloropropiophenones. The success of Colonge[2] in chloromethylating aliphatic ketones by treatment with formalin in the presence of hydrogen chloride and zinc chloride suggested that a similar procedure might prove effective in the aromatic series. We therefore attempted to adapt his method to serve our purpose. In order to minimize the amount of water present, and thus enhance the solubility of the ketones, paraformaldehyde was used in place of formalin. Preliminary experiments on acetomesitylene showed that zinc chloride was not necessary to bring about the reaction. However, the product was not the expected β-chloropropiomesitylene (I) but a chloroacetoisodurene (II). The chloromethyl group had entered the ring instead of the side-chain. In other words, we appeared to have a method for nuclear chloromethylation similar to that developed by Blanc[3] for aromatic hydrocarbons and extended by others, notably Quelet,[4] to other types of aromatic compounds.



Experiments with other aromatic ketones have substantiated this surmise. The method appears to be general for ketones in which the aryl radical carries two or more alkyl groups. Acetophenone and benzophenone failed to react under these conditions.

The reaction provides an indirect method of methylation; this is shown by the fact that acetoisodurene and pentamethylacetophenone were obtained in 80 and 90% yields, respectively, by reducing the corresponding chloromethyl derivatives according to the method of v. Braun and Nelles.[5]

TABLE OF RESULTS

Compound	Time, hr.	Yield, %	M. p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Chlorine, % Calcd.	Chlorine, % Found
5-Chloromethyl-2,4-dimethylacetophenone[a]	41	50	68.5–69	67.17	67.03	6.66	6.75	18.02	17.94
3-Chloromethylacetomesitylene[b]	12	80	74.5–75.5	68.42	68.55	7.18	7.04		
3-Chloromethylacetoisodurene[b]	12	75	88.5–90	69.48	69.14	7.62	7.81		
3-Chloromethylpropiomesitylene	15	88	75–76	69.48	69.50	7.62	7.75	15.78	15.73
3-Chloromethylisobutyromesitylene[c]	36	78		70.43	70.23	8.02	8.09		
3-Chloromethylpivalylmesitylene[b,d]	15	25	54–55	71.27	71.11	8.37	8.34	14.02	14.29
3-Chloromethylbenzoylmesitylene[b]	150	35	90–91	74.85	74.87	6.28	6.20		
3-Chloromethyl-2,4,6-triethylacetophenone	60	57	57–58	71.27	71.41	8.37	8.27	14.02	14.29

[a] The reaction mixture was kept at 80°. The position of the chloromethyl group in this compound was not proved. [b] The yield here is calculated on the original amount of ketone, in all other cases on the amount of ketone that reacted. [c] This compound is a liquid, b. p. 140° (2 mm.); $n^{20}D$ 1.5395; d^{20}_{20} 1.0785. [d] Pivalylmesitylene is a new compound. It was prepared from mesitylene and pivalyl chloride by the Friedel-Crafts method; b. p. 97–97.5° (2.5 mm.); $n^{20}D$ 1.5093; d^{20}_{20} 0.9531. *Anal.* Calcd. for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.33; H, 9.83.

Procedure.—A mixture of 0.1 mole of the ketone, 0.11 mole of paraformaldehyde and 100 cc. of concentrated hydrochloric acid was shaken for fifteen to seventy-two hours at 25–85° depending upon the nature of the ketone. The solid which precipitated was removed by filtration, washed thoroughly and recrystallized from high-boiling petroleum ether or methyl alcohol.

In some cases the chloromethyl derivative did not sepa-

(1) Röhm and Haas Research Assistant.
(2) Colonge, *Bull. soc. chim.*, [5] **3**, 2116 (1936).
(3) Blanc, *ibid.*, **33**, 313 (1923).
(4) For a leading reference see Quelet and Allard, *Compt. rend.*, **205**, 238 (1937).
(5) v. Braun and Nelles, *Ber.*, **67**, 1094 (1934).

rate from the reaction mixture. It was then necessary to pour the mixture into 500 cc. of water and extract with benzene or ether. After the extracts were washed several times with water and dried over calcium chloride, the solvent was removed and the residue distilled *in vacuo*. The chloromethyl derivative was separated easily from the parent ketone by this method.

All but one of the chloromethylated ketones prepared were low-melting solids which, although very soluble in organic solvents, could be recrystallized from low-boiling petroleum ether or methyl alcohol.

Summary

A method has been developed for nuclear chloromethylation of certain types of aromatic ketones.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF HARVARD UNIVERSITY]

Hexahydroacetomesitylene[1]

BY E. P. KOHLER, THOMAS L. JACOBS[2] AND H. M. SONNICHSEN[3]

In continuation of a series of investigations made in this Laboratory[4] as to the effect of hindrance on the stability of enols of aliphatic monoketones, it appeared of interest to study the behavior of hexahydroacetomesitylene and its derivatives from this same point of view. The results of such a study are presented herewith.

It was decided to undertake the preparation of hexahydroacetomesitylene by catalytic hydrogenation of the mesitylene nucleus because that method seemed likely to involve the fewest stereochemical complications, although it is probable that there are other easier routes to that substance.

Preliminary experiments showed that the carbonyl group of acetomesitylene is reduced catalytically before nuclear hydrogenation begins, and the alcohol produced is dehydrated under much less drastic conditions than are necessary for the hydrogenation of the ring; consequently it was necessary to find another derivative of mesitylene which could be hydrogenated in the nucleus and later transformed into an acetyl derivative, and for this purpose mesitylene carboxylic acid seemed the logical choice. The sodium salt of this acid was successfully hydrogenated in water solution using Raney nickel catalyst activated with ammonium chloroplatinate.

It was not possible to separate the isomeric hexahydromesitylene carboxylic acids by simple crystallization, due partly to their great solubility in common organic solvents, and sublimation also failed. The acids were therefore converted into a mixture of amides from which a pure amide melting at 230° and a mixture melting sharply at 167° were obtained. The mixture was shown to contain the 230° amide.

When the residues from the amide preparation were distilled under reduced pressure the principal product was the nitrile, 2,4,6-trimethylhexahydrobenzonitrile, and from the solid residue in the distillation flask was recovered more of the mixture of amides melting at 167°. The structure of the nitrile was proved by the fact that methyl alcoholic potassium hydroxide hydrolyzed it to the 230° amide. The failure of the nitrile to be hydrolyzed past the amide stage by heating with methyl alcoholic potassium hydroxide for several hours was our first indication of the hindered nature of these derivatives of trimethylcyclohexane.[5] The amide also resisted concentrated phosphoric acid and was remarkably inert toward nitrous acid, although by this means it was possible to obtain enough pure trimethylhexahydrobenzoic acid (m. p. 85–87°) for an analysis.

The mixture of amides melting at 167° gave an acid melting at 114–117° when partially hydrolyzed with nitrous acid, and the material remaining unattacked was a mixture of the 230° amide and the 167° mixture. A mixture of the acid

(1) Abstracted from a thesis entitled "Mesitylenic and Hexahydromesitylenic Ketones" presented by H. M. Sonnichsen to the Faculty of Arts and Sciences of Harvard University in partial fulfillment of the requirements for the degree of Doctor of Philosophy, June, 1939. The work described herein was begun under the direction of Professor Kohler and completed after his death under the direction of Dr. Jacobs.—H. M. S.

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(4) Kohler, Tishler and Potter, THIS JOURNAL, **57**, 2517 (1935); Kohler and R. B. Thompson, *ibid.*, **59**, 887 (1937); D. T. Rogers, Harvard Ph.D. Thesis, 1938.

(5) Similar cases may be found in the following references: (a) Jacobsen, *Ber.*, **22**, 1219 (1889); (b) Küster and Stallberg, *Ann.*, **278**, 207 (1893); (c) Hantzsch and Lucas, *Ber.*, **28**, 748 (1895); (d) Sudborough, Jackson and Lloyd, *J. Chem. Soc.*, **71**, 229 (1897); (e) Sachs, *Ber.*, **35**, 3325 (1902); (f) Klages, *ibid.*, **36**, 4192 (1903); (g) Knoevenagel, *ibid.*, **37**, 4091 (1904); (h) Reich, *Bull. soc. chim.*, **21**, 222 (1917); (i) Tiemann, *Ber.*, **31**, 889 (1898).