

sium permanganate was finally titrated. The accuracy of this oxidation method was checked by oxidation of chalcone.²

An unusual compound was isolated in one determination where manganous chloride was used as a catalyst. The ethereal solution was evaporated, and the residue crystallized from alcohol. A solid which melted at 136° was obtained.

Anal. Calcd. for $\text{C}_{22}\text{H}_{20}\text{O}_2$: C, 85.71; H, 7.14; mol. wt., 448. Found: C, 85.82; H, 7.14; mol. wt., 470.

This compound could possibly be formed by the condensation of β -phenylvalerophenone and chalcone in a manner similar to the substance obtained from β -phenylbutyrophenone and chalcone. This compound yielded a 2,4-dinitrophenylhydrazone.

Anal. Calcd. for $\text{C}_{28}\text{H}_{28}\text{O}_6\text{N}_4$: N, 8.92. Found: N, 9.11.

The compound could not be synthesized by condensing β -phenylvalerophenone with chalcone when either pyridine or ethylmagnesium bromide was used as a condensing agent.

Addition of Benzophenone to Ethylmagnesium Bromide.—Benzophenone (0.5 mole) in 40 cc. of anhydrous benzene was added slowly to a 100% excess of ethylmagnesium bromide containing 6 mole per cent. of cobaltous chloride. The temperature of the reaction was kept below 20° . A mixture of diphenylethylcarbinol and diphenylpropylene was obtained. The reaction product was dehydrated to diphenylpropylene by distillation with a trace of iodine. The yield was quantitative.

Benzophenone, 0.05 mole, in 40 cc. of anhydrous benzene containing 6 mole per cent. of cobaltous chloride was slowly added to 100% excess of ethylmagnesium bromide; the

reaction temperature was kept at -12° . The reaction mixture was then stirred for two hours at -12° , and allowed to stand overnight at room temperature. By the usual methods of isolation, benzopinacol (45%) and diphenylethylcarbinol (55%) were obtained from this mixture.

Summary

1. The effect of some metallic chlorides on the reaction of Grignard reagents with benzalacetophenone has been studied.

2. It has been shown that manganous chloride has little catalytic effect on the reaction between ethylmagnesium bromide or iodide and chalcone. Cobalt chloride is a powerful catalyst for the formation of reduction dimers. Cuprous and ferric chlorides are intermediate in their catalytic effect.

3. Metallic halides do not markedly affect the reaction between ethylmagnesium bromide and chalcone; they slightly favor 1,2 addition. Variations in temperature and in the order of addition of the reagents also produce only a slight effect.

4. Benzophenone at 25° reacts with ethylmagnesium bromide containing cobalt chloride to give only the addition product. Benzophenone at -12° reacts with ethylmagnesium bromide containing cobalt chloride to give both benzopinacol and diphenylethylcarbinol.

CHICAGO, ILLINOIS

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[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY, THE UNIVERSITY OF CHICAGO]

Carboxylation. IV. Direct Introduction of the Chloroformyl ($-\text{COCl}$) Group into Alicyclic and Aliphatic Acid Chlorides

BY M. S. KHARASCH, KENNETH EBERLY AND MORTON KLEIMAN

In the course of work on the introduction of the chloroformyl ($-\text{COCl}$) group¹ into cyclohexane by the use of trichloromethyl chloroformate, there was obtained under optimum conditions (six hours of heating at 225°) a 3% yield of a disubstitution product, identified as 1,1-dichloroformylcyclohexane by hydrolysis to cyclohexane-1,1-dicarboxylic acid. Despite careful search, no hexahydrobenzoyl chloride could be detected.

This rather striking result suggested that diphosgene reacts more readily with hexahydrobenzoyl chloride than with cyclohexane. Upon further investigation, it was found that ten hours

of heating of hexahydrobenzoyl chloride with diphosgene in a sealed tube at 225° , subsequent hydrolysis of the reaction product, and crystallization of the hydrolyzate from an ether-ligroin mixture, gave an 81% yield of cyclohexane-1,1-dicarboxylic acid.

In a like manner, diphosgene reacts with isobutyryl chloride to give a 70% yield of dimethylmalonyl chloride; with α -ethylbutyryl chloride to give a 90% yield of diethylmalonyl chloride; and with α -ethylhexoyl chloride to give a 30% (or possibly higher) yield of ethylbutylmalonyl chloride. In many experiments with propionyl chloride and diphosgene, however, the maximum yield of methylmalonic acid was only 15%. No

(1) For previous references, see Kharasch, Kane and Brown, *THIS JOURNAL*, **64**, 1621 (1942).

malonic acid was obtained from acetyl chloride. With phenylacetyl chloride, the best yield of phenylmalonic acid so far obtained is only 2%.

From these findings, it appears that a chloroformyl group derived from diphosgene readily replaces a tertiary hydrogen atom on the α carbon atom of an acid chloride. The same reagent replaces secondary hydrogen atoms with considerable difficulty (if low yield be regarded as a criterion). Replacement of a primary hydrogen atom by this method seems to be impossible.

Experimental

Reaction of Cyclohexane with Diphosgene.—A mixture of 7 g. of cyclohexane and 8.3 g. of diphosgene was sealed in a bomb-tube and heated for ten hours at 225°. The tube was then allowed to come to room temperature, cooled by immersion in liquid nitrogen, and opened. After allowing the volatile products to boil away, the content of the tube was poured into water, allowed to stand for a few hours at room temperature, and finally evaporated to dryness on a steam-bath. A solid material (0.2 g.) which melted at 172° (dec.) was thus obtained. This substance, after crystallization from a mixture of ether and ligroin, melted at 178° (dec.) and did not depress the melting point of a known sample of cyclohexane-1,1-dicarboxylic acid.²

Anal. Calcd. for $C_6H_{10}O_4$: C, 55.78; H, 7.03. Found: C, 55.59; H, 6.96.

The cyclohexane-1,1-dicarboxylic acid was further identified by decarboxylation (at 200°) to the hexahydrobenzoic acid and conversion of the latter substance (with the aid of thionyl chloride and ammonia) to the known hexahydrobenzamide (m. p. 186°).

Anal. Calcd. for $C_7H_{13}ON$: N, 11.02. Found: N, 11.01.

The volatile components were distilled from the mixture obtained by the interaction of cyclohexane and diphosgene. In order to prepare the diamide of cyclohexane-1,1-dicarboxylic acid, the residue was poured into a large excess of aqueous ammonia. The dark sludge which separated was taken up in hot dilute alcohol, treated with bone black, and filtered. The filtrate was reduced to a small volume and allowed to stand. Small, colorless crystals melting at 261° were obtained. The melting point of this material was not altered by further crystallization from dilute alcohol. *Anal.* Calcd. for $C_6H_{14}O_2N_2$: N, 16.47. Found: N, 16.21. The melting point of this diamide recorded by Dox and Yoder² is 237°. The reason for this discrepancy is unknown.

Preparation of Cyclohexane-1,1-dicarboxylic Acid from Hexahydrobenzoyl Chloride.—A mixture of 4 g. of hexahydrobenzoyl chloride and 5.4 g. of diphosgene was heated for ten hours in a sealed tube at 225°. The bomb-tube, after being cooled in the usual manner, was opened, and the volatile products were allowed to boil away. The residue was then hydrolyzed with water. When the water solution was evaporated to dryness, 3.8 g. of crude cyclo-

hexane-1,1-dicarboxylic acid (m. p. 170°) was obtained. This yield is 81% of that calculated on the basis of the amount of hexahydrobenzoyl chloride used. Recrystallization (with bone black) of the crude product from an ether-ligroin mixture gave colorless crystals of the acid melting at 176° (dec.).

Synthesis of Dimethylmalonyl Chloride by Interaction of Isobutyryl Chloride with Diphosgene.—A mixture of 3 g. of isobutyryl chloride and 2 g. of diphosgene was sealed *in vacuo* in a heavy glass bomb-tube and heated for ten hours at 225°. The bomb-tube was cooled to -80° before opening. The combined products of eleven such bomb reactions, when fractionated, yielded unreacted isobutyryl chloride (5.2 g.) and dimethylmalonyl chloride (31 g.), b. p. 153-159° (749 mm.). The dimethylmalonyl chloride was further identified by hydrolyzing it to the corresponding dimethylmalonic acid, m. p. 187°. The yield of dimethylmalonyl chloride, based upon the amount of isobutyryl chloride consumed in the reaction, was 70%.

Synthesis of Diethylmalonyl Chloride by the Interaction of α -Ethylbutyryl Chloride with Diphosgene.—A mixture of 4 g. each of α -ethylbutyryl chloride and diphosgene was sealed *in vacuo* in a heavy glass bomb-tube and heated at 225° for ten hours. The combined products of ten such bomb-tube reactions, when fractionated, yielded 9 g. of unreacted ethylbutyryl chloride and 39.4 g. of diethylmalonyl chloride (b. p. 190-194°). This yield is 90% of that calculated from the amount of ethylbutyryl chloride consumed in the reaction. The diethylmalonyl chloride was further identified by preparing the known diamide, m. p. 224-226° (cor.).

Synthesis of Ethylbutylmalonyl Chloride by the Interaction of α -Ethylhexoyl Chloride with Diphosgene.—Many attempts were made to carry out this reaction in glass bomb-tubes; however, except when extremely small amounts of reactants were used, the bomb-tubes exploded. A steel bomb proved more satisfactory. But, unfortunately, despite all efforts to make this bomb gas-tight, it leaked slightly at the high pressure produced during the reaction. In this steel bomb, a mixture of 25 g. of ethylhexoyl chloride and 35 g. of diphosgene was heated ten hours at 225°. The reaction mixture when fractionated yielded 3.5 g. of unreacted ethylhexoyl chloride, and 9 g. of crude ethylbutylmalonyl chloride, b. p. 190-220°; the latter was identified by hydrolyzing it to the known ethylbutylmalonic acid, m. p. 116-117°. Since the yield of ethylbutylmalonyl chloride (based upon the amount of the ethylhexoyl chloride consumed in the reaction) was 30%, it seems likely that, with satisfactory apparatus, a higher yield of this acid chloride may be obtained.

Reaction of Propionyl Chloride with Diphosgene.—A mixture of 3.5 g. of propionyl chloride and 7.5 g. of diphosgene was heated in a bomb-tube for ten hours at 225°. After cooling and opening the tube in the usual manner, the content was hydrolyzed with water and the solution evaporated to dryness on a water-bath. A 15% yield (0.65 g.) of crude methylmalonic acid was thus obtained. Crystallization (with bone black) of this product from an ether-ligroin mixture gave colorless crystals of methylmalonic acid [m. p. 132-133° (dec.)].

Reaction of Phenylacetyl Chloride with Diphosgene.—A mixture of 4 g. of phenylacetyl chloride with 5.1 g. of

(2) Dox and Yoder, *THIS JOURNAL*, **43**, 1366 (1921); Vogel, *J. Chem. Soc.*, **123**, 1487 (1929), report a melting point of 179.5° (dec.).

diphosgene was heated in a bomb-tube for ten hours at 150–175°. After cooling and opening the tube in the usual manner, the reaction mixture was hydrolyzed with water (over a period of twelve hours at room temperature), and evaporated to dryness on a water-bath. Since phenylmalonic acid is readily decarboxylated, the last traces of water were removed by drying the product over phosphorus pentoxide *in vacuo*. The mixture of phenylacetic acid and phenylmalonic acid thus obtained (3.8 g.) was decarboxylated at 220°. The carbon dioxide evolved was collected quantitatively. From the amount of carbon dioxide formed, it is estimated that the phenylmalonic acid present in the reaction mixture amounted to a 1.4% yield.

Summary

1. It has been demonstrated that the chloroformyl (—COCl) group can be directly introduced (at the α carbon atom) into aliphatic and

aryl-substituted-aliphatic acid chlorides by the use of trichloromethylchloroformate (diphosgene) as the "carboxylating" agent.

2. The experimental conditions requisite for carrying out this type of carboxylation have been determined.

3. The syntheses with good yields of several di-substituted malonyl chlorides have been described.

4. The chloroformyl group (derived from diphosgene) replaces hydrogen atoms attached to the α carbon atoms of acid chlorides most easily when these α carbon atoms are tertiary and least easily when they are primary.

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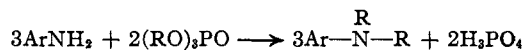
Alkylation of Amines. I¹

BY JOHN H. BULLMAN, A. RADIKE AND B. W. MUNDY

The esters of sulfuric,² sulfurous,³ and *p*-toluenesulfonic acids⁴ have been used frequently for the alkylation of amines. Now that the methyl, ethyl and *n*-butyl esters of orthophosphoric acid have become readily available within recent years,⁵ it was of interest to investigate the possibility of using these esters as alkylating agents for amines since Noller⁶ has shown that they may be used to alkylate phenols.

All of the esters investigated appeared to be non-toxic under normal conditions and were quite stable toward hydrolysis. Three-quarters of an hour was required to saponify triethyl phosphate completely when boiled with the calculated amount of sodium hydroxide.

It was found that all three groups in the ester could be utilized in the alkylation. The reaction may be represented by the equation



Several attempts to alkylate *p*-nitroaniline by this method resulted in failure. The conditions necessary to effect alkylation resulted in decomposition.

(1) Original manuscript received April 13, 1942.

(2) Claesson and Lundwall, *Ber.*, **13**, 1700 (1880); Ullmann and Wenner, **33**, 2476 (1900); Cade, *Chem. Met. Eng.*, **29**, 319 (1923).

(3) Voss and Blanke, *Ann.*, **485**, 258 (1931).

(4) Marvel and Sekera, *This Journal*, **55**, 345 (1933).

(5) Commercial Solvents Corporation, Terre Haute, Indiana.

(6) Noller and Dutton, *This Journal*, **55**, 424 (1933).

When branched chain alkyl orthophosphates such as isopropyl phosphate were used, practically pure isopropylaniline was obtained.

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Experimental

Preparation of Orthophosphate Esters.—The *n*-propyl and the isopropyl esters of orthophosphoric acid were prepared from phosphorus oxychloride and the proper alcohol similar to the method described in "Organic Syntheses."⁷ The yield of *n*-propyl phosphate was 54%, while that of the isopropyl phosphate was 65%.

Procedure for Alkylation of Amines.—A mixture of 0.3 mole of the amine and 0.2 mole of trialkyl phosphate in a 500-cc. flask provided with a condenser and boiling chips was refluxed at a moderate rate for two hours. In most cases, during the early stages of heating, the reaction became vigorous and the temperature rose sharply. As soon as rapid boiling ceased the stream of water in the condenser jacket was replaced by one of air. The mixture was then cooled to 50°, 25 g. of sodium hydroxide in 100 ml. of water added and the whole refluxed one hour, and then poured into a 400-cc. beaker where it was allowed to cool to room temperature. The oily layer of amine, which formed on top, was poured off from the solid sodium phosphate. The latter was extracted with ether and the combined extracts and oil dried over anhydrous sodium sulfate. The ether was then removed, the residue treated with an equal volume of acetic anhydride and allowed to stand overnight.

(7) *Organic Syntheses*, **16**, 10 (1936).