

Reactions of Methylcalcium Iodide. II. Carboxylation, Metalation, and Metal-Halogen Exchange Reactions

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(Received March 22, 1974)

Utility of methylcalcium iodide in several organic reactions in tetrahydrofuran was shown. Carboxylation of methylcalcium iodide at -70°C gave acetic acid in 57–63% yield. Metallation of indene and fluorene by methylcalcium iodide at -30°C gave 3-indenyl- and 9-fluorenylcalcium iodides in 99 and 93% yields, respectively. Metal-halogen exchange reactions of methylcalcium iodide with halobenzenes were rather slow.

Although reactions of organocalcium halides have been studied, available data are limited. Yields of products are generally low, particularly in the reactions of aliphatic organocalcium halides. We demonstrated that methylcalcium iodide is a useful organometallic reagent in several organic reactions in tetrahydrofuran.¹⁾ Reactions with ketones, aldehydes and esters gave the corresponding addition products in good yields. Both coupling and addition reactions were observed in the reactions with acid halides. They gave the corresponding ketones in low yields by the reaction with nitriles, reacting slowly with benzyl chloride and 1,1-diphenylethylene, but not reacting with cyclohexene. We have examined the utility of methylcalcium iodide in carboxylation, metalation, and metal-halogen exchange reactions.

Results and Discussion

Bryce-Smith and Skinner²⁾ reported that carboxylation of phenylcalcium iodide at -50 to -30°C in tetrahydrofuran afforded benzoic acid in a high yield, whereas that of *n*-butyl- and *n*-pentylcalcium iodides at 20 – 25°C in diethyl ether gave the corresponding carboxylic acids in only 10 and 9% yields, respectively. They observed the formation of the corresponding ketones and carbinols besides the carboxylic acids. However, we found that carboxylation of methylcalcium iodide at -70°C in tetrahydrofuran gave acetic acid in 53–57% yield based on methyl iodide used in the preparation of methylcalcium iodide. Since the yield of methylcalcium iodide was in the range 91–93% based on methyl iodide, the yield of acetic acid based on methylcalcium iodide would be 57–63%. Gas chromatographic analyses also showed the presence of acetone and *tert*-butyl alcohol in 17 and 11% yields based on methyl iodide (18 and 12% yields based on methylcalcium iodide), respectively. The discrepancy of our results with those of Bryce-Smith and Skinner²⁾ could be partly attributed to the difference in the reaction temperature. The addition of alkylcalcium iodide to calcium carboxylate formed by the reaction of alkylcalcium iodide with carbon dioxide might be more significant at higher temperature.

Kocheshkov and co-workers^{3,4)} reported that metallation of indene and fluorene by phenylcalcium iodide

followed by carboxylation gave the corresponding carboxylic acids in good yields. They stated that metallation of indene, fluorene and related hydrocarbons by alkylcalcium iodides followed by carboxylation afforded the corresponding carboxylic acids in very low yields.³⁾ However, we found that metalation of indene by methylcalcium iodide at -30°C followed by carboxylation gave indene-3-carboxylic acid in 99% yield, mp 161°C .

We used an excess amount of calcium metal in the preparation of methylcalcium iodide. Indene-3-carboxylic acid could be partly derived from the direct metalation of indene by the excess calcium metal. We found that direct metallation of indene by metallic calcium in tetrahydrofuran under similar reaction conditions gave only a trace of indene-3-carboxylic acid after carboxylation. Direct metallation seems to be a rather slow reaction, *e.g.*, Fischer and Stölzle⁵⁾ obtained bis(cyclopentadienyl)calcium in 27% yield from calcium metal and cyclopentadiene in 3–4 hr in refluxing tetrahydrofuran.

Kocheshkov and co-workers^{3,4)} described the formation of indene-1-carboxylic acid. However, the melting point 154°C shows that the product was indene-3-carboxylic acid. The melting points of indene-1- and indene-3-carboxylic acids were reported to be 73.5 – 74°C ⁶⁾ and 159.5 – 161°C ,⁷⁾ respectively.

We also found that fluorene-9-carboxylic acid was formed in 93% yield by the metallation of fluorene with methylcalcium iodide at -30°C followed by carboxylation.

Thus the metalation of indene and fluorene by methylcalcium iodide provides an excellent method for preparation of 3-indenyl- and 9-fluorenylcalcium iodides, which is in contrast to that described.^{3,4)} The discrepancy could be ascribed to low purity of alkylcalcium iodides.

Bryce-Smith and Skinner²⁾ reported that the reaction of α -bromonaphthalene with phenylcalcium iodide gave α -naphthylcalcium iodide in an excellent yield. However, no information can be found in literature on the metal-halogen exchange reaction of alkylcalcium halides. We found that the reactions of methylcalcium iodide with halobenzenes were rather slow. Reactions of methylcalcium iodide with bromobenzene in tetrahydrofuran at -30°C gave a trace of benzoic acid after carboxylation. Gas chromatographic analysis also indicated the presence of a nearly quantitative amount of unchanged bromobenzene in the reaction products.

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Neither toluene nor biphenyl was detected.

On the other hand, longer reaction time and higher reaction temperature improved the yield to some extent. The reaction at 20 °C for 24 and 45 hr gave benzoic acid in 11 and 36% yields, respectively, after carboxylation. The reactions of methylcalcium iodide with chlorobenzene, bromobenzene and iodobenzene at 23 °C for about 50 hr gave benzoic acid in 21, 42, and 38% yields, respectively. The reaction of *n*-propylcalcium iodide with bromobenzene at 20 °C for 40 hr gave benzoic acid in 80% yield. We used excess calcium metal in the preparation of methyl- and *n*-propylcalcium iodide. The reaction of unchanged calcium metal with halobenzenes to give phenylcalcium halides was significant under these reaction conditions. Still longer reaction time and higher reaction temperature would not markedly improve the yield, since the loss of organocalcium halides by the reaction with the solvent, tetrahydrofuran, becomes significant under the conditions.^{1,2)}

Experimental

Gas chromatographic analyses were carried out on a Shimadzu GC-4A or GC-4B gas chromatograph using columns of Chromosorb 101 (80—100 mesh) and 20% polyethylene glycol 6000 on Celite 545 (60—80 mesh) for carboxylic acids and other products, respectively. Proton magnetic resonance spectra were obtained with a Varian T-60-A spectrometer using dimethyl-*d*₆ sulfoxide or carbon tetrachloride as the solvent and tetramethylsilane as an internal standard.

Materials. Methylcalcium iodide and *n*-propylcalcium iodide were prepared in tetrahydrofuran.⁸⁾ Tetrahydrofuran was purified by distillation in the presence of benzophenone sodium ketyl under a nitrogen atmosphere. Nitrogen was purified by being passed through a tube containing copper turnings in a furnace at 170 °C followed by drying with phosphorus pentoxide. Methyl iodide, *n*-propyl iodide, chlorobenzene, bromobenzene, iodobenzene, and indene were dried over calcium hydride and distilled. Fluorene was dried by being kept over phosphorus pentoxide in a desiccator. Carbon dioxide was dried by being passed through calcium chloride, silica gel, and concentrated sulfuric acid. Commercial authentic samples and other chemicals were used without further purification.

Procedure. The reaction vessel was a two- or one-necked flask equipped with three-way cocks. Each cock was connected with a nitrogen inlet and a rubber serum cap. Methylcalcium iodide and *n*-propylcalcium iodide were prepared in the flask under nitrogen atmosphere. Various reactants were added to this organocalcium compound with a hypodermic syringe under nitrogen atmosphere. Carboxylation was carried out by passing carbon dioxide through a stainless steel needle.

Reaction of Methylcalcium Iodide with Carbon Dioxide. Carbon dioxide was passed through a suspension of methylcalcium iodide in tetrahydrofuran at -70 °C for 2 hr, after which water was added. The precipitate was washed with diethyl ether, and 20% hydrochloric acid was added to the precipitate. Extraction with diethyl ether and elimination of the solvents and other materials of lower boiling points under a reduced pressure gave a mixture of acetic acid and water. Its NMR spectrum indicated the absence of impurity other than water, and showed the yield of acetic acid to be 57% based on the methyl iodide used in the preparation of methylcalcium iodide.

In another run, carbon dioxide was passed through a suspension of methylcalcium iodide in tetrahydrofuran at -70 °C for 1 hr, and then water and 20% hydrochloric acid were added. The reaction mixture was subjected to gas chromatographic analyses. The yield of acetic acid was 53% based on methyl iodide. Gas chromatographic analyses also showed the presence of acetone and *tert*-butyl alcohol in 17 and 11% yields, respectively, based on methyl iodide in the reaction mixture.

Metallation of Indene by Methylcalcium Iodide. To methylcalcium iodide prepared from 0.35 g (8.8 mmol) of calcium and 0.98 g (6.9 mmol) of methyl iodide was added 0.57 g (4.9 mmol) of indene in 2.0 ml of tetrahydrofuran. The reaction mixture was allowed to stand at -30 °C for 2.5 hr under stirring, and carbon dioxide was passed through the reaction mixture at -70 °C for 1 hr, and then 10.0 ml of 20% hydrochloric acid was added. Extraction with diethyl ether and evaporation of the solvent under reduced pressure left a solid, which was washed with carbon tetrachloride and dried over phosphorus pentoxide under reduced pressure in a desiccator. Purity of the product was checked by its NMR spectrum. Yield of indene-3-carboxylic acid was 0.78 g (99% based on indene), mp 161 °C (lit.⁷⁾ 159.5—161 °C). The reaction of 0.12 g (3.0 mmol) of calcium metal with 0.69 g (5.9 mmol) of indene in 15.0 ml of tetrahydrofuran under similar conditions gave a trace of indene-3-carboxylic acid after carboxylation. The result shows that direct metallation of indene by the excess calcium metal, used in the preparation of methylcalcium iodide, was not significant under the above reaction conditions.

Metallation of Fluorene by Methylcalcium Iodide. To methylcalcium iodide prepared from 0.30 g (7.4 mmol) of calcium and 0.82 g (5.8 mmol) of methyl iodide was added, 0.77 g (4.6 mmol) of fluorene in 3.0 ml of tetrahydrofuran, and the mixture was kept at -30 °C for 3 hr under stirring. Carbon dioxide was passed through the mixture at -70 °C for 1 hr, and the reaction mixture was treated in a similar manner to that in the metallation of indene. Yield of fluorene-9-carboxylic acid was 0.91 g (93% based on fluorene), mp 225 °C. Melting points were reported to be in the range 225—232 °C.⁹⁻¹²⁾

Reaction of Methylcalcium Iodide with Halobenzenes. To methylcalcium iodide prepared from 0.31 g (7.7 mmol) of calcium and 0.89 g (6.2 mmol) of methyl iodide was added, 0.56 g (5.0 mmol) of chlorobenzene in 2.0 ml of tetrahydrofuran and the mixture was allowed to react at 23 °C for 49 hr under stirring. Passage of carbon dioxide at -70 °C for 1 hr led to the formation of benzoic acid. Gas chromatographic analyses indicated the yield of benzoic acid to be 21% based on chlorobenzene, and the presence of trace of benzene in the reaction products. The reaction of 0.054 g (1.3 mmol) of calcium metal with 0.32 g (2.9 mmol) of chlorobenzene in 6.8 ml of tetrahydrofuran under similar conditions gave a trace of benzoic acid after carboxylation.

To methylcalcium iodide prepared from 0.30 g (7.4 mmol) of calcium metal and 0.85 g (6.0 mmol) of methyl iodide was added 0.75 g (4.8 mmol) of bromobenzene in 2.0 ml of tetrahydrofuran, and the mixture was allowed to react at 23 °C for 49.5 hr under stirring. The reaction mixture was treated in a similar manner. The yield of benzoic acid determined by gas chromatography was 42% based on bromobenzene. Gas chromatographic analysis showed the presence of benzene in 0.4% yield based on bromobenzene. The reaction of 0.12 g (3.0 mmol) of calcium metal with 1.04 g (6.6 mmol) of bromobenzene in 15.0 ml of tetrahydrofuran under similar conditions gave a trace of benzoic acid after carboxylation.

To methylcalcium iodide prepared from 0.27 g (6.7 mmol)

of calcium and 0.83 g (5.8 mmol) of methyl iodide was added 0.89 g (4.4 mmol) of iodobenzene in 2.0 ml of tetrahydrofuran. The mixture was allowed to react at 23 °C for 49.5 hr under stirring, and treated in a similar manner. Gas chromatographic analyses showed the formation of benzoic acid in 38% yield based on iodobenzene, as well as a trace of benzene. The reaction of 0.056 g (1.4 mmol) of calcium metal with 0.59 g (2.9 mmol) of iodobenzene in 7.0 ml of tetrahydrofuran under similar conditions gave 0.64 mmol of benzoic acid (22% based on iodobenzene and 46% based on metallic calcium) after carboxylation. The result indicates the formation of phenylcalcium iodide under the above reaction conditions by the direct reaction of iodobenzene with excess calcium metal.

Reaction of n-Propylcalcium Iodide with Bromobenzene.

To *n*-propylcalcium iodide prepared from 0.11 g (2.7 mmol) of calcium and 0.36 g (2.1 mmol) of *n*-propyl iodide was added 0.16 g (1.0 mmol) of bromobenzene and the mixture was allowed to react at 20 °C for 40 hr under stirring. A similar treatment of the mixture led to the formation of benzoic acid in 80% yield based on bromobenzene. The yield was determined by gas chromatography.

The authors are grateful to Mr. Akira Matsumura for his assistance in the preliminary experiments of this work.

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