and distillation of the oily residue gave 17.5 g (75% yield) of clear, colorless oil: bp 119–123°; mp 27–28°; ir (film) 1720, 915, 835 cm^{-1}.

Anal. Calcd for C$_{12}$H$_{22}$O$_2$: C, 72.69; H, 11.18. Found: C, 71.92; H, 11.13.

Reaction of Lithium Dimethylcuprate with 10,11-Epoxy-2-dodecanone.—To a solution of 5.34 mmol of lithium dimethylcuprate in 15 ml of absolute ether at −50° was added dropwise 2.67 mmol (506 mg) of 10,11-epoxy-2-dodecanone in 30 ml of ether. Following the 10-min addition, the reaction mixture was stirred for 30 min and then quenched with 40 ml of saturated ammonium chloride solution. The reaction mixture was warmed to ambient and stirred for 0.5 hr. The ether layer was decanted, shaken with 20 ml of water and 20 ml of brine solution, and then dried over sodium sulfate. Removal of the ether and column chromatography of the residue on silica gel G using 2% ether–98% methylene chloride as eluent gave 372 mg (68% yield) of 11-hydroxy-2-tridecanone: mp 44–45° (recrystallized from hexane); ir (CCl$_4$) 3500, 1720, 1355, 1160 cm^{-1}.

Anal. Calcd for C$_{13}$H$_{26}$O$_2$: C, 72.85; H, 12.23. Found: C, 72.74; H, 12.20.

Reaction of Lithium Diphenylcuprate with 2,3-Epoxy-3-methylbutyronitrile.—To a solution of 10 mmol of lithium diphenylcuprate in 20 ml of ether and 10 ml of benzene at 0° was added 2,3-epoxy-3-methylbutyronitrile[27] (485 mg, 5 mmol) in 10 ml of ether over a 10-min period. After addition was complete the mixture was stirred for an additional 20 min. The usual work-up yielded a liquid residue which upon chromatography on a silica gel column, eluting with pentane–ether, yielded 3-hydroxy-3-methyl-2-phenylbutyronitrile (295 mg, 34%) [ir (film) 3400, 2225, 1150, 730, 690 cm^{-1}, nmr (CDCl$_3$) δ 7.37 (s, 5), 3.80 (s, 1), 2.56 (s, 1), 1.30 (s, 6)] and 2,2-dimethyl-3-benzoyloxirane (50 mg, 6%) [ir (neat) 1690, 1220, 680, 700 cm^{-1}, nmr (CDCl$_3$) δ 7.8 (m, 5), 4.15 (s, 1), 1.63 (s, 3), 1.28 (s, 3)].

Reaction of Lithium Dimethylcuprate with *exo*-Norbornene Oxide.—To a solution of 0.5 mmol (95 mg) of cuprous iodide and 20.0 mmol of methyllithium in 30 ml of anhydrous dimethoxyethane at 0° under nitrogen was added dropwise with stirring 9.0 mm (0.990 g) of *exo*-norbornene oxide. The reaction was warmed to 55° and maintained there for 5 hr. The reaction mixture was cooled to 0° and hydrolyzed with 10 ml of aqueous

ammonium chloride. Fifty milliliters of ether and 30 ml of water were added to the mixture and shaken. The ether layer was collected and treated consecutively with 20 ml of water, 20 ml of saturated sodium chloride solution, and solid anhydrous Na$_2$CO$_3$. Solvent removal *in vacuo* gave a white solid which after sublimation (60°, 7 mm) gave 0.65 g (58%) of *endo*-3-methyl-*exo*-2-norbornanol: mp 96–100° (lit.[28] mp 95.5–97°); ir (CCl$_4$) 3300, 1070 cm^{-1}.

Reaction of *exo*-norbornene oxide (9 mmol) with methyllithium (20 mmol) in 30 ml of dimethoxyethane at 70° for 5 hr resulted in a recovery of 93% of starting material and 7% conversion to *endo*-3-methyl-*exo*-2-norbornanol and a trace of norcamphor.

Reaction of Lithium Dimethylcuprate with 5α-Cholestane 2α,3α-Oxide.—To a solution of lithium dimethylcuprate (5 mmol) in 20 ml of ether at 0° was added dropwise 387 mg (1.0 mmol) of 5α-cholestane 2α,3α-oxide[29] in 20 ml of ether. After addition was completed, the reaction mixture was warmed to room temperature and allowed to stir for 24 hr. Work-up gave 341 mg of a white solid which showed two major spots on tlc on silica gel. Column chromatography on silica gel using pentane–ether as eluent gave 5α-cholestan-2-one (82 mg, 22%), mp 128.5–129.5°, [α]^{25}D +50.6° (c 1.97, EtOH) (lit.[29] mp 130°, [α]D +50.7°), and 2β-methyl-5α-cholestan-3α-ol (260 mg, 65%), mp 117.5–118.0°, [α]^{25}D +42.9° (c 2.0, CHCl$_3$), ir (CCl$_4$) 3400 cm^{-1}. Oxidation of this alcohol with chromic anhydride–pyridine gave 2β-methyl-5α-cholestan-3-one,[30] mp 98.5–99° (lit.[15] mp 97.5–98.5°), ir (CS$_2$) 1715 cm^{-1}, [α]^{25}D +122° (c 1.51, CHCl$_3$).

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# Preparation of Organocalcium Halides in Hydrocarbon Solvents

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Contrary to the description in the literature, the reaction of alkyl halides with calcium metal in hydrocarbon solvents was found to give the corresponding alkylcalcium halides in good yields. The reaction was not restricted to primary alkyl iodides. Bromides and chlorides also afforded alkylcalcium halides. Isopropyl halides were also converted into organocalcium halides. In the reaction with *tert*-butyl halides, however, the disproportionation to form the corresponding alkane and alkene far exceeded the formation of *tert*-butylcalcium halides. The reaction of calcium with aryl halides gave arylcalcium halides in poor yields.

In the preceding paper,[1] we demonstrated that the reaction of organic halides with calcium metal in tetrahydrofuran gave the corresponding organocalcium halides in much better yields than those available in the literature. The key ingredient appeared to be the

$$RX + Ca \longrightarrow RCaX \qquad (1)$$
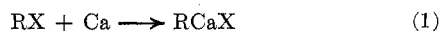
availability of higher purity calcium metal than was previously obtainable. The lower content of sodium in the calcium metal seemed to be an important factor in this improvement. Reaction 1 was shown to be not restricted to aryl and primary alkyl iodides

contrary to the description in the literature. Bromides and chlorides also afforded organocalcium halides. In addition, isopropyl halides were first converted into organocalcium halides by the reaction.

Our experimental procedure showed several additional advantages. Previous authors described various approaches to the activation of calcium metal, *e.g.*, treatment with Grignard reagent,[2] amalgamation,[3–5] use of calcium–magnesium alloy,[3] and heating with

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magnesium and mercury.[6-13] Therefore, there would be some organomercury or organomagnesium compounds mixed in with their organocalcium halides. On the other hand the amount of such extraneous organometallics would be minimized under our experimental conditions, because the activation of calcium metal was not necessary.[1] The yields of organocalcium iodides by previous workers were generally low especially in the aliphatic series, and a considerable amount of calcium iodide produced by the Wurtz-type coupling was present.[5,14] This too was avoided in our case due to the more reactive calcium metal. Thus, our experimental procedure would result in the formation of organocalcium halides in much purer state than was reported before by previous authors.

Nevertheless, a serious disadvantage of reaction 1 remained unsolved, which is the use of ethereal solvents as the reaction media. Although tetrahydrofuran and other ethereal solvents are convenient media for the preparation of organocalcium halides, they are readily cleaved by organocalcium reagents. Bryce-Smith and Skinner[3] reported the half-lives of phenyl- and methylcalcium iodide at 20° in tetrahydrofuran to be 13.5 and 13 days, respectively. According to our experiments,[15,16] about 77% of methylcalcium iodide was consumed by the reaction with tetrahydrofuran during a storage of 20 hr at 28° under a nitrogen atmosphere following the procedure described previously. This calcium compound was found to be somewhat more stable at lower temperature, about 25% being consumed by the reaction during a storage of 20 hr at −70°.[16] Therefore, it is necessary to use the organocalcium halides for further reactions immediately after the preparation in tetrahydrofuran. The present study was aimed at preparing organocalcium halides both in high yields and in a more stable state.

Results and Discussion

We first attempted to prepare methylcalcium iodide in diethyl ether using the calcium metal of higher purity, since diethyl ether appeared to be cleaved less readily than tetrahydrofuran by organocalcium halides. The preparation of organocalcium halides in the absence of ethereal solvents is quite desirable, but we felt at first that the preparation would be extremely difficult, because Bryce-Smith and Skinner[3] described that no reaction could be induced in the absence of ethereal media even between the activated calcium and various organic iodides.

These authors obtained methylcalcium iodide in 37% yield by the reaction of methyl iodide with their

activated calcium in refluxing diethyl ether. The reaction of methyl iodide with the calcium metal of higher purity was very slow in diethyl ether at low temperature, while the reaction in tetrahydrofuran proceeded smoothly even at −70°.[1] The reaction in diethyl ether proceeded very slowly at low temperature even after the initiation by the addition of a small amount of the organic iodide at 35°. However, the reaction proceeded smoothly at 35° to give methylcalcium iodide in 61% yield over 3 hr. The activation of calcium metal was not necessary, but the yield was lower than that of the corresponding reaction in tetrahydrofuran at −70°. Since relatively higher temperature was necessary for the reaction in diethyl ether, the Wurtz-type coupling and the cleavage of ethereal bond were rather significant.

Contrary to our expectation, the stability of methylcalcium iodide in diethyl ether was still rather low. For example, about 40% of the calcium compound was consumed by the reaction with diethyl ether during a storage of 20 hr at 28° after the preparation.

It seemed, therefore, to be absolutely necessary to carry out reaction 1 in the absence of ethereal solvent in order to obtain organocalcium halides in a stable state. Kocheshkov and coworkers[17,18] prepared several organocalcium iodides by the treatment of calcium shavings with organic iodides in ethereal solvent. They isolated solvated organocalcium iodides and removed the ethereal solvent by heating under vacuum. Such a procedure would be, however, inconvenient for the practical use of organocalcium halides in organic syntheses.

Contrary to the description in the literature, we found that reaction 1 proceeded smoothly in toluene or benzene to give alkylcalcium halides in good yields when the higher purity calcium metal was used. The initiation of the reaction was not difficult, and the activation of calcium metal was not necessary even in toluene and benzene. Although a higher reaction temperature was necessary, the Wurtz-type coupling was not significant under our reaction conditions. Generally, a small amount of alkyl halide remained unchanged in the reaction mixture at the end of our preparation of alkylcalcium halide. Reaction 1 in the hydrocarbon solvents was found not to be restricted to primary alkyl iodides. Bromides and chlorides also afforded the corresponding organocalcium halides. Isopropyl halides were also converted into the corresponding organocalcium halides in good yields by the reaction in toluene. These alkylcalcium halides were found to be insoluble in hydrocarbon solvents.

It would be noteworthy that reaction 1 with isopropyl bromide in toluene proceeded smoothly without initiation by the addition of a small amount of the corresponding iodide. Isopropyl bromide appeared to be more reactive than *n*-propyl bromide in the reaction. Usually, organic bromides and chlorides are much less reactive than the corresponding iodides, and the initiation of reaction 1 by the addition of a small amount of the corresponding iodide is helpful. We adopted this

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technique throughout the preparation of organocalcium bromides and chlorides in tetrahydrofuran.[1]

On the other hand, the disproportionation to form the corresponding alkane and alkene was an important side reaction in reaction 1 with *tert*-butyl halides in toluene, and the yields of *tert*-butylcalcium halides were negligible as in the corresponding reaction in tetrahydrofuran.[1] Reaction 1 with benzyl halides in benzene gave the corresponding organocalcium halides in poor yields. Wurtz-type coupling was an important side reaction in this case.

The hydrocarbon solvents useful for reaction 1 are not restricted to aromatic compounds. We found that reaction 1 with several alkyl iodides proceeded smoothly in cyclohexane to give the corresponding alkylcalcium iodides in good yields. Initiation of the reaction was not difficult and the activation of calcium metal was again not necessary.

Unlike reaction 1 in hydrocarbon solvents with alkyl halides, that with aryl halides gave the corresponding organocalcium halides in poor yields. For example, the reaction of calcium with iodobenzene in toluene at 100° for 91 hr gave a trace of phenylcalcium iodide, and almost all of the iodobenzene remained unchanged in the reaction system. The reaction at 180° for 30 hr in tetralin gave phenylcalcium iodide but in only 15% yield. This is a disadvantage of reaction 1 in hydrocarbon solvents. Some of the main results are given in Table I.

TABLE I

PREPARATION OF ORGANOCALCIUM HALIDES BY REACTION 1 IN HYDROCARBON SOLVENTS[a]

Halide, RX	Registry no. (RX)	Solvent	Temp, °C	Time, hr	Yield, %[b]	Registry no. (RCaX)
CH₃I	74-88-4	Toluene	40	25.5	61–68[e]	20458-43-9
CH₃I		Toluene	40	43	77–84[e]	
CH₃I		Cyclohexane	40	43	71–76[f]	
C₂H₅I	75-03-6	Toluene	60	27	64	20458-44-0
C₂H₅I		Cyclohexane	60	45	70	
n-C₃H₇I	107-08-4	Toluene	95	41	88	20458-45-1
n-C₃H₇I		Cyclohexane	75	44	77	
n-C₃H₇Br[c]	106-94-5	Toluene	65	29	72	42282-72-4
n-C₃H₇Br[d]		Toluene	65	48	Trace	
n-C₃H₇Cl[c]	540-54-5	Toluene	45	46	50	42282-73-5
n-C₃H₇Cl[d]		Toluene	45	48	Trace	
i-C₃H₇I	75-30-9	Toluene	85	28	78	42177-27-5
i-C₃H₇Br[c]	75-26-3	Toluene	55	45	75	42398-30-1
i-C₃H₇Br[d]		Toluene	55	48	66	
i-C₃H₇Cl[c]	75-29-6	Toluene	33	47	75	42282-75-7
t-C₄H₉I		Toluene	95	17	0	
t-C₄H₉Cl[c]		Toluene	70	19	0	
C₆H₅CH₂I	620-05-3	Benzene	90	99	6	42282-76-8
C₆H₅CH₂Br[c]	100-39-0	Benzene	90	145	6	42282-77-9
C₆H₅CH₂Cl[c]	100-44-7	Benzene	90	94	2	42282-78-0
C₆H₅I	591-50-4	Toluene	120	96	3	24488-76-4
C₆H₅I		Toluene	160	46	3	
C₆H₅I		Tetralin	180	30	15	
C₆H₅Br[c]	108-86-1	Toluene	160	45	5	42282-79-1
C₆H₅Cl[c]	108-90-7	Toluene	130	43	3	42282-80-4

[a] Reaction conditions: organic halides, 5.0 mmol; calcium, 6.5 mmol; solvent, 10 ml. [b] Based on the organic halide. [c] In these cases, reaction 1 was initiated by the addition of 1 mol % of the corresponding iodides, respectively. [d] The initiation by the addition of the corresponding iodides was not adopted. [e] Three runs were carried out. [f] Two runs were carried out.

Experimental Section

Vapor phase chromatographic analyses were performed on a Shimadzu GC-4A gas chromatograph.

Materials.—Benzyl and *tert*-butyl iodides were prepared by a conventional procedure.[19] Commercial products of the other organic halides were purified by usual methods.[20] Calcium metal of higher purity was provided by Mitsuwa Chemicals, Ltd., Osaka. As was described in the preceding paper,[1] the calcium contained 0.493% magnesium and 0.0019% sodium. The calcium was rasped in dry liquid paraffin. Nitrogen was purified by passing through a tube containing copper turnings in a furnace at 170° followed by drying with phosphorus pentoxide. Tetrahydrofuran, diethyl ether, benzene, toluene, tetralin, and cyclohexane were purified by distillation in the presence of benzophenone sodium ketyl under a nitrogen atmosphere. Other chemicals were commercial products and were used without further purification.

Preparation of Organocalcium Halides by Reaction 1 in Hydrocarbon Solvents (General Procedure).—The reaction vessel was a two-necked flask equipped with two three-way cocks. Each three-way cock was connected with a nitrogen inlet and a rubber serum cap. The rasped calcium was placed in the flask. The reaction vessel was evacuated and filled with dry nitrogen, and the calcium was washed with the hydrocarbon used as the solvent for reaction 1 under a nitrogen atmosphere.

In the preparation of organocalcium iodides, about 1% of a solution of organic iodide (5.0 mmol) in the solvent (3.0 ml) was added *via* a hypodermic syringe at the prescribed temperature to this rasped calcium (0.26 g, 6.5 mmol) in the solvent (5.0 ml) without stirring. The mixture did not show the change in color noted in the preparation in tetrahydrofuran. After about 0.5 hr, 2.0 ml of the solvent was added. The rest of the organic iodide was then added *via* a hypodermic syringe over a period of 1 hr while stirring at the same temperature. Stirring was continued for several hours at this temperature. The reaction system afforded a fine black powder as the reaction proceeded. After the preparation, organocalcium iodide was decomposed by the addition of methanol, acetic acid, or a 2:1 mixture (volume ratio) of water and ethanol to the reaction mixture, and the products were analyzed. In the case of methyl, ethyl, and propyl derivatives, the total amount of the gas evolved after the decomposition was determined by a gas buret. The gas was analyzed by vapor phase chromatography. The gas usually contained a small amount (less than 1 mol %) of hydrogen. In other cases, the amount of hydrocarbon evolved after the decomposition was determined by vapor phase chromatography. Yield of organocalcium iodides was determined by the amount of hydrocarbon evolved after the decomposition.

Preparation of organocalcium bromides and chlorides was carried out in a similar manner. In some cases, however, the reaction was initiated by the addition of 1 mol % of the corresponding iodide. Such an initiation was very helpful in the preparation of n-propylcalcium bromide and chloride, but was not necessary in the preparation of isopropylcalcium bromide.

Preparation of Methylcalcium Iodide in Ether.—About 1% of a solution of methyl iodide (5.0 mmol) in diethyl ether (3.0 ml) was added at 35° without stirring. After the reaction started, 2.0 ml of the ether was added, and the remainder of methyl iodide was slowly added to the reaction system. Three runs of the preparation at 35° for 1.5 hr gave methylcalcium iodide in 54% yield in each case. The preparation at 35° for 3 hr gave the compound in 61% yield.

Registry No.—Calcium, 7440-70-2.

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