Selective Direct Fluorination of Organolithium and Organomagnesium Compounds

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The first successful selective monofluorination of organolithium and organomagnesium compounds with elemental fluorine has been achieved in hydrocarbon ether solvents at low temperatures.

The direct fluorination of organometallic compounds using elemental fluorine has been studied in recent years.[1–7] We have studied the selective direct fluorination of organolithium[8] and organomagnesium compounds. Various aliphatic and aromatic organolithium and organomagnesium compounds were fluorinated in hydrocarbon ether solvents at −60 °C (to increase selectivity and avoid reaction of fluorine with the solvent), see eqn. (1).† The results are summarized in Table 1.

$$\text{R–M} + \text{F}_2 \xrightarrow{-60\ ^\circ\text{C}} \text{R–F} + \text{M–F} \qquad (1)$$

Fluorine gas, diluted with helium, was delivered slowly to a stirred solution of the organometallic compound. The fluorination was terminated when 2.2 times the theoretical amount of fluorine was delivered to the reaction mixture. The excess fluorine gas was not recycled. The yields listed in Table 1, therefore, are almost proportional to the rate of fluorination —lower yields are due to slower reactions between organometallic substrates and fluorine gas. An attempt was made to accelerate the fluorination by raising the reaction temperature but this was unsuccessful as the solvents reacted with fluorine gas. No obvious side reactions such as polyfluorination or polymerizations were observed and unconverted organometallic compounds were recovered after fluorination. Practical quantities of the monofluorine target compounds were isolated and there appears to be no reason why this reaction cannot be run on a larger scale.

The key for accomplishing the selective direct monofluorination was the use of hydrocarbon ether solvents. It was found that the ethereal solvents were surprisingly unreactive with diluted fluorine gas at −60 °C. The use of a homogeneous system was also essential to obtain satisfactory results. For example, when phenylmagnesium bromide suspended in diethyl ether at −60 °C was fluorinated, no reaction took place and the organomagnesium compound remained unchanged.

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† Typically, an organometallic compound was dissolved in the specified solvent (Table 1) at −60 °C. Fluorine gas (diluted with helium) was bubbled through at 4 $\text{cm}^3\ \text{min}^{-1}$. The n-butyl- and *sec*-butyl-fluorides were trapped at −196 °C. With aromatic reactions, fluorobenzene was trapped at −78 °C. Crude products were purified by preparative gas chromatography. The yields have not been optimized.

Table 1

Reaction	R–M[a]	Solvent	Product[b]	Yield (%)[c]
1	BuLi	THF	BuF	49
		Bu$_2$O	BuF	55
2	Bu^{s}Li	Bu$_2$O	Bu^{s}F	42
3	Bu^{t}Li	Bu$_2$O	Bu^{t}F	<5
4	PhLi	Et$_2$O	PhF	42
5	BuMgCl	THF	BuF	28
		Bu$_2$O	BuF	37
6	Bu^{s}MgCl	Bu$_2$O	Bu^{s}F	33
7	Bu^{t}MgCl	Bu$_2$O	Bu^{t}F	0
8	PhMgCl	Et$_2$O	PhF	25

[a] All the organolithium and organomagnesium reagents were obtained from Aldrich. The original solvents were removed under vacuum and replaced with the specified solvents to prepare a 0.2 mol dm^{-3} solution for the fluorination. Typically, 100 ml of the 0.2 mol dm^{-3} solution (20 mmol) was used in this study. The dialkyl ether solvents were chosen so that those solvents were easily separated from the fluorinated products. Thus, nonvolatile dibutyl ether was used for the aliphatic organometallic compounds to isolate volatile butyl fluorides. Volatile diethyl ether was used for the aromatic organometallic compounds to isolate relatively nonvolatile fluorobenzene. [b] Products were identified by comparing their GC–MS spectra and ^{19}F NMR spectra. The fluorobenzene standard was obtained from Aldrich, Inc. *tert*-Butylfluoride standard was prepared from 2-methylpropan-2-ol and hydrogen fluoride. The n-fluorobutane and 2-fluorobutane standards were prepared as in ref. 10 and 11, respectively. [c] Isolated yield.

In contrast, the more soluble phenylmagnesium chloride gave monofluorobenzene in 25% yield. A slight decrease in yields was observed when tetrahydrofuran (THF) was used in place of dialkyl ethers (reactions 1 and 5). Experiments using THF as solvent produced significantly more of the corresponding hydrocarbon (butanes from the aliphatic organometallic compounds and benzene from the aromatic organometallic compounds) in the products than the dialkyl ether experiments. The reaction of elemental fluorine with THF alone at −60 °C was found to produce a very small amount of fluorinated organic compounds and hydrogen fluoride. Any HF produced in such side reactions reacted immediately with the organometallic compound to give the corresponding hydrocarbons.

In these experiments, the organolithium compounds were found to be more reactive than the organomagnesium compounds and yields were generally higher for the organolithium compounds. Aliphatic organometallic compounds were slightly more reactive than the aromatic organometallic compounds and gave higher yields. Only a slight difference was observed in yields between primary and secondary organometallic compounds (reactions 2 and 6). The fluorination of *tert*-butyllithium produced isobutene, isobutane, and a low yield of *tert*-butylfluoride (reaction 3). A coupling reaction of *tert*-butyllithium and *tert*-butylfluoride occurs during fluorination. It is known that *tert*-butyllithium reacts with *tert*-butylchloride to give a mixture of isobutene and isobutane.[9] *tert*-Butyl magnesium chloride, on the other hand, was found to be non-reactive with fluorine gas at −60 °C.

We are grateful for support of this work by the US Air Force Office of Scientific Research (AFOSR-88-0084).

Received 23rd October 1991; Com. 1/05406E

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