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DECOMPOSITION AND BYPRODUCTS FROM REACTIONS INVOLVING PENTAFLUOROPHENYL-GRIGNARD AND LITHIUM REAGENTS. A GC/MS STUDY[†]

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SUMMARY

Decomposition and side reactions of pentafluorophenylmagnesium bromide and pentafluorophenyllithium, when used in syntheses, have been investigated using GC/MS techniques. Reactions with reagents such as C_6F_5X ($X = H, F, Cl, Br, I$), $C_6F_4X_2$ ($X = H, Cl$), $C_6F_3Cl_3$, C_6H_6 , $(C_6X_5)_3P$ ($X = H, F$), $(C_6X_5)_3P=O$ ($X = H, F$), $(C_6X_5)Si(CH_3)_3$ ($X = H, F$) and $(CH_3)_{4-n}SiCl_n$, $n = 1, 2$, in ether or ether/n-hexane were studied.

In addition to the principal reaction of synthetic use, namely the replacement of a halogen by a pentafluorophenyl group, two types of side reactions were observed. These were (i) intermolecular loss of LiF via a nucleophilic substitution, and (ii) intramolecular loss of LiF, followed by the addition of either, inorganic salts such as lithium or magnesium halides, or organometal compounds such as organolithium or Grignard reagent present in the system. GC/MS proved to be an ideal method of monitoring such organometallic reaction systems, although it was sometimes not possible to identify byproducts as a particular isomer.

INTRODUCTION

Grignard and organolithium reagents are extensively used as synthetic reagents with little thought to the byproducts and decomposition products

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produced during the reactions. In the case of pentafluorophenyl Grignard or lithium reagents the presence of these unwanted materials is clearly shown by the dark tarry residues remaining after purification of the desired product. In pentafluorophenyl chemistry, the lithium reagent [1,2] is often used in preference to the Grignard [2] since it is more reactive, and thus unwanted products can be reduced by carrying out the reaction at lower temperature, though if the pentafluorophenyl lithium is allowed to warm too rapidly it decomposes via tetrafluorobenzene [3,4].

In the course of our study of the mass spectra of some methyl-pentafluorophenyl silanes [5] we observed some anomalous peaks in the spectra of a sample of $(C_6F_5)_2Si(CH_3)_2$ which we had been sent. This sample, although having satisfactory elemental analyses, and apparently pure by NMR criteria, was shown, when subjected to a GC/MS analysis, to be contaminated by seven identifiable impurities [6] suggesting an interesting chemistry involving the side reactions. These observations thus prompted the present GC/MS study of reactions of pentafluorophenyl Grignard and lithium reagents, with emphasis not on the expected product, but on the byproducts, especially in cases where the exact stoichiometric ratio of reactants was not present.

EXPERIMENTAL

All reactions were carried out under nitrogen in 50 or 100 ml three-necked flasks, all glassware being carefully dried beforehand. Sampling was via syringe and a silicone septum.

Pentafluorophenylmagnesium bromide was prepared by reacting 10 mmoles each of C_6F_5Br and Mg in 15 ml of dry ether followed by 1 hour of reflux (Solution A). Pentafluorophenyllithium was prepared either by the addition of 10 mmoles of n-butyllithium in hexane (\approx 5 ml) to 10 mmoles of bromopentafluorobenzene in 15 ml of dry ether at $-78^\circ C$, the mixture being allowed to react at this temperature for 1 hour (Solution B), or alternatively by addition of the n-butyllithium to pentafluorobenzene under the same conditions, except for a two-hour reaction period (Solution C).

Reagents were commercially available, and were dried and/or redistilled before use except for the pentafluorophenyl silanes and phosphines which were prepared by reaction of C_6F_5Li with the corresponding silyl halide or PCl_3 .

The gas chromatography/mass spectrometry analyses were carried out on an AEI Ms-30 double beam double focussing mass spectrometer interfaced with

a Pye 104 gas chromatograph through a silicone membrane separator to beam 2 and a Biemann glass frit separator to beam 1. Either separator could be used, or both simultaneously. Biemann was used most often. The gas chromatograms were recorded from the total ion monitor, and mass spectra were initiated manually when desired, being recorded at either 3 or 10 seconds/mass decade, at a 4 Kv acceleration voltage, 1000 resolution, 70 ev ionization voltage, 100 μ amp trap current. The source was held at 200°C, the separator and connecting lines at 250°C, and the GC column was programmed linearly for 50°C to 300°C at either 10° or 15°C/minute, with a helium flow of 40 ml/minute through a 5 ft x $\frac{1}{4}$ inch glass column packed with 3% SE-30 in Chromosorb W. PFK (perfluorokerosene) was used as a chemical mass marker in beam 2 simultaneously recorded with, but not overlapping the unknown spectra from the GC in beam 1.

RESULTS

The byproducts of synthetic reactions involving C_6F_5MgBr and C_6F_5Li (prepared by two routes) are shown in Table I. In Table II typical results are shown for C_6F_5Li allowed to react with various haloaromatic derivatives a situation likely to arise in synthetic reactions, since in preparation of the pentafluorophenyl reagents it is often the case that a slight excess of the fluoroaromatic is used. These reactions represent both side reactions and the decomposition products of unreacted C_6F_5Li as it warms to room temperature. In Table III the product of the reaction of C_6F_5Li with various organometallics are shown, as would be typical of the side reaction that could occur in the preparation of C_6F_5 -organometallic derivatives. As controls, the corresponding phenyl derivatives have been compared as well.

DISCUSSION

The most common reactions involving substitution of C_6F_5X derivatives, constitute displacement of a fluorine atom para to the substituent group X (where X = H, CH_3 , CF_3 , NO_2 , C_6F_5 etc.), though X = NH_2 is meta directing and X = OCH₃, or $NHCH_3$ leads to both meta and para substitution [7-9], with ortho attack being rather rare.

We observe two principal reaction pathways involving pentafluorophenyl lithium with C_6F_5X (X = H, F, Cl, Br, I), the first being nucleophilic attack of a pentafluorophenyl anion at the para position leading to species

TABLE I
Byproducts from the reactions of C_6F_5MgBr and C_6F_5Li with Me_3SiCl and Me_2SiCl_2

No.	C_6F_5 from Solution	Reactant	Solvent	Temp† °C	Byproduct*
1	A	Me_3SiCl	Et_2O	29	a, b, c, d (n = 1), e (n = 1), f
2	A	Me_3SiCl	dioxane	60	a, b, c, d (n = 2), e (n = 1), f, g (n = 2-3)
3	A	Me_2SiCl_2	Et_2O	25	a, b, c, d (n = 2), e (n = 1), h, i (n = 3-12), j (n = 1-6)
4	A	Me_2SiCl_2	C_6H_6	45	a, b, c, d (n = 2), e (n = 1), h, i (n = 3-12), j (n = 1-6)
5	A	Me_2SiCl_2	dioxane	60	a, b, c, d (n = 2), e (n = 1), h, i (n = 3-12), j (n = 1-6)
6	A	Me_2SiCl_2	C_6H_5Cl	80	a, b, c, d (n = 2), e (n = 1), h, i (n = 3-12), j (n = 1-6)
7	A	Me_2SiCl_2	<i>o</i> - $C_6H_4Cl_2$	100	a, b, c, d (n = 2), e (n = 1), h, i (n = 3-12), j (n = 1-6)
8	C**	Me_3SiCl	Et_2O /hexane	25	a, b, g (n = 2), k
9	B	Me_3SiCl	Et_2O /hexane	25	a, b, g (n = 2), k
10	C	Me_3SiCl	toluene/hexane	80	a, b, g (n = 2), k, m, o
11	B	Me_3SiCl	toluene/hexane	80	a, b, e (n = 1), g (n = 2), k, o
12	C	Me_2SiCl_2	Et_2O /hexane	25	a, i (n = 3-7), p (n = 0-3), q
13	B	Me_2SiCl_2	Et_2O /hexane	25	a, i (n = 3-7), p (n = 0-3), q, s
14	C	Me_2SiCl_2	toluene/hexane	80	a, i (n = 3-7), p (n = 0-3), q
15	B	Me_2SiCl_2	toluene/hexane	80	a, i (n = 3-7), p (n = 0-3), q
16	B	Me_3SiCl + excess C_6F_5Br	Et_2O /hexane ₂	25	b, d (n = 2), e, t (n = 1), u (n = 1-3), w (n = 1-3)
17	C	Me_3SiCl + excess C_6F_5H	Et_2O /hexane	25	b, t (n = 1), u (n = 1-3), v (n = 1, 3)

Table I, continued:

† Reactions were carried out for 6 hours at the specific temperature.
 * Products were worked up by standard procedures after dilute acid hydrolysis and extraction.
 ** Solutions B and C were reacted at -78°C and slowly allowed to warm to room temperature and allowed to react 6 hours at the specified temperature.

a. $\text{C}_6\text{F}_5\text{H}$	b. $\text{Me}_3\text{SiOSiMe}_3$
c. $\text{C}_6\text{F}_4\text{BrH}$	d. $\text{C}_6\text{n}^{\text{F}}_4\text{n}$
e. $\text{C}_6\text{n}^{\text{F}}_4\text{nBr}_2$	f. $\text{C}_{12}\text{F}_9\text{H}$
g. $\text{Me}_3\text{SiO}(\text{SiMe}_2\text{O})_n\text{SiMe}_3$	h. $\text{C}_6\text{F}_6\text{SiMe}_3$
i. $(\text{Me}_2\text{SiO})_2$	j. $\text{C}_6\text{F}_5(\text{SiMe}_2\text{O})_n\text{SiMe}_2\text{C}_6\text{F}_5$
k. $\text{C}_4\text{H}_9\text{OSiMe}_3$	l. $\text{C}_6\text{F}_5\text{SiMe}_2\text{O}-\text{SiMe}_3$
m. $\text{C}_4\text{H}_9\text{C}_6\text{F}_4\text{SiMe}_3$	o. $(\text{C}_6\text{F}_5)_2\text{SiMe}_2$
p. $\text{C}_6\text{F}_5(\text{SiMe}_2\text{O})_n\text{SiMe}_2\text{OH}$	q. $(\text{Me}_2(\text{C}_4\text{H}_4)\text{SiC}_6\text{F}_5$
r. $(\text{C}_4\text{H}_9\text{C}_6\text{F}_4(\text{C}_6\text{R}_5)\text{SiMe}_2$	s. $(\text{C}_4\text{H}_9\text{C}_6\text{F}_4)_2\text{SiMe}_2$
t. $\text{C}_6\text{n}^{\text{F}}_4\text{nH}_2$	u. $\text{C}_6\text{n}^{\text{F}}_4\text{nHCl}$
v. $\text{C}_6\text{n}^{\text{F}}_4\text{n+1H}$	w. $\text{C}_6\text{n}^{\text{F}}_4\text{n+1Br}$

TABLE II
Reactions of C_6F_5Li with Haloaromatics

No.	Solution C Reacted with	Products†	Additional Products if Solution B is used
18	C_6H_6	t (n = 2-4), v (n = 1-4), x (n = 1, 2)	
19	C_6F_5H	t (n = 1-3), v (n = 1-5)	w (n = 2, 3), y (n = 2, 3)
20	C_6F_6	d (n = 1-4), t (n = 1-4), v (n = 1-4), z, aa	w (n = 2, 3)
21	C_6F_5Cl	t (n = 1-4), u (n = 1-5), v (n = 1-5)	e (n = 2, 3), w (n = 2-5)
22	C_6F_5Br	e (n = 1-3), v (n = 1-4), w (n = 2-4)	v (n = 5), w (n = 1)
23	C_6F_5I	v (n = 1-2), bb (n = 2, 3), cc (n = 1-2)	v (n = 3), w (n = 1-3), dd (n = 1-2), ee (n = 1)
24	$C_6F_4H_2$	d (n = 2-4), t (n = 1-4), v (n = 1-4)	e (n = 2-3), w (n = 2-4)
25	$C_6F_4Cl_2$	t (n = 2, 3), v (n = 1-4), ff (n = 2-4), gg (n = 1-3)	e (n = 3), w (n = 2-4)
26	$C_6F_3Cl_3$	t (n = 3, 4), v (n = 1-4), ff (n = 3, 4), hh (n = 1-4)	e (n = 3), w (n = 2-4)

† All reactions were for 6 hours at 25°C after slowly warming the solution from -78°, in ether/hexane, 1:1 mole equivalents being used.

a-w as in Table I

x. $C_6nF_{4n}C_6H_6$	y. $C_6nF_{4n}HBr$	z. $C_4H_9C_6F_5$
aa. $(C_4H_9)_2C_6F_4$	bb. $C_6nF_{4n+1}I$	cc. $C_6nF_{4n}I_2$
dd. $C_6nF_{4n}BrI$	ee. $C_6nF_{4n}HI$	ff. $C_6nF_{4n+1}Cl$
gg. $C_6nF_{4n}Cl_2$	hh. $C_6nF_{4n-1}Cl_3$	

TABLE III

Reactions of C_6F_5Li with other organometallics

No.	Solution C* reacted with	Productst	Additional products if Solution B is used
27	$C_6H_5SiMe_3$	t (n = 1-4), v (n = 1-5)	none
28	$C_6F_5SiMe_3$	d (n = 2-4), m, t (n = 1), v (n = 1-4)	e (n = 1-3), w (n = 2-4), y (n = 2)
29	$(C_6H_5)_3P$	t (n = 1-4), v (n = 1-4)	ii, jj, w (n = 2-3), g (n = 1-2),
30	$(C_6F_5)_3P$	t (n = 2, 3), v (n = 1-4), ii, jj, kk	d (n = 2, 3), e (n = 1-3), w (n = 1-4), y (n = 2)
31	$(C_6H_5)_3PO$	v (n = 1-4)	w (n = 2-4)
32	$(C_6F_5)_3PO$	d (n = 2), v (n = 1-4), ii, jj	w (n = 1-4), y (n = 2)
33	$(\pi C_5H_5)_2Fe$	t (n = 1-4), v (n = 1-5), ll	e (n = 3), w (n = 2-5)

* Reaction conditions as in Table II

† Products a-z, aa-hh as in Tables I and II

ii. $(C_6F_5)_3P$ jj. $C_{12}F_9(C_6F_5)_2P$ ll. $(C_5H_4C_6F_4H)C_5H_5Fe$ kk. $(C_{12}F_9)_2(C_6F_5)P$

of the type $C_6F_5(C_6F_4)_n C_6F_4X$ (species f, u, v, w, bb, ff). An alternate scheme involves lithiation of the X group of the polymers formed and attack of this species on C_6F_5X . At higher temperatures loss of LiF occurs resulting in addition of C_6F_5Li across the tetrafluorobenzene formed. This reaction, followed by hydrolysis or Li/X exchange leads to species of the type $C_{6n}F_{4n}H_2$, or $C_{6n}F_{4n}HX$ and $C_{6n}F_{4n}X_2$ (species c, d, e, t, u, y, cc, dd, ee, gg, hh). Li/X exchange, or LiX addition across the benzyne is obviously possible as seen by the byproducts of the reaction of C_6F_5Li with $(CH_3)_3SiCl$ when excess C_6F_5X is present.

The formation of $C_{6n}F_{4n}H_2$ (species t) involves either Li/F exchange followed by hydrolysis, or the possible addition of LiH (formed by the coupling reaction of $n-C_4H_9Li$ with $n-C_4H_{10}$) across a benzyne type species. Significant amounts of $C_6F_5(n-C_4H_9)$ and $C_6F_4(n-C_4H_9)_2$ species are also surprisingly detected.

The observation of $C_{6n}F_{4n}H_2$ ($n = 2-4$) in $C_6F_4H_2/C_6F_5Li$, $C_{6n}F_{4n}Cl_2$ ($n = 2-3$) in $C_6F_4Cl_2/C_6F_5Li$ and $C_{6n}F_{4n-1}Cl_3$ ($n = 2-4$) in the $C_6F_5Cl_3/C_6F_5Li$ system suggest replacement of fluorine para to the substituent is a favoured pathway for these reactions.

In reactions with the phosphines and silanes, it is interesting that nucleophilic attack on the C_6F_6 substituent does occur though rupture of the C_6F_5P or C_6F_5Si bond cannot be ruled out, since it could be reformed under the reaction conditions. It appears that the $(C_{12}F_9)_3P$ species result from the attack of $C_6F_5^-$ on a para fluorine, since all other reactions would be ruled out for steric reasons. Further work will be required, including product isolation, since it has been suggested that the substitution pattern may be solvent dependent [10]. However, more recently, using other nucleophiles on $(C_6F_5)_3P$ we have observed one hundred percent para substitution [11,12].

The reactions of ferrocene suggest that rather than nucleophilic attack on ferrocene, the $(C_5H_5)_2Fe$ has become lithiated, and this in turn reacts with the haloaromatics present.

The reaction with the silanes are as expected, siloxanes being the by-products of incomplete reaction. There are however interesting reactions involving the substitution of C_4H_9 groups for a fluorine on the C_6F_5 attached to Si, this reaction being more prevalent at higher temperatures. Similarly, when partial substitution of C_6F_5 has occurred prior to hydrolysis we are then left with C_6F_5 substituted siloxane species.

In conclusion, most of the products observed are readily explained, and not particularly surprising. However, this study does point out the necessity of careful control of reagent proportions and reaction conditions if products are not to be contaminated by unwanted materials. GC/MS has proven to be an ideal tool to monitor such reactions. Generally, the C_6F_5Li reactions, if the temperature is kept low, produce fewer objectionable byproducts than do the Grignard reagents.

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