REACTIONS OF HEXAFLUOROBENZENE WITH SOME ORGANO-METALLIC REAGENTS

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Summary

The inverse addition of trichloro-2-thienyl-lithium to hexafluorobenzene in THF or ether has given 1,4-bis(trichloro-2-thienyl)tetrafluorobenzene in addition to the tetrakis(trichloro-2-thienyl)difluorobenzene. n-Butyl-lithium with hexafluorobenzene gave mono, bis, tris and tetrakis compounds whereas t-BuLi afforded only 1,4-bis(t-butyl)tetrafluorobenzene in excellent yield. Other organolithium and organomagnesium reagents gave the expected products. IR, ^{19}F NMR and UV spectral data are presented for the several new compounds.

Introduction

Hexafluorobenzene undergoes nucleophilic displacement of fluorine with a variety of nucleophiles [1]. Potassium thiophenoxide [2] and *N*-lithium-*N*-methylanilide [3] with hexafluorobenzene gave 1,2,4,5-tetrasubstituted compounds whereas the thiolate anion [4] yielded 1,2,3,5-tetrasubstitution under suitable conditions. There has recently been reported the preparation of 1,2,4,5-tetrakis(trichloro-2-thienyl)difluorobenzene in good yield from trichloro-2-thienyl-lithium and hexafluorobenzene [5]. The present paper deals with an extension of this earlier work on hexafluorobenzene.
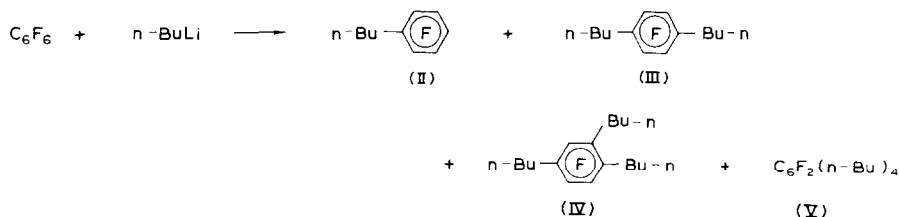
Results and discussion

In the preparation of 1,2,4,5-tetrakis(trichloro-2-thienyl)difluorobenzene *via* normal addition of hexafluorobenzene to trichloro-2-thienyl-lithium in THF at —78 °C, there was no evidence for the formation of mono-, di- or tri-substituted products even with a 1:1 molar ratio of hexafluorobenzene and trichloro-2-thienyl-lithium [5]. We have found that the inverse addition with a 2:1 molar ratio at —78 °C in THF gives, in addition to the tetrakis compound (52.8%), the 1,4-bis(trichloro-2-thienyl)tetrafluorobenzene (I) (13.3%).

$$2 - C_4Cl_3SLi \ + \ C_6F_6 \ \longrightarrow \ 2 - SCl_3C_4 - \langle F \rangle - C_4Cl_3S - 2$$

<div align="center">(I)</div>

A similar reaction in ether at −15 to −20 °C also gave the tetrakis (43.5%) and the bis (20.4%) compounds. The ^{19}F NMR spectrum, in $CCl_4/CFCl_3$, of the bis compound consisted of a singlet at 141.7 ppm, indicative of 1,4-di-substitution.

An *in situ* reaction of hexafluorobenzene with tetrachlorothiophene and Mg in THF (employing 1 equiv. of 1,2-dibromoethane) gave 1,2,4,5-tetrakis-(trichloro-2-thienyl)difluorobenzene (19.6%).

Reaction of hexafluorobenzene with 6.1 equiv. of n-BuLi gave four products, identified as n-butylpentafluorobenzene (II) (14.3%), 1,4-bis(n-butyl)-tetrafluorobenzene (III) (20.6%), 1,2,4-tris(n-butyl)trifluorobenzene (IV) (31.3%) and tetrakis(n-butyl)difluorobenzene (V) (14.8%). Compound (V) is believed to have 1,2,4,5-tetrasubstitution as has been reported for other tetra-substituted difluorobenzenes [2, 3, 5]. However, it was not possible to ex-clude 1,2,3,5-tetrasubstitution on the basis of comparison of the ^{1}H NMR spectra of compounds (III) - (V).

$$C_6F_6 \ + \ n-BuLi \ \longrightarrow \ n-Bu - \langle F \rangle \ + \ n-Bu - \langle F \rangle - Bu-n$$

<div align="center">(II)   (III)</div>

$$+ \ n-Bu - \langle F \rangle \overset{Bu-n}{-} Bu-n \ + \ C_6F_2(n-Bu)_4$$

<div align="center">(IV)   (V)</div>

The ^{19}F NMR spectra, in $CCl_4/CFCl_3$, of (III) and (V) consisted of singlets at 135.5 ppm and 127.2 ppm, respectively, while (IV) showed three reson-ances at 126.0, 144.2 and 147.7 ppm, in agreement with the assigned struc-tures. No pentakis or hexakis products were isolated. It appears that the total electron-releasing effect of four n-butyl groups coupled with steric effects make the remaining nuclear fluorines somewhat inert to additional nucleo-philic attack. Reaction of hexafluorobenzene with 2.01 equiv. of n-BuLi gave n-butylpentafluorobenzene (9.8%) and 1,4-bis(n-butyl)tetrafluoro-benzene (51.9%). No tris or tetrakis compounds were obtained under these conditions.

A similar reaction of hexafluorobenzene with 4.05 equiv. of t-BuLi in THF at −78 °C gave 1,4-bis(t-butyl)tetrafluorobenzene (VI) (91.6%), iden-tified by its ^{19}F NMR spectrum which showed a singlet at 135.5 ppm, con-sistent with a symmetrical structure.

$$C_6F_6 \ + \ t-BuLi \ \longrightarrow \ t-Bu - \langle F \rangle - Bu-t$$

<div align="center">(VI)</div>

The yields of the bis compound (VI) were 85% with 2.05 equiv. of t-BuLi in THF and 41.8% with 4.05 equiv. in ether. The lower yield in ether is probably due to the decreased polarity of the medium. No tris or tetrakis products could be isolated. It appears that steric effects are important in preventing polysubstitution.

n-Octyl-lithium [6, 7] and hexafluorobenzene (1:1.1) in ether/THF gave n-octylpentafluorobenzene (58.5%), whereas 2.1 equiv. of n-octyl-lithium afforded n-octylpentafluorobenzene (8.9%) and 1,4-bis(n-octyl)tetra-fluorobenzene (59.8%). No tris or tetrakis products were isolated from these experiments.

Trimethylsilylsodium [8] with hexafluorobenzene (2.1:1) in HMPT gave pentafluorophenyltrimethylsilane (20.6%). No bis compound was ob-tained under our conditions.

n-Butylmagnesium bromide and hexafluorobenzene in ether/THF af-forded n-butylpentafluorobenzene (41.2%). A similar reaction in THF gave 55.8% of n-butylpentafluorobenzene. The higher yield in THF is consistent with the observation made earlier [9].

n-Octylmagnesium bromide and perfluoro-n-octylmagnesium halide with hexafluorobenzene in ether did not give any alkylated product. The failure of these organomagnesium halides to react with hexafluorobenzene is attributed to the less polar nature of the solvent and the instability of perfluoro-n-octyl-magnesium halide at higher temperatures. n-Octylmagnesium bromide is known to cleave some cyclic ethers at elevated temperatures [10]. No solvent cleavage by n-octylmagnesium bromide was observed when the reaction of hexafluorobenzene with the Grignard reagent was carried out in ether/THF at ambient temperatures.

Experimental

All reactions were carried out in an atmosphere of dry, oxygen-free nitrogen. Ethereal solvents were dried over sodium and THF was further pu-rified by distillation from a sodium benzophenone–ketyl mixture. n-Butyl-lithium and t-butyl-lithium were obtained from the Foote Mineral Company. The reactions were performed in THF at $-78\,^{\circ}$C unless otherwise stated.

IR spectra were determined on Beckman IR-18A as Nujol or HCB mulls or as thin films. UV spectra were recorded on a Cary Model 14R recording spectrometer. ^{19}F NMR spectra were run on Varian HA-100 tuned to 94.075 MHz using solutions in carbon tetrachloride with fluorotrichloro-methane as an internal standard. Molecular weights were determined mass spectrometrically.

General procedure

To hexafluorobenzene in THF at $-78\,^{\circ}$C was added the appropriate organolithium or organomagnesium compound, and the mixture was stirred at this temperature until Color Test I [11] was negative. In reactions where

TABLE 1

Reaction of hexafluorobenzene with some organometallic reagents

Hexafluorobenzene /mol	RM/mol	Method	Compounds isolated (% yield)	B.p./m.p. (°C/mmHg)	n_D^{20}	Mol. wt. found (calcd.)	Analysis: Found (Calc.)		
							C	H	F
0.05	0.305[a]	A	$n\text{-}C_4H_9C_6F_5$ (14.3)	54 - 55/2	1.4220[b]				
			$1,4\text{-}(n\text{-}C_4H_9)_2C_6F_4$ (20.6)	86 - 87/2	1.4490	262 (262.3)	63.86 (64.11)	6.92 (6.92)	28.32 (28.97)
			$1,2,4\text{-}(n\text{-}C_4H_9)_3C_6F_3$ (31.3)	126 - 127/2	1.4648	300.5 (300.4)	71.41 (71.96)	9.56 (9.06)	19.40 (18.97)
			$1,2,4,5\text{-}(n\text{-}C_4H_9)_4C_6F_2$ (14.8)	153 - 155/2	1.4782	338 (338.5)	78.60 (78.06)	10.40 (10.72)	10.99 (11.22)
0.05	0.055[c]	A	$n\text{-}C_8H_{17}C_6F_5$[d] (58.5)	69 - 70/1	1.4332	281 (280.6)	60.22 (59.99)	6.11 (6.11)	34.24 (33.90)
0.06	0.125[c]	A	$n\text{-}C_8H_{17}C_6F_5$ (8.9)	69 - 70/1					
			$1,4\text{-}(n\text{-}C_8H_{17})_2C_6F_4$[e] (59.8)	148 - 150/1	1.4575	375 (374.5)	70.59 (70.55)	9.20 (9.16)	19.91 (20.29)
0.025	0.105[f]	A	$1,4\text{-}(t\text{-}C_4H_9)_2C_6F_4$[g] (91.6)	94 - 95		262 (262.3)	63.84 (64.11)	6.93 (6.92)	28.80 (28.97)
0.05	0.1[h]	A	$1,4\text{-}(2\text{-}C_4Cl_3S)_2C_6F_4$[i] (20.4)	196 - 197		521 (521.0)	32.51 (32.28)	—	14.59 (14.58)
			$1,2,4,5\text{-}(2\text{-}C_4Cl_3S)_4C_6F_2$ (43.5)	345 - 347[j]				—	
0.05	0.1[h]	A	$1,4\text{-}(2\text{-}C_4Cl_3S)_2C_6F_4$[k] (13.3)	196 - 197					
			$1,2,4,5\text{-}(2\text{-}C_4Cl_3S)_4C_6F_2$ (52.8)	345 - 347					
0.5	0.1[l]	B	$(CH_3)_3SiC_6F_5$[m] (20.6)	94 - 95/57					
0.05	0.22[n]	A	$n\text{-}C_4H_9C_6F_5$ (41.2)	54 - 55/2	1.4219				

TABLE 2

Spectral data of substituted fluorobenzenes

No.	Compound	IR spectral data/cm^{-1}		UV spectra data
		Skeletal vibrations of fluorinated ring	C—F stretching	$\lambda_{max.}/m\mu$ (ϵ)
(I)	1,4-Bis(trichloro-2-thienyl)tetrafluorobenzene*	1465, 1485	985, 1325	298, (12 200) 264 (9740)
(III)	1,4-Bis(n-butyl)tetrafluorobenzene	1460, 1485	980, 1125, 1275	265, (870) 215 (9055)
(IV)	1,2,4-Tris(n-butyl)trifluorobenzene	1470, 1485	975, 1125, 1250	266, (840) 217.5 (9760)
(V)	1,2,4,5-Tetrakis-(n-butyl)difluorobenzene	1440, 1455	960, 1120, 1240	275.5, (905) 268, (1760) 219 (962)
(VI)	1,4-Bis(t-butyl)tetrafluorobenzene	1475, 1485	965, 1050, 1285	269, (910) 212 (9330)
(VII)	n-Octylpentafluorobenzene	1470, 1485	975, 1125, 1250	259.5, (890) 217.5 (9250)
(VIII)	1,4-Bis(n-octyl)tetrafluorobenzene	1460, 1485	970, 1125, 1275	264, (880) 212 (8925)

* The compound is insoluble in hexane and hence UV data were determined in CCl$_4$. The UV spectra of all other compounds were run in hexane.

Footnotes to Table 1

A = inverse addition; B = normal addition.
[a] RM = n-BuLi.
[b] Cited [12]: 85 °C/35 mmHg, n_D^{20} = 1.4219.
[c] RM = n-C$_8$H$_{17}$Li; see refs. 6 and 7 for the preparation and estimation, respectively, of n-C$_8$H$_{17}$Li.
[d, e] Carbonated before work-up; di-n-octyl ketone (8.1%, identified by IR spectroscopy $>$C = O: 1710 cm^{-1} and m.p. 49 - 50 °C. cited [13]: 50.5 °C) and n-hexadecane (7.7%; b.p. 96 °C/1 mmHg, n_D^{20} = 1.4343).
[e] Di-n-octyl ketone (7.8%) and n-hexadecane (3.1%).
[f] RM = t-BuLi.
[g] Yield 85% with 2.05 equiv. of t-BuLi in THF, and 41.8% with 4.05 equiv. in ether.
[h] RM = 2-C$_4$Cl$_3$SLi [14].
[i] In ether at —15 °C to —20 °C. The bis compound was separated from the tetrakis compound by extraction with hot petroleum ether (b.p. 60 - 80 °C), sublimed at 150 °C/5 mmHg and crystallized from petroleum ether. (Found: Cl, 41.02%. C$_{14}$Cl$_6$F$_4$S$_2$ requires Cl, 40.83%.)
[j] Cited: 345 - 347 °C.
[k] In THF at —78 °C.
[l] RM = (CH$_3$)$_3$SiNa [8].
[m] Cited [15]: 93 °C/57 mmHg.
[n] RM = n-BuMgBr in ether was added to hexafluorobenzene in THF.

Color test I was positive even after *ca.* 24 h, the reaction mixture was carbonated before work-up. The work-up consisted of hydrolysis with cold 3 mol l^{-1} HCl, separation of the organic layer and extraction of the aqueous layer with ether. The combined extract was dried over $MgSO_4$. The crude product, obtained after removal of solvent, was purified by crystallization or distillation. All liquids were further purified by preparative VPC.

The relevant data are recorded in Table 1. UV and IR spectral data are listed in Table 2.

Acknowledgments

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