

Received: August 8, 1989; accepted February 6, 1990

REACTIONS OF PERFLUOROAROMATIC COMPOUNDS
WITH ETHEREAL SOLUTIONS OF METHYLMAGNESIUM IODIDE
IN THE PRESENCE OF SILVER(I) AND COPPER(I) SALTS

A.A. BOGACHEV, L.S. KOBRINA and G.G. YAKOBSON

Institute of Organic Chemistry, Novosibirsk, 630090 (U.S.S.R.)

SUMMARY

The reactions of hexafluorobenzene, octafluorotoluene, decafluorodiphenyl, and octafluoronaphthalene with ethereal solutions of methylmagnesium iodide in the presence of AgCl or CuI gave the products of the methylation and 1-ethoxy-ethylation of the perfluorinated substrates, whose formation has been suggested to occur with participation of free radicals. Substitution of fluorine atoms by the 1-ethoxyethyl radicals in $C_6F_5CF_3$ and $C_6F_5C_6F_5$ proceeds with predominant para-orientation; in $C_{10}F_8$, 1- and 2-orientations take place to an equal extent, whereas the methyl radicals attack mainly the 1-position of octafluoronaphthalene and show a low selectivity in the reaction with octafluorotoluene.

INTRODUCTION

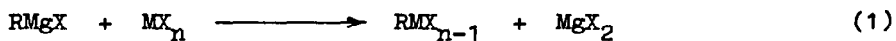
Studies [1] on the homolytic reactions of polyfluoroaromatic compounds have shown that perfluorinated derivatives of aromatic hydrocarbons react with carbon radicals by the addition mechanism with subsequent dimerisation of radical σ -complexes, but not by the substitution mechanism, typical for the non-fluorinated aromatic compounds [2]. It was found in this case that electrophilic radicals attack perfluoroaromatic compounds of the benzene series having electron-accepting substituents other than fluorine (e.g., CF_3 or C_6F_5)

exclusively at the meta-position. As for octafluoronaphthalene, it reacts under mild conditions (85°C) with the electrophilic pentafluorobenzoyloxy radical to give the dimerization product of 1-addition σ -complexes of this radical, whereas with nucleophilic methyl and electrophilic pentafluorophenyl radicals it reacts under more vigorous conditions (140-200°C) to form the products of homolytic fluorine substitution in the 2-position. The lack of selectivity in the reactions of octafluoronaphthalene with nucleophilic and electrophilic radicals was attributed to the reversible character of the addition of these radicals to octafluoronaphthalene at high temperatures and the irreversible rearrangement of σ -complexes of addition of the radicals at the 2-position of octafluoronaphthalene [3].

RESULTS AND DISCUSSION

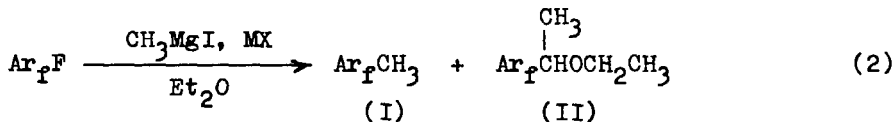
This paper studies orientations in the reactions of perfluorinated aromatic hydrocarbons (hexafluorobenzene, octafluorotoluene, decafluorodiphenyl, and octafluoronaphthalene) with nucleophilic radicals (methyl and 1-ethoxyethyl) under conditions close to kinetic. For the generation of these radicals under mild conditions (25-35°C), a system consisting of methylmagnesium iodide and silver(I) or copper(I) salts in diethyl ether was used.

The one-electron oxidation of Grignard reagents ($RMgX$) by transition metal salts (MX_n) is known to involve a metal exchange reaction [4], whereby (1) the resultant organometallic compound (RMX_{n-1}) may decompose by a free-radical mechanism at temperatures below 0°C. For instance, methylsilver quickly decomposes below -30°C [5], and the more stable methylcopper does so at room temperature [6].



Previously we have reported [7] the use of oxidation of methylmagnesium iodide by silver chloride or copper iodide in diethyl ether for the homolytic substitution of fluorine atoms by alkyl groups in perfluoroaromatic compounds. Along with the methyl-substituted derivatives, the reaction gave 1-ethoxyethylation products, due to participation of secondary

radicals in the reaction. Similarly, the reactions of perfluoroaromatic substrates with methylmagnesium iodide - AgCl or CuI - diethyl ether systems, studied in the present paper, led to the formation of methyl- and 1-ethoxyethyl-derivatives (I and II) of polyfluoroaromatic compounds (2):



Ar_f = (a) C₆F₅, (b) CF₃C₆F₄, (c) C₆F₅C₆F₄, (d) C₁₀F₇;
 MX = AgCl, CuI.

The reactions were carried out at different mole ratios of methylmagnesium iodide to perfluoroaromatic substrate. In all experiments, a 2.5 M diethyl ether solution of CH₃MgI, and equimolar amounts of AgCl or CuI relative to methylmagnesium iodide were used. Table 1 lists the results of the reactions of perfluorinated aromatic compounds with ethereal solutions of methylmagnesium iodide in the presence of silver chloride (at 25°C) and copper iodide (at 35°C). Product yields for the experiments with hexafluorobenzene and octafluorotoluene are given on the basis of the GLC analysis of the reaction mixtures; and for the experiments with decafluorodiphenyl and octafluoronaphthalene, on the basis of the silica gel column chromatography.

As seen from Table 1, the use of either AgCl or CuI as oxidants for methylmagnesium iodide is equally effective, as judged by the results of the reactions. In the case of hexafluorobenzene, a decreased mole ratio of CH₃MgI to substrate (from 1:1 to 1:10) leads to an increased conversion degree of the substrate. The latter reaction gives increased relative yields of 2,3,4,5,6-pentafluorotoluene (Ia), and, accordingly, decreased relative yields of (1-ethoxyethyl)pentafluorobenzene (IIa), which may be the result of a reduced concentration of 1-ethoxyethyl radicals as a consequence of the diminished possibility for methyl radicals to eliminate hydrogen atoms from diethyl ether. Upon replacement of one fluorine atom in hexafluorobenzene by the CF₃ or C₆F₅ groups, a dependence of the methyl- to 1-ethoxyethyl-derivative ratio on the character

TABLE 1

Interaction of perfluoroaromatic compounds
with ethereal solutions of methylmagnesium iodide
in the presence of silver and copper salts

Substrate (Ar _F)	Mole ratio of CH ₃ MgI substrate	Salt (MX)	Yields of products (%), considerings the converted substrate		Conversion of the substrate (%)
			Ar _F CH ₃ (I)	Ar _F CHOCH ₂ CH ₃ CH ₃ (II)	
C ₆ F ₆ *	1:1	CuI	23	62	1.3
	1:5	CuI	65	32.5	26
	1:5	AgCl	68	30	26
	1:10	CuI	80	17	31
	1:10	AgCl	81	17	31.5
C ₆ F ₅ CF ₃ *	1:1	CuI	37.5	56.5	1.1
	1:5	CuI	41	54	2.4
	1:5	AgCl	44	52	2.5
	1:10	CuI	53	29.5	1.7
C ₆ F ₅ C ₆ F ₅ **	1:2	CuI	-	96	1.4
	1:5	CuI	6	91	11.5
	1:5	AgCl	5	90	11
	1:10	CuI	11.5	86	5.2
C ₁₀ F ₈ **	1:2	CuI	35	63	22
	1:5	CuI	65	32	39
	1:5	AgCl	67	31	39
	1:10	CuI	64	33	46
	1:10	AgCl	79	19	55

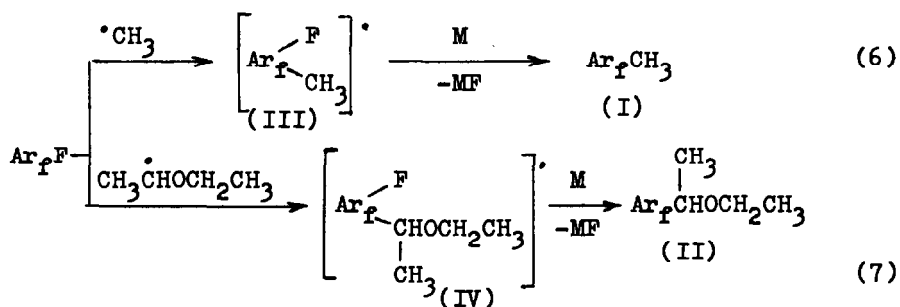
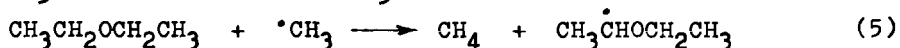
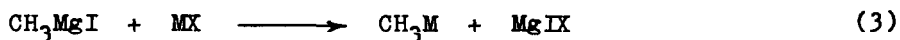
* Yields calculated from the GLC data;

** Considering the isolated products.

of the substituent is observed. For the reactions with an excess of perfluoroaromatic substrate in the series of C_6F_6 , $C_6F_5CF_3$, $C_6F_5C_6F_5$, the yield of the methyl-substituted derivatives (Ia)-(Ic) decreases, whereas that of the 1-ethoxyethyl-derivatives (IIa)-(IIc) increases, with (1-ethoxyethyl)nonafluorodiphenyl (IIc) being formed almost exclusively in the case of decafluorodiphenyl.

In the effect of the CH_3MgI - substrate ratio on the relative yields of methylation and 1-ethoxyethylation products, octafluoronaphthalene is similar to hexafluorobenzene in this reaction, but of all the compounds considered here it reacts to the greatest extent both with methyl and 1-ethoxyethyl radicals, and is most sensitive to the nature of the metal in the halide. Thus, at a 1:10 mole ratio of CH_3MgI to $C_{10}F_8$, on passing from CuI to $AgCl$, the yield of methylheptafluoronaphthalenes (Id) relative to (1-ethoxyethyl)heptafluoronaphthalenes (IIId) somewhat increases.

For the formation of products (I and II) in the reactions of perfluoroaromatic compounds with ethereal solutions of methylmagnesium iodide in the presence of silver chloride or copper iodide, the following scheme may be suggested, where the first stage is the metal exchange process (3):



As a result of the decomposition of the organometallic intermediate CH_3M with the homolytic cleavage of the carbon-metal bond (4), methyl radicals are produced, which may eliminate the

α -hydrogen atoms from diethyl ether (5), generating thus the 1-ethoxyethyl radicals. Addition of methyl (6) and 1-ethoxyethyl (7) radicals to the perfluoroaromatic substrate gives the respective radical σ -complexes (III and IV), whose defluorination by the reduced metal M leads to the homolytic substitution products (I and II). The absence of radical σ -complex dimerisation products, which are typical for the homolytic reactions of polyfluoroaromatic compounds [1], may be explained by the efficiency of defluorination of radical σ -complexes (III and IV) by the reduced metals.

The isomeric mixtures of 1-ethoxyethylation products (IIb and IIc), obtained in the reactions of octafluorotoluene and decafluorodiphenyl, are characterised by the high content of para-isomers. The ortho:meta:para ratio, determined from the GLC and ^{19}F NMR data, does not practically depend on the CH_3MgI - substrate ratio, being 8:18:74 for the reactions of octafluorotoluene, and 2:16:82 for those of decafluorodiphenyl. In the methylation of octafluorotoluene, a mixture of 2-, 3-, and 4-methylheptafluorotoluenes (Ib) is formed, with a certain predominance of ortho- and para-isomers (the ortho:meta:para ratio being 37:24:39). The isomer ratio of the methylation products of decafluorodiphenyl (Ic), formed in small amounts, has not been determined. The low selectivity of the methyl radical as compared to the 1-ethoxyethyl one in the reaction with octafluorotoluene probably results from its less nucleophilic character [2], though one should not exclude possible steric hindrance in the attack of the bulky 1-ethoxyethyl radical at the ortho-position of perfluorinated substrates $\text{C}_6\text{F}_5\text{CF}_3$ and $\text{C}_6\text{F}_5\text{C}_6\text{F}_5$.

In the reaction of octafluoronaphthalene with methyl radicals, generated from methylmagnesium iodide in the presence of AgCl or CuI at 25-35°C, predominant orientation in the 1-position is observed. The ratio of 1- to 2-isomer in the mixture of methylheptafluoronaphthalenes (Id) is approximately 90:10, and is opposite to the ratio obtained in the thermolysis of di-tert-butyl peroxide in octafluoronaphthalene at 140-160°C. The reversal of orientation depending on the reaction temperature may support our suggestion about the reversibility of addition

of methyl radicals to octafluoronaphthalene at higher temperatures and the occurrence of the irreversible rearrangement with fluorine atom migration in the respective σ -complexes [3]. In the case of the 1-ethoxyethyl radical, which is more nucleophilic [8], the proportion of attack in the 2-position of octafluoronaphthalene increases. The resulting mixture of the (1-ethoxyethyl)heptafluoronaphthalenes (IIId) contains approximately equal amount of 1- and 2-isomers.

The free-radical mechanism was proposed here for interpreting the reactions of perfluoroaromatic compounds with methyl and 1-ethoxyethyl radicals, generated by the use of methylmagnesium iodide - silver or copper salts - diethyl ether systems, on the basis of the following considerations. The free-radical mechanism seems to be confirmed by participation of the secondary-generated (5) 1-ethoxyethyl radicals, as well as by the isomer ratio of products(I and II), and the dependence of their relative yields on the reagent-substrate ratio. These facts disagree with the radical-ion mechanism of substitution or the mechanism involving coordination of a metal with perfluoroaromatic substrate.

Thus, it has been shown in the case of the reactions of perfluoroaromatic compounds with the methylmagnesium iodide - AgCl or CuI - diethyl ether systems that, when one fluorine atom in hexafluorobenzene is exchanged for an electron-accepting substituent (CF_3 or C_6F_5), substitution by nucleophilic radicals is characterised by the predominant para-orientation, and orientation in the radical reactions of octafluoronaphthalene depends not only on the polarity of attacking radical but also on the reaction temperature (Table 2).

EXPERIMENTAL

The 1H and ^{19}F NMR spectra were recorded on a Varian A56/60A spectrometer at 60 and 56.4 MHz respectively, without a solvent (external standard was TMS; internal, C_6F_6). Mass-spectra were recorded on a Finnigan MAT 8200 instrument. The GLC analysis was carried out on a chromatograph with

TABLE 2

Isomer distributions in the reactions
of perfluoroaromatic compounds with some carbon radicals

Substrate	Radical	T °C	Isomer ratio (%)			Ref.
			o-	m-	p-	
$C_6F_5CF_3$	$CH_3\dot{C}HOCH_2CH_3$	25-35	8	18	74	this paper*
	$CH_3\dot{C}$	25-35	37	24	39	this paper*
	$C_6H_5\dot{C}$	80	5	71	24	9
	$C_6F_5\dot{C}$	80	6	90	4	10
$C_6F_5C_6F_5$	$CH_3\dot{C}HOCH_2CH_3$	25-35	2	16	82	this paper*
	$C_6F_5\dot{C}$	80	13	60	27	11
$C_{10}F_8$	$CH_3\dot{C}HOCH_2CH_3$	25-35	50	50		this paper*
	$CH_3\dot{C}$	25-35	90	10		this paper*
	$CH_3\dot{C}$	160	12	88		3
	$C_6H_5\dot{C}$	110	70	30		12
	$C_6F_5\dot{C}$	160	0	100		3

* The isomer ratio does not practically depend on the reagent-substrate ratio.

4000 x 4 mm steel columns, at 50-250°C (programmed heating 10°/min), stationary phase 15% QF-1 on the Chromaton N-AW carrier (0.20-0.25 mm); the detector was a catharometer; the carrier gas, helium. Isolation of products by column chromatography was carried out on silica gel (0.140-0.315 mm); eluents were hexane and chloroform.

Interaction of hexafluorobenzene and octafluorotoluene
with ethereal solutions of methylmagnesium iodide

(a) In the presence of silver chloride

A 2.5 M solution of methylmagnesium iodide in diethyl ether was added dropwise (during 0.5-1 h) to a suspension of silver chloride in the substrate at room temperature with vigorous stirring. The reaction mixture was then diluted with ether (4- or 5-fold excess), the inorganic precipitate was filtered off, the filtrate washed with water, 5% HCl solution, saturated sodium thiosulphate solution, again with water, and dried with CaCl_2 . The ether was evaporated off without vacuum, excess of the substrate distilled off at atmosphere pressure, and the residue analysed by GLC. Distillation of the methyl-substituted derivatives (Ia and Ib) from the residue gave the 1-ethoxyethylation products (IIa and IIb).

(b) In the presence of copper iodide

A 2.5 M solution of methylmagnesium iodide in diethyl ether was added at room temperature to a suspension of copper iodide in the substrate with vigorous stirring and the mixture was refluxed for 2 h. Further treatment was similar to that described above.

Table 3 lists the experimental data on the reactions of hexafluorobenzene and octafluorotoluene with ethereal solutions of methylmagnesium iodide in the presence of AgCl and CuI. (1-Ethoxyethyl)pentafluorobenzene (IIa) has been described earlier in ref. [7]. The mixture of (1-ethoxyethyl)heptafluorotoluenes (IIb) is a colourless liquid. Found %: C 45.52, 45.55; H 3.02, 3.09; F 45.98, 45.90. Mol. wt. 290.0550. $\text{C}_{11}\text{H}_9\text{F}_7\text{O}$ requires %: C 45.52, H 3.10, F 45.86; Mol. wt. 290.0541. ^1H NMR spectrum, ppm: 1.11 (triplet, CH_3), 1.53 (doublet, CH_3), 3.35 (quartet, CH_2), 4.83 (quartet, CH). ^{19}F NMR spectrum, ppm: -1.3 (F^5), 25.5 and 34.0 (F^4 and F^6), 45.2 (F^2), 107.0 (CF_3) are the signals assigned to the meta-isomer; 21.7 (F^3 , F^5), 23.6 (F^2 , F^6), 107.2 (CF_3) are the signals assigned to the para-isomer.

TABLE 3

Reaction of hexafluorobenzene and octafluorotoluene with ethereal solutions of methylmagnesium iodide in the presence of AgCl and CuI

Substrate	Charge of the starting compounds		Substrate distillate (g)	Residue (g)	The content of the residue (g)*				
	substrate (g)	CuI (g)			substrate methylation products (Ia and Ib)	1-ethoxy-ethylation products (IIa and IIb)			
	2.5 M of CH ₃ MgI (ml)								
C ₆ F ₆	9.30	-	9.52	20	8.97	0.39	0.21	0.02	0.10
	46.52	7.18	-	20	38.11	9.60	6.90	1.59	0.94
	46.50	-	9.50	20	37.68	10.38	7.29	1.53	1.02
	46.53	3.58	-	10	38.40	8.32	6.68	1.16	0.32
	46.48	-	4.79	10	38.82	7.95	6.26	1.12	0.33
C ₆ F ₅ CF ₃	11.80	-	9.53	20	10.31	1.58	1.35	0.05	0.09
	59.02	7.20	-	20	56.02	3.18	2.70	0.13	0.19
	58.97	-	9.52	20	57.96	1.07	0.70	0.12	0.19
	118.03	-	9.50	20	117.25	0.77	0.54	0.10	0.07

* Calculated from GLC data.

Interaction of decafluorodiphenyl and octafluoronaphthalene with ethereal solutions of methylmagnesium iodide

(a) In the presence of silver chloride

A 2.5 M ethereal solution of methylmagnesium iodide was added dropwise (during 0.5-1 h) to a suspension of silver chloride in an ethereal solution of the substrate (at room temperature) with vigorous stirring, whereupon the mixture was stirred during further 1 h. Then the reaction mixture was diluted with ether (4- or 5-fold excess), the inorganic precipitate was filtered off, and the filtrate washed with water, 5% HCl solution, the saturated solution of sodium thiosulphate, again with water, dried with CaCl_2 , and the ether evaporated. Part of the substrate was crystallised off from chloroform (if necessary), and the mother solution evaporated. After evaporation, the residue was passed through a silica gel chromatography column. Elution with hexane yielded the substrate and a fraction containing the substrate and methyl-derivatives (Ic and Id); elution with chloroform gave the 1-ethoxyethylation products (IIc and IID). The mixed fraction was additionally separated on a silica gel column, and the residue of the substrate and the methylation products (Ic and Id) were isolated.

(b) In the presence of copper iodide

A 2.5 M solution of methylmagnesium iodide in diethyl ether was added at room temperature to a suspension of copper iodide in an ethereal solution of the substrate with vigorous stirring, whereupon the mixture was refluxed for 2 h, and subsequently treated similarly to the method described above.

Table 4 presents the experimental data for the reactions of decafluorodiphenyl and octafluoronaphthalene with ethereal solutions of methylmagnesium iodide in the presence of AgCl and CuI. The mixture of (1-ethoxyethyl)nonafluorodiphenyls (IIc) is a colourless viscous liquid. Found %: C 49.57, 49.40; H 2.49, 2.33; F 44.35, 44.00. Mol. wt. 388.0487. $\text{C}_{16}\text{H}_3\text{F}_9\text{O}$ requires %: C 49.48, H 2.32, F 44.07. Mol. wt. 388.0509.

^1H NMR spectrum, ppm: 1.23 (triplet; CH_3), 1.68 (doublet, CH_3),

TABLE 4

Reaction of decafluorodiphenyl and octafluoronaphthalene with ethereal solutions of methylmagnesium iodide in the presence of AgCl and CuI

Substrate	Charge of the starting compounds				Returned		Chromatographically isolated products (g)	
	substrate (g)	AgCl (g)	CuI (g)	2.5 M Et ₂ O solution (ml)	substrate (g)	methylation products (Ic and Id)	1-ethoxyethylation products (IIc and IIId)	
C ₆ F ₅ C ₆ F ₅	33.42	-	9.50	20	40	33.22	-	0.21
	41.78	3.61	-	10	50	40.88	0.05	0.97
	41.80	-	4.75	10	50	40.65	0.06	1.22
	84.03	-	4.81	10	100	83.52	0.05	0.43
C ₁₀ F ₈	13.61	-	4.78	10	15	12.11	0.58	1.04
	68.03	7.22	-	20	75	62.72	3.42	2.03
	68.00	-	9.49	20	75	62.71	3.32	2.11
	67.98	3.60	-	10	75	64.77	2.51	0.71
	68.02	-	4.76	10	75	64.52	2.16	1.37

3.53 (quartet, CH₂), 5.04 (quartet, CH). ¹⁹F NMR spectrum, ppm: -0.8 (F⁵), 1.4 (F^m), 11.1 (F^p), 20.3 (F^o), 30.1 and 31.0 (F⁴ and F⁶), 45.4 (F²) are the signals assigned to the meta-isomer; 1.4 (F^m), 11.6 (F^p), 20.3 (F^o), 23.8 (F³, F⁵), 25.2 (F², F⁶) are the signals assigned to the para-isomer. The mixture of (1-ethoxyethyl)heptafluoronaphthalenes (IId) has been described [7].

The products (Ia) - (Id) of methylation of perfluoro-aromatic compounds have been identified chromatographically by authentic samples.

REFERENCES

- 1 L.S. Kobrina, Usp. Khim., 46 (1977) 660.
- 2 M. Tiecco and L. Testaferri, "Reactive Intermediates", ed. by R.A. Abramovitch, Plenum Press, New York 1983, v.3, p.61.
- 3 A.A. Bogachev, L.S. Kobrina and G.G. Yakobson, Zh. Org. Khim., 20 (1984) 1063.
- 4 A.N. Kashin and I.P. Beletskaya, Usp. Khim., 51 (1982) 881.
- 5 G. Semerano and L. Riccoboni, Ber., 74 (1941) 1089.
- 6 H. Gilman and R.G. Jones, J. Org. Chem., 17 (1952) 1630.
- 7 A.A. Bogachev, L.S. Kobrina and G.G. Yakobson, Zh. Org. Khim., 20 (1984) 218.
- 8 F. Minisci, Top. Curr. Chem., 62 (1976) 1.
- 9 R. Bolton, J.P.B. Sandall and G.H. Williams, J. Fluorine Chem., 4 (1974) 355.
- 10 L.S. Kobrina, V.L. Salenko and G.G. Yakobson, Zh. Org. Khim., 13 (1977) 1693.
- 11 L.S. Kobrina, V.L. Salenko and G.G. Yakobson, J. Fluorine Chem., 8 (1976) 193.
- 12 L.V. Vlasova, L.S. Kobrina and G.G. Yakobson, Zh. Org. Khim., 7 (1971) 1224.