

Chloro- and Bromo-defluorination of Hexafluorobenzene and Octafluorotoluene

A.I. Shipilov, E.E. Zolotkova, and S.M. Igumnov

Perm Effiliation of the Federal State Unitary Enterprise Russian Scientific Center
“Applied Chemistry”, Perm, 614034 Russia
e-mail: shipilov@perm.ru

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Abstract—Halo(chloro, bromo)defluorination of perfluorobenzene and toluene efficiently occurs under the action of appropriate alkali metal halides in the presence of hexaethylguanidinium chloride in catalytic amount. The relative efficiency of halide anions and metal cations in these reactions was established.

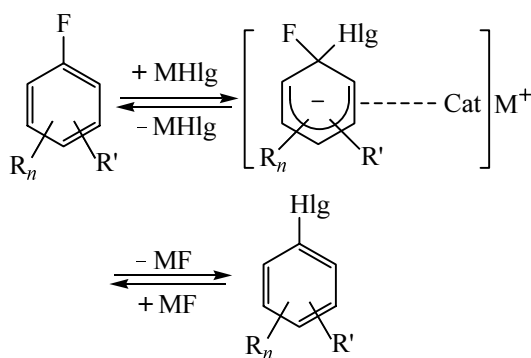
Nucleophilic substitution in perfluoro- or polyfluorobenzenes is a well known and widely used procedure for preparation of various functionally-substituted aromatic derivatives. A large number of papers was dedicated to the studies of this class reactions that was summarized in recent reviews [1–3]. However we believe that the nucleophilic halogenation of perfluorobenzenes has not attracted sufficient attention. A successful realization of these reactions obviously extends the synthetic opportunities and gives better insight into the nature of the chemical processes occurring in nucleophilic aromatic substitution.

The fluorine atom is successfully replaced by other halogens (here and hereinafter we mean by halogens chlorine or bromine) in reactions with alkali metal halides even in highly electrophilic substrates like tetrafluorophthalodinitrile [4] and pentafluorobenzo-nitrile [5]. The presence of a powerful electron-withdrawing group in the perfluorinated ring significantly increases the activity of the polyfluoroaromatic ring toward the nucleophilic substitution, in particular, to substitution with weak nucleophiles like halide ions. Although the hexafluorobenzene and octafluorotoluene as a rule are highly active in nucleophilic substitution reactions, we have not come across successful attempts of halodefluorination of these compounds.

We formerly demonstrated [6] that the use of highly efficient “onium” catalysts, like hexaethylguanidinium chloride or tetra(diethylamino)phosphonium bromide, resulted in considerable activation of aromatic

compounds in nucleophilic substitution due to reduction of the activation energy of the reaction caused by stabilization of the intermediate anionic σ -complex. By this procedure the chlorodefluorination was carried out with as relatively inactive substrate as dichlorotetrafluorobenzene.

In this study we continued the investigation of catalytic halodefluorination. The experimental data obtained in reactions of sodium and potassium halides with hexafluorobenzene and octafluorotoluene in the presence of hexaethylguanidinium chloride are presented in Tables 1 and 2.



$n = 5, \text{R}_n = \text{F}; n = 4, \text{R}_n = \text{F}, \text{R}' = \text{CF}_3; \text{M} = \text{K}, \text{Na}; \text{Hlg} = \text{Cl}, \text{Br}; \text{Cat} = (\text{Et}_2\text{N})_3\text{CCl}.$

It was proved by special experiments that in the absence of the hexaethylguanidinium chloride no chlorodefluorination of hexafluorobenzene and octafluorotoluene was effected by sodium chloride under the conditions under study. At the same time as show the

Table 1. Chlorodefluorination of hexafluorobenzene (molar ratio C₆F₆–MCl–Cat, 0.5:1:0.1)

Run no.	MCl	T, °C	Time, h	Composition of reaction products, % ^a				
				C ₆ F ₆	C ₆ F ₅ Cl	C ₆ F ₄ Cl ₂	C ₆ F ₃ Cl ₃	C ₆ F ₂ Cl ₄
1	NaCl	100–110	48	95.4	4.3	0.3	–	–
			93	93.2	5.6	1.1	–	–
2	NaCl	130–140	24	87.6	11	1.4	Traces	–
			48	78.5	16.9	3.8	0.8	–
3 ^b	NaCl	130–140	24	61.8	17.2	11.8	8.2	1.0
			48	25.4	15	20	29.7	9.9
4	NaCl	160–170	24	69.1	20	8.8	2.1	Traces
			48	52	28.7	13.5	5.1	0.7
5	KCl	130–140	24	90.5	9.1	0.4	–	–
			48	89.3	10.5	0.2	–	–
6	KCl	160–170	24	87	12.3	0.7	–	–
			48	77.4	20.1	2.5	–	–
7 ^c	–	160–170	24	91	9	–	–	–
			48	90.5	9.5	–	–	–

^a C₆F₄Cl₂ contained ~95% of 1,3-dichlorotetrafluorobenzene, C₆F₃Cl₃ contained ~98% of 1,3,5-trichlorotrifluorobenzene, C₆F₂Cl₄ was pure 1,3-difluorotetrachlorobenzene.

^b The synthesis was carried out at stirring in a metallic reactor of about 1 liter capacity.

^c Molar ratio C₆F₆–hexaethylguanidinium chloride, 1:1.

Table 2. Halodefluorination of octafluorotoluene (molar ratio C₆F₅CF₃–MHLg–Cat, 0.5:1:0.1, 140–145°C)

Run no.	MHLg	Time, h	Composition of reaction products, % ^a				
			Ar _F CF ₃	Br–Ar _F CF ₃	Cl–Ar _F CF ₃	Cl ₂ –Ar _F –CF ₃	Cl ₃ –Ar _F –CF ₃
1	NaCl	7	60.1	–	38.1	1.8	–
		14	40.4	–	54.3	5.3	–
		24	9.9	–	77	9.2	3.9
2	KCl	7	88.4	–	10.1	1.5	–
		14	85.1	–	12.3	2.6	–
		24	80.2	–	18.3	1.0	0.5
3	NaBr	7	84.4	6.1	9.4	–	–
		14	77.5	13.0	9.4	–	–
		24	72	18	9.9	–	–
4	KBr	7	86.8	5.9	7.3	–	–
		14	83.6	9.0	7.4	–	–
		24	81	11.2	7.8	–	–
5 ^b	–	7	85.3	–	15.7	–	–
		14	84.1	–	15.8	Traces	–

^a Br–Ar_FCF₃: pure *para*-isomer; Cl–Ar_FCF₃: ratio of *para*-, *ortho*-, and *meta*-isomers ~1:0.5:0.3; Cl₂–Ar_F–CF₃: pure 2,4-dichlorohexafluorotoluene; Cl₃–Ar_F–CF₃: pure 2,4,6-trichloropentafluorotoluene.

^b Molar ratio C₆F₅CF₃–hexaethylguanidinium chloride, 1:1.

results from Table 1 sodium chloride brings about the chlorodefluorination in hexafluorobenzene in the presence of catalytic amounts of hexaethylguanidinium chloride already at 100–110°C. However the conversion

under these conditions reached only 7% in 90 h. The process occurred more efficiently at higher temperature and at vigorous stirring. The conversion at 130–140°C within 24 h was 20% without stirring and ~40% at

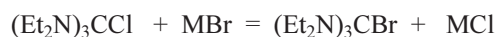
stirring the reaction mixture, whereas at 160–170°C in 48 h the conversion of hexafluorobenzene attained nearly 50% even without stirring. As expected, the catalytic halodefluorination proceeded more efficiently with a more active substrate, octafluorotoluene, since the trifluoromethyl group activated additionally the aromatic ring with respect to nucleophilic substitution and directed the reaction predominantly into the *para*-position. In the chlorodefluorination both of hexafluorobenzene and octafluorotoluene alongside the monosubstituted arise also di- and trisubstituted products.

The data obtained show that the reactivity of a metal bromide is considerably less than that of the respective chloride, in keeping with the known activity series manifested by the halide anions in the halodefluorination reactions in aprotic solvents: $F^- > Cl^- > Br^- > I^-$. For instance, in the highly reactive substrates (perfluorobenzonitriles) [4, 5] the fluorine replacement occurs the most easily with chlorine, worse with bromine, and the most difficultly with iodine. The fluoride ion is capable of isotope exchange in as relatively inactive substrate as chloropentafluorobenzene [7].

The process of halodefluorination in hexafluorobenzene and octafluorotoluene is notably affected by the salt cation. The yield of nucleophilic halogenation products significantly decreases in going from sodium to potassium cation. The hexaethylguanidinium chloride taken as reagent also effects chlorodefluorination as efficiently as the system $KCl-[(Et_2N)_3C]Cl$ as show our studies. Thus with increasing cation size the replacement of fluorine by halogen is decelerated in a series $Na^+ > K^+ \sim (Et_2N)_3C^+$ apparently due to several reasons. Firstly, apparently the yield of halodefluorinated products would be considerably affected by the reverse fluorodehalogenation process. The metal fluorides in reactions of halogen exchange for fluorine in aromatic compounds are known to compose the following activity series: $NaF \ll KF < CsF$ [8]. Secondly, in catalytic halodefluorination (especially at low conversions where the contribution of the reverse reaction cannot be significant) the successful occurrence of the process strongly depends apparently on the electrophilic assistance by cation to the rupture of the C–F bond and on efficient stabilization of the σ -complex. The electrophilic assistance decreases depending on the salt cation (in keeping with the Lewis acidity) in the following order: $Na^+ > K^+ > (Et_2N)_3C^+$ [9]. It is therefore presumable that in the halodefluorination of hexafluorobenzene and octafluorotoluene the second

reaction stage, elimination of the fluoride anion, possesses a higher energy barrier than the first one, nucleophilic addition of a halide anion to the aromatic ring affording σ -complex. Consequently this stage proves to be the rate-determining one. This reasoning considering the data on the mechanism of fluorodehalogenation of perfluorohalobenzenes where as the rate-determining stage is known to be regarded the first one, fluoride ion addition [7], demonstrates the reversibility of catalytic halogen exchange in aromatic compounds under the effect of metal halides in the absence of solvents (see figure). Besides we believe that the above reasoning additionally confirms the previous statement that the principal role of the catalyst (hexaethylguanidinium chloride) in the halogen exchange reactions consists in reducing the activation energy of the reaction by stabilizing the σ -complex and to lesser degree in activating the halide ion by the guanidinium cation [6].

In reaction of $C_6F_5CF_3$ with sodium and potassium bromides in the presence of the catalyst (hexaethylguanidinium chloride) alongside bromo derivatives were obtained also chlorinated products. It is not yet clear whether the chlorodefluorination is effected by hexaethylguanidinium chloride proper or a metal chloride formed by ion exchange acts as a reagent.



The observed phenomenon can obviously be caused by simultaneous occurrence of both processes, i.e., the chlorodefluorination of octafluorotoluene can be due to the action both of the metal chloride and hexaethylguanidinium chloride.

Hence the investigation performed established that halodefluorination in hexafluorobenzene and octafluorotoluene efficiently occurred under the influence of metal halides in the presence of catalytic quantities of hexaethylguanidinium chloride. We showed that the relative efficiency grew in going from metal bromide to chloride and from hexaethylguanidinium cation to potassium and sodium. The data obtained demonstrate that the catalytic halogen exchange in perhaloaromatic compounds in the absence of solvent is a reversible process.

EXPERIMENTAL

^{19}F NMR spectra were registered on spectrometer Bruker WP-80 (75.398 MHz) in deuteroacetone, internal

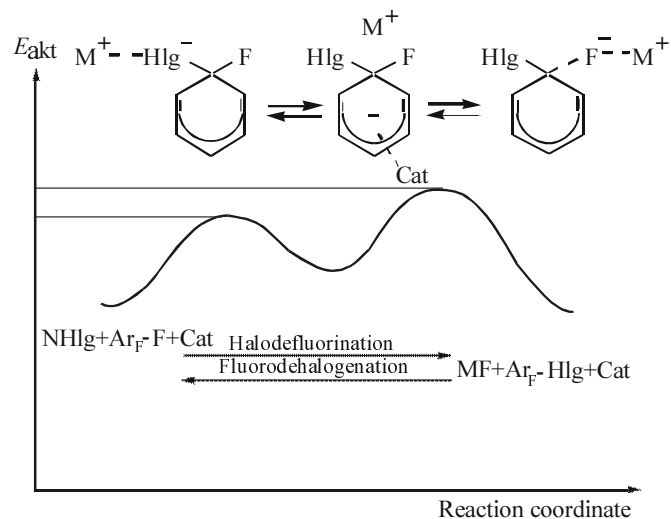
reference hexafluorobenzene. Chromatographic analyses were performed on chromatograph Hewlett-Packard 5890 equipped with detector by thermal conductivity and a capillary column (30 m × 0.25 mm) with stationary phase SE-54 in isothermal mode (100°C), carrier gas helium, flow rate 20 ml/min.

Octafluorotoluene and hexafluorobenzene were manufactured at the Pilot Plant of the Perm Effiliation of the Federal State Unitary Enterprise Russian Scientific Center "Applied Chemistry" and were used without further purification. Hexaethylguanidinium chloride, produce of the same Plant, was additionally recrystallized from dichloromethane. Sodium and potassium bromides of "pure" grade were dried at ~250°C for 8 h.

Halodefluorination of hexafluorobenzene and octafluorotoluene. Hexafluorobenzene or octafluorotoluene, metal halide (KCl, KBr, NaCl, NaBr), and hexaethylguanidinium chloride in appropriate quantities were thoroughly mixed and charged into metallic pressure reactors of capacity ~12 ml. The reactors were closed air-tightly and placed into an electric oven where they were maintained at a required constant temperature. After a preset time the reactor was removed from the oven, cooled, and discharged. The reaction mixture was weighed. When the final weight of the reaction mixture was the same as that of the charge, it was subjected to centrifugation on a laboratory centrifuge, the liquid organic phase was separated from solid salts, and analyzed by GLC and ^{19}F NMR. The reaction conditions and compositions of products are given in Tables 1 and 2. ^{19}F NMR spectra of all compounds were consistent with the published data [10].

REFERENCES

1. Rodionov, P. and Furin, G., *J. Fluor. Chem.*, 1990, vol. 47, p. 361.
2. Rodionov, P.P. and Furin, G.G., *Izv. SO Akad. Nauk SSSR*,



Scheme of halogen exchange reaction in perfluoro-halobenzenes under the action of metal halides in the presence of catalyst. M = K, Na; Hlg = Br, Cl; Ar_F = -C₇F₇, -C₆F₅; Cat = Et₂N₃C-Cl.

Ser. Khim., 1990, vol. 4, no. 4, p. 3.

3. Brooke, G.M., *J. Fluor. Chem.*, 1997, vol. 86, p. 1.
4. Birchall, J.M. and Haszeldine, R.N., *J. Chem. Soc. (C)*, 1970, p. 456.
5. Bichall, J.M., Haszeldine, R.N., and Jones, M.E., *J. Chem. Soc. (C)*, 1971, p. 1343.
6. Shipilov, A.I., Karyukalova, N.N., and Igumnov, S.M., *Zh. Org. Khim.*, 2002, vol. 38, p. 240.
7. Cacace, F., Speranza, M., Wolf, A.P., and Macgregor, R.R., *J. Fluor. Chem.*, 1982, vol. 21, p. 145.
8. Vorozhtsov, N.N., *Zh. Vses. Khim. Obshch.*, 1970, vol. 15, p. 52.
9. Dneprovskii, A.S. and Temnikova, T.I., *Teoreticheskie osnovy organicheskoi khimii* (Theoretical Bases of Organic Chemistry), Leningrad: Khimiya, 1991, 559 p.
10. *Nuclear Magnetic Resonance Spectroscopy*, Emsley, J.W., Ed., New York: Pergamon press, 1971, 529 p.