



## Perfluorocarbon-Hydrocarbon Self-Assembly. Part 3.<sup>1</sup> Liquid Phase Interactions between Perfluoroalkylhalides and Heteroatom Containing Hydrocarbons.

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**Abstract:** In the liquid phase a specific and attractive intermolecular interaction exists between iodo- or bromo-perfluoroalkanes ( $R_f-X$ ,  $R_f$  = perfluorinated chain,  $X = Br, I$ ) and heteroatom containing hydrocarbons (El) and it is robust enough to overcome the low affinity between perfluorocarbons and hydrocarbons. The interaction results in the formation of  $R_f-X \cdots El$  complexes and this formation strongly affects  $^{14}N$  and  $^{19}F$  NMR spectra of the partners. An association constant of  $10.7 \pm 1 \text{ mol}^{-1}$  has been determined. © 1998 Elsevier Science Ltd. All rights reserved.

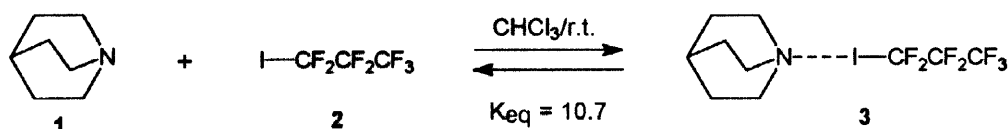
Halogens (mainly  $I_2$  and  $Br_2$ ),<sup>2</sup> interhalogens (e.g.  $ICl$  and  $IBr$ ),<sup>3</sup> and pseudohalogens (mainly  $ICN$ )<sup>4</sup> are known to behave as electron acceptors when interacting with organic bases. Attractive intermolecular interactions between a variety of carbon-bound halogens and electronegative atoms ( $C-X \cdots El$ ,  $X = Cl, Br, I$ ;  $El = N, O, \dots$ ) have been observed since the early sixties.<sup>5</sup> Recently, the iodine atom of iodoarenes and the oxygen, or nitrogen atom of nitro, or cyano, residues have been identified as acceptor and donor motifs robust enough to be employed reliably in the design of supramolecular architectures.<sup>6</sup>

We have already described how the specific  $I \cdots N$  intermolecular interaction occurring between  $\alpha,\omega$ -diiodoperfluoroalkanes and hydrocarbon diamines gives rise to co-crystalline infinite chains, the *solid state* architectures of which have been established by X-ray analyses.<sup>1,7</sup> In this paper we prove how the ability of perfluoroalkyl halides and heteroatom substituted hydrocarbons to work as complementary motifs in the *liquid phase* is quite general. Specifically, both iodo- and bromoperfluoroalkanes can work as acceptor motifs and not only nitrogen but also sulphur and oxygen atoms can work as electron donors. This interaction opens new opportunities in the design and manipulation of molecular aggregation processes and useful exploitations can be anticipated in several fields (supramolecular chemistry, drug design, etc.).

The specific and attractive intermolecular interaction occurring between quinuclidine **1** and 1-iodoperfluoropropane **2** has been studied by using spectroscopic methods. On addition of equimolar amounts of **2** to deuteriochloroform solutions of **1**, the  $^1H$  and  $^{13}C$  NMR spectra of the electron donor **1** showed changes and observed chemical shift variations gave a first indication of a specific interaction between the two

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## Scheme.



solutes ( $n \rightarrow \sigma^*$  donation)<sup>8</sup> to give the complex 3. Strong evidence of a specific C-I $\cdots$ N interaction came from  $^{19}\text{F}$  and  $^{14}\text{N}$  NMR spectra. On complete complexation of 1 (2/1 ratio  $\cong$  150), a 7 ppm upfield shift for the  $^{14}\text{N}$  chemical shift was observed and signal width passed from 960 Hz to 2160 Hz. The significant line broadening observed in the  $^{14}\text{N}$  NMR spectrum is a clear indication of an increase in the quadrupolar relaxation due to a specific I $\cdots$ N intermolecular association. As for the iodoperfluoropropane 2, a several ppm shift to higher fields of the signal of the  $-\text{CF}_2\text{I}$  group in  $^{19}\text{F}$  NMR spectra was observed on complex 3 formation. The quinuclidine induced change of the chemical shifts of the other two signals in  $^{19}\text{F}$  spectra decreased with increasing distance from the iodine atom. This is consistent with the generalisation that the specific I $\cdots$ N intermolecular interaction, firmly established in the solid phase,<sup>1</sup> is the driving force for perfluorocarbon-hydrocarbon self-assembling in the liquid phase. On varying the iodide/amine ratio in a 1 M solution of the complex 3 in deuteriochloroform, the chemical shift of the  $-\text{CF}_2\text{I}$  group changed from -61.13 ppm ( $\delta_{\text{free}}$ ) to -77.80 ( $\delta_{\text{max}}$ ) and by following this variation as a function of the 1/2 ratio an equilibrium constant of  $10.7 \pm 0.4 \text{ l mol}^{-1}$  has been derived for the complex formation at 25 °C.<sup>9</sup> This association constant could be considered as an apparent binding constant since chloroform has been suggested to interact with quinuclidine.<sup>10</sup> To the best of our knowledge, this is the first reported association constant of an amine-perfluoroalkyl iodide complex.

The  $^{19}\text{F}$  NMR spectra of 1,2-diiodo- and 1,2-dibromotetrafluorobutanes, 4 and 5, respectively, have been recorded by using a wide set of structurally different solvents<sup>11</sup> in order to prove that intermolecular interactions, similar to that described above between 1 and 2, occur in the liquid phase when other donor and acceptor motifs are involved. In Tables 1 and 2 the chemical shift differences of the  $-\text{CF}_2\text{I}$  and  $-\text{CF}_2\text{Br}$  groups between values observed in *n*-pentane and in hydrocarbon solvents containing an electron donor motif are reported ( $\Delta\delta_{\text{used solvent}} = \delta_{n\text{-pentane}} - \delta_{\text{used solvent}}$ ).<sup>12</sup> Some trends revealed by the Tables are worth noting. As far as the acceptor motif  $\text{R}_f\text{-X}$  is concerned, the tendency to form strong complexes ( $\text{I} > \text{Br}$ ) parallels the order of

Table 1.  $^{19}\text{F}$  NMR chemical shift differences of 1,2-dihalotetrafluoroethanes 4 and 5 in different solvents.<sup>a</sup>

Run	Solvent	I(CF <sub>2</sub> ) <sub>2</sub> I <sup>b, c</sup>		Run	Solvent	Br(CF <sub>2</sub> ) <sub>2</sub> Br <sup>b, d</sup>	
		$\Delta\delta_{\text{CF}_2\text{I}}$	$\Delta\delta_{\text{CF}_2\text{Br}}$			$\Delta\delta_{\text{CF}_2\text{I}}$	$\Delta\delta_{\text{CF}_2\text{Br}}$
1	Piperidine	11.23	2.40	10	1,3-Propanediol	4.30	0.90
2	<i>N</i> -Methylpiperidine	8.89	2.07	11	1,3-Propanedithiol	3.45	0.58
3	Morpholine	10.59	1.95	12	Pyridine	7.32	1.12
4	<i>N</i> -Methylmorpholine	8.39	1.71	13	Furan	1.11	0.13
5	Thiomorpholine	9.94	1.62	14	Thiophene	1.41	0.26
6	Tetrahydrofuran	4.13	0.95	15	Acetone	3.63	0.90
7	Tetrahydrothiophene	5.38	0.76	16	DMSO	7.22	2.03
8	3,6-Dioxaoctane	3.36	0.96	17	HMPA	8.23	2.76
9	3,6-Dithiaoctane	5.50	0.77	18	Acetonitrile	2.74	0.45

<sup>a</sup>  $\text{CFCl}_3$  was used as internal standard. <sup>b</sup>  $\Delta\delta = \delta_{n\text{-pentane}} - \delta_{\text{used solvent}}$ . <sup>c</sup>  $\delta_{\text{ICF}_2\text{CF}_2\text{I}}$  in *n*-pentane = -52.42 ppm.

<sup>d</sup>  $\delta_{\text{BrCF}_2\text{CF}_2\text{Br}}$  in *n*-pentane = -63.32 ppm.

**Table 2.** Electronic and steric effects on  $\Delta\delta_{\text{-CF}_2\text{I}}$  values shown by 1,2-diiodotetrafluoroethane **4**.<sup>a</sup>

Run	Solvent	$\text{I}(\text{CF}_2)_2\text{I}^{\text{b,c}}$ $\Delta\delta_{\text{CF}_2\text{I}}$	Run	Solvent	$\text{I}(\text{CF}_2)_2\text{I}^{\text{b,c}}$ $\Delta\delta_{\text{CF}_2\text{I}}$
1	<i>Cis</i> -2,6-dimethylpiperidine	8.29	9	Ethyl isonicotinate	5.68
2	2,2,6,6-Tetramethylpiperidine	6.92	10	Ethyl acetate	2.80
3	1,2,2,6,6-Pentamethylpiperidine	2.64	11	Ethyl monofluoroacetate	2.12
4	2-Methylpyridine	7.20	12	Ethyl difluoroacetate	1.30
5	2,6-Dimethylpyridine	5.86	13	Ethyl trifluoroacetate	0.72
6	4-Methylpyridine	7.62	14	Ethyl monochloroacetate	1.82
7	4-Isopropylpyridine	7.71	15	Ethyl dichloroacetate	1.54
8	4-Acetylpyridine	5.87	16	Ethyl monoiodoacetate	2.41

<sup>a</sup>  $\text{CFCl}_3$  was used as internal standard. <sup>b</sup>  $\Delta\delta = \delta_{n\text{-pentane}} - \delta_{\text{used solvent}}$ . <sup>c</sup>  $\delta_{\text{I}(\text{CF}_2)_2\text{I}}$  in *n*-pentane = -52.42 ppm

halogen atom polarisabilities, consistent with a key-role of halogen polarisation (and/or charge-transfer energies) in the interaction. The same order ( $\text{I} > \text{Br}$ ) has been established in the solid state for the  $\text{R}_\text{H} - \text{X} \cdots \text{El}$  interaction that, while being definitively weaker, has been firmly recognised through searches of the Cambridge Structural Database.<sup>13</sup> The ranking of the electron donor ability of the different solvents obtained with diiodide **4** parallels perfectly that obtained with dibromide **5**, thus implying that similar self-assembling processes are occurring.

As for the electron donor motif  $\text{El}$ , the order in which the  $\text{R}_\text{F}-\text{X} \cdots \text{El}$  interaction becomes weaker is  $\text{N} > \text{S} \geq \text{O}$ . *n*-Donors work better than  $\pi$ -donors (Table 1, runs 6, 7, 13, 14) and for a given heteroatom, stronger interactions are observed in higher hybridization states (Table 1, runs 18, 12, 2; 14, 7; 13, 6, respectively). Both steric and electronic effects affect the strength of the  $\text{R}_\text{F}-\text{X} \cdots \text{El}$  intermolecular interaction. More crowded environments around the donor site make it less accessible at shorter distances for the incoming halogen atom (Table 2: runs 1-5) and an electron withdrawing environment around the donor motif diminishes its donor ability (Table 1: run 12; Table 2: runs 8, 9, 10-16). In both cases weaker interactions result. The presence of electron releasing residues on the donor molecule induce an opposite effect on the intermolecular interaction (Table 1: run 12; Table 2: runs 6, 7). Secondary amines are better donors than tertiary amines (Table 1: runs 1-4) while further experiments are required before general statements about the relative donor ability of alcohols/ethers or thiols/thioethers can be made (Table 1: runs 6-11).

In conclusion, <sup>14</sup>N and <sup>19</sup>F NMR spectroscopy proves that a wide variety of electron donors  $\text{El}$  and electron acceptors  $\text{R}_\text{F}-\text{X}$  give rise in the liquid phase to strong and specific attractive interactions and form the  $\text{R}_\text{F}-\text{X} \cdots \text{El}$  adducts. The association constant has been established in one case and quite different heteroatom containing hydrocarbon motifs have been ranked according to their ability to self-assemble. Single  $\Delta\delta_{\text{-CF}_2\text{X}}$  values reported in Tables 1 and 2 are highly consistent with each other and with the electronic and steric effects expected for a  $n \rightarrow \sigma^*$  electron donation in the  $\text{R}_\text{F}-\text{X} \cdots \text{El}$  adducts. Studies of weak molecular interactions in solution constitute a difficult experimental problem. The  $\Delta\delta_{\text{-CF}_2\text{X}}$  value is a simple, effective, and sensitive tool to grade the donor and acceptor abilities of the interacting partners, strong interactions resulting in large values.

The "halogen bonding"<sup>14</sup> is proven as an attractive interaction robust enough to overcome the low affinity existing between fluorocarbons and hydrocarbons<sup>15</sup> and to drive effectively their self-assembly in the liquid phase. As for the nature of the attractive  $\text{R}_\text{F}-\text{X} \cdots \text{El}$  interaction, charge transfer probably plays a key role, but electrostatic effects, polarisation, and dispersion contributions all might be influential and further studies are required in order to establish their relative relevance.

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9. A quite similar  $R_F-I \cdots N$  interaction has been observed in solution, among others, when mixtures of 1,4-diazabicyclo[2,2,2]octane and 1,6-diiodoperfluorohexane were studied. Indeed, the structure of both these compounds allows the  $C-I \cdots N$  interaction observed between **1** and **2** to be doubled at either ends of diazabicyclooctane and diiodoperfluorohexane. As a result of this double lock, diazabicyclooctane and diiodoperfluorohexane give rise, on mixing, to infinite and crystalline chains (ref. 1). The same spectral properties ( $^1H$ ,  $^{13}C$ ,  $^{14}N$ ,  $^{19}F$  NMRs) were shown by a given solution when it was obtained either dissolving the co-crystal or immediately after dissolving equimolar amounts of diamine and diiodide. Moreover,  $^1H$  and  $^{19}F$  NMR spectra of highly diluted solutions of the co-crystal were identical to those shown by pure diamine and pure diiodide while  $^{19}F$  NMR spectra of concentrated solutions showed for the  $CF_2I$  group a high-field shift of several ppm relative to pure diiodoperfluorohexane. All these observations are consistent with a rapid association equilibrium which gives dimeric, trimeric, etc. adducts. A similar rapid equilibrium is present in all other donor-acceptor interactions discussed in this paper.
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12. Measured  $\Delta\delta_{-CF_2X}$  values are mainly related to the strength of the  $R_F-X \cdots El$  interaction. Upfield shifts, relative to pure **4**, similar to those reported in Table 1 have been measured also for the co-crystals formed by **4** with  $N,N,N',N'$ -tetramethylethylenediamine and kryptofix 2.2.2. where the  $N \cdots I$  interaction has been proved by X-ray (ref. 1). This is consistent with ascribing  $\Delta\delta_{-CF_2X}$  values of Table 1 mainly to the  $R_F-X \cdots El$  interaction. Moreover, the larger the observed  $\Delta\delta_{-CF_2X}$  values are, the easier it is to isolate these complexes as solid and crystalline systems. For instance, both 1,4-diiodoperfluorobutane and  $N,N'$ -dimethylpiperazine and dioxane are liquid compounds. The  $CF_2I$  group of diiodoperfluorobutane shows  $\Delta\delta_{N,N'-dimethylpiperazine} = 10.32$  ppm,  $\Delta\delta_{dioxane} = 3.11$  ppm. When diiodoperfluorobutane and dimethylpiperazine are mixed, a crystalline complex immediately separates while no crystal is formed starting from diiodoperfluorobutane and dioxane. This proves further that large  $\Delta\delta_{-CF_2X}$  values reflect strong  $R_F-X \cdots El$  interactions. A grading of the strength of donor and acceptor motifs similar to that reported in Table 1 is obtained by using other techniques, for instance the shifts of donors C-H stretching modes and/or acceptors C-F (or C-X) stretching modes in IR spectra.
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