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Noncovalent paramagnetic complexes: detection of halogen bonding in solution by ESR spectroscopy

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Abstract—Halogen-bonded complexes between aliphatic and aromatic iodoperfluorocarbons and persistent nitroxide radicals have been detected by ESR spectroscopy in solution. Quantitative data indicate that nitroxides behave as strong electron donors in halogen bonding, giving rise to interactions whose strength is close to that of strong hydrogen bonds. These results point to a novel design of supramolecular paramagnetic species.

It has been known for a long time that halogen atoms can act as Lewis acids. Thus, they can be involved in electron donor–acceptor interactions with atoms possessing lone pairs, such as nitrogen, oxygen, and sulfur, or anions like bromide and iodide.[1] This interaction is now referred to as halogen bonding (XB) by analogy to hydrogen bonding (HB), with which it shares numerous properties.[2,3] XB is currently exploited in supramolecular chemistry and in the engineering of new materials via self-assembly of organic compounds.[4] Several analytical methods (solution calorimetry, IR, NMR) have been used to detect XB in solution, to define its nature, to establish its energetic and geometric characteristics, and to reveal the striking similarities between XB and HB.[2]

The existence of halogen-bonding interactions between persistent free radicals and electron acceptor moieties has been the subject of very limited studies.[5,6] Recently, the first report on the use of XB for the construction of novel nitroxide supramolecular assemblies appeared in the literature.[7] In this communication, the XB between persistent free radicals (electron donor species) and halogenated molecules (electron acceptor species) has been detected in solution. The modes of electron spin transfer from the radical XB acceptor to the XB donors are examined resorting to the study of the ESR spectroscopic induced variations. The energetic parameters of XB have also been determined.

As a part of our continuing studies on the interactions between closed-shell and open-shell molecules,[8,9] we report here a study on the interactions between nitroxide radicals and perfluorocarbon halides. These interactions have been interpreted in terms of the formation of halogen-bonded complexes. Iodoperfluoroalkanes and iodoperfluorobenzenes were chosen as electron acceptors as it was demonstrated that molecules having strong electron withdrawing substituents close to the interacting halogen atoms behave as particularly strong XB donors.[2]

The addition of a iodoperfluorocarbon to a perfluorocarbon solution (perfluoro-octane, -hexane, or -benzene) of 2,2,6,6-tetramethyl-1-piperidinyloxy free radical (TEMPO) causes a substantial increase of the nitrogen hyperfine splitting, a_N, of the nitroxide. Figure 1 reports the experimental dependence of a_N for solutions of TEMPO in C_6F_6 at 298 K, as a function of the C_6F_5I concentration. Table 1 lists the a_N values of TEMPO in different halocarbon solvents.

It is well established that the nitrogen hyperfine splitting constant of nitroxides is sensitive to the nature of the

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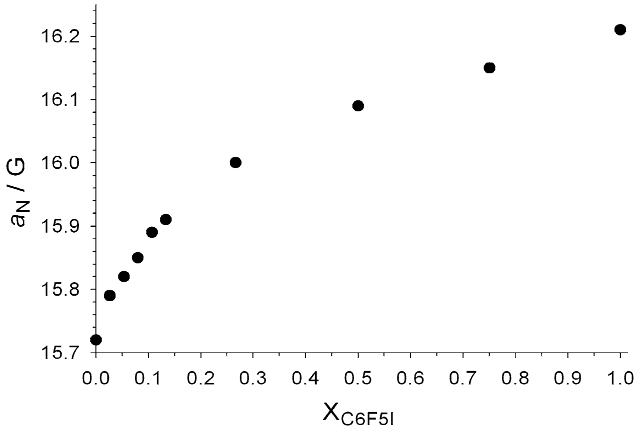


Figure 1. Experimental dependence of a_N on C_6F_5I mole fraction at 298 K in hexafluorobenzene.

Table 1. ESR spectral parameters of TEMPO at rt

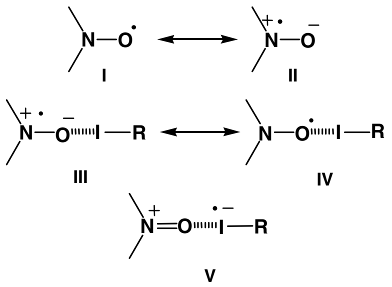
Solvent	a_N (G)	Line width (pp)[a] (*G*)	*g*-Factor
n-C_8F_{18} or n-C_6F_{14}	15.37	1.47	2.0063_0
n-$C_7F_{15}Br$	15.54	1.35	2.0062_2
n-$C_8F_{17}I$	16.17	4.33	2.0063_4
$(CF_3)_2CHOH$ 0.1 M[b]	16.31	1.45	2.0060_5
i-C_3H_7I	15.46	0.93	2.0061_8
$CHF_2CF_2CH_2I$	15.96	0.96	2.0060_3
CF_3CH_2I	15.93	1.33	2.0059_1
i-C_3F_7I	16.72	2.05	2.0063_0
C_6F_6	15.72	1.29	2.0062_3
C_6H_5I	15.84	1.23	2.0061_9
C_6F_5I	16.19	3.28	2.0064_5

[a] Peak-to-peak experimental line width.

[b] Solvent: n-C_8F_{18}.

solvent used.[10] This dependence can be explained on the basis of the two canonical forms I and II of the nitroxide function (Scheme 1).

a_N is proportional to the unpaired electron spin density on nitrogen. Thus, solvents favoring the dipolar structure II, where the electron is delocalized on the nitrogen atom, will give rise to an increase in the magnitude of nitrogen splitting. Observed data are consistent with the formation of a halogen-bonded complex wherein the iodine atom of C_6F_5I interacts with the nitroxidic oxygen[11] of TEMPO (Scheme 1, structures III and IV).



Scheme 1.

The larger spin density on nitrogen in structure III is responsible for the increase of the a_N value. Bromoperfluoroalkanes and iodocarbons give smaller changes than iodoperfluorocarbons, confirming the role of the polarizability of the halogen atom and the degree of fluorination around it.[3b]

Clearly, the ability of a halocarbon to give rise to strong XB parallels its ability to increase a_N. The larger increase in the a_N values induced by iodoperfluorocarbons, with respect to corresponding iodocarbons, is even more remarkable if we consider the typically low polarity of perfluorocarbon derivatives.

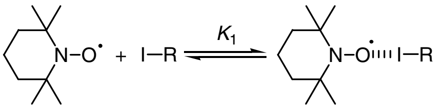
Unexpected results were obtained when measuring the *g*-value of the radical in the halogen-bonded complex. Actually, when TEMPO is dissolved in iodoperfluoro solvents, the corresponding ESR spectra are characterized by *g*-values very close to those measured in the corresponding perfluorinated solvents (see Table 1). This behavior is different from that generally shown by nitroxides dissolved in hydrogen bonding donor solvents. In fact, in the latter case, the coordinated species show both smaller *g*-values and larger nitrogen splitting than the noncoordinated ones.[8] The *g*-value in organic radicals is expected to differ from that of the free electron by an amount that is proportional to the product between the probability of finding the unpaired electron on a given atom and the corresponding spin–orbit coupling constant. Since the latter constant is smaller for nitrogen ($73.3\ cm^{-1}$) than for oxygen ($151\ cm^{-1}$), all the factors increasing the weight of the dipolar structure II give rise to a reduction of the *g*-value. Actually, this phenomenon is observed when the nitroxidic oxygen accepts a hydrogen bond (see Table 1, data referring to 1,1,1,3,3,3-hexafluoro-2-propanol, HFIP).[8] In the present case, the similarity of the *g*-factors between the free and halogen-bonded nitroxide might be attributed to the transfer of some of the unpaired spin density from the nitroxidic moiety to the iodine atom (Scheme 1, structure V). Since the iodine atom is characterized by a very large spin–orbit coupling constant ($4303\ cm^{-1}$),[12] structure V is expected to induce an increase of the *g*-factor. This compensates the opposite effect due to the larger weight of the dipolar structure III upon XB occurrence.

Structure V may represent a pre-reactive state of the complex,[3a] which seems considerably stable in the solid state. In solution, the complex is stable enough to record the ESR spectra. However, decomposition occurs after several days at rt, reasonably as a consequence of inner sphere electron-transfer from the nitroxyl radical to the iodoperfluorocarbon. A similar interesting example of pre-reactive complex involving nitroxyl radicals is based on the interaction between TEMPO and ClO_2.[13] This complex then evolves to the formation of the oxammonium salt.

A more convincing evidence for the formation of the halogen-bonded complex was provided by the marked broadening of the ESR lines observed when the nitroxide spectra were recorded in iodoperfluorocarbon solvents. This effect is particularly evident in the ESR spectra of diphenylnitroxide (DPNO), whose hyperfine structure completely disappears upon addition of the iodoperfluoro derivatives (see Fig. 2). This effect is caused by the delocalization of spin density from the nitroxide to the iodine atom and by the consequent additional splitting due to ^{127}I ($I = 5/2$). Hyperfine coupling to iodine in the ESR spectra of organic radicals has rarely been detected. The difficulty in observing this coupling is probably due to the large nuclear quadrupole moment of this element. Fluctuations in the electric-field gradient at the halogen nuclei, due to molecular tumbling, produce nuclear spin relaxation, which is fast with respect to hyperfine splitting and leads to averaging of the magnetic field contributions of the nuclear spin states.[14]

The line broadening extent is proportional to the XB donor concentration and depends also on its nature. To further prove the correlation between XB and line broadening, weaker XB donors[15] were used (see Supplementary data). Non-fluorinated iodoarenes, as well as n-$C_8F_{17}Br$, did not lead to any observable change in the ESR spectrum of the nitroxide, apart from the small increase of a_N discussed above.

On the other hand, addition of HFIP to a sample containing n-$C_8F_{17}I$ and TEMPO resulted in a narrowing of the nitroxide spectral lines, which was proportional to the alcohol concentration. Clearly, the occurrence of XB in solution can be reverted by addition of a strong HB donor, which is able to compete with the iodoperfluorocarbon by interaction with the nitroxidic oxygen.[16]



(1)

In order to determine the strength[17] of the XB between TEMPO and the different iodoperfluoro derivatives, we established the equilibrium constants for the formation of the corresponding complexes (Eq. 1).[18] Since the rate of formation and breakdown of XB is very fast in the time scale of ESR spectroscopy, the experimental spectrum represents the concentration-weighted average of the spectra due to the free and halogen-bonded nitroxides. Under these conditions, we could obtain the ratio between the free species and the complexed ones by simulation of the experimental spectra in the fast exchange regime. This has been possible in the case of n-$C_8F_{17}I$, i-C_3F_7I, C_6F_5I, as their intrinsic ESR line shape is known. The equilibrium constants (K_1) for the formation of the halogen-bonded complexes are reported in Table 2 and were obtained by plotting the ratio between the concentration of the complexed species and free ones as a function of the concentration of the electron acceptor.

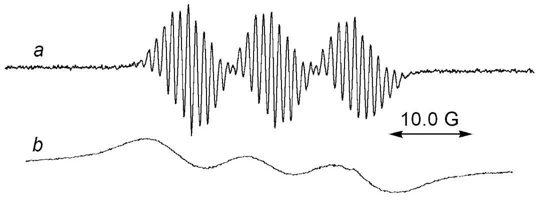


Figure 2. ESR spectra of DPNO recorded in C_6F_6 in the absence (a) and in the presence (b) of n-$C_8F_{17}I$ (0.57 M). In the latter case the nitroxide concentration has been raised to get a better signal to noise ratio. The nitroxide was generated by in situ oxidation of the parent amine with m-chloroperbenzoic acid.

The data reported in Table 2 confirm that fluorination promotes the XB donor ability of iodocarbons[19] and indicate that iodoperfluoroalkanes form stronger XB than C_6F_5I. Secondary iodoperfluoroalkanes give an equilibrium constant slightly smaller than their primary analogue. This observation is opposite to that observed when other XB acceptors were used.[20] This can be related to the steric hindrance[3b] around the oxygen atom in TEMPO, which disfavors the approach of iodine when the more hindered secondary iodide is used. Substitution of iodobenzene for perfluorobenzene as solvent gives rise to a smaller value for the equilibrium constant, indicating that the nitroxide can be weakly involved in interactions with the former solvent.

By measuring the variation of the equilibrium constant for the TEMPO/n-$C_8F_{17}I$ complex in the temperature range between 298 and 328 K (see Fig. 3) we obtained the corresponding thermodynamic parameters $\Delta H^\circ = -7.0 \pm 0.4$ kcal/mol and $\Delta S^\circ = -18.1 \pm 1.4$ e.u.

The value of enthalpy of formation (7 kcal/mol) reported here nicely compares with the experimental

Table 2. Equilibrium constants (298 K) for the formation of the halogen-bonded complexes of TEMPO, K_1, determined by ESR spectroscopy

XB donor	Solvent	K_1 (M^{-1})
n-$C_8F_{17}I$	n-C_8F_{18}	15.4 ± 0.6
i-C_3F_7I	n-C_6F_{14}	5.7 ± 0.2
CF_3CH_2I	n-C_6F_{14}	<0.1
C_6F_5I	C_6F_6	0.38 ± 0.016
C_6F_5I	C_6H_5I	0.18 ± 0.010

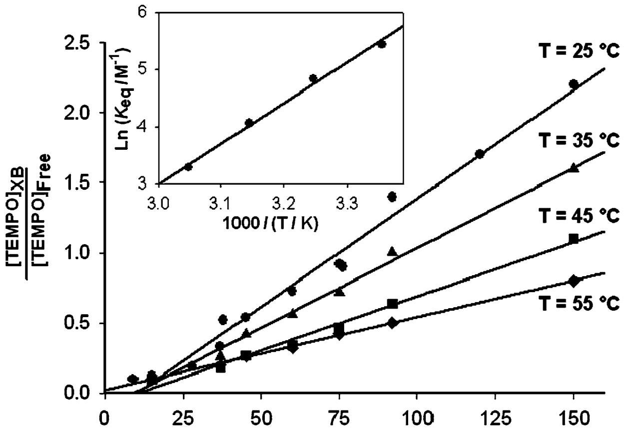


Figure 3. Plot of the ratio between the concentration of the free and halogen bonded TEMPO as a function of n-$C_8F_{17}I$ concentration at different temperatures. Inset: van't Hoff plot.

value of 7.4 kcal/mol found for the association of 1-iodoperfluorohexane and 2,2,6,6-tetramethylpiperidine (measured with an adiabatic accelerating rate calorimeter).[16] The ESR value of 7 kcal/mol is quite remarkable and indicates that iodoperfluoro compounds form with TEMPO interactions whose strength is similar to those formed with strong HB donors. For instance, a value of 5.75 kcal/mol has been measured for the formation of TEMPO-HFIP hydrogen-bonded complex.[8] The relatively small value of the affinity constant for the halogen-bonded complex at room temperature (15.4 M^{-1}) can be explained by the large negative value of the entropy of reaction (−18.1 e.u.), which derives from the freezing of the translational freedom of the complex.

In conclusion, the formation in solution of stable halogen-bonded complexes between nitroxides and different XB donors was detected for the first time by ESR spectroscopy. Some structural aspects of the complexes, the equilibrium constants, and the thermodynamic parameters for the formation of complexes involving TEMPO, a prototype persistent radical, were established. Thus, ESR spectroscopy adds to the palette of analytical methods affording useful pieces of information on the formation of halogen-bonded complexes. Indeed, by using nitroxide derivatives, ESR spectroscopy could become a useful competitive method to determine the equilibrium constants for the formation of halogen-bonded complexes also with diamagnetic species. Finally, the results described in this paper may be quite helpful in designing new organic radical solids exhibiting magnetic properties where XB control both the crystal packing and generate, or propagate, ferromagnetic interactions.[21]

Acknowledgments

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Supplementary data

ESR control experiments, detailed radical ratios determined from the ESR spectra. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.03.033.

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18. In principle equilibrium constants could be determined by reporting the dependence of a_N value on the concentration of the iodoperfluoro derivative. However, two distinct effects contribute to the solvent effect on the a_N value: the electrostatic contribution and that one due to XB formation with the solvent. The dependence of ESR nitrogen hyperfine splitting on solvent properties can be expressed

as a linear combination of these two terms and estimation of the electrostatic term is required to isolate the specific halogen-bonding effect from the general medium effect.[8]

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