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Heavy Halogen Atom Effect on ¹³C NMR Chemical Shifts in Monohalo Derivatives of Cyclohexane and Pyran. Experimental and Theoretical Study

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Abstract: As a first step, a qualitative analysis of the spin−orbit operator was performed to predict the kind of organic compounds, where it could be expected that the SO/FC (spin−orbit/Fermi contact) and SO/SD (spin−orbit/spin dipolar) yield unusually small contributions to the "heavy atom effect" on ¹³C SCSs (substituent chemical shifts). This analysis led to the conclusion that compounds presenting strong hyperconjugative interactions involving the $\sigma^{\star}_{C-X}$ orbital (X = halogen) are good examples where such effects can be expected to take place. On the basis of such results, the following set of model compounds was chosen: 2-*eq*-halocyclohexane (**2-eq**), 2-*ax*-halocyclohexane (**2-ax**), and 2-*ax*-halopyran (**3**), to measure ¹³C SCSs. Such experimental values, as well as those of methane and halomethanes taken from the literature, were compared to calculated values at a nonrelativistic approach using B3LYP, and at a relativistic approach with BP86 using scalar ZORA, spin−orbit ZORA, scalar PAULI, and spin−orbit PAULI. Results from relativistic calculations are in agreement with the trends predicted by the qualitative model discussed in this work.

I. Introduction

The heavy halogen atom effect on carbon chemical shifts has now been known for about three decades.[1−7] In the past decade, many articles appeared[8−20] where calculations of this effect are reported using different levels of approximation. The interesting work by Kaupp et al.[21] can be distinguished from the others, because it provides important insights on how the cross term due to SO and FC interactions (SO/FC) is transmitted through the molecule. It was concluded that its propagation is closely analogous to the well-established mechanisms for the transmission of the FC term in indirect spin−spin coupling constants (SSCCs). Although the results reported by Kaupp et al.[21] substantiate this

interpretation, it is suggested here that when intending to generalize such results, the role played by the SO operator in defining the SO/FC interaction is somewhat overlooked.

It is easy to obtain a qualitative pictorial representation of some factors affecting the contribution of the SO operator to the heavy atom effect on the ¹³C substituent chemical shifts (SCS), for C_1 bonded to a halogen atom, σ_{C1-X} (X = Cl, Br, I). Thus, in the next section, a qualitative description of interactions affecting the SO part of the SO/FC and SO/SD terms is given. Such analysis provides an intuitive base to detect the kind of compounds where the "the heavy atom effect" on the ¹³C_1 chemical shift could be notably influenced by intramolecular interactions affecting the SO part of both contributions.

On the basis of the discussion presented in section II, it was possible to predict some features, which must be exhibited by some compounds, to show the effects of the heavy halogen atom on ¹³C_1 SCSs important enough to be

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amenable to measurement. According to these ideas, the following compounds were chosen for the experimental determination of their ^{13}C$_1$ SCSs: *eq-* and *ax*-halo-cyclohexanes and 2-halo-tetrahydropyran; and the corresponding experimental ^{13}C$_1$–SCSs values for the halo-methanes were taken from literature. The experimental results were compared to scalar ZORA, spin–orbit ZORA (SO-ZORA), scalar PAULI, and spin–orbit PAULI (SO-PAULI)[22–24] calculations to verify if the qualitative trends predicted by the approach presented in section II were well-found. For completeness sake, ^{13}C$_1$ SCSs GIAO-DFT calculations (Gauge-including atomic orbitals[25] within the framework of nonrelativistic density functional theory) were also performed and compared to those obtained with the ZORA and PAULI methods, which incorporate the relativistic effects into the GIAO-DFT calculation of NMR shielding tensors.

II. Qualitative Analysis of Factors Affecting the SO Part of the SO/FC and SO/SD Terms

Electrons and nuclei are described separately within the Born–Oppenheimer approximation, and an interesting example of its validity is found in NMR spectroscopy. In fact, NMR spectra are obtained inducing transitions between nuclear spin states, which can be described by the Hamiltonian given in eq 1.

$$\hat{H} = -\frac{1}{2\pi} \sum_N \gamma_N \bar{\mathbf{I}}_N \cdot (\overleftrightarrow{1} - \overleftrightarrow{\sigma}_N) \cdot \bar{\mathbf{B}} +$$
$$\sum_{N \neq M} \bar{\mathbf{I}}_N \cdot (\overleftrightarrow{J}_{NM} + \overleftrightarrow{D}_{NM}) \cdot \bar{\mathbf{I}}_N \quad (1)$$

In the first term of this Hamiltonian, the nuclear magnetic shielding tensor is bilinear both in magnetic moment as in the spectrometer static magnetic field. Therefore, the study of nonrelativistic nuclear magnetic shielding tensors from the electronic molecular part perturbation theory yields

$$\sigma_{\alpha\beta}^N = \left. \frac{\partial^2 E(\mu_N, \mathbf{B})}{\partial \mu_{N,\alpha} \partial B_\beta} \right|_{\mu_N=0; \mathbf{B}=0} \quad (2)$$

where $E(\mu_N, \mathbf{B})$ is the perturbed molecular energy and involves the magnetic field dependent momentum: $\pi = \mathbf{p} + \mathbf{A}$, where $\mathbf{A}$ includes the vector potential of the spectrometer static magnetic field, as well as the sum of those corresponding to the nuclear magnetic moments; N is the nucleus under consideration, whose magnetic moment is μ_N; and $\mathbf{B}$ is the spectrometer static magnetic field. Equation 1 gives the two different contributions, its diamagnetic and paramagnetic parts, $\sigma_{\alpha\beta}^N = \sigma_{\alpha\beta}^{N,p} + \sigma_{\alpha\beta}^{N,d}$.

To take into account the effect of a heavy atom, relativistic corrections are thought to be obtained from approximate solutions of the nonrelativistic Schrödinger equation;[26] that is, the Hamiltonian is taken as

$$H = H_{N-e} + H_{KE}^{NR} + H^{Darwin-1} + H^{SO} \quad (3)$$

where H_{N-e} is the nonrelativistic nucleus–electron attraction; H_{KE}^{NR} is the nonrelativistic kinetic energy term; $H^{Darwin-1}$ is the one-electron Darwin term; and $H^{SO} = H^{SO(1)} + H^{SO(2)}$

corresponds to the one- and two-electron contributions to the spin–orbit Hamiltonian, respectively. The spin–orbit contribution to nuclear magnetic shielding tensor arises from the Hamiltonian operator given in eq 4.

$$H^{SO} = \frac{e^2\hbar}{4m_e^2}\frac{\mu_0}{4\pi}g_e\left(\sum_N Z_N \sum_i \frac{\mathbf{s}_i \cdot \mathbf{l}_{iN}}{r_{iN}^3} - \sum_{i \neq j} \frac{(\mathbf{s}_i + 2\mathbf{s}_j) \cdot \mathbf{l}_{ij}}{r_{ij}^3}\right) \quad (4)$$

where $\mathbf{s}_i$ is the ith electron spin operator; Z_N is the charge of the Nth nucleus; g_e is the electron g-factor; r_{iN} is the distance from the i electron to the N nucleus, $\mathbf{r}_i - \mathbf{R}_N$; $\mathbf{l}_{iN} = (\mathbf{r}_i - \mathbf{R}_N) \times [-i\nabla_i + \mathbf{A}_0(\mathbf{r}_i)]$ is the ith electron angular momentum taken from nucleus N and $\mathbf{l}_{ij} = (\mathbf{r}_i - \mathbf{r}_j) \times [-i\nabla_i + \mathbf{A}_0(\mathbf{r}_i)]$ is its angular momentum with respect to the jth electron. $\mathbf{A}_0$ is the vector potential corresponding to the spectrometer static magnetic field.

The first term in square brackets in $\mathbf{l}_{iN} = (\mathbf{r}_i - \mathbf{R}_N) \times [-i\nabla_i + \mathbf{A}_0(\mathbf{r}_i)]$ is magnetic field independent and, within triple perturbation theory, connects the singlet ground state with triplet excited states, allowing interactions with both the Fermi contact, FC, eq 5, and the spin-dipolar, SD, eq 6, operators:

$$H_{FC}^N = \frac{4\pi}{3}\frac{e\hbar}{m_e}\frac{\mu_0}{4\pi}g_e \sum_i \delta(\mathbf{r}_{iN})\mu_N \cdot \mathbf{s}_i \quad (5)$$

$$H_{SD}^N = \frac{e\hbar}{m_e}\frac{\mu_0}{4\pi}g_e\mu_N \cdot \sum_i \frac{3\mathbf{r}_{iN}\mathbf{r}_{iN}^T - \mathbf{1}r_{iN}^2}{r_{iN}^5} \cdot \mathbf{s}_i \quad (6)$$

yielding third-order terms that undergo orbital interactions with the spectrometer static magnetic field $\mathbf{B}_o$ obtaining four different contributions; see eqs 4–6.

However, keeping in mind that, in this work, only a qualitative description of the heavy atom effect on ^{13}C nuclear magnetic shielding is sought, it can be suggested that only two of those four terms, that is, the one-electron contributions, are considered more important than the two-electron contributions. They will be labeled here as SO/FC and SO/SD contributions to the ^{13}C magnetic shielding constant. In the studied compounds (see below), it is expected that the SO/FC term should be more important than the SO/SD contribution.

Therefore, because this qualitative analysis will be applied mainly to the leading term, the present study is restricted to the SO/FC term. It is recalled that the influence of the FC interaction on the SO/FC term was clearly discussed by Kaupp et al.,[19] and no further comment, is worth to be given here. This by no means suggests that in this work the FC contribution to the SO/FC term is being undervalued.

The above considerations indicate that the first step must be a close look at the one-electron part of the H^{SO} Hamiltonian of eq 4, as given in eq 7:

$$H^{SO} = \frac{e^2\hbar}{4m_e^2}\frac{\mu_0}{4\pi}g_e\left(\sum_N Z_N \sum_i \frac{\mathbf{s}_i \cdot \mathbf{l}_i}{r_{iN}^3}\right) \quad (7)$$

It will be assumed that the triple perturbation theory is applied to both occupied and vacant localized molecular orbitals, LMOs, which were localized through separate procedures.

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It is also important to recall that the main aim of this work is to verify if hyperconjugative interactions from bonding or antibonding orbitals involving the carbon atom, whose substituent chemical shift (SCS) value is being analyzed, can affect the "heavy atom" effect. Qualitatively, it can be considered that the valence occupied LMOs behave like the NBO (natural bond orbitals) bonding and lone-pair orbitals, while the valence vacant LMOs behave like the NBO antibonding orbitals, as given by Weinhold et al.'s method.[27,28] To allow an easier way for the qualitative analysis of the SO operator, the gauge origin is taken at the site of the heavy nucleus, and in this way the l_i operator is, for the present purpose, essentially equal to the rotation operator centered at that nucleus. Therefore, the SO part of the SO/FC cross term must have a significant value whenever the following two conditions hold:

(a) The overlap of a 90° rotated occupied LMO, for example, the lone pairs $LP_2(X)$ or $LP_3(X)$, and the antibonding orbital corresponding to the $\sigma^*_{C_1-X}$ must be significant. A similar contribution originating in $LP_1(X)$, that is, the X lone-pair deepest in energy, is neglected on account of the following two reasons. (i) The rotated $LP_1(X)$ and the $\sigma^*_{C_1-X}$ antibonding orbital overlap to a much lesser extent than the ones involving the rotated $LP_2(X)$ and $LP_3(X)$ LMOs; (ii) the energy gap between $\sigma^*_{C_1-X}$ and $LP_1(X)$ is much larger than the energy gaps between the $\sigma^*_{C_1-X}$ antibonding orbital with either $LP_2(X)$ or $LP_3(X)$.

(b) The relevant energy gaps between the $\sigma^*_{C_1-X}$ antibonding orbital and $LP_2(X)$ and $LP_3(X)$ occupied LMO orbitals are not "very large".

Even though this last assertion cannot be precisely defined, an intuitive description of factors affecting the SO part of the SO/FC term can be sought. Point b indicates that, on the one hand, "heavy atom" effects on ^{13}C chemical shifts are more important for lone-pair bearing atoms like X = iodine than, for instance, X = tetra-coordinated tin atoms because bonding orbitals are much deeper in energy than orbitals representing lone pairs. It is important to recall that in a previous paper,[29] it was observed that in 1-I-bicyclo-[1.1.1]pentane the heavy atom effect on $^{13}C_1$ was estimated as ca. 43.4 ppm, while the analogous value for 1-Sn(CH₃)₃-bicyclo[1.1.1]pentane was estimated as ca. −10 ppm. It is important to note that the different sign can be rationalized as originated in the FC part of the SO/FC term [see ref 21] because the Sn magnetogyric ratio is negative for the two most abundant Sn isotopes. On the other hand, any hyperconjugative interaction that increases a relevant energy gap must decrease the corresponding SO part of the SO/FC and the SO/SD cross terms. The simple perturbed molecular orbital theory (PMO)[30] can be used to determine the type of hyperconjugative interactions that affect significantly the relevant energy gaps between the $\sigma^*_{C_1-X}$ antibonding orbitals and the $LP_2(X)$ and $LP_3(X)$ occupied orbitals. They are as follows: (i) any hyperconjugative interaction transferring charge into the $\sigma^*_{C_1-X}$ antibonding orbital, and (ii) hyperconjugative interactions like $LP_2(X) \rightarrow \sigma^*_{C_1-Y}$ and $LP_3(X) \rightarrow \sigma^*_{C_1-Y}$, where Y stands for any atom bonded to C_1 other than X. Interactions of type I push up the σ^*_{C1-X} orbital
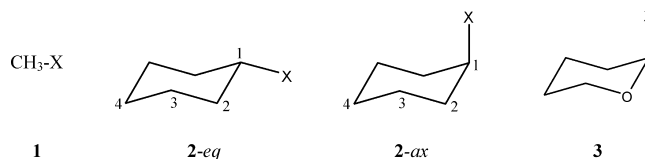

Figure 1. Structures of the studied compounds.

energy, while those of type ii push down the $LP_2(X)$ and $LP_3(X)$ orbital energies.

Moreover, it is recalled that the FC term of one-bond SSCCs might be affected by several factors like, for instance, the inductive effect of Y atoms bonded to C_1, the C_1 hybridization, hyperconjugative interactions involving either any bond attached to C_1 or the $\sigma^*_{C_1-X}$ antibonding orbital,[31] etc. This suggests that a competition can take place between the two opposite factors affecting the SO and FC parts of the SO/FC term. Apparently, a case in point is the "heavy atom" effect on C_1 SCSs in 1-X-bicyclo-[1.1.1]pentane (X = F, Cl, Br, I) previously reported.[29,32] Here, in fact, despite the strong hyperconjugative interactions into the $\sigma^*_{C_1-X}$ antibonding orbital, the heavy atom effect on C_1 SCSs is similar to those in halomethanes. It is experimentally known that $^1J_{C1,F}$ in 1-F-bicyclo[1.1.1]-pentane is notably larger, in absolute value, than in other less strained F-alkane derivatives.[33]

III. Selected Compounds To Verify the Qualitatively Predicted Trends in Section II

On the basis of the considerations presented in section II, four representative classes of halo-compounds were chosen to analyze how the "heavy atom" effect on ^{13}C SCSs is affected by changes originating in the SO operator [eq 1], X-methanes (**1**), *eq-* and *ax*-X-cyclohexanes (**2-*eq*** and **2-*ax***), and 2-halo-tetrahydropyrans (**3**), for X = F, Cl, Br, and I (Figure 1).

It is expected that in **1** very small hyperconjugative interactions transferring charge into $\sigma^*_{C_1-X}$ take place. However, important interactions of type $LP(X) \rightarrow \sigma^*_{C-H}$ must be operating, as commented above, widening the relevant energy gaps between the energies of the σ^*_{C-X} antibonding and those occupied $LP_2(X)$ and $LP_3(X)$ lone-pair orbitals.

Comparing **2-*eq*** and **2-*ax*** conformers, it is expected that a hyperconjugative interaction involving the σ^*_{C1-X} antibonding orbital is weaker in the former than in the latter. In compound **3**, the anomeric effect involving the ring oxygen atom defines a strong hyperconjugative interaction into the $\sigma^*_{C_1-X}$ antibonding orbital. Besides, the $\sigma^*_{O-C_1}$ and $\sigma^*_{O-C_5}$ antibonding orbitals in **3** are notably better electron acceptors than $\sigma^*_{C_1-C_1}$ and $\sigma^*_{C_1-C_1}$ antibonding orbitals, in either **2-*eq*** or **2-*ax***. A similar assertion holds for $\sigma^*_{C_{sp^3}-H}$ antibonding orbitals in **1** when comparing their electron acceptor ability with **3**. For this reason, it is expected that interactions $LP_2(X) \rightarrow \sigma^*_{C_{sp^3}-Y}$ and $LP_3(X) \rightarrow \sigma^*_{C_{sp^3}-Y}$ are stronger in **3** than either in **2** or in **1** (Figure 2).

IV. Experimental and Computational Details

Compounds **2** with X = Cl, Br, and I were commercially available, while the fluoro-derivative was synthesized ac-
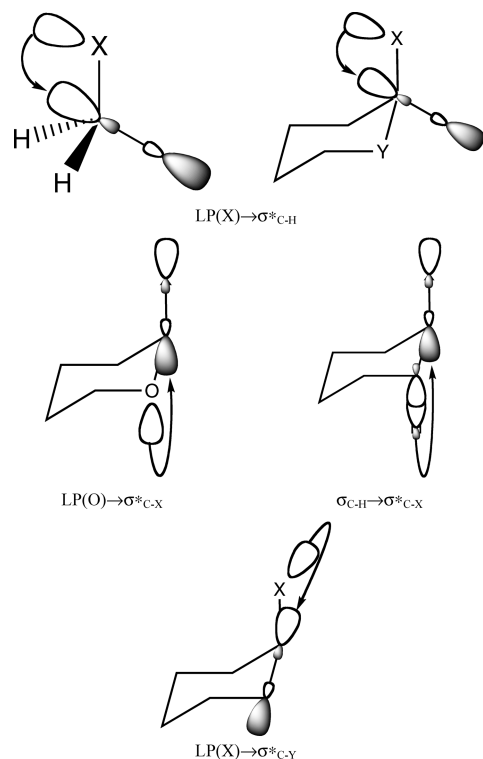
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Figure 2. Relevant NBO interactions for methane, cyclohexane, and pyran derivatives, where X = F, Cl, Br, and I, and Y = CH$_2$ and O.

cording to a literature procedure.[34] Compounds **3** with X = Cl, Br, and I were also synthesized according to literature procedures,[35] and only their *axial* conformers were experimentally observed. Compound **3** with X = F was not studied in this work, because it was not possible to synthesize this compound.

Nonrelativistic calculations, that is, geometry optimization, NBO, and NMR shielding, were carried out at B3LYP level, using cc-pVTZ basis set[36,37] for C, H, O, F, Cl, and Br and Sadlej pVTZ for I.[38] Moreover, the $^1J_{CF}$ SSCCs were also calculated with the B3LYP functional using the EPR-III basis set for C and F, while for H and O the cc-pVTZ basis set was applied using the Gaussian 03 program.[39]

In the relativistic framework, the calculations of ground-state geometries in the relativistic scalar ZORA approach were carried out with the BP86 functional using a triple-ζ doubly polarized Slater-type basis set (TZ2P) with the Amsterdam Density Functional (ADF) package.[40] The corresponding NMR shielding constants were calculated using four different levels of theory: scalar ZORA, SO-ZORA, scalar PAULI, and SO-PAULI.

The ^{13}C substituent chemical shifts (SCS) were obtained as the difference between nuclear shielding constants calculated for each halo-derivative and for the corresponding parent compound and were reported in three different approaches: nonrelativistic at B3LYP level, and the relativistic levels at BP86/TZ2P, which was previously mentioned.

V. Results and Discussion

Experimental and calculated ^{13}C$_1$ SCSs for compounds **1**, **2-eq**, **2-ax**, and **3** are collected in Table 1, where experimental

Table 1. Experimental and Theoretical^a ^{13}C SCS for **1**, **2**, and **3** Halocompounds

		H	F	Cl	Br	I
1^a	SCS$_{exp}$	0.0	77.7	27.4	12.3	−18.4
	SCS$_{B3LYP}$	0.0	81.4	43.5	34.3	18.3
	SCS$_{ZORA}$^{b}	0.0	84.0	40.3	33.2	13.8
	SCS$_{SO-ZORA}$^{c}	0.0	83.4	38.1	20.7	−16.1
	σ_{SO}		0.5	2.2	10.1	29.9
	SCS$_{PAULI}$^{b}	0.0	84.07	40.32	34.18	66.03
	SCS$_{SO-PAULI}$^{d}	0.0	83.56	38.18	22.20	45.33
	σ_{FC}		0.5	2.1	11.9	20.1
	D^e		57	54	41	34
2-eq	SCS$_{exp}$	0.0	66.7	32.8	25.1	6.1
	SCS$_{B3LYP}$	0.0	67.5	45.6	43.5	37.6
	SCS$_{ZORA}$^{b}	0.0	69.7	41.8	43.7	35.1
	SCS$_{SO-ZORA}$^{c}	0.0	69.1	39.9	33.7	12.1
	σ_{SO}		0.6	1.9	10.0	22.8
	SCS$_{PAULI}$^{b}	0.0	69.71	41.80	44.40	98.12
	SCS$_{SO-PAULI}$^{d}	0.0	69.14	39.74	33.76	75.75
	σ_{FC}		0.6	2.1	10.6	21.8
	D^e		95	103	100	91
2-ax	SCS$_{exp}$	0.0	63.5	33.1	28.4	13.8
	SCS$_{B3LYP}$	0.0	64.7	45.4	44.6	39.8
	SCS$_{ZORA}$^{b}	0.0	66.3	41.5	44.8	37.9
	SCS$_{SO-ZORA}$^{c}	0.0	65.9	40.1	37.6	21.9
	σ_{SO}		0.5	1.5	7.2	15.8
	SCS$_{PAULI}$^{b}	0.0	66.31	41.48	45.34	94.28
	SCS$_{SO-PAULI}$^{d}	0.0	65.75	39.63	36.05	74.85
	σ_{FC}		0.6	1.9	9.2	18.4
	D^e		101	114	109	108
3	SCS$_{exp}$	0.0		26.0	25.9	16.7
	SCS$_{B3LYP}$	0.0	42.2	24.7	34.1	43.6
	SCS$_{ZORA}$^{b}	0.0	42.7	36.6	42.7	42.2
	SCS$_{SO-ZORA}$^{c}	0.0	42.2	35.0	35.2	26.9
	σ_{SO}		0.5	1.6	7.5	15.3
	SCS$_{PAULI}$^{b}	0.0	42.76	36.61	42.86	81.50
	SCS$_{SO-PAULI}$^{d}	0.0	42.15	34.63	33.74	64.11
	σ_{FC}		1.0	2.3	9.4	16.9
	D^e		154	176	190	212

^{a} Experimental values for halomethanes were taken from ref 36. ^{b} $\sigma = \sigma_{dia} + \sigma_{para}$. ^{c} $\sigma_{SO-ZORA} = \sigma_{dia} + \sigma_{para} + \sigma_{so}$. ^{d} $\sigma_{SO-PAULI} = \sigma_{dia} + \sigma_{para} + \sigma_{FC}$. ^{e} D: "Descriptor" of hyperconjugative interactions affecting the SO part of the SO/FC term (see Table 2).

values for series **1** were taken from the literature,[41] while those for the remaining compounds were measured as part of this work. In Table 1 are also shown the SCS calculated using the following approaches: nonrelativistic B3LYP, scalar ZORA, scalar PAULI, SO-ZORA, and SO-PAULI. For scalar ZORA and scalar PAULI, the NMR shielding was computed by summing the diamagnetic and paramagnetic contributions, and for SO-ZORA and SO-PAULI the SO and FC interaction was taken into account together with diamagnetic and paramagnetic contributions to each SCS, respectively, and it was plotted in Figure 3 for compounds **1**, **2-eq**, **2-ax**, and **3**, versus the halogen atom, where it can be observed that the calculated SO contributions are notably smaller for compounds **2-eq**, **2-ax**, and **3** than in **1**.

Relevant NBO analyses carried out for **1**, **2-eq**, **2-ax**, and **3** compounds. For the qualitative analysis described in section II, it is important to evaluate hyperconjugative interactions (a) involving the $\sigma^*_{C_1-X}$ antibonding orbital, and (b) involving the LP$_2$(X) and LP$_3$(X) lone pair orbitals. In this qualitative study, the former interactions (a) are taken into account globally considering the occupancy of the $\sigma^*_{C_1-X}$ antibonding orbital, while for the latter (b), by considering the sum of the occupancies of both lone-pairs.
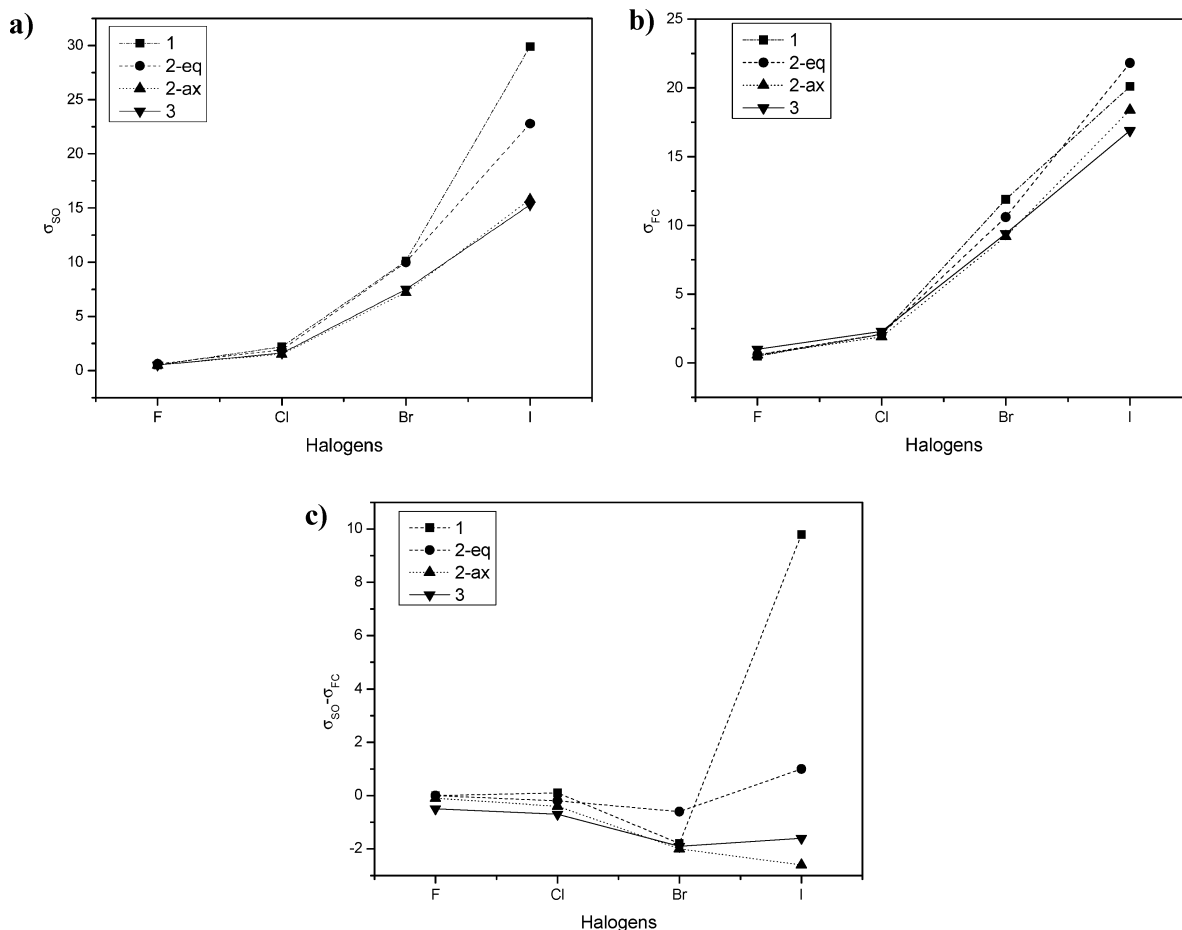
a)

b)

c)

Figure 3. Calculated contribution to ^{13}C SCS for different halo-substituents in methane, **1**, cyclohexane-eq, **2-eq**, cyclohexane-ax, **2-ax**, and pyran, **3**: (a) σ_{SO} contribution; (b) σ_{FC} contribution; and (c) its difference, $\sigma_{SO} - \sigma_{FC}$.

Table 2. Relevant NBO Occupancies To Study the Relative Influence of the SO Part of the SO/FC Contribution to the $^{13}C_\alpha$ SCSs in **1**, **2-eq**, **2-ax**, and **3-ax**[a]

	occupancy[b]	F	Cl	Br	I
1	$\sum nx$	−54	−50	−38	−32
	σ^*_{CX}	3	4	3	2
	$\sigma^*_{CX} - \sum nx$	+57	+54	+41	+34
2-eq	$\sum nx$	−56	−57	−48	−40
	σ^*_{CX}	39	46	50	51
	$\sigma^*_{CX} - \sum nx$	+95	+103	+100	+91
2-ax	$\sum nx$	−56	−55	−45	−39
	σ^*_{CX}	45	59	64	69
	$\sigma^*_{CX} - \sum nx$	+101	+114	+109	+108
3	$\sum nx$	−66	−90	−63	−39
	σ^*_{CX}	89	86	127	173
	$\sigma^*_{CX} - \sum nx$	+154	+176	+190	+212

[a] Each LP occupancy was obtained by subtracting 2.000 from the calculated occupancy (in units of 10^{-3}), that is, the occupancy of an ideally occupied NBO. σ^*_{C-X} occupancies are also given in units of 10^{-3}. [b] $\sum nx$ stands for the sum of the $LP_2(X)$ and $LP_3(X)$ occupancies. $\sigma^*_{CX} - \sum nx = D$, which stands for "descriptor of hyperconjugative interactions affecting the SO part of the SO/FC term" (see Table 1).

In Table 2, such occupancies are given in units of 10^{-3} for the $\sigma^*_{C_1-X}$ antibonding orbital, and for the lone-pair orbitals they are given as the difference between the sum of the calculated occupancies of both lone-pairs and 4.000, which corresponds to the sum of the occupancies of two ideally occupied NBO orbitals. These differences are negative, and

they are also expressed in units of 10^{-3}. As commented in section II, both types of interactions tend to decrease the absolute value of the SO/FC term due to the SO influence. Therefore, the sum of the absolute values of both types of occupancies, given in units of 10^{-3}, is taken as a significant, although qualitative, "descriptor" (D), of the influence of hyperconjugative interactions on the SO part of the SO/FC contribution to $^{13}C_1$ SCSs. For this reason, in Table 2, such sums of occupancies (D) are also displayed for the four chosen compounds for X = F, Cl, Br, I. It is recalled that for the same halogen atom, the SO contribution decreases with the increase of the D "descriptor". In all cases, for the same halogen atom, D increases monotonously from compounds **1** to **3**, and, therefore, the qualitative description presented above suggests that the SO decreases along the same series of compounds. In general, this observation is in line with the results displayed in Figure 3, with the exception of compounds **3** where the SO-ZORA calculated SO terms are quite similar to those calculated in **2-ax**. This observation suggests that two opposite effects are taking place in halogen derivatives of compound **3**; that is, while the SO part of the SO/FC term is notably reduced due to the strong hyperconjugative interactions that take place in this compound, the FC contribution is increased due to the strong inductive effect produced by the ring oxygen atom placed α to C_1. To test if this suggestion is supported by available data, in Table 3 are displayed calculated $^1J_{CF}$ SSCCs (in Hz) at the B3LYP//

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Table 3. $^1J_{CF}$ SSCCs (in Hz) Calculated at the B3LYP// EPR-III/aug-cc-pVTZ for the Fluorinated Compounds of Series **1**, **2-eq**, **2-ax**, and **3**

	1	2-eq	2-ax	3
FC	−280.3	−279.0	−273.0	−320.0
SD	23.3	23.4	24.1	24.5
PSO	35.9	29.5	30.6	42.9
DSO	0.4	0.9	0.9	1.1
$J_{calc}{}^a$	−220.7	−225.2	−217.4	−251.5
J_{exp}	−157.5	−169.5	−164.6	

^{a} J_{calc} = FC + SD + PSO + DSO.

EPR-III/aug-cc-pVTZ level for the fluorinated compounds of series **1**, **2-eq**, **2-ax**, and **3**. In fact, it is observed that the absolute value of the FC term of $^1J_{CF}$ SSCC in **3** is notably larger than for the remaining compounds. It is recalled that $^1J_{CF}$ SSCCs, in general, are not reproduced accurately within the DFT framework.[42] However, because in this work only a qualitative approach is applied, it is considered that the trend of the calculated FC contribution to $^1J_{CF}$ SSCCs is adequate to validate this qualitative analysis on the influence of the SO contribution to the "heavy atom effect" on ^{13}C SCSs.

VI. Concluding Remarks

For the results described in this Article, the spin−orbit operator is analyzed from a qualitative point of view, to estimate how certain types of hyperconjugative interactions would affect the performance of the SO operator to define a notably small "heavy atom effect" on the ^{13}C SCS bonded to a heavy halogen atom. The SO/FC contribution to ^{13}C SCS was calculated within the scalar ZORA, SO-ZORA, scalar PAULI, and SO-PAULI approaches, and the results are compared in Figure 3. It is observed that the SO and FC parts of the SO/FC term are sensitive enough to show observable differences for both *equatorial* and *axial* cyclohexane conformers. It is also important to highlight those strong hyperconjugative effects, which yield an important decrease on the SO part of the SO/FC term, and sometimes can be masked by strong inductive effects increasing the corresponding FC term of spin−spin coupling constants, as in compound **3**.

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