EFFECTS OF INTRAMOLECULAR INTERACTIONS ON NMR $J(^{13}C,^{1}H)$ SPIN-SPIN COUPLING CONSTANTS. A DFT-B3LYP CALCULATION AND EXPERIMENTAL STUDY

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Dedicated to Prof. Imre G. Csizmadia on the occasion of his 75th birthday

Abstract

Two different types of interactions affecting both $^{1}J(C,H)$ and longer range $^{n}J(C,H)$ spin-spin coupling constants, SSCCs, are studied from a theoretical point of view in model compounds. The study, based on the DFT methodology, was supplemented with measurements of several $^{n}J(C,H)$ couplings. The studied interactions are, on the one hand, those of electrostatic origin caused by proximity of either an electronegative atom or of an H atom and a C—H bond on the corresponding $^{1}J(C_{sp2},H)$ SSCC. In agreement with previous observations it was determined that the former interaction yields an increase while the latter a decrease in the corresponding $^{1}J(C,H)$ SSCC. Both of these changes are notably shielded by the dielectric effect of the solvent. On the other hand, the influence of the strong negative hyperconjugative interactions that take place in the aldehyde moiety on the corresponding $^{1}J(C_C,H_f)$ and $^{2}J(C,H_f)$ SSCCs, are studied. These negative hyperconjugative interactions are inhibited by, for instance, the intramolecular hydrogen bond in salicylaldehyde, the dielectric effect of the solvent, or the electrostatic effect of an aproximate electronegative atom close to the formyl proton of the H_f—C_C bond.

Resumen

En el presente trabajo se estudian compuestos modelos, desde un punto de vista teórico, dos tipos de interacciones diferentes que afectan las constantes de acoplamiento spin-spin, SSCCs, $^{1}J(C,H)$ y las de mayor rango $^{n}J(C,H)$. El estudio, basado en metodología DFT, fue complementado con la medición de varios acoplamientos $^{n}J(C,H)$. Las interacciones *estudiadas son, por una parte, aquellas de origen electrostático causadas ya sea por la proximidad de un átomo electronegativo o bien por un átomo de H y un enlace C—H en el correspondiente* $^1J(C_{sp2},H)$ *SSCC. En acuerdo con observaciones previas, se determinó que la interacción nombrada en primer término, conduce a un incremento en el correspondiente* $^1J(C_C,H_f)$ *SSCC mientras que la última causa disminución en el mismo. Ambos cambios están notablemente apantallados por el efecto dieléctrico del solvente. Por otra parte, se estudia la influencia de las interacciones hiperconjugativas fuertemente negativas que tienen lugar en la mitad aldehídica sobre los correspondientes* $^1J(C_C,H_f)$ *y* $^2J(C,H_f)$ *SSCCs. Las interacciones hiperconjugativas fuertemente negativas son inhibidas, por ejemplo, por el enlace hidrógeno intramolecular en aldehído salicílico, el efecto dieléctrico del solvente o el efecto electrostático de un átomo electronegativo cercano al protón formílico del enlace* H_f—C_C.

Introduction

Nuclear spin-spin coupling constants, SSCCs, as measured by high resolution NMR spectroscopy, are very sensitive parameters to many intra- and inter- molecular interactions. For this reason these parameters are considered to be excellent probes to gauge such interactions. However, to fully appreciate such a capability, it is important to understand how subtle changes in the molecular electronic structure affect SSCCs. To achieve such an understanding, it is important to calculate SSCCs with reasonable accuracy for some model compounds; however, for many years such a calculations were a difficult task for Quantum Chemistry. An important breakthrough took place during the last decade when the first attempts to calculate them within the framework of the Density Functional Theory, DFT, [1] were reported. It is now common to find in the literature papers where SSCCs are thus calculated in polyatomic compounds, with a good agreement between calculated and experimental values. It is important to recall that, according to the non-relativistic Ramsey's formulation, isotropic SSCCs, i.e. measured in isotropic phases, [2] are contributed by four terms, namely, Fermi contact, FC, spin-dipolar, SD, paramagnetic spin-orbit, PSO, and diamagnetic spin-orbit, DSO, eq. (1),

$$J_{CH} = {}^{FC}J_{CH} + {}^{SD}J_{CH} + {}^{PSO}J_{CH} + {}^{DSO}J_{CH} \tag{1}$$

In many cases for light atoms like ^1H, ^{13}C and ^{15}N, SSCCs are by far dominated by the FC term. However, to make a correct analysis all four terms should be included.

In previous papers it was reported that $^1J(C,H)$ SSCCs are notably affected by electrostatic interactions[3,4,5,6] and by hyperconjugative interactions either from the corresponding C—H bond or its antibond. The main purpose of this paper is to get a deeper insight into how these effects operate, and how other $^nJ(C, H)$ SSCCs can also be used as excellent probes to investigate at least part of such interactions. To study $^1J(C, H)$ SSSCs five mono- di- and tri-substituted benzenes are taken as model compounds, **1** to **5 (X=NO$_2$)**. It should be noted that side chains in **1** to **4** correspond to substituents bearing compound **5(X=NO$_2$)**. To study a few longer range $^nJ(C,H)$ SSCCs ($n > 1$), in adittion to compound **5**, five additional 5-X-salicylaldehyde derivatives were selected, and a set of $^nJ(C,H)$ SSCCs were measured and calculated within the DFT framework. Within an aldehyde group, CHO, very strong negative hyperconjugative interactions [7] take place, corresponding to charge transfer interactions from the oxygen non-bonding electron pair of p symmetry into the $(C_C$—$H_f)^*$ and $(C_C$—$C_1)^*$ antibonds [6]. The consequences of these negative hyperconjugative interactions on NMR parameters are really remarkable; for instance, this is the origin of the very large *geminal* SSCCs observed across a carbonyl group [8] and the present evidence indicates that such couplings show a strong dielectric solvent effect. The following three examples are typical of a *geminal* coupling through a carbonyl group (experimental values), e.g. in acetaldehyde $^{2}J(C,H)$ = 29.74 Hz, in gas phase, and $^{2}J(C,H)$ = 26.25 Hz in DMSO solution [9]; in formamide [10] $^{2}J(^{15}N,^{1}H)$ = -20.14 and -15.30 Hz, for gas-phase and DMSO solution, respectively; $|^{2}J(^{17}O,^{1}H)| \cong 40$ Hz in methyl formate [11]. Such SSCCs originate mainly from the FC term and it is known that for *geminal* SSCCs, hyperconjugative interactions into the coupling pathway yield an algebraic increase in the FC term [12]. On the other hand, hyperconjugative interactions from the coupling pathway yield an algebraic decrease in such a term. It is also important to recall that negative hyperconjugative interactions are known to be slightly inhibited by the dielectric effect of the solvent [13,14]. This was also found to be the origin of the inhibition of the lone-pair orientation effect [15], and the solvent dependence of $^{2}J(C,H)$ SSCC in acetaldehyde [16]. For this reason, in this work special attention is also paid to $^{2}J(C_1,H_f)$ SSCCs in **1**, **3**, **4**, and **5**(**X**), where X = H, OCH_3, Br, Cl, OH, NO_2. First of all, compounds **1** to **5**, $^{1}J(C,H)$ SSCCs were calculated where, for the sake of completeness, all four terms of eq. (1) were included. In compound **3**, two different conformations were taken into account, $\alpha = 0^{o}$ and $\alpha = 180^{o}$; similarly, in compound **4**, two conformations were considered, $\beta = 0^{o}$ and $\beta = 180^{o}$. Medium effects were taken into account by performing calculations on each isolated compound and considering a solvent with a dielectric constant of 46.7, which corresponds to an infinitely diluted dimethylsulfoxide, DMSO, solution. This choice was made since solutions of these polar compounds were prepared at high concentrations in a polar solvent, and therefore, when taking $\varepsilon = 46.7$, it was not intended to reproduce qualitatively the experimental conditions, but to represent only a strong polar solution.

Experimental

NMR measurements

All ^{1}H and ^{13}C NMR spectra were recorded, using 5 mm sample tubes, on a Bruker AM500 instrument operating at 500.138 and 125.760 MHz. 64 K data points were acquired with a spectral width of 1939 Hz. FIDs were zero filled to 128K data points, corresponding to a digital resolution of 0.2 Hz. Samples were prepared using CD_3CN as solvent, at concentrations *ca.* 80 % w/w. In order to identify the coupling nuclei in each J(C,H) SSCC, selective double resonance experiments were carried out on each of the ring proton signals. All spectra were recorded at the LANAIS NMR-500 facility in the Department of Physics, FCEyN, University of Buenos Aires. Compounds **5** (X= H, OCH_3, Br, Cl, OH, NO_2) were available commercially and their identities and purities were checked by recording their ^{1}H and ^{13}C NMR spectra.

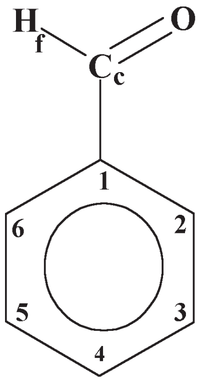
DFT calculations

Geometry optimizations and calculations of all four terms of SSCCs, FC, SD, PSO and DSO, were carried out within the DFT framework. The CP-DFT [17,18] perturbative approach was used (as implemented in the Gaussian 03 package of programs [19]) for calculating all the three second-order terms of SSCCs, i.e. FC, SD, and PSO; the DSO term was evaluated as an expectation value over the electronic ground state. The functional employed is the hybrid B3LYP of Lee *et al.* [20], where the exchange part is treated according to the Becke's three parameter approach [21,22]. For geometry optimizations the 6-311G** basis set was employed, while for calculating SSCCs the EPR-III basis set [23] was chosen, with triple-zeta quality including diffuse and polarization functions. The s part of this basis set is enhanced with tight s functions to better reproduce the electronic density in the nuclear regions; this point is particularly important when calculating the FC term. It is important to stress that coupling constants calculated at the B3LYP/EPR-III level are close to their basis-set converged values [24]. Dielectric solvent effects were taken into account using the SCRF-PCM version of the polarization continuum model, PCM, of Tomasi *et al.* [25,26,27]. Calculation of SSCCs including dielectric solvent effects were performed using optimized geometries obtained within the SCRF-PCM model. All DFT calculations were carried out with the Gaussian 03 package of programs. Hyperconjugative interactions were studied using the NBO approach [28,29].

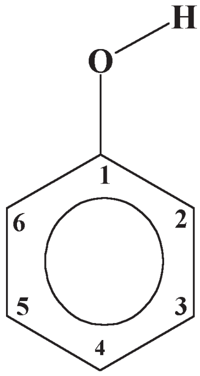
Results and Discussion

A good starting point to study how different interactions affect $^1J(C_{sp^2},H)$ SSCCs is to consider such couplings in benzaldehyde, **1**, and in phenol, **2**. For these two compounds, total calculated $^1J(C,H)$ SSCCs considering two different solvents, $\varepsilon = 1$ and $\varepsilon = 46.7$, i.e. an isolated molecule, and an infinitely diluted solution in dimethylsulphoxide, DMSO, are compared in Table 1 with the respective experimental values, taken from Ref.[30]. It should be recalled that in **1** and **2** both planar rotamers are equally populated and, therefore, experimental $^1J(C,H)$ SSCCs for ring positions 2 and 6, and for 3 and 5, correspond to their respective average value. It is expected that for the former two, i.e *ortho* positions, the inductive and resonance effects be almost the same; a similar assertion should hold for the latter two, *meta* positions. Therefore, the large differences between $^1J(C_2, H_2)$ and $^1J(C_6, H_6)$ SSCCs, $\Delta(^1J_o) = 7.6$ Hz in **1,** and $\Delta(^1J_o) = -6.8$ Hz in **2**, Table 1, suggest that they originate mainly from an electrostatic effect arising from the proximity between the side chain and the *ortho* protons. It is to be noted the opposite sign for calculated $\Delta(^1J_o)$ in **1** and **2**, i.e. in **1** the proximity of H_2 to the oxygen O=C is similar to that of the oxygen O—H in **2**, and vice versa. To estimate such an effect, in this Table the NBO natural atomic charges on the H atoms are also shown. In this study it will be neglected any effect from σ-hyperconjugative interactions involving the respective side-chain and the (C—H)* antibond. As observed previously, [5] in aromatic compounds the proximity of an oxygen atom to an H—C bond yields an increase in the FC term of its $^1J(C,H)$ SSCC. On the other hand, the proximity between two H atoms yields a decrease in the corresponding $^1J(C,H)$ SSCC [32,33]. It is important to note that in **1** and **2** solvent effects on $^1J(C,H)_o$ (*ortho* to the side-chain) SSCCs are of opposite signs. This trend is consistent with the fact that differences $\Delta(^1J_o)$ in both compounds are of electrostatic origin, and dielectric solvent effects should shield such interactions. A similar conclusion is reached comparing the NBO atomic charges at H_2 and H_6; it is also interesting to note that for calculations in a very polar solvent both atomic charges tend to give the same value. The asymmetry between $^1J(C_3,H_3)$ and $^1J(C_5,H_5)$, $\Delta(^1J_m)$, is small both in **1** and **2**; however, a slight difference between their solvent effect is still observed, which is assumed to originate on the opposite electrostatic effects of the side–chain on both C_3—H_3 and C_5—H_5 bonds. In the same Table 1 it is observed that in **1** the $LP(O_p) \rightarrow (C_C—H_f)^*$ negative hyperconjugative interaction is inhibited, due to the dielectric effect of the solvent, by 2.7 kcal/

mol. It is also noted that the SSCC where the largest solvent effect takes place is $^{1}J(C_C,H_f)$; although the inhibition of such an interaction yields a direct increase of this coupling, the total effect should also originate in the inhibition of the $LP(O_p) \rightarrow (C_C—C_1)^*$ negative hyperconjugative interaction.



1



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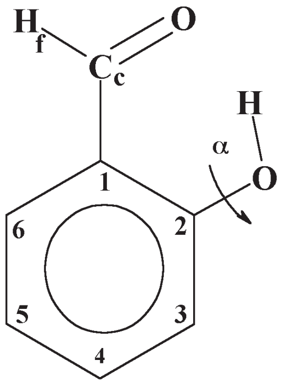

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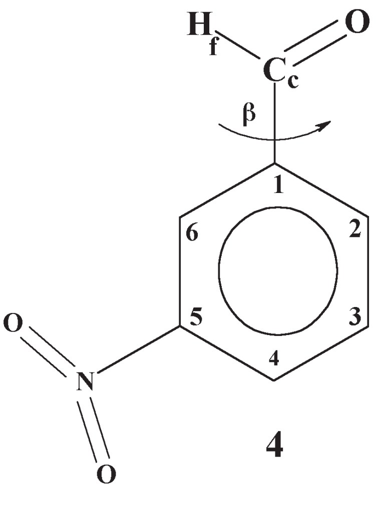

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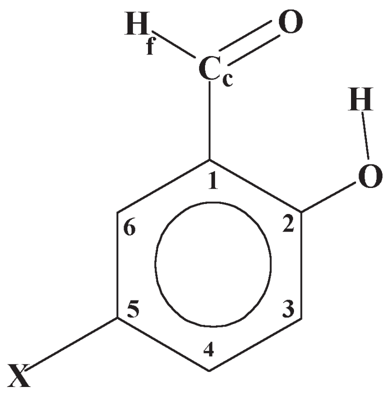

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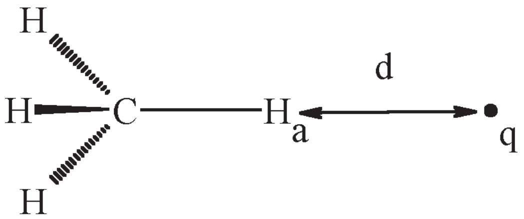
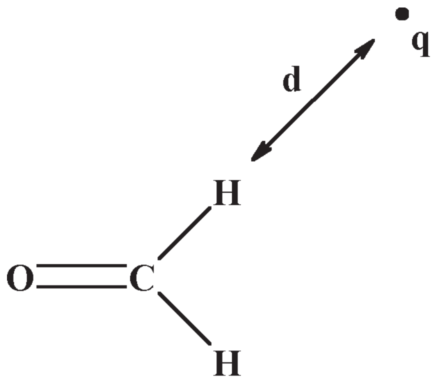


6a



6b

***Table 1**. Comparison between calculated and experimental values of $^1J(C,H)$ SSCCs (in Hz) in compounds **1** and **2**. The NBO atomic charges on each proton are also shown (in 10^{-3} au). S.E. stands for solvent effect on calculated SSCCs and NBO atomic charges, it is given by the difference $F(\varepsilon = 46.7) - F(\varepsilon = 1)$, where F stands for either J or Q_H.*

	(**1**)				(**2**)			
		Theo.		Exp^a.		Theo.		Exp^a.
	ε = 1	ε = 46.7	S.E.		ε = 1	ε = 46.7	S.E.	
$^1J(C_2,H_2)$	168.4	167.7	-0.7	161.0	158.4	163.1	1.4	159.0
Q_{H2}	753	748	-5	—	781	775	-6	—
$^1J(C_3,H_3)$	164.0	167.3	3.3	161.9	163.0	164.8	1.8	158.4
Q_{H3}	770	752	-18	—	775	759	-16	—
$^1J(C_4,H_4)$	162.5	165.9	3.4	160.4	166.1	167.4	1.3	159.0
Q_{H4}	771	752	-19	—	773	760	-13	—
$^1J(C_5,H_5)$	164.1	167.7	3.6	161.9	162.8	164.8	2.0	158.4
Q_{H5}	770	751	-19	—	774	760	-14	—
$^1J(C_6,H_6)$	160.8	165.2	4.4	161.0	165.2	164.4	-0.8	159.0
Q_{H6}	772	751	-21	—	763	754	-9	—
$^1J(C_C,H_f)$	175.8	181.9	6.1	176.9	—	—	—	—
Int^b	23.6	20.9	-2.7	—	—	—	—	—

a) Taken from Ref. [30]
b) Int stands for $LP(O_p)\rightarrow(C_C—H_f)^*$ negative hyperconjugative interaction

In Table 2 calculated $^1J(C,H)$ SSCCs are compared for conformers **3a** and **3b**; in **3a** calculated SSCCs are also compared with experimental values. It is important to note that in **3b** the intra-molecular hydrogen bond is broken. The behavior of $^{1}J(C_3,H_3)$ SSCC can easily be rationalized since in **3a** the C_3—H_3 bond is close to the in-plane electron pair of the hydroxyl-oxygen non-bonding and therefore a significant contribution to the calculated SSCC originates in this electrostatic interaction.

Table 2. *Effect of the O—H conformation on $^{1}J(C,H)$ SSCCs (in Hz) in (**3**). S.E. stands for solvent effect on calculated SSCCs and NBO atomic charges (in 10^{-3} au), it is given by the difference $F(\varepsilon = 46.7) - F(\varepsilon = 1)$, where F stands either for J or Q_{H}.*

	(**3a**)				(**3b**)		
	Theo.			Exp.[a]	Theo.		
J(C,H)	ε = 1	ε = 46.7	S.E.		ε = 1	ε = 46.7	S.E.
$^{1}J(C_3,H_3)$	166.1	167.5	1.4	162.2	157.7	164.4	6.7
Q_{H3}	7.58	744	-14	—	777	749	-28
$^{1}J(C_4,H_4)$	161.6	165.4	3.8	159.7	162.5	165.6	3.1
Q_{H4}	770	751	-19	—	770	751	-19
$^{1}J(C_5,H_5)$	167.1	170.2	3.1	169.1	167.1	169.9	2.8
Q_{H5}	768	750	-18	—	768	752	-16
$^{1}J(C_6,H_6)$	160.8	165.8	5.0	159.3	160.2	163.8	3.6
Q_{H6}	773	750	-23	—	773	753	-202
$^{1}J(C_C,H_f)$	177.1	184.6	7.5	177.7	175.2	179.6	4.4
Q_{Hf}	855	823	-32.0	—	882	851	-31
Int.[b]	20.9	18.9	-2.0	—	24.0	21.1	-2.9

a) Taken from Ref. [30].

b) Int stands for $LP(O_p)\rightarrow(C_C$—$H_f)^*$ negative hyperconjugative interaction.

Therefore, when changing the O—H conformation this effect is "quenched" and a decrease in the $^{1}J(C_3,H_3)$ SSCC is expected, which is further magnified since in **3b** the hydroxyl-proton is close to H_3. In this way a total decrease of 8.4 Hz is observed when calculations are carried out for an isolated molecule (ε = 1). This rationalization is further supported by the following considerations: in 3**a** a solvent effect of only 1.4 Hz is observed for $^{1}J(C_3,H_3)$. This is consistent with the effect of the oxygen proximity being partially shielded by the dielectric effect of the solvent.

***Table 3**. Effect of the CHO conformation on $^{1}J(C,H)$ SSCCs (in Hz) in (**4**). S.E. stands for solvent effect on calculated SSCCs (in Hz) and NBO atomic charges, Q_{H}, (in 10^{-3} au), it is given by the difference $F(\varepsilon = 46.7) - F(\varepsilon = 1)$, where F stands either for J or Q_{H}.*

	(**4a**)			(**4b**)		
	Theo.			Theo.		
	$\varepsilon = 1$	$\varepsilon = 46.7$	S.E.	$\varepsilon = 1$	$\varepsilon = 46.7$	S.E.
$^{1}J(C_2,H_2)$	170.7	171.9	1.2	163.0	169.3	6.3
Q_{H2}	746	736	-10	765	739	-26
$^{1}J(C_3,H_3)$	168.9	174.3	5.4	168.8	174.6	5.8
Q_{H3}	760	737	-23	760	737	-23
$^{1}J(C_4,H_4)$	173.0	175.4	2.4	173.3	175.4	2.1
Q_{H4}	736	724	-12	736	724	-12
$^{1}J(C_6,H_6)$	170.9	174.1	3.2	177.8	176.3	-1.5
Q_{H6}	738	723	-15	721	720	-1
$^{1}J(C_C,H_f)$	182.8	191.0	8.2	175.2	179.6	4.4
Q_{Hf}	866	834	-22	870	833	-37
Int.[a]	23.3	20.8	-2.5	23.6	20.8	-2.8

a) Int stands for $LP(O_p)\rightarrow(C_C—H_f)^*$ *negative hyperconjugative interaction.*

On the other hand, the "solvent effect", S.E., on $^{1}J(C_3,H_3)$ in 3**b** is increased to 6.7 Hz, with a partial dielectric shielding of the proton proximity effect on $^{1}J(C_3,H_3)$ SSCC. For an isolated molecule, ($\varepsilon = 1$), the **a**→**b** conformation change yields a change in $^{1}J(C_4,H_4)$ SSCC of 0.9 Hz, and this difference is reduced to 0.1 Hz for $\varepsilon = 46.7$. On the other hand, such a conformational change yields a change in $^{1}J(C_6,H_6)$ of only 0.6 Hz (isolated molecule), which, although small, suggests that, in **3a** the intra-molecular hydrogen bond somewhat inhibits the $n(O_p)\rightarrow(C_C—H_f)^*$ interaction. When the hydrogen bond is broken, **3b**, that negative hyperconjugative interaction is increased (from 20.9 to 24.0 kcal/mol), affecting the $C_6—H_6$---$H_f—C_C$ proximity effect on $^{1}J(C_6,H_6)$ There is a substantial change in the solvent effect on this SSCC, i.e. from 5.0 to 3.6 Hz, for **3a**→**3b**. This trend is consistent with a dielectric solvent inhibition of the strong $n(O_p)\rightarrow(C_C—H_f)^*$ negative hyperconjugative interaction, i.e. it seems that this is an indirect effect: when such hyperconjugative interaction is inhibited, then the $C_6—H_6$---$H_f—C_C$ proximity effect is enhanced. In **3a** this negative hyperconjugative interaction is also inhibited by the intra-molecular hydrogen bond; for $\varepsilon = 1$ this inhibition goes from 24.0 kcal/mol (without the intra-molecular hydrogen bond, **3b**) to 20.9 kcal/mol, when the hydrogen bond is operating, **3a,** which is weakened by the dielectric effect of the solvent. For this reason it is not surprising to observe a decrease in the $^{1}J(C_6,H_6)$ solvent effect in **3b**.

In Table 3, calculated $^{1}J(C,H)$ SSCCs for conformers **4a** and 4**b** are compared. The effects of such a conformational change on $^{1}J(C_2,H_2)$ and $^{1}J(C_6,H_6)$ SSCCs are quite similar to the difference between $^{1}J(C_2,H_2)$ and $^{1}J(C_6,H_6)$ in **1**. As it could be expected, $^{1}J(C_3,H_3)$ and $^{1}J(C_4,H_4)$ are only slightly affected. A change quite remarkable is observed for $^{1}J(C_C,H_f)$ SSCC; as discussed previously, [5] it seems to originate from a "*meta*-NO_2" electrostatic effect, which creates an electric field along the C_C—H_f of this polarity $C_C(+)$—$H_f(-)$. This result is compatible with the strong solvent effect calculated for $^{1}J(C_C,H_f)$ SSCC in **4a**, S.E = 8.2 Hz, which is reduced to 4.4 Hz in **4b**. According to results previously published [5], this observation can be rationalized on the following grounds. The electrostatic field produced by the NO_2 along the C_C—H_f bond affects, on one hand, the electronic distribution along that bond, and, on the other hand, such an electric field inhibits the $n(O_p)\rightarrow(C_C\rightarrow H_f)^*$ negative hyperconjugative interaction. As discussed previously through the model systems **7a** and **7b**, with $q < 0$, these two effects are intertwined and difficult to consider separately [6].

As noted previously, aromatic $^{1}J(C,H)$ SSCCs calculated at the B3LYP/EPR-III level, appear to be overvalued. Following Helgaker *et al.*, [34,35] and Oddershede *et al.* [36] the inclusion of nuclear motion effects, assuming such effects originating mainly in the Zero Point Vibrational correction, ZPV, the overall overvaluation seems to be about ca. 10 Hz. However, results displayed in Tables 1 and 2, suggest that for SSCCs undergoing electrostatic effects the ZPV correction could be smaller than for other C—H bonds without such a proximity interaction.

According to comments made in the Introduction's section, $^{2}J(C_C,H_f)$ SSCCs in benzaldehyde derivatives could be sensitive to several interactions. These effects are compared in Table 4, for conformations **a** and **b**, calculated $^{2}J(C_C,H_f)$ SSCCs for **3** and **4** compounds. The respective calculated $LP(O_p)\rightarrow(C_C—H_f)^*$ and $LP(O_p)\rightarrow(C_C—C_1)^*$ negative hyperconjugative interactions as well as the occupancy of the respective $(C_C—H_f)^*$ and $(C_C—C_1)^*$ antibonds are also shown. The following features of data listed in Table 4 are worth noting. The intra-molecular hydrogen bond in **3a** inhibits both the $LP(O_p)\rightarrow(C_C—H_f)^*$ and $LP(O_p)\rightarrow(C_C—C_1)^*$ negative hyperconjugative interactions, and the dielectric effect of the solvent yields a further inhibition of such interactions. No experimental $^{2}J(C_C,H_f)$ SSCC is known for compound **4**, nonetheless, it is observed that the dielectric effect of the solvent yields inhibitions slightly different than those observed for compound **3**, and such inhibitions are somewhat stronger in **4b** than in **4a**.

Table 4. *Side-chain conformation effect on $^{2}J(C_1,H_f)$ SSCC (Hz) in compounds **3** and **4**. The intensity of the negative hyperconjugative interactions of type $LP(O_p)\rightarrow(C_C—H_f)^*$ and $LP(O_p)\rightarrow(C_C—C_1)^*$ are also shown (in kcal/mol). Occ. stands for the occupancy of the respective antibonding orbital (times 10^3).*

	3				**4**			
	a		**b**		**a**		**b**	
ε	1	46.7	1	46.7	1	46.7	1	46.7
$^{2}J(C_C,H_f)$	21.1	20.3	27.7	24.7	27.7	25.8	28.2	26.3
$LP(O_p)\rightarrow(C_C—H_f)^*$	20.9	18.9	24.0	21.1	23.3	20.8	23.6	20.8
Occ. $(C_C—H_f)^*$	58	51	72	61	66	57	67	57
$LP(O_p)\rightarrow(C_C—C_1)^*$	15.4	14.8	22.4	20.6	21.5	20.4	21.6	20.4
Occ. $(C_C—C_1)^*$	50	49	65	59	66	62	66	62

In Table 5 several experimental $^{n}J(C,H)$ SSCCs are compared for compounds **5(X=H, OCH$_3$, OH, Cl, Br, NO$_2$)**. For the last compound, **X** = NO$_2$, theoretical values calculated for ε = 1 and ε = 46.7 are also shown. The important variation of $^{1}J(C_C,H_f)$ SSCC along this series of compounds is in agreement with the important sensitivity of this SSCC to different interactions. The rather large solvent effect, 8.2 Hz, calculated for that SSCC is also in line with the *meta* electrostatic NO$_2$ effect discussed in Table 3 for compound **4**. $^{2}J(C_1,H_f)$ SSCCs are also sensitive to a *meta* substitution, in agreement with discussions made above about this large *geminal* coupling defined mainly by the negative hyperconjugative interactions of types $LP(O_p) \rightarrow (C_C—H_f)^*$ and $LP(O_p) \rightarrow (C_C—C_1)^*$. Experimentally, the $^{2}J(C_2,H_3)$ SSCCs are only determined as absolute values; however, calculations for **5(X=NO$_2$)** indicate that this value is negative, it is also accepted, for all other compounds, that the coupling is negative. The *vicinal* couplings $^{3}J(C_2,H_f)$ and $^{3}J(C_6,H_f)$ correspond to *trans* and *cis* arrangements of their coupling pathway. These values are notably different from "normal" values for such coupling pathways [6]. Anomalous behaviors for *vicinal* SSCCs whose coupling pathways undergo strong negative hyperconjugative interactions were commented elsewhere. It is noteworthy how different are $^{3}J(C_2,H_f)$ and $^{3}J(C_2,H_4)$ SSCCs for compounds displayed in Table 5; similar comments hold for $^{3}J(C_2,H_6)$, $^{3}J(C_2,H_4)$ and $^{3}J(C_5,H_3)$ SSCCs. The two four-bond J(C,H) couplings, $^{4}J(C_1,H_4)$ and $^{4}J(C_6,H_3)$ are calculated as negative in **5(X=NO$_2$)**, and therefore the experimental values are assumed to be negative. It is interesting to remark that such values are compatible with couplings dominated by the FC term and transmitted through the π–electronic system [37].

***Table 5**. Selected $^{n}J(C,H)$ SSCCs (in Hz) in **5(X=H, OCH$_3$, OH, Br, Cl, NO$_2$)** experimental values measured as part of this work. For **X = NO$_2$** they are compared with the corresponding calculated values for ε = 1 and 46.7.*

						NO$_2$		
	H	**OMe**	**OH**	**Cl**	**Br**	1	46.7	Exp.
$^{1}J(C_C,H_f)$	176.9	178.0	178.9	182.0	182.1	182.8	191.0	185.1
$^{2}J(C_1,H_f)$	20.4	20.2	21.3	20.8	20.7	22.2	21.7	21.3
$^{2}J(C_2,H_3)$	-2.7	-2.8	-2.5	-2.7	-2.8	-1.8	-1.7	-2.2
$^{3}J(C_2,H_f)$	4.7	4.5	1.7	4.3	n.o.	4.9	4.9	4.3
$^{3}J(C_6,H_f)$	1.9	1.5	n.o	1.5	1.2	1.8	1.8	1.3
$^{3}J(C_2,H_4)$	9.9	10.0	9.7	9.7	9.6	10.3	10.2	10.0
$^{3}J(C_2,H_6)$	7.5	7.3	7.8	7.7	7.6	8.1	8.2	7.9
$^{3}J(C_5,H_3)$	7.9	9.6	9.5	11.2	11.3	9.8	10.1	n.o.
$^{4}J(C_1,H_4)$	-1.1	-0.9	-1.0	-1.1	-1.1	-0.8	-0.8	-0.8
$^{4}J(C_6,H_3)$	-1.0	-1.2	-1.2	-1.1	-1.2	-1.0	-1.0	-1.0

Concluding Remarks

Benzaldehyde (**1**) and phenol (**2**) are excellent model compounds to understand the electrostatic proximity effects on $^1J(C,H)$ SSCCs for aromatic C—H bonds. The proximity to an electronegative atom brings about an increase of the coupling, while the proximity to an H atom (with positive charge) originate a decrease of the coupling. For an isolated molecule, the sum of the absolute value of both effects amounts to 7.6 Hz in (**1**) and 6.8 Hz in (**2**). These two values are notably reduced to 2.5 Hz and 1.3 Hz, respectively, when calculations are carried out in a polar solvent. These results suggest that the assumption commonly made about the ZPV correction for any aromatic $^1J(C,H)$ SSCC, close to 5 Hz, could be notably wrong when the coupling under consideration is subject to a strong proximity effect. In general the study of the influence of nuclear motions on SSCCs is computationally demanding [34,35,36]; for this reason, calculations were carried out in some model compounds and results are thus generalized to bonds of similar hybridizations. The influence of strong electrostatic effects on the ZPV correction was not addressed.

$^1J(C_C,H_f)$ and $^2J(C_1,H_f)$ SSCCs in benzaldehyde derivatives depend strongly on the $LP(O_p)\rightarrow(C_C—H_f)^*$ and $LP(O_p)\rightarrow(C_C—C_1)^*$ negative hyperconjugative interactions. These hyperconjugative interactions are affected by several factors like the C=O---H—O hydrogen bonds in compounds **3** and **5**; dielectric effects of the solvent and proximity factors like the *meta* NO_2 effect on **4a** and **5(X=NO$_2$)**. In this case it would also be interesting to carry out detailed studies on how the effect of nuclear motion strongly affects SSCCs and its dependence on negative hyperconjugative interactions like $^1J(C_C,H_f)$ and $^2J(C_1,H_f)$ in benzaldehyde derivatives. The combination of nuclear motion and the dielectric effect of solvent on SSCCs is a subject not yet dealt with in the literature.

Although longer range SSCCs were not studied in detail in this work, results presented in Table 5 suggest that *vicinal* J(C,H) SSCCs may take quite unusual values when part of the coupling pathway is involved in strong negative hyperconjugative interactions. This observation is consistent with some anomalous *vicinal* SSCCs commented in two recent reviews [32,33].

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References

[1] Helgaker, T.; Jaszunski, M.; Ruud, K., *Chem. Rev.*, **1999**, *99*, 293.

[2] Kowalewski, J., *Prog. NMR Spectrosc.*, **1977**, *11*, 1.

[3] Vizioli, C.; Ruiz de Azúa, M. C.; Giribet, C. G.; Contreras, R. H.; Turi, L.; Dannenberg, J. J.; Rae, I. D.; Weigold, J. A.; Malagoli, M.; Zanasi, R.; Lazzeretti, V., *J. Phys. Chem.*, **1994,** *98*, 8858**.**

[4] Giribet, C. G.; Vizioli, C. V.; Ruiz de Azúa, M. C.; Contreras, R. H.; Dannenberg, J. J.; Masunov, A., *J. Chem. Soc., Faraday Trans*.,**1996**, *92*, 3029.

[5] de Kowalewski, D. G.; Kowalewski, V. J.; Peralta, G. J.; Eskuche, E.; Contreras, R. H.; Esteban, A L.; Galache, M. P.; Díez, E., *Magn. Reson. Chem.*, **1999**, *37*, 227.

[6] Contreras, R. H.; Peralta, J. E., *Prog. NMR Spectrosc.,* **2000**, *37*, 321.

[7] Reed, A. E.; Schleyer, P. V. R., *J. Am. Chem. Soc.*, **1990**, *112*, 1434.

[8] Hansen, P. E., In *The Chemistry of Double-bonded Functional Groups*, S. Patai, Ed.; Wiley, New York, **1989**, Ch. 3.

[9] Ando, I.; Inoue, Y.; Watanabe, S.; Sakamoto, Y.; Webb, G. A., *J. Mol Liquids*, **1984**, *27*, 179.

[10] Taha, A. N.; True, N. S., *J. Phys. Chem. A,* **2000**, *104*, 2985.

[11] de Kowalewski, D. G.; Kowalewski, V. J.; Contreras, R. H.; Díez, E.; Esteban, A., *Magn. Reson. Chem.*, **1998**, *36*, 336.

[12] Tormena, C. F.; Rittner, R.; Contreras, R. H.; Peralta, J. E., *J. Phys. Chem. A*, **2004**, *108*, 7762.

[13] Eliel, E. L.; Giza, G. A., *J. Org. Chem.,* **1968**, *33*, 3754.

[14] Lemieux, R. U.; Pavia, A. A.; Marti, J. C.; Watanabe, K. A., *Can. J. Chem.* **1969**, *47*, 4427.

[15] Zaccari, D. G.; Snyder, J. P.; Peralta, J. E.; Taurian, O. E.; Contreras, R. H., V. Barone, *Molec. Phys.*, **2002**, *100*, 705.

[16] Zaccari, D. G.; Barone, V.; Peralta, J. E.; Contreras, R. H.; Taurian, O. E.; Díez, E.; Esteban, A., *Int. J. Mol. Sci.*, **2003**, *4*, 93.

[17] Sychrovský, V.; Gräfenstein, J.; Cremer, D., *J. Chem. Phys*., **2000**, *113*, 3530.

[18] Helgaker, T.; Watson, M.; Handy, N. C., *J. Chem. Phys*., **2000**, *113*, 9402.

[19] Gaussian 03, Revision B.05, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C. and Pople, J. A. *Gaussian 03, Revision B.05* **2003**, Gaussian, Inc., Pittsburgh PA.

[20] Lee, C.; Yang, W.; Parr, R.G.; *Phys. Rev.*, *B* **1988**, *37*, 785.

[21] Becke, A. D., *Phys. Rev. A,* **1988**, *38,* 3098.

[22] Becke, A. D., *J. Chem. Phys*., **1993**, *98*, 5648.

[23] Barone, V., *J. Chem. Phys*., **1994**, *101*, 6834.

[24] Peralta, J. E.; Scuseria, G. E. ; Cheeseman, R.; Frisch, M. J., *Chem. Phys. Lett.*, **2003**, *375*, 452.

[25] Cancs, M. T.; Mennucci, B.; Tomasi, J., *J. Chem. Phys*., **1997**, *107*, 3032.

[26] Cossi, M.; Barone, V.; Mennuci, B.; Tomasi, J., *Chem. Phys. Lett*., **1998**, *286*, 253.

[27] Mennucci, B.; Tomasi, J., *J. Chem.. Phys*., **1997**, *106*, 5151.

[28] Reed, A. E.; Curtiss, L. A.; Weinhold, V., *Chem. Rev.*, **1988**, *88*, 899.

[29] NBO version 3.1; Glendening, E. D.; Reed, A. E.; Carpenter, J. E.; Weinhold, F. (Included in the GAUSSIAN 03 package of programs).

[30] Ernst, L.; Wray, V.; Chertkov, V. A.; Sergeyev, N. M., *J. Magn. Reson.*, **1977,** *25*, 123.

[31] Biekofsky, R. R.; Pomilio, A. B.; Contreras, R. H., *J. Mol. Struct. Theochem*, **1990**, *210*, 211.

[32] Contreras, R. H.; Peralta, J. E.; Giribet, C. G.; Ruiz de Azúa, M. C. ; Facelli, J. C., *Ann. Rep. NMR Spectrosc.*, **2000**, *41*, 55.

[33] Contreras, R. H. ; Barone, V.; Facelli, J. C.; Peralta, J. E., *Ann. Reps. NMR Spectrosc*., **2003**, *51*, 167.

[34] Lutnæs, O. B.; Ruden, T. A.; Helgaker, T.; Ruud, K., *J. Chem. Phys*. **2003,** *118*, 9572.

[35] Lutnæs, O. B.; Ruden, T. A.; Helgaker, T., *Magn. Reson. Chem*., **2004,** *42*, S117.

[36] Wigglesworth, R. D.; Raynes, W. T.; Kirpekar, S.; Oddershede, J.; Sauer, S. P. A., *J. Chem. Phys*., **2000,** *112*, 3735.

[37] Barfield, M.; Chakrabarti, B., *Chem. Rev.*, **1969**, *69*, 757.