

Fluorine–Fluorine Spin–Spin Coupling Constants in Aromatic Compounds: Correlations with the Delocalization Index and with the Internuclear Separation

Norberto Castillo, Chérif F. Matta, and Russell J. Boyd*

Department of Chemistry, Dalhousie University, Halifax, Nova Scotia, Canada B3H 4J3

Received September 30, 2004

This paper describes a new empirical approach for the evaluation of fluorine–fluorine spin–spin coupling constants (J_{FF}) in aromatic compounds. The correlations between J_{FF} and the delocalization index calculated within the framework of the theory of atoms in molecules (AIM) and with the fluorine–fluorine internuclear separation are investigated. Both the internuclear separation and the delocalization index are found to be highly correlated with J_{FF} . A regression model in which the experimental J_{FF} coupling constant is fitted exponentially to the internuclear separation and linearly to the delocalization index yields a squared correlation coefficient as high as 0.96 for a data set consisting of 33 coupling constants spread over a range of 85 Hz.

INTRODUCTION

In view of its importance in the elucidation of long-range interactions in organic and bioorganic rigid molecules the fluorine–fluorine coupling constant (J_{FF}) is a particularly interesting property to calculate (see, for example, Gakh et al.¹ and references therein). In general, the Fermi contact interaction is the dominant mechanism by which spin information is transmitted between nuclei with spin $I = 1/2$ (such as ^1H , ^{13}C , ^{15}N , and ^{19}F) and thus determines, in large part, the magnitude of their J -coupling interaction (also known as scalar spin coupling).^{2–4} The electron density at or near such a nucleus is perturbed to favor an antiparallel orientation of electron spins with respect to the spin of the nucleus. In other words, near a spin $1/2$ nucleus, there is a net excess of α - or β -spin density. This spin information is then transmitted through space by means of the mechanism of exchange, which embodies the Pauli exclusion principle. When a second nucleus senses this perturbation in its immediate vicinity, it responds by adopting either a parallel or antiparallel orientation, which differ in energy, and thus leads to an energy splitting observed as the J -coupling constant. The coupling constant can be positive or negative depending on whether the state with antiparallel or parallel nuclear spins is the lower in energy, respectively.

In general, the calculation of J -coupling constants is not trivial.^{5–7} The prediction of NMR properties, especially coupling constants, usually requires very large basis sets with at least triple- ζ quality and supplemented with diffuse and polarization functions. One important factor to consider is the behavior of the basis set near and at the nuclei, since that is where the Fermi contact interaction takes place. The electron density exhibits marked maxima at the positions of the nuclei, maxima that constitute cusps if one neglects the finite nuclear size, as is the common practice in quantum chemistry. The presence of nuclear cusps poses a challenge to contracted Gaussian basis functions and necessitates the use of a large number of primitives or the use of Slater-type

basis functions. This problem is encountered specifically in the calculation of spin–spin coupling and does not arise for instance in the calculation of nuclear shielding constants.⁵ The convergence of spin–spin coupling constants with the extension of the basis set has been analyzed at the multi-configurational self-consistent-field level for HF and H₂O. It was found that only correlation-consistent basis sets augmented with tight s functions converge smoothly and yield accurate indirect nuclear spin–spin couplings.⁸ Additional challenges arise from the high computational costs associated with the calculation of the other interactions contributing to the scalar coupling constant, namely, the paramagnetic spin–orbit, diamagnetic spin–orbit, and spin–dipolar interactions.^{5,7}

The calculation of the coupling constants involving fluorine is generally more problematic than for other nuclei in view of the possible relative importance of contributions other than the Fermi contact interactions in some of its compounds.^{9–11} These difficulties led several groups to propose empirical approaches for the fast estimation of J -coupling constants such as J_{FF} correlations with distance^{12,13} or with properties derived from the topology of the electron density.¹⁴ The primary goal of this paper is to describe an alternative empirical model, but with foundations in physics, which has the potential to provide a fast prediction of the J_{FF} coupling constants. In the present paper we use the standard Pople basis sets that behave well *on average* (as opposed to specifically at the position of the nuclei), and thus we circumvent a major problem in the calculation of spin–spin coupling constants.

THEORY

The extent of spatial localization or delocalization of electrons has long been known to be determined by the Fermi hole.¹⁵ The Fermi hole is the physical manifestation of the Pauli exclusion principle, it measures the extent of same-spin density exclusion at a point \mathbf{r}_2 given a reference electron is present at \mathbf{r}_1 .¹⁵ If the density of the Fermi hole is localized near the reference point, then all other same-spin electrons

* Corresponding author phone: (902)494-8883; fax: (902)494-1310; e-mail: russell.boyd@dal.ca.

are excluded from this region and the reference electron is *localized* at \mathbf{r}_1 . In contrast, if the Fermi hole is spread into a region around \mathbf{r}_2 far from \mathbf{r}_1 , the location of the reference electron, then there is a significant reduction in the probability of finding other same-spin electrons in the vicinity of \mathbf{r}_2 , which implies that the reference electron is “smeared” or *delocalized* between \mathbf{r}_1 and \mathbf{r}_2 . In Hartree–Fock (H–F) theory, the Fermi hole is equal to the exchange density (the quantity in the curly brackets in eq 1) divided by the corresponding spin-density $\rho^\sigma(\mathbf{r})$. Thus, the Fermi hole is given by:¹⁵

$$h^\sigma(\mathbf{r}_1, \mathbf{r}_2) = - \sum_i \sum_j \{ \phi_i^*(\mathbf{r}_1) \phi_j(\mathbf{r}_1) \phi_j^*(\mathbf{r}_2) \phi_i(\mathbf{r}_2) \} / \rho^\sigma(\mathbf{r}_1) \quad (1)$$

where $\sigma = \alpha$ or β , the double sum runs over σ -spin-orbitals ϕ . The Fermi hole when integrated over all space of the second electron yields $-1e$ corresponding to the complete removal of one electronic charge. At $\mathbf{r}_1 = \mathbf{r}_2$ this quantity reduces to $-\rho^\sigma(\mathbf{r}_1)$ and thus excludes same-spin density from the position of electron 1. When the exchange density ($\rho^\sigma(\mathbf{r}_1)h^\sigma(\mathbf{r}_1, \mathbf{r}_2)$) is integrated over all space with respect to the coordinates of both electrons it yields $-N^\sigma$, the negative of the total number of σ -electrons (i.e., the total Fermi correlation of σ -spin electrons). If now the integration is performed over a bounded region of space, it will yield the total Fermi correlation within this region denoted by $F^\sigma(A, A)$ and given by:¹⁵

$$\begin{aligned} F^\sigma(A, A) &= \int_A d\mathbf{r}_1 \int_A d\mathbf{r}_2 \rho^\sigma(\mathbf{r}_1) h^\sigma(\mathbf{r}_1, \mathbf{r}_2) \\ &= - \sum_i \sum_j \int_A d\mathbf{r}_1 \int_A d\mathbf{r}_2 \{ \phi_i^*(\mathbf{r}_1) \phi_j(\mathbf{r}_1) \phi_j^*(\mathbf{r}_2) \phi_i(\mathbf{r}_2) \} \\ &= - \sum_i \sum_j S_{ij}^2(A) \end{aligned} \quad (2)$$

where $S_{ij}(A) = S_{ji}(A)$ denotes the overlap of a pair of spin-orbitals over a region A . The limiting value of $F^\sigma(A, A)$ is $-N^\sigma(A)$, the negative of the σ -spin population of A implying a complete localization of N σ -electrons within A since these electrons do not exchange with electrons outside A . The total number of electrons localized within A is called the *localization index*, $\lambda(A)$, and is given by:¹⁶

$$\lambda(A) = |F^\sigma(A, A)| + F^\beta(A, A) \quad (3)$$

The limit of total localization, where the localization index equals the total electron population contained within A , i.e., $\lambda(A) = N(A)$, can never be reached as the electrons will always be delocalized to some extent outside of region A .

The measure of electron delocalization from region A to region B is determined by:¹⁶

$$\begin{aligned} F^\sigma(A, B) &= \int_A d\mathbf{r}_1 \int_B d\mathbf{r}_2 \rho^\sigma(\mathbf{r}_1) h^\sigma(\mathbf{r}_1, \mathbf{r}_2) \\ &= - \sum_i \sum_j \int_A d\mathbf{r}_1 \int_B d\mathbf{r}_2 \{ \phi_i^*(\mathbf{r}_1) \phi_j(\mathbf{r}_1) \phi_j^*(\mathbf{r}_2) \phi_i(\mathbf{r}_2) \} \\ &= - \sum_i \sum_j S_{ij}(A) S_{ji}(B) \end{aligned} \quad (4)$$

in which it is clear that $F^\sigma(A, B) = F^\sigma(B, A)$. The total extent of exchange between two regions A and B is given by the

delocalization index $\delta(A, B)$ which measures the number of electron pairs shared between A and B and which is given by:¹⁶

$$\delta(A, B) = 2|F^\alpha(A, B)| + 2|F^\beta(A, B)| \quad (5)$$

When these ideas are used in conjunction with the theory of atoms in molecules (AIM), a theory which defines atomic regions (basins) in a molecule unambiguously, one can then quantify localization of electrons within an atom or between two atoms in a molecule.¹⁶ The AIM theory is well-known and has been extensively reviewed on a number of occasions,^{17–21} and we only recap the quantum condition defining the boundary of an atomic basin in a molecule given by:¹⁷

$$\nabla \rho(\mathbf{r}) \cdot \mathbf{n}(\mathbf{r}) = 0, \quad \text{for all } \mathbf{r} \text{ on the surface} \quad (6)$$

where $\nabla \rho(\mathbf{r})$ is the gradient of the electron density ρ , and $\mathbf{n}(\mathbf{r})$ is a vector normal to the surface.

The relationship between the hydrogen-to-hydrogen delocalization index $\delta(\text{H}, \text{H})$ and the experimental proton–proton spin-coupling constants (J_{HH}) has been recently investigated.²² It has been shown that J_{HH} is linearly correlated with $\delta(\text{H}, \text{H})$. The theoretical basis for this correlation is the proportionality of $\delta(\text{H}, \text{H})$ determined over the volume of two *hydrogen atoms* to the product of the electron spin densities at the positions of the two *protons*, a product proportional to the coupling constant. Thus, the expression relating the Fermi contact contribution to the coupling constant between two nuclei $J_{nn'}$ to the exchange between the positions of the two nuclei is given by:²³

$$J_{nn'} = - \frac{2}{3h} \left(\frac{16\pi\beta\hbar}{3} \right)^2 \gamma_n \gamma_{n'} \frac{1}{\Delta E} \times \sum_i \sum_j \langle \phi_i(\mathbf{r}_1) \delta(\mathbf{r}_{1n}) \phi_j(\mathbf{r}_1) \rangle \langle \phi_j(\mathbf{r}_2) \delta(\mathbf{r}_{2n'}) \phi_i(\mathbf{r}_2) \rangle \quad (7)$$

in standard notation, where $\delta(\mathbf{r}_{kn})$ is a Dirac δ function which picks out the value at $\mathbf{r}_{kn} = 0$ (i.e., at the position of nucleus n) in any integration over the coordinates of the k th electron. The contribution described by eq 7 is termed the “contact term” because it is evaluated at the nuclei.²³

If, as in the case of hydrogen, one assumes that density at a fluorine nucleus is, on average, proportional to the density within the basin of the fluorine atom one can then write:²²

$$\begin{aligned} \langle \phi_i(\mathbf{r}_1) \delta(\mathbf{r}_{1n}) \phi_j(\mathbf{r}_1) \rangle \langle \phi_j(\mathbf{r}_2) \delta(\mathbf{r}_{2n'}) \phi_i(\mathbf{r}_2) \rangle &\propto \\ \langle \phi_i(\mathbf{r}_1) \phi_j(\mathbf{r}_1) \rangle_F \langle \phi_j(\mathbf{r}_2) \phi_i(\mathbf{r}_2) \rangle_{F'} &\propto S_{ji}(F) S_{ij}(F') \end{aligned} \quad (8)$$

Expression 8 is a reasonable approximation in the case of proton spin–spin coupling since the basin of the hydrogen atom is primarily described by spherically symmetric s -functions, which is not the case for the fluorine atom. Thus, there is no a priori reason to assume that eq 8 will apply to fluorine or to any atom other than hydrogen. Quite to the contrary, one would expect that the approximation in eq 8 will generally fail for non-hydrogen atoms due to the presence of basis functions with nonzero angular momentum in a primary (rather than polarizing) role. These nonzero angular momentum functions increase the contributions of the other terms responsible for the J -coupling, namely, the paramagnetic spin–orbit, the diamagnetic spin–orbit, and

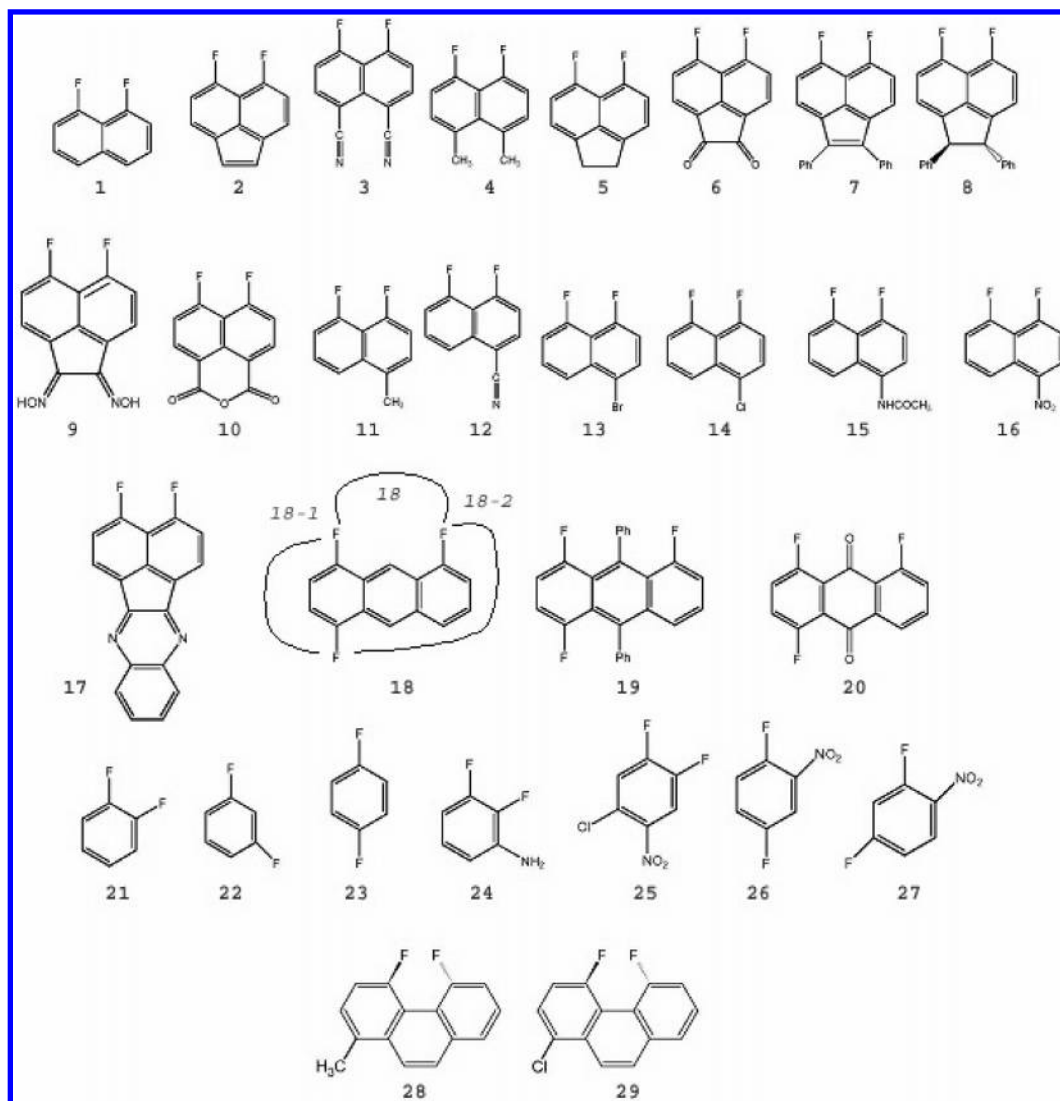


Figure 1. Chemical structures of the compounds constituting the data set employed in this study. For compounds **18**–**20**, three different F–F coupling interactions exist. These are labeled on the chemical structure of **18** in italics, and similar labeling convention applies to **19** and **20**. The labeling of these interactions corresponds to that used in Table 1.

the spin–dipolar interactions. It is therefore quite surprising that the approximation in eq 8 appears to hold for fluorine–fluorine coupling, as will be shown phenomenologically in this paper.

The correlation between the experimental J_{FF} and $\delta(\text{F},\text{F}')$ was studied for the 29 aromatic fluorine derivatives (and 35 coupling constants) shown in Figure 1. While strictly speaking, the above formalism only acquires physical meaning within the context of H–F theory and can be readily extended to configuration interaction (CI) theories,¹⁶ we have used here delocalization indexes calculated from Kohn–Sham (KS)²⁴ orbitals. It has been shown on a number of occasions that delocalization indexes obtained using KS orbitals exhibit similar numerical values and trends as those obtained from H–F and are systematically slightly higher than those obtained from CI wave functions. (See Poater et al.²⁵ and references therein.)

COMPUTATIONAL METHOD

The geometries of all molecules have been fully optimized at the B3LYP/6-31G(*d*) level. Single-determinant KS “wave-functions” were obtained at the B3LYP/6-311++G(*d,p*)/

B3LYP/6-31G(*d*) level. The resulting wave functions were then integrated using the PROAIM suite of programs^{26,27} to obtain the atomic overlap matrices, which were then processed using AIMDELOC²⁸ to obtain the delocalization indexes. All electronic structure calculations were performed using the Gaussian 03 package.²⁹ Statistical analyses were carried out using the Minitab³⁰ and the Origin³¹ packages.

RESULTS AND DISCUSSION

Large spin–spin coupling between two fluorine atoms separated by more than three bonds but which are spatially close is known as “through space coupling”. Ernst and Ibrom proposed that the magnitude of J_{FF} is related to the distance of separation of the two coupled fluorine atoms (d_{FF}) in a simple way:¹²

$$J_{\text{FF}} \approx ae^{bd_{\text{FF}}} \quad (9)$$

where a and b are the fitting constants, and $b < 0$. Mallory et al.¹³ reported a strong correlation ($r^2 = 0.991$) of the form of eq 9 for several 1,8-difluoronaphthalenes. These workers included 13 data points in the fitting, all chosen from a set

of 18 closely related derivatives of 1,8-difluoronaphthalenes. Significantly, however, five compounds that could not be fitted to the above equation were excluded from the fitting. The authors argue that the origin of this correlation is the sidewise overlap of the fluorine 2p orbitals.¹³ (See also ref 32.) In a more recent study, Peralta et al.¹⁰ concluded that the inability of fittings to eq 9 to accommodate these five outliers is due to significant contributions from terms other than the Fermi contact term, especially the paramagnetic spin–orbit coupling. These authors predict that enlarging the data set is not likely to improve the regression model described in eq 9.¹⁰

A different approach was recently adopted by Alkorta and Elguero,¹⁴ who relied on the theory of atoms in molecules to predict J_{FF} coupling constants from the total electron density at the bond critical point (ρ_{BCP}). These workers report a strong linear correlation between the coupling constants and ρ_{BCP} ($r^2 = 0.983$), but their expression also includes a term proportional to the cosine of the dihedral angle F–C···C–F as a second regressor. Alkorta and Elguero¹⁴ used a very small data set in their regression (only 6 data points) leading to an elevated ratio of parameters to data points (1:3). Their approach, while certainly very appealing, depends on the presence of a bond path linking the two fluorine atoms, which often occurs in these compounds when the F–F distance and angular orientations are favorable for F–F bonding. It is not clear how one can use their expression when there is no bond path linking the nuclei in question. In contrast, the delocalization index discussed in the Theory section has a nonvanishing value between any two atoms in a molecule whether bonded or not (i.e., whether they share a bond path and an interatomic zero-flux surface (eq 6) or not). In the case when two atoms do share a bond path, the delocalization index has been shown to provide the basis for the definition of a bond order.^{16,33,34} The delocalization index between atoms sharing a bond path has also been shown to be highly correlated with several bond properties including ρ_{BCP} .³³

In this paper, we follow a new empirical approach that incorporates and extends the data sets used in previous related studies.¹³ Thus we included Mallory et al.'s¹³ set of 1,8-difluoronaphthalenes, benzene derivatives, compounds with three and four fused rings including those where the coupling occurs through an intervening phenyl ring or oxygen atom³⁵ (**19** and **20**, respectively).

We first tested the purely geometrical correlation. We fitted 35 data points to an expression of the same form of eq 9 and obtained the following:

$$J_{\text{FF}} = 7.897 \times 10^7 e^{-5.461 \times d_{\text{FF}}} \quad (10)$$

where J_{FF} is in Hz and F–F interatomic distances are in Å and which yields a calculated–experimental linear relationship with $r^2 = 0.94$, $\text{SD} = 8.55$, and an average absolute deviation of 7.25 Hz. Figure 2a displays the correlation between J_{FF} calculated from eq 10 and experimental F–F distances. As one can see from the figure and the statistical indicators, the correlation is excellent. The ability of distance alone to predict the experimental values with such a high correlation coefficient is quite surprising, as mentioned at the beginning of this section, due to the contribution of terms other than the Fermi term in the coupling interaction.¹⁰

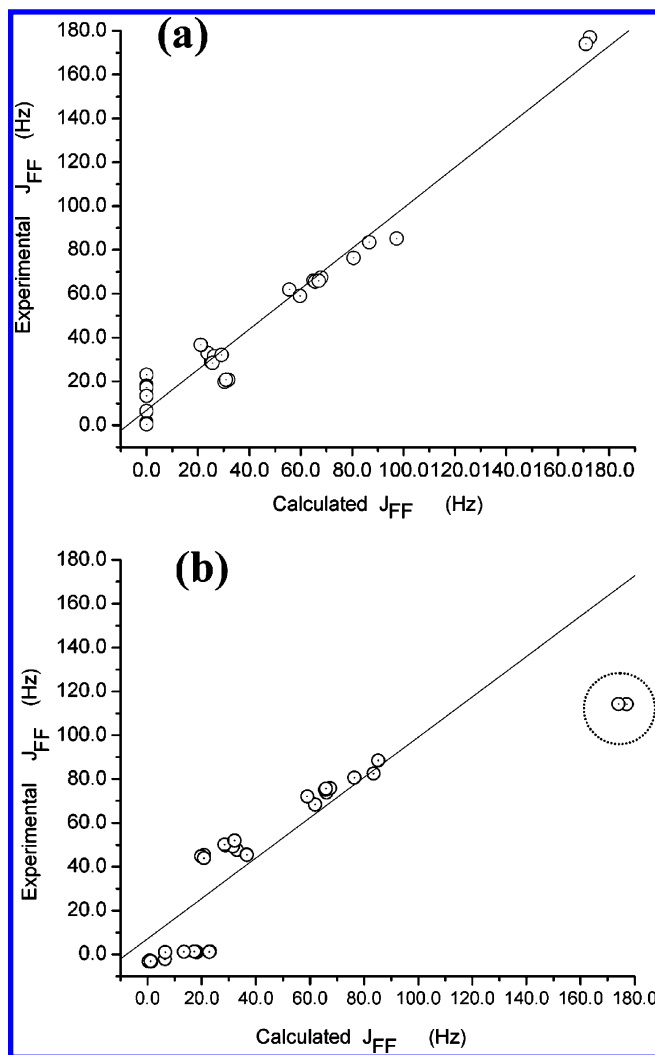


Figure 2. (a) Plot of experimental J_{FF} coupling constants vs those calculated from eq 10, which uses the F–F distance (d_{FF}) as the sole predictor. The plot corresponds to the following fit: $J_{\text{FF}}^{\text{Exptl.}} = 6.89 + 0.92 \times J_{\text{FF}}^{\text{Calc.}}$. [$r^2 = 0.96$, $\text{SD} = 8.35$, $n = 35$]. (b) Plot of experimental J_{FF} coupling constants vs those calculated from eq 12, which uses the delocalization indexes ($\delta(\text{F},\text{F}')$) as the sole predictor (outliers are encircled). The plot corresponds to the following fit: $J_{\text{FF}}^{\text{Exptl.}} = 0.37 + 1.00 \times J_{\text{FF}}^{\text{Calc.}}$. [$r^2 = 0.77$, $\text{SD} = 20.58$, $n = 35$].

We have also attempted the correlation of J_{FF} coupling constants with the delocalization indexes, not knowing a priori whether the approximation embodied in eq 8 would hold in the case of the F–F coupling. If the approximation holds as in the case of proton–proton coupling, then one expects a linear correlation of the form:²²

$$J_{\text{FF}} \approx a + b \times \delta(\text{F},\text{F}') \quad (11)$$

where a and b are constants. Fitting our 35 data points to the linear model of eq 11 leads to

$$J_{\text{FF}} = -3.284 + 1303 \times \delta(\text{F},\text{F}') \quad (12)$$

where J_{FF} is in Hz, $r^2 = 0.77$, $\text{SD} = 20.58$, and the mean absolute deviation between the calculated and experimental J_{FF} coupling constants is 14.66 Hz. The presence of two outlying data points (see Figure 2b) reduces the overall quality of the fit. If one excludes the two outliers from the correlation, one obtains a regression equation ($a = 3.696$, b

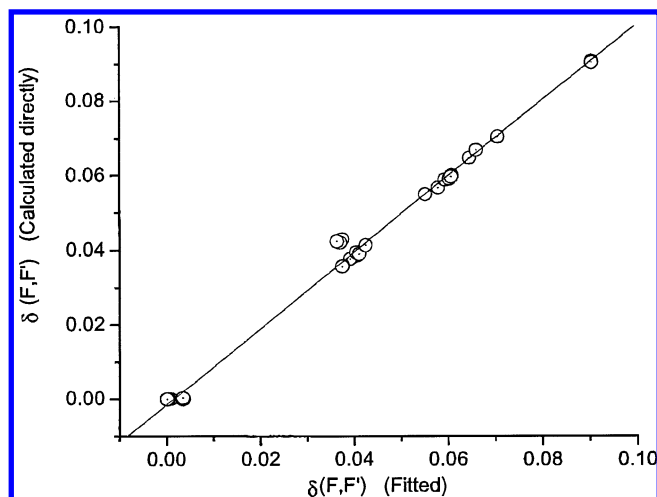


Figure 3. Delocalization indices ($\delta(F,F')$) calculated directly and those obtained through the exponential fit with distance (eq 13). $\delta(F,F') = -0.0015 + 1.0232 \times \delta(F,F')^{\text{fitted}}$ [$r^2 = 1.00$, SD = 0.0022, $n = 35$].

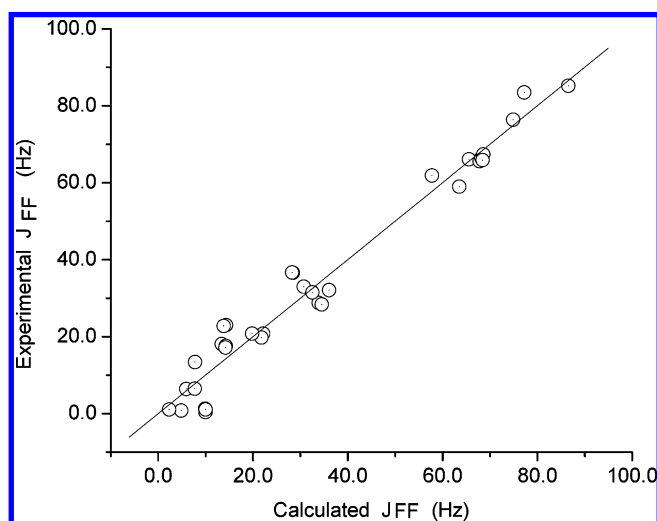


Figure 4. Plot of experimental J_{FF} coupling constants vs those calculated from eq 14, which uses both the F–F distance (d_{FF}) and the delocalization indexes ($\delta(F,F')$) as predictors. The plot corresponds to the following fit: $J_{FF}^{\text{Exptl.}} = 0.02 + 1.00 \times J_{FF}^{\text{Calc.}}$ [$r^2 = 0.96$, SD = 5.15, $n = 33$].

= 959.953) for which the fit is improved substantially with higher correlation coefficient, a standard deviation cut by half ($r^2 = 0.85$, SD = 10.38, $n = 33$), and an average absolute deviation of 8.35 Hz. The two outliers are data collected from difluorophenanthrene derivatives **28** and **29** where the two fluorine atoms are located in the bay region. In view of the larger size of fluorine (compared to hydrogen), these molecules are highly twisted to accommodate the two fluorine atoms in the bay region. The lack of space around the fluorine is likely to cause significant departure from spherical symmetry of its electron density distribution. When the electron density of an atom adopts a nonspherical distribution, the basin integral can no longer be assumed to be proportional to the density at the nucleus. Thus, in cases of crowded fluorine atoms, the working assumption behind eq 11 (namely, eq 8) is no longer valid, which provides an explanation for the irregular behavior of the coupling constants of compounds such as **28** and **29**.

Table 1. Comparison of Calculated and Experimental J_{FF} Spin Coupling Constants in Hz, Listed along with the Internuclear Separations in Å, and the Delocalization Indexes

F–F interaction	d_{FF}	$10^2 \times \delta(F,F')$	$J_{FF}^{\text{Exptl. } a}$	$J_{FF}^{\text{Calc. } b}$	residuals
1	2.5810	5.78	59.00	63.51	4.51
2	2.7721	3.74	36.70	28.24	8.46
3	2.5128	6.59	83.50	77.22	6.28
4	2.4916	7.04	85.20	86.53	1.33
5	2.7357	4.10	28.40	34.50	6.10
6	2.7314	4.03	31.50	32.53	1.03
7	2.7702	3.75	36.60	28.43	8.17
8	2.7394	4.06	28.80	33.86	5.06
9	2.7120	4.24	32.10	36.05	3.95
10	2.5943	5.50	61.90	57.74	4.16
11	2.5638	6.02	65.60	67.79	2.19
12	2.5655	5.92	66.10	65.57	0.53
13	2.5573	6.07	67.40	68.58	1.18
14	2.5589	6.05	66.50	68.17	1.67
15	2.5600	6.06	65.90	68.43	2.53
16	2.5262	6.44	76.40	74.89	1.51
17	2.7497	3.90	33.00	30.71	2.29
18 ^c	4.9276	0.02	1.10	2.31	1.21
18-1 ^c	5.4703	0.34	22.80	13.82	8.98
18-2 ^c	7.3578	0.01	1.10	9.99	8.89
19 ^c	5.1923	0.09	6.40	5.91	0.49
19-1 ^c	5.4523	0.36	23.00	14.30	8.70
19-2 ^c	7.4881	0.00	1.30	9.89	8.59
20 ^c	5.2054	0.04	0.80	4.85	4.05
20-1 ^c	5.4290	0.33	18.10	13.40	4.70
20-2 ^c	7.4983	0.01	0.40	9.96	9.56
21	2.6964	3.73	20.80	22.16	1.36
22	4.7034	0.33	6.50	7.71	1.21
23	5.4435	0.36	17.60	14.27	3.33
24	2.7049	3.69	19.80	21.76	1.96
25	2.7016	3.62	20.80	19.81	0.99
26	5.4438	0.36	17.20	14.19	3.01
27	4.6706	0.34	13.40	7.75	5.65
28 ^d	2.3884	9.02	174.0		
29 ^d	2.3868	9.02	177.0		

^a Experimental values were collected from refs 13 and 35–37.

^b Calculated according to eq 14. ^c More than one J_{FF} coupling interaction exists in the molecule. Labels of these interactions are indicated in Figure 1. ^d Outliers, not included in the fitting, see text.

Within the exponential model, the correlation with internuclear distance provides better statistics than the correlation with the delocalization index. The two models, however, are not independent (though not collinear) and one finds:

$$\delta(F,F') = 29.337 \times e^{-2.422 \times d_{FF}} \quad (13)$$

in which distances are in Å. Figure 3 shows the correlation between the delocalization index calculated directly and that calculated using the fit in eq 13.

Using 33 data points (after excluding the two outliers around $J_{FF} \sim 175$) and combining the two regressors into one model leads to

$$J_{FF} = 10.5 - 1216e^{-d_{FF}} + 2509 \times \delta(F,F'), \quad (14)$$

which is exponential with respect to distance and linear with respect to the delocalization indexes, and where J_{FF} is in Hz and d_{FF} is in Å. Equation 14 leads to a good agreement between calculated and experimental J_{FF} as can be seen from the statistics, Table 1, and Figure 4 and a relatively small mean absolute deviation (4.05 Hz).

CONCLUSIONS

Contrary to expectations, both the internuclear distance and the delocalization index yield strong correlations with the experimental J_{FF} coupling constants, except in compounds with crowded fluorine atoms. The correlations described in this paper span a wide range of coupling constants (84 Hz) and a variety of aromatic compounds, including ones with phenyl groups or oxygen atoms intervening between the coupled fluorine atoms and also including fluorines that are meta and para with respect to each other in a ring. When the two descriptors are combined, they yield a regression model capable of accurately reproducing the experimental J_{FF} coupling constants.

ACKNOWLEDGMENT

The authors acknowledge the Natural Sciences and Engineering Research Council of Canada (NSERC) for funding. The authors also acknowledge the Killam Trusts for a Killam Postdoctoral Fellowship to one of them (C.F.M.).

REFERENCES AND NOTES

- Gakh, Y. G.; Gakh, A. A.; Gronenborn, A. M. Fluorine as an NMR probe for structural studies of chemical and biological systems. *Magn. Reson. Chem.* **2000**, *38*, 551–558.
- Ramsey, N. F. Electron coupled interactions between nuclear spins in molecules. *Phys. Rev.* **1953**, *91*, 303–307.
- Stephen, M. J. A variational method for calculating nuclear spin-spin interactions in molecules. *Proc. R. Soc. (London) A* **1957**, *243*, 274–280.
- Wilkens, S. J.; Westler, W. M.; Markley, J. L.; Weinhold, F. Natural J-coupling analysis: interpretation of scalar J-couplings in terms of natural bond orbitals. *J. Am. Chem. Soc.* **2001**, *123*, 12026–12036.
- Helgaker, T.; Jaszuński, M.; Ruud, K. Ab initio methods for the calculation of NMR shielding and indirect spin–spin coupling constants. *Chem. Rev.* **1999**, *99*, 293–352.
- Watson, M. A.; Salek, P.; Macak, P.; Jaszuński, M.; Helgaker, T. The calculation of indirect nuclear spin–spin coupling constants in large molecules. *Chem. Eur. J.* **2004**, *10*, 4627–4639.
- Alkorta, I.; Elguero, J. Review on DFT and *ab initio* calculations of scalar coupling constants. *Int. J. Mol. Sci.* **2003**, *4*, 64–92.
- Helgaker, T.; Jaszuński, M.; Ruud, K.; Górska, A. Basis-set dependence of nuclear spin–spin coupling constants. *Theor. Chem. Acc.* **1998**, *99*, 175–182.
- Peralta, J. E.; Contreras, R. H.; Snyder, J. P. Natural bond orbital dissection of fluorine–fluorine through-space NMR coupling (J_{F} , F) in polycyclic organic molecules. *Chem. Commun.* **2000**, 2025–2026.
- Peralta, J. E.; Barone, V.; Contreras, R. H.; Zaccari, D. G.; Snyder, J. P. Through-bond and through-space J_{FF} spin–spin coupling in peridifluoronaphthalenes: Accurate DFT evaluation of the four contributions. *J. Am. Chem. Soc.* **2001**, *123*, 9162–9163.
- San Fabián, J.; Westra Hoekzema, A. J. A. Vicinal fluorine–fluorine coupling constants: Fourier analysis. *J. Chem. Phys.* **2004**, *121*, 6268–6276.
- Ernst, L.; Ibrom, K. A new quantitative description of the distance dependence of through-space ^{19}F , ^{19}F spin–spin coupling. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1881–1882.
- Mallory, F. B.; Mallory, C. W.; Butler, K. E.; Lewis, M.-B.; Qian Xia, A.; Luzik, E. D. Jr.; Fredenburgh, L. E.; Ramanjulu, M. M.; Van, Q. N.; Franci, M. M.; Freed, D. A.; Wray, C. C.; Hann, C.; Nerz-Stormes, M.; Carroll, P. J.; Chirlian, L. E. Nuclear spin–spin coupling via nonbonded interactions. 8. The distance dependence of through-space fluorine–fluorine coupling. *J. Am. Chem. Soc.* **2000**, *122*, 4108–4116.
- Alkorta, I.; Elguero, J. Fluorine–fluorine interactions: NMR and AIM analysis. *Struct. Chem.* **2004**, *15*, 117–120.
- Bader, R. F. W.; Stephens, M. E. Spatial localization of the electronic pair and number distributions in molecules. *J. Am. Chem. Soc.* **1975**, *97*, 7391–7399.
- Fradera, X.; Austen, M. A.; Bader, R. F. W. The Lewis model and beyond. *J. Phys. Chem. A* **1999**, *103*, 304–314.
- Bader, R. F. W. *Atoms in Molecules: A Quantum Theory*; Oxford University Press: Oxford, U.K., 1990.
- Bader, R. F. W. A quantum theory of molecular structure and its applications. *Chem. Rev.* **1991**, *91*, 893–928.
- Bader, R. F. W.; Nguyen-Dang, T. T. Quantum theory of atoms in molecules—Dalton revisited. *Adv. Quantum Chem.* **1981**, *14*, 63–123.
- Bader, R. F. W. 1997 Polanyi Award Lecture: Why are there atoms in chemistry?. *Can. J. Chem.* **1998**, *76*, 973–988.
- Popelier, P. L. A. *Atoms in Molecules: An Introduction*; Prentice Hall: London, 2000.
- Matta, C. F.; Hernández-Trujillo, J.; Bader, R. F. W. Proton spin–spin coupling and electron delocalisation. *J. Phys. Chem. A* **2002**, *106*, 7369–7375.
- Pople, J. A.; Schneider, W. G.; Bernstein, H. J. *High-Resolution Nuclear Magnetic Resonance*; McGraw-Hill Book Co. Inc.: New York, 1959.
- Kohn, W.; Sham, L. J. Self consistent equations including exchange and correlation effects. *Phys. Rev. A* **1965**, *140* (4A), 1133–1138.
- Poater, J.; Solà, M.; Duran, M.; Fradera, X. The calculation of electron localization and delocalization indices at the Hartree–Fock, density functional and post-Hartree–Fock levels of theory. *Theor. Chem. Acc.* **2002**, *107*, 362–371.
- Bader, R. F. W. AIMPAC; <http://www.chemistry.mcmaster.ca/aimpac/>.
- Biegler-König, F. W.; Bader, R. F. W.; Tang, T.-H. “Calculation of the average properties of atoms in molecules. II. *J. Comput. Chem.* **1982**, *13*, 317–328.
- Matta, C. F. AIMDELOC: Program to calculate AIM localization and delocalization indices (QCPE0802); Quantum Chemistry Program Exchange, Indiana University, 2001; (<http://qcpe.chem.indiana.edu/>).
- 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.; Pople, J. A. *Gaussian 03*, revision B.01; Gaussian, Inc.: Pittsburgh, PA, 2003.
- Minitab. MINITAB, Release 13 for Windows; Minitab Inc.: 2000.
- Microcal. Origin v.6.0; Microcal Software, Inc.: 1999.
- Mallory, F. B. A theory regarding the role of lone-pair interactions in “through-space” fluorine–fluorine nuclear spin–spin coupling. *J. Am. Chem. Soc.* **1973**, *95*, 7747–7752.
- Matta, C. F.; Hernández-Trujillo, J. Bonding in polycyclic aromatic hydrocarbons in terms of the electron density and of electron delocalization. *J. Phys. Chem. A* **2003**, *107*, 7496–7504.
- Austen, M. A. A New Procedure for Determining Bond Orders in Polar Molecules, with Applications to Phosphorus and Nitrogen Containing Systems. Ph.D. Thesis, McMaster University, Hamilton, ON, Canada, 2003.
- Mallory, F. B.; Mallory, C. W.; Baker, M. B. Nuclear spin–spin coupling via nonbonded interactions. 6. F–F Coupling through an intervening phenyl group. *J. Am. Chem. Soc.* **1990**, *112*, 2577–2581.
- Berger, S.; Braun, S.; Kalinowski, H. *NMR Spectroscopy of the Non-Metallic Elements*; John Wiley & Sons: New York, 1997.
- Mallory, F. B.; Mallory, C. W.; Ricker, W. M. Nuclear spin–spin coupling via nonbonded interactions. 4. F–F and H–F coupling in substituted benzo[*a*]phenanthrenes. *J. Org. Chem.* **1985**, *50*, 457–461.

CI0497051