19F-NMR Diastereotopic Signals in Two N-CHF<sub>2</sub> Derivatives of (4S,7R)-7,8,8-Trimethyl-4,5,6,7-
tetrahydro-4,7-methano-2H-indazole †

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Abstract: In this paper, we report the anisochrony of the fluorine atoms of a CHF<sub>2</sub> group when linked to a pyrazole ring. The pyrazole is part of (4S,7R)-7,8,8-trimethyl-4,5,6,7-tetrahydro-4,7-methano-2H-indazole also known as (4S,7R)-campho[2,3-c]pyrazole, which has two stereogenic centers. Gauge-Independent Atomic Orbital (GIAO)/Becke, 3-parameter, Lee-Yang-Parr (B3LYP)/6-311++G(d,f) calculated 19F chemical shifts of the minimum energy conformations satisfactorily agree with the experimental data. The energy differences between minima need to consider solvent effects (continuum model) to be satisfactorily reproduced.

Keywords: 19F-NMR; diastereotopic; anisochrony; pyrazoles; indazoles; GIAO; B3LYP; PCM

1. Introduction

Anisochrony in NMR is observed when a prochiral group is linked to a molecule possessing a stereogenic center. In these conditions, the studied nuclei became diastereotopic [1–4]. In the majority of cases, the literature reports concern 1H-NMR and often the protons of CH<sub>2</sub>X groups (e.g., benzyl groups) [5,6]. The phenomenon can be observed on the methyl groups of Me<sub>2</sub>X substituents (e.g., isopropyl groups), with both 1H- and 13C-NMR [7]. Much less common is the observation of the anisochrony of phenyl substituents in CPh<sub>2</sub>X groups, also with 1H- and 13C-NMR [8,9].

The observation of diastereotopic signals for other nuclei have been reported less often, but, for instance 31P [10–18] is much more common than for 15N, where only one example has been described [19]. Other seldom-explored nuclei are 2H [20], 3H [21], 7Li [22], and 17O [23].

In the present paper, we present our results concerning the observation of 19F diastereotopic signals. In 1957, anisochronous signals were already observed for F<sub>2</sub>BrC–C=HBrPh, before the phenomenon was clearly understood [24]. Since then, the phenomenon has been repeatedly described, mainly for CHF<sub>2</sub> groups [25–27], but also for CRF<sub>2</sub> groups [28,29] as well as CRAr<sub>2</sub> (Ar = meta and para substituted with F atoms) and CR(CH<sub>2</sub>F)<sub>2</sub> [30].

None of the examples reported in the preceding paragraph concern a chiral molecule containing an N-CHF<sub>2</sub> substituent. There are many examples of azoles bearing a C-CHF<sub>2</sub> substituent, mainly in agrochemistry [31–33], the field of N-CHF<sub>2</sub> and N-CRF<sub>2</sub> azoles is less studied although there are several articles dealing with the structures presented in Figure 1.
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Figure 1. N-CHF₂, N-CCIF₂, and N-CBrF₂ azoles and benzazoles.

Imidazoles 1 and benzimidazoles 2 [34–36], pyrazoles 3 [37,38], indazoles 4 and 5 [35,39], benzo-triazole 6 [34–36] were reported. Related compounds 9–12 with CXF₂ substituents are described in reference [40].

The compounds we have prepared (Scheme 1) and studied, 13 and 14, are derivatives of (4S,7R)-7,8,8-trimethyl-4,5,6,7-tetrahydro-4,7-methano-2H-indazole also known as (4S,7R)-camphopyrazole, a compound we have previously investigated [41–44].

Scheme 1. Synthesis of the N-difluoromethyl derivatives 13 and 14 of (4S,7R)-campho[2,3-c]pyrazole. SCDA: sodium chlorodifluoroacetate.

2. Results and Discussion

2.1. Chemistry

As indicated in Scheme 1, compounds 13 and 14 were prepared for the first time by direct difluoromethylation of camphopyrazole 15 with sodium chlorodifluoroacetate (SCDA) [45], according to the Mehta and Greaney conditions [46] or by adding a phase transfer catalyst [47], in both cases using N,N′-dimethylformamide as solvent and K₂CO₃ as base. Both isomers were obtained in an 85:15 ratio (see Experimental Section). The only other paper where the N-substitution of 15 was reported (with 1,2-dichloroethane) yielded a 50:50 mixture of both isomers [48]. The structure elucidation of compounds 13 and 14 was based on the close correlation of the ¹³C chemical shifts of the pyrazole ring with those of a reference compound [48].

2.2. NMR Spectroscopy

In both configurational isomers, the fluorine atoms are diastereotopic, and two distinct signals were observed for each one. From the spectra (Figures 2 and 3 and data given in Supplementary Materials), ²J(H–¹⁹F) and ²J(¹⁹F–¹⁹F) coupling constants can be measured.
Figure 2. $^{19}$F-NMR spectrum of 13 in CDCl$_3$ at 300 K with signals at $-89.16$ ppm (ddd, $^2J_F = 226.6$, $^2J_H = 60.6$, $^6J_H = 1.4$), and $-91.64$ (dd, $^2J_F = 226.6$, $^2J_H = 59.4$); the red arrows correspond to the amplification of the left and right side of the signal at $-89.16$ ppm.

Figure 3. $^{19}$F-NMR spectrum of 14 in CDCl$_3$ at 300 K with signals at $-90.80$ ppm (dd, $^2J_F = 225.5$, $^2J_H = 61.3$), and $-92.05$ (dd, $^2J_F = 225.4$, $^2J_H = 60.7$).

The $^2J_{FF}$ SSCC (spin-spin coupling constant) in F-C-F compounds is very sensitive to structural aspects, especially the C atom hybridization; for sp$^3$ carbons range between 3.5 and 340 Hz [49].
There are no $^2J_{\text{FF}}$ values published for $N$-azolyl derivatives, and thus the values we have measured (about 225 Hz) are the only representatives of this kind of compound.

In $^1$H-NMR (see experimental part and Supplementary Material), the most interesting information concerning the CHF$_2$ group where when the anisochrony is larger (compound 13) the two $^2J_{\text{HF}}$ couplings are different and when the anisochrony is smaller (compound 14) they are identical. Moreover, the signal of the 9-CH$_3$ group in compound 13 shows a long-distance $^6J_{\text{HF}}$ coupling of 1.4 Hz (also measured in the $^{19}$F-NMR spectrum, see Figure 2); in compound 14, this coupling is not observed due to the additional bond (it would be a $^7J_{\text{HF}}$).

2.3. Computational Results

We have calculated the energy of compounds 13 and 14 as a function of the torsion angle $\theta$ about the $N$-(CHF$_2$) bond (defined as H-C-N1-N2, 30-29-7-3 or 30-29-3-7). There are two minima (0 imaginary frequencies)—one near 0° and the other near 180° (Figure 4).

According to the calculations, the 2-substituted isomer 14 is more stable than the 1-substituted isomer 13 by 10.8 kJ·mol$^{-1}$ (both in their minima; i.e., having 0 imaginary frequencies). Note that in camphopyrazole, tautomer 2H is more stable than tautomer 1H [41,43,44] due to the Mills–Nixon effect [50,51]; once again, tautomerism and isomerism behave similarly.

When the energy was calculated as a function of the torsion angle $\theta$ about the $N$-(CHF$_2$) bond, in both cases, the minimum energy conformation corresponds to $\theta = 0^\circ$; i.e., the H atom of the CHF$_2$ group eclipsing the “pyridine-like” N atom of pyrazole, the so-called syn-periplanar conformation (Figure 5). The difference between the 0° and the 180° minima are for 13 15.7 kJ·mol$^{-1}$ and for 14...
11.8 kJ·mol⁻¹, and the transition states are for 13 23.6 (θ = 104.4°) and 26.6 kJ·mol⁻¹ (θ = 255.8°) and for 14 23.5 (θ = 114.9°) and 23.1 kJ·mol⁻¹ (θ = 242.9°).

This conformational preference can most probably be explained by the dominance of vicinal hyperconjugation, with electron donation from the electron-rich sigma N-N bonding orbital into both of the very electron deficient vicinal C-F anti-bonding orbitals [52–55].

A natural bond orbital (NBO) analysis shows that the energetic difference between the conformations minima at 0° and 180° can be explained based on the stabilization due to the sum of the charge transfer between the lone pair of the pyridine-like nitrogen and the σ* C-H bond and between the σ N-N and the σ* C-F bonds. This stabilization amount is 6.6 kJ·mol⁻¹ in the minima at 0° of 13 and 14, while in the minima at 180° it is between 1.1 and 1.0 kJ·mol⁻¹, respectively.

Figure 5. Energy profiles in kJ·mol⁻¹ vs. the dihedral angle θ.

Gauge-Independent Atomic Orbital (GIAO) calculated parameters (absolute shieldings) accounted for the experimental results obtained by multinuclear NMR (¹H, ¹³C, ¹⁵N, and ¹⁹F) (see Supplementary Materials). We will focus on the ¹⁹F chemical shifts (Table 1).

| Comp. | θ (°) | ¹⁹F (31) | ¹⁹F (32) | Δδ (31–32) | ¹⁹F (a) | ¹⁹F (b) | Δδ (a–b) |
|-------|-------|-----------|-----------|-------------|---------|---------|----------|
| 13    | –3.6  | –93.18    | –89.73    | –3.45       | –91.64  | –89.16  | –2.48    |
| 13    | –179.3| –90.07    | –98.52    | +8.45       | –92.05  | –90.80  | –1.25    |
| 14    | 11.1  | –92.83    | –88.66    | –4.17       | –92.05  | –90.80  | –1.25    |
| 14    | 179.3 | –85.73    | –97.40    | +11.67      |         |         |          |

Table 1. Calculated (gas phase) and experimental ¹⁹F-NMR chemical shifts (CDCl₃).

The four experimental values (−91.6, −89.2, −92.0, −90.8, ppm) are close to the calculated ones for 13 (0°) (−93.2, −89.7 ppm) and for 14 (0°) (−92.8, −88.7 ppm) than for the 180° assignment (−98.5, −90.1, −97.4, −85.7 ppm). Assuming the simplification that only the two minima contribute to the experimental values, a simple interpolation of the type Exp = a × (Calc. abs minima) + (1–a) × (Calc. second minima) lead to 13 = 91.8% of conformer θ ≈ 0° and 8.2% of conformer θ ≈ 180°, and 14 = 81.6% of conformer θ ≈ 0° and 18.4% of conformer θ ≈ 180°. This corresponds at 298.15 K to −6.0 and −3.7 kJ·mol⁻¹, respectively—lower than the calculated differences between both rotamers, but of the same sign. To see if the inclusion of solvent effects improves the agreement, we calculated the differences of energy between minima in CHCl₃ (Polarizable continuum model, PCM) obtaining for 13 and 14, −7.6 and −5.1 kJ·mol⁻¹, respectively—much closer to the experimental results (the TS have
very close values: 19.8 and 19.2 kJ mol\(^{-1}\)); the solvent slightly modifies the geometries, see \(\theta\) values in Table 2.

We have calculated the chemical shifts in CHCl\(_3\), obtaining the values reported in Table 2. With these values, we have calculated that the difference of energies for 13 and 14 are \(-4.9\) and \(-4.3\) kJ mol\(^{-1}\), respectively, comparable to those obtained for the gas phase (\(-6.0\) and \(-3.7\) kJ mol\(^{-1}\)) to be compared with \(-7.6\) and \(-5.1\) kJ mol\(^{-1}\).

### Table 2. Calculated (CHCl\(_3\)) and experimental \(^{19}\)F-NMR chemical shifts (CDCl\(_3\)).

| Comp. | \(\theta\) (\(^{\circ}\)) | \(^{19}\)F (31) | \(^{19}\)F (32) | \(\Delta\delta\) (31–32) | \(^{19}\)F (a) | \(^{19}\)F (b) | \(\Delta\delta\) (a–b) \(^a\) |
|-------|----------------|----------------|----------------|-------------------|----------------|----------------|----------------|
| 13    | -4.0           | -94.07         | -90.23         | -3.84             | -91.64         | -89.16         | -2.48          |
| 14    | -179.5         | -91.97         | -99.34         | +7.37             | -92.05         | -90.80         | -1.25          |

\(^{a}\) The sign is arbitrary because the assignment of a and b is also arbitrary.

We have also calculated the \(^{13}\)C chemical shifts of the three carbon atoms of the pyrazole ring (C3, C3a, C7a named C4, C9, and C11 in Figure 3). The results are reported in Table 3 and correlates well with the experimental carbon signal shifts, and aided the assignment of the pyrazole ring carbons.

### Table 3. Comparison of experimental and calculated \(^{13}\)C chemical shifts.

| Comp.  | 13 exp. CDCl\(_3\) | 13 calc. Gas | 13 calc. CHCl\(_3\) | 14 exp. CDCl\(_3\) | 14 calc. Gas | 14 calc. CHCl\(_3\) |
|--------|-------------------|--------------|---------------------|-------------------|--------------|---------------------|
| C3 (C4)| 134.3             | 133.2        | 134.4               | 117.9             | 117.3        | 118.2               |
| C3a (C9)| 132.1             | 133.0        | 133.9               | 130.2             | 132.3        | 133.6               |
| C7a (C11)| 153.6             | 153.7        | 155.2               | 169.1             | 167.5        | 169.3               |

### 3. Experimental Section

#### 3.1. Chemistry

**General**

All chemicals cited in the synthetic procedure are commercial compounds. Melting points were determined by differential scanning calorimetry (DSC) with a SEIKO DSC 220 C connected to a model SSC5200H disk station. Thermograms (sample size 0.003–0.005 g) were recorded with a scan rate of 5.0 \(^{\circ}\)C. Column chromatography was performed on silica gel 60 (Merck KGaA, Darmstadt, Germany), 70–230 mesh), and elemental analyses using a Perkin-Elmer 240 apparatus (Madrid, Spain).

Preparation of (4\(^S\),7\(^R\))-1-(Difluoromethyl)-7,8,8-trimethyl-4,5,6,7-tetrahydro-4,7-methano-1\(H\)-indazole (13) and (4\(^S\),7\(^R\))-2-(Difluoromethyl)-7,8,8-trimethyl-4,5,6,7-tetrahydro-4,7-methano-1\(H\)-indazole (14).

Procedure A from Ref. [46]. Into a 100-mL round-bottom three-necked flask equipped with reflux condenser and magnetic stirring, 2 equivalents of sodium chlorodifluoroacetate (SCDA) and 1.5 equivalents of the base (K\(_2\)CO\(_3\)) were introduced. The vacuum was established for 15 min and then purged with argon for another 15 min (this process was repeated three times). Six milliliters of \(N, N\)-dimethylformamide (DMF) was added slowly with stirring and under an argon stream, and then 1 equivalent of (4\(^S\),7\(^R\))-7,8,8-trimethyl-4,5,6,7-tetrahydro-4,7-methano-1\(H\)-indazole (13) and (4\(^S\),7\(^R\))-2-(Difluoromethyl)-7,8,8-trimethyl-4,5,6,7-tetrahydro-4,7-methano-1\(H\)-indazole (14) dissolved in 2 mL of DMF was added from an addition funnel over 15 min. The flask was immersed in a silicone bath previously heated to 100 \(^{\circ}\)C and left stirring for 8 h. To control the temperature, a thermometer was used which was connected to the heating plate and immersed in the silicone oil bath. After the reaction time was completed, it was cooled to room temperature and EtOAc (15 mL) and water (15 mL) were added to the mixture. The organic fraction was washed with brine, and the aqueous fraction was extracted with EtOAc. The organic fractions were combined, dried over anhydrous MgSO\(_4\), and the
solvent evaporated off. The yield of the reaction crude—in which both isomers are present in a ratio (85% of 13: 15% of 14)—is quantitative. The purification was carried out by column chromatography using dichloromethane/hexane (1:1) as eluent. Compound 14 was eluted first.

Procedure B from Ref [47]. Into a 100-mL round-bottom flask equipped with reflux condenser and magnetic stirring, 2 equivalents of SCDA, 3 equivalents of the base (K$_2$CO$_3$), 1 equivalent of (4S,7R)-7,8,8-trimethyl-4,5,6,7-tetrahydro-4,7-methano-1H-indazole (15), and 0.3 equivalents of tetraethylammonium bromide (TEAB) were dissolved in 10 mL of DMF and the mixture was stirred at 100 °C for 3 h. The resulting mixture was poured into water and extracted with EtOAc, the organic extract containing again an 85:15 mixture of both isomers (overall yield 90%) was treated as previously described in procedure A.

(4S,7R)-1-(Difluoromethyl)-7,8,8-trimethyl-4,5,6,7-tetrahydro-4,7-methano-1H-indazole (13). m.p.: 45.4 °C; 1H-NMR: (400.13 MHz, CDCl$_3$) $\delta$ = 7.27 (s, H$_3$), 7.14 (dd, $^{2}J_F$ = 59.5, $^{1}J_F$ = 60.5, CHF$_2$), 2.81 (d, $^{3}J_F$ = 3.8), 2.05 (cm, H$_{sec}$), 1.03 (cm, H$_{ax}$), 1.81 (cm, H$_{sec}$), 1.18 (cm, H$_{ax}$), 1.37 (dd, $^{5}J_F$ = 1.4, CH$_3$-9), 0.92 (s, CH$_3$-10), 0.77 (s, CH$_3$-11); 13C-NMR: (100.61 MHz, CDCl$_3$) $\delta$ = 153.6 (dd, $^{2}J_C$ = 1.6, C7a), 134.3 (dd, $^{4}J_C$ = 2.3, C3), 132.1 (C3a), 111.6 (dd, $^{1}J_F$ = 246.0, $^{1}J_F$ = 248.7, CHF$_2$), 63.2 (C8), 53.7 (C7), 47.6 (C4), 33.0 (C6), 27.4 (C5), 20.1 (C11-14), 19.5 (CH3-10), 11.6 (dd, $^{5}J_F$ = 1.4, CH$_3$-9); 19F NMR: (376.50 MHz, CDCl$_3$) $\delta$ = −89.16 (dd, $^{2}J_F$ = 226.6, $^{2}J_H$ = 60.6, $^{6}J_{HF}$ = 1.4), −91.64 (dd, $^{2}J_F$ = 226.6, $^{2}J_H$ = 59.4); 15N-NMR: (40.54 MHz, CDCl$_3$) $\delta$ = −177.4 (dd, $^{2}J_F$ = $^{2}J_{HF}$ = 27.9, N1), −79.9 (N2). Anal. calcd. for C$_{12}$H$_{16}$F$_{2}$N$_{2}$: C 63.70, H 7.13, N 12.38. Found: C 63.45, H 7.45, N 12.13.

(4S,7R)-2-(Difluoromethyl)-7,8,8-trimethyl-4,5,6,7-tetrahydro-4,7-methano-1H-indazole (14). m.p.: 40.7 °C; 1H-NMR: (400.13 MHz, CDCl$_3$) $\delta$ = 7.28 (s, H$_3$), 7.11 (dd, $^{2}J_F$ = $^{2}J_{HF}$ = 60.9, CHF$_2$), 2.79 (d, $^{3}J_F$ = 4.1), 2.10 (cm, H$_{sec}$), 1.22 (cm, H$_{ax}$), 1.88 (cm, H$_{sec}$), 1.35 (cm, H$_{ax}$), 1.29 (s, CH$_3$-9), 0.97 (s, CH$_3$-10), 0.65 (s, CH$_3$-11); 13C-NMR: (100.61 MHz, CDCl$_3$) $\delta$ = 169.1 (dd, $^{4}J_C$ = 2.2, C7a), 130.2 (C3a), 117.9 (C3), 111.2 (dd, $^{1}J_F$ = 246.4, $^{1}J_F$ = 246.5, CHF$_2$), 60.4 (C8), 50.1 (C7), 46.9 (C4), 33.3 (C6), 27.2 (C5), 20.4 (C11-14), 18.9 (CH3-10), 10.4 (CH$_3$-9); 19F NMR: (376.50 MHz, CDCl$_3$) $\delta$ = −90.80 (dd, $^{2}J_F$ = 225.5, $^{2}J_{HF}$ = 61.3), −92.05 (dd, $^{2}J_F$ = 225.4, $^{2}J_{HF}$ = 60.7); 15N-NMR: (40.54 MHz, CDCl$_3$) $\delta$ = −177.2 (dd, $^{2}J_F$ = $^{2}J_{HF}$ = 24.9, N2), N1 not detected. Anal. calcd. for C$_{12}$H$_{16}$F$_{2}$N$_{2}$: C 63.70, H 7.13, N 12.38. Found: C 63.37, H 7.48, N 11.98.

3.2. NMR

NMR spectra were recorded on a Bruker (Bruker Biospin GmbH, Rheinstetten, Germany) DRX 400 (9.4 Tesla, 400.13 MHz for 1H, 100.61 MHz for 13C and 40.54 MHz for 15N using a 5-mm inverse-detection H-X probe equipped with a z-gradient coil, at 300 K. Chemical shifts ($\delta$ in ppm) are given from internal solvent, CDCl$_3$ 7.26 for 1H and 77.0 for 13C and for 15N, nitromethane (0.00) was used as external reference. Signals were characterized as s (singlet), d (doublet), and cm (complex multiplet) and the $J$ coupling constants are given in Hz.

Typical parameters for 1H-NMR spectra were spectral width 4800 Hz and pulse width 9.5 μs at an attenuation level of 0 dB. Typical parameters for 13C-NMR spectra were spectral width 21 kHz, pulse width 12.5 μs, at an attenuation level of −6 dB and relaxation delay 2 s, WALTZ-16 was used for broadband proton decoupling; the Free Induction Decays (FIDs) were multiplied by an exponential weighting (ib = 1 Hz) before Fourier transformation.

Inverse proton detected heteronuclear shift correlation spectra, ($^1$H-$^1$H) gs-HMQC, and ($^1$H-$^{13}$C) gs-HMBC were acquired and processed using standard Bruker NMR software and in non-phase-sensitive mode. Gradient selection was achieved through a 5% sine truncated shaped pulse gradient of 1 ms.

Selected parameters for ($^1$H-$^{13}$C) gs-HMQC and ($^1$H-$^{13}$C) gs-HMBC spectra were spectral width 4800 Hz for 1H and 20.5 kHz for $^{13}$C, 1024 × 256 data set, number of scans two (gs-HMQC) or four (gs-HMBC) and relaxation delay 1 s. The FIDs were processed using zero filling in the $F_1$ domain and a sine-bell window function in both dimensions was applied prior to Fourier transformation. In the
gs-HMQC experiments, Globally Optimized Alternating Phase Rectangular Pulse (GARP) modulation of \(^{13}\)C was used for decoupling. Selected parameters for \((^{1}\text{H}-^{15}\text{N})\) gs-HMQC, and \((^{1}\text{H}-^{15}\text{N})\) gs-HMBC spectra were spectral width 3500 Hz for \(^{1}\text{H}\) and 12.5 kHz for \(^{15}\text{N}\), 1024 \(\times\) 256 data set, number of scans four, relaxation delay 1 s, 37–60 ms delay for evolution of the \(^{15}\text{N}-^{1}\text{H}\) long-range coupling. The FIDs were processed using zero filling in the \(F_1\) domain and a sine-bell window function in both dimensions was applied prior to Fourier transformation.

\(^{19}\text{F}\)-NMR spectra were recorded on the same spectrometer (376.50 for \(^{19}\text{F}\)) using a 5 mm Quattro Nucleus Probe (QNP) direct-detection probehead equipped with a z-gradient coil, at 300 K. Chemical shifts (\(\delta\) in ppm) are given from CFCl\(_3\) as external reference (one drop of CFCl\(_3\) in CDCl\(_3\) (0.00)). Typical parameters for \(^{19}\text{F}\) NMR spectra were spectral width of 55 kHz, pulse width of 13.75 \(\mu\)s at attenuation level of \(-6\) dB and relaxation delay of 1 s. WALTZ-16 was used for broadband proton decoupling \(^{19}\text{F}\{^{1}\text{H}\}\), the FIDs were multiplied by an exponential weighting (lb = 1 Hz) before Fourier transformation.

### 3.3. Computational Details

Calculations were carried out at the B3LYP/6-311++G(d,p) level [56,57]. Subsequent frequency calculations verify that the structures obtained correspond to energetic minima (imaginary frequencies = 0) or to transition states (imaginary frequencies = 1). In the optimization process, the 0\(^\circ\) and 180\(^\circ\) angles get slightly modified (Tables 1 and 2). These resulting geometries have been used for the calculation of the absolute chemical shieldings with the GIAO method [58,59]. Solvent effects were calculated within the PCM approximation (continuum model) [60–62]. All the calculations have been performed with the Gaussian-09 package [63].

Equations (1)–(4) [64–66] have been used to transform absolute shieldings into chemical shifts:

\[\delta^{1}\text{H} = 31.0 - 0.97 \times \sigma^{1}\text{H}, \text{(reference TMS, 0.00 ppm)} \]  
\[\delta^{13}\text{C} = 175.7 - 0.963 \times \sigma^{13}\text{C}, \text{(reference TMS, 0.00 ppm)} \]  
\[\delta^{15}\text{N} = -152.0 - 0.946 \times \sigma^{15}\text{N}, \text{(reference TMS, 0.00 ppm)} \]  
\[\delta^{19}\text{F} = 162.1 - 0.959 \times \sigma^{19}\text{F}, \text{(reference CFCl\(_3\), 0.00 ppm)} \]

The natural bond orbital (NBO) method [67] has been used to obtain the stabilizing charge-transfer interactions in complexes using the NBO-6 program [68].

### 4. Conclusions

In summary, we have found a new and original example of diastereotopic fluorine atoms, measured two values of \(^2J_{\text{FF}}\) in an original environment and successfully carried out GIAO/B3LYP/6-311++G(d,p) calculations of \(^{19}\text{F}\) chemical shifts that agree with the calculated energies of the two minima of the potential energy curve when solvent was taken into account.

**Supplementary Materials:** Supplementary materials are available online: Tables S1–S3 and Figures S1–S14.

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**Conflicts of Interest:** The authors declare no conflict of interest.
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**Sample Availability:** Samples of the compounds 13, 14, 15, are available from the authors.