MAGNETIC RESONANCE IN CHEMISTRY, VOL. 35, 868–876 (1997)

^{1}H, ^{13}C and ^{19}F NMR Study of *ar*,*ar*′-Difluoro[2.2]paracyclophanes, *ar*,*ar*′-Difluoro-2,11-dithia[3.3]paracyclophanes and their Monofluoro Analogues. Long-Range ^{19}F,^{19}F Spin–Spin Coupling

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The four isomeric difluoro-2,11-dithia[3.3]paracyclophanes, $3F_2$, with one fluorine substituent per aromatic ring were prepared as a 1:1:1:1 mixture. They were converted into the bissulphones, which were pyrolysed to yield the *ar*,*ar*′-difluoro[2.2]paracyclophanes, $2F_2$, as a mixture of *pseudogeminal*, *pseudoortho*-, *pseudometa*- and *pseudopara*-isomers in a ratio of 1:2:3:2. The ^{1}H, ^{13}C and ^{19}F NMR spectra of the mixture of starting materials, $3F_2$, and of the mixture of products, $2F_2$, were analyzed by the use of two-dimensional shift correlations (^{1}H,^{1}H-COSY, ^{13}C,^{1}H- and ^{19}F,^{1}H-HETCOR) and by comparing the experimental ^{1}H and ^{13}C chemical shifts with those predicted by assuming additivity of substituent chemical shifts (SCS). The SCS values were derived from the spectra of the monofluoro compounds, 2F and 3F. Large through-space ^{19}F,^{19}F coupling constants were observed for the *pseudogeminal* isomers of $2F_2$ (13.7 Hz) and $3F_2$ (7.2 Hz). Smaller *J*(F,F) values were found for the *pseudoortho*- (0.6 Hz) and, surprisingly, for the *pseudopara*-isomer (2.8 Hz) of $2F_2$. The latter coupling is probably transmitted through the π-electron system(s) of the [2.2]paracyclophane deck. A number of through-space *J*(F,C) and *J*(F,H) couplings were also observed. © **1997 John Wiley & Sons, Ltd.**

Magn. Reson. Chem. **35**, 868–876 (1997) No. of Figures: 5 No. of Tables: 5 No. of References: 34

Keywords: NMR; ^{13}C NMR; ^{19}F NMR; cyclophanes; through-space coupling; long-range coupling

Received 21 May 1997; accepted 22 July 1997

INTRODUCTION

Scalar spin–spin coupling through space[1–3] is particularly well known for cases in which one of the interacting nuclei is fluorine. Recently we have derived an equation[4] that describes the distance dependence of through-space ^{19}F,^{19}F coupling constants, *J*(F,F), distinctly better than earlier relationships.[5,6] The compounds that we examined[4,7] covered F,F distances between 318 and 242 pm. The shorter of these distances were realized in *syn*-[*n.n*]metacyclophanes, **1**, carrying a fluorine substituent between the bridges at each benzene ring. The benzene rings in these compounds are inclined towards each other. The corresponding paracyclophanes with *pseudogeminal* fluorine substituents, ψg-$\mathbf{2F_2}$ and ψg-$\mathbf{3F_2}$, in which the rings are parallel, were prepared to achieve the larger distances. The syntheses gave mixtures of $\mathbf{2F_2}$ and $\mathbf{3F_2}$, respectively, containing the four possible diastereomers with one fluorine atom per benzene ring. In this paper, we describe the analysis of the ^{1}H, ^{13}C and ^{19}F NMR spectra of these isomeric mixtures and, for comparison, of the monofluoro derivatives, **2F** and **3F**. The preparation, by a different method, and ^{19}F NMR chemical shifts only (without assignments) of a $\mathbf{2F_2}$ mixture were previously described by Huang *et al.*[8]

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Contract grant sponsor: Fonds der Chemischen Industrie.

EXPERIMENTAL

NMR spectra were recorded at *ca.* 296 K on a Bruker AM-400 spectrometer at 400.1 MHz (^{1}H) and 100.6 MHz (^{13}C) and on a Bruker AC-200 spectrometer at 50.3 MHz (^{13}C) and 188.3 MHz (^{19}F). The solvent was $CDCl_3$ in all cases. Chemical shifts were referenced to internal TMS in the ^{1}H spectra, to $CDCl_3$ ($\delta = 77.05$) in the ^{13}C spectra and to $\Xi = 94.094\,056$ MHz, simulating internal $CF^{35}Cl_3$, in the ^{19}F spectra. The ^{19}F frequency had been determined from a sample containing *ca.* 5% (v/v) $CFCl_3$ in $CDCl_3$. ^{13}C and ^{19}F spectra were recorded with ^{1}H decoupling. In addition, some of the ^{19}F spectra were obtained with selective proton decoupling at an irradiation power level of 52 dB below 0.2 W (nominal). For precise determinations of ^{19}F,^{13}C and ^{19}F,^{19}F coupling constants the digital resolution of the ^{13}C and ^{19}F spectra was usually better than 0.1 Hz per point and Gaussian window functions plus one or two

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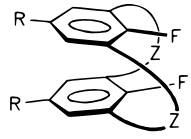

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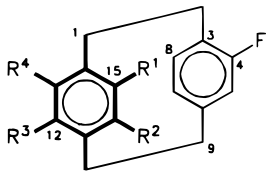
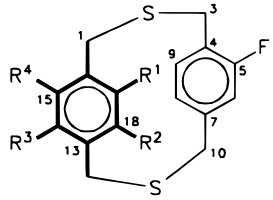
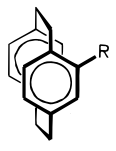
Z = CH_2CH_2 or CH_2SCH_2
R = H or *t*Bu

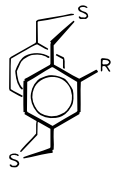




$2F_2$ $3F_2$

R^1	R^2	R^3	R^4	Stereochemical designation
F	H	H	H	*ψg (pseudogeminal)*
H	**F**	H	H	*ψo (pseudoortho)*
H	H	**F**	H	*ψp (pseudopara)*
H	H	H	**F**	*ψm (pseudometa)*





2F, R = F
2H, R = H

3F, R = F
3H, R = H

levels of zero-filling were employed. Multiplicities given with the ^{13}C spectra refer to splittings that would be caused by ^1J(C,H) coupling and were determined by DEPT-135 experiments.[9] NOE difference spectra[10] were recorded with saturation times of 6 s, irradiation power levels of 40–42 dB below 0.2 W (nominal) and either with irradiation at a single frequency or with multiple irradiations of individual lines per multiplet,[11] depending on the selectivity required.

^{1}H,^{1}H-COSY[12] experiments and their variants optimized for small long-range couplings (^{1}H,^{1}H-COSY-LR[13]) were performed with relaxation delays of 0.4–0.8 s. The delay for the evolution of small couplings in the COSY-LR pulse sequence was set to 80 ms. ^{13}C,^{1}H-HETCOR spectra[14,15] were run with suppression of ^{1}H,^{1}H coupling in the F_1 dimension.[16,17] The relaxation delay was 0.4 s and the polarization transfer and refocusing delays were both 3.23 ms for the aromatic carbon atoms whereas for the aliphatic carbon atoms they were 3.45–4.00 and 1.72–2.00 ms respectively. In the ^{13}C,^{1}H-COLOC experiments[18] a relaxation delay of 0.8 s was chosen and the polarization transfer and refocusing delays were set to 30 and 37.5 ms, respectively.

^{19}F,^{1}H correlation[19] experiments were carried out with fluorine detection and without suppression of ^{1}H,^{1}H-couplings in the F_1 dimension. Relaxation delays were 0.8 s and polarization transfer and refocusing delays were set to 55 and 27.5 ms, respectively.

For all 2D experiments digital resolutions were chosen to be good enough to permit the separation of close chemical shifts in both dimensions. Data were multiplied with sine-bell or shifted sine-bell window functions in both dimensions, zero-filled in F_1 and processed in the magnitude or power mode. For data acquisition standard spectrometer software (Bruker DISR91 and earlier versions) was used throughout. Data processing was performed with the same software or with Bruker UXNMR, version 911101 or earlier. Iterative analyses of spin systems were carried out with the NUMMRIT[20] program for Bruker X32 workstations.

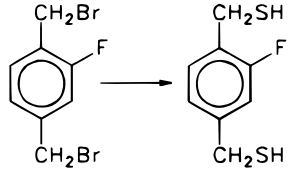
Electron impact mass spectra were recorded on a Finnigan MAT 8430 spectrometer at 70 eV. High-resolution mass determinations were performed by peak matching at a resolution of 10 000. UV spectra were recorded on a Hewlett–Packard Model 8452 diode-array spectrometer and infrared spectra on a Nicolet Model 320 FT-IR spectrometer (KBr pellets).

Syntheses

Scheme 1 depicts the reaction sequence by which the fluorinated cyclophanes were prepared.

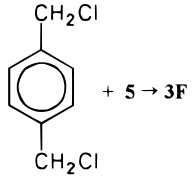
1,4-Bis(bromomethyl)-2-fluorobenzene (4). This has been reported previously[21] but not characterized. M.p. 101–102 °C (EtOH); ^{1}H NMR, δ = 7.36 [t, J(F,H) = J(H,H) = 7.8 Hz, 1H, H-6], 7.16–7.10 (m, 2H, H-3,5), 4.49 (br.s, 2H, 1-CH_2), 4.42 (s, 2H, 4-CH_2); ^{13}C-NMR, δ = 160.4 [s, J(F,C) = 251.5 Hz, C-2], 140.6 [s, J(F,C) = 7.9 Hz, C-4], 131.6 [d, J(F,C) = 3.7 Hz, C-6], 125.4 [s, J(F,C) = 14.6 Hz, C-1], 125.1 [d, J(F,C) = 3.5 Hz, C-5], 116.5 [d, J(F,C) = 22.1 Hz, C-3], 31.8 [t, J(F,C) = 1.8 Hz, 4-CH_2], 25.6 [t, J(F,C) = 4.2 Hz, 1-CH_2]; ^{19}F NMR, δ = −116.5.

(2-Fluoro-4-mercaptomethylphenyl)methanethiol (5). Dibromide **4** was converted into dithiol **5** by reaction[22] with thiourea in boiling ethanol and hydrolysis of the resulting isothiouronium bromide with boiling aqueous sodium hydroxide. Dithiol **5** was obtained as a colourless oil (76%); ^{1}H NMR, δ = 7.26 [t, J(F,H) = J(H,H) = 8.0 Hz, 1H, H-6], 7.06–7.01 (m, 2H, H-3,5), 3.72 [d, J(H,H) = 8.0 Hz, 2H, 1-CH_2], 3.69 [t, J(H,H) = 7.7 Hz, 2H, 4-CH_2], 1.86 [t, J(H,H) = 8.0 Hz, 1-CH_2SH], 1.77 [t, J(H,H) = 7.7 Hz, 4-CH_2SH]; ^{13}C NMR, δ = 160.2 [s, J(F,C) = 247.6 Hz, C-2], 142.4 [s, J(F,C) = 7.6 Hz, C-4], 130.2 [d, J(F,C) = 4.4 Hz, C-6], 127.1 [s, J(F,C) = 14.8 Hz, C-1], 123.9 [d, J(F,C) = 3.3 Hz, C-5], 115.2 [d, J(F,C) = 22.2 Hz, C-3], 28.3 [t, J(F,C) = 1.5 Hz, 4-CH_2], 21.9 [t, J(F,C) = 3.7 Hz, 1-CH_2]; the ^{1}H and ^{13}C spectra were mutually assigned by 2D ^{13}C,^{1}H-HETCOR and -COLOC experiments; ^{19}F NMR, δ = −118.4; MS, *m/z* (%) 188 (54) (M^+), 155 (100) (M^+ − SH), 122 (90) (M^+ − 2SH), 109 (22), 101 (12), 46 (10); HRMS, calculated for $C_8H_9FS_2$, 188.0130, found 188.0129.



4 **5**

4 + 5 → 3F$_2$ → 2F$_2$



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Scheme 1

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Mixture of isomeric 5,*x*-difluoro-2,11-dithia[3.3]paracyclophanes ($3F_2$; $x = 14, 15, 17, 18$). The preparation followed loosely that described for 2,11-dithia[3.3]metaparacyclophane.[23] A solution of 6.71 g (23.8 mmol) of **4** and 4.49 g (23.8 mmol) of **5** in 2 l of toluene was deoxygenated ('degassed') by bubbling nitrogen gas through it. Over a period of 24 h it was then slowly added dropwise to a 'degassed' boiling solution of 5.60 g (100.0 mmol) of KOH in 1 l of *ca.* 90% ethanol. Refluxing was continued for a further 1 h. The volume of the reaction mixture was reduced to one tenth by rotary evaporation and 150 ml of water were added. The mixture was extracted three times with CH_2Cl_2 and the combined organic phases were washed with water, aqueous saturated $NaHCO_3$ solution and water. The solvent was removed by rotary evaporation and the product purified by column chromatography (silica gel, CH_2Cl_2) and crystallized from CCl_4 to yield 3.49 g (48%) of a 1:1:1:1-mixture of $3F_2$ isomers, m.p. 162–165.5 °C; UV/Vis (EtOH), λ_{max} (log ε), 214 nm (4.34), 228, sh (3.92), 260 (3.50), 272 (3.41); IR (KBr), ν 1621 cm^{-1} (m), 1577 (m), 1502 (m), 1426 (s), 1261 (m), 1096 (m), 958 (m), 866 (m), 813 (m); ^1H and ^{13}C NMR, see Table 5; ^{19}F NMR, see Table 4.

Mixture of isomeric 4,*x*-difluoro[2.2]paracyclophanes ($2F_2$; $x = 12, 13, 15, 16$). A 2.00 g (6.5 mmol) amount of the isomeric mixture $3F_2$ was stirred for 3 days at room temperature with 27 ml of 50% hydrogen peroxide and 163 ml of glacial acetic acid. The precipitate formed was filtered off, washed with diethyl ether and dried under vacuum to yield 2.17 g (90%) of bissulphones, m.p. >300 °C. A 1.10 g (3.0 mmol) amount of this bissulphone mixture was pyrolysed in an apparatus according to Haenel and Staab[24] under a nitrogen atmosphere of 5 Pa at 450 °C in the pyrolysis oven and 250 °C (initially, then gradually raised to 280 °C) in the evaporation oven. The condensate was purified by chromatography on silica gel plates, developed twice with light petroleum, then once with CH_2Cl_2; yield 0.37 g (50%) of $2F_2$, approximate isomer ratio 1:2:2:3 ($\psi g:\psi o:\psi p:\psi m$); m.p. 212–214 °C (lit.[8] 211–213 °C); ^1H and ^{13}C NMR, see Table 3; ^{19}F NMR, see Table 4.

4-Fluoro[2.2]paracyclophane (2F):[25] ^1H and ^{13}C NMR, see Table 1; ^{19}F NMR, see Table 4.

5-Fluoro-2,11-dithia[3.3]paracyclophane (3F). This was prepared similarly to $3F_2$ using 2.63 g (15.0 mmol) of 1,4-bis(chloromethyl)benzene (**6**), 2.82 g (15.0 mmol) of **5**, 1 l of toluene, 500 ml of EtOH and 2.30 g (50.0 mmol) of KOH. Purification of the product was achieved by adsorption on five times its weight of silica gel, extraction with CH_2Cl_2, crystallization from $CHCl_3$ and sublimation at *ca.* 150 °C and 33 Pa; yield 1.73 g (40%), m.p. 178–179 °C; UV/Vis (EtOH), λ_{max} (log ε) 214 nm (4.26), 224, sh (4.04), 258 (3.44), 274, sh (3.18); IR (KBr), ν 1578 cm^{-1} (m), 1504 (m), 1425 (s), 1260 (m), 1099 (m), 956 (m), 810 (m); ^1H and ^{13}C NMR, see Table 2; ^{19}F NMR, see Table 4; MS, *m/z* (%) 290 (100) (M^+), 168 (10) ($SCH_2C_6H_4CH_2S^+$), 153 (8), 136 (10), 123 (34), 105 (52) ($C_8H_9^+$), 91 (23) ($C_7H_7^+$). Analysis: calculated for $C_{16}H_{15}FS_2$, C 66.17, H 5.21, S 22.08; found, C 66.17, H 5.25, S 22.16%.

2,11-Dithia[3.3]paracyclophane (3H).[26] ^1H NMR, $\delta = 6.85$ (s, 8H, H_{ar}), 3.81 (s, 8H, CH_2); ^{13}C NMR, $\delta = 135.5$ (s, quat. C_{ar}), 129.6 (d, $C_{ar}H$), 38.3 (t, CH_2).

RESULTS AND DISCUSSION

Monofluoro[2.2]paracyclophane, 2F

In the ^{13}C NMR spectrum of **2F**, the signals of the carbon atoms in the fluorine-bearing ring can be assigned in a straightforward manner from the combination of their characteristic fluorine couplings with the signal phase in the DEPT-135 spectrum.[9] Of the ^{13}C signals for the second aromatic ring, the one of the carbon in the *pseudogeminal* position relative to the fluorine substituent, C-15, is readily recognized by its relatively strong shielding, $\Delta\delta_C = -3.90$, with respect to the parent hydrocarbon **2H** and by the deshielding, $\Delta\delta_H = +0.45$, of its connected proton. We have observed[27] this upfield-^{13}C/downfield-^1H shift also for substituents such as CH_3 and Br and the substituent-induced deshielding of the *pseudogeminal* proton was described long ago by Reich and Cram.[28] The remaining protons on the second aromatic ring were assigned by homodecoupling of H-15. Two-dimensional $^{13}C,^1H$-HETCOR and -COLOC spectra then completed the assignment of the proton and carbon NMR spectra (Table 1). The bridge proton multiplets could not be analysed because they overlap strongly. The bridge proton chemical shifts given in Table 1 were extracted from the $^{13}C,^1H$-HETCOR spectrum.

Table 1. ^{13}C and ^1H NMR data (δ, ppm and *J*, Hz) for compound 2F

Carbon	δ_C	$\Delta\delta_C$[a]	*J*(F,C)	Carbon	δ_C	$\Delta\delta_C$	*J*(F,C)
1	34.3	−1.5	1.00	9	34.8	−0.9	1.77
2	30.1	−5.7	0.71	10	35.3	−0.5	0.63
3	125.9	−13.8	17.87	11	138.9	−0.8	0.15
4	161.1	28.1	245.30	12	132.9	−0.1	0.39
5	122.2	−10.8	22.34	13	133.6	0.5	⩽0.05
6	142.9	3.2	7.20	14	139.8	0.1	0.17
7	128.0	−5.1	2.75	15	129.2	−3.9	1.57
8	135.4	2.4	6.36	16	132.5	−0.6	0.28
Proton[b]	δ_H	$\Delta\delta_H$[a]	*J*(F,H)	**Proton**	δ_H	$\Delta\delta_H$	*J*(F,H)
1	3.05/3.10			9	2.97/2.99		
2	3.38/2.65[c]			10	3.02/3.08		
5	5.89	−0.59	11.1	12	6.51	0.04	
7	6.38	−0.09		13	6.39	−0.09	
8	6.45	−0.02	8.0	15	6.92	0.45	3.1
				16	6.50	0.03	

[a] Obtained by subtracting the chemical shifts of **2H** from those of **2F** and rounding the result to one (^{13}C) or two (^1H) decimal places.
[b] Coupling constants between aromatic protons: $^3J(H,H) = 7.7–7.9$, $^4J(H,H) = 1.8–2.0$ Hz.
[c] Lower value for the *anti*-proton with respect to fluorine. No *syn*/*anti* assignment implied for protons connected to C-1, C-9 and C-10.

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Takemura and Mori[29] had previously investigated the ^{13}C NMR spectrum of **2F** with respect to possible *pseudogeminal* through-space ^{19}F,^{13}C spin coupling. They concluded that no such coupling was observable. Our present results do show, however, that not only can their missing J(F,C) value be found very easily (it amounts to 1.57 Hz) but also that, with one exception (C-13), all carbon nuclei of the fluorine-free aromatic ring plus the four bridge carbon atoms are indeed coupled to fluorine. Good magnetic field homogeneity, sufficient digital resolution and the application of Gaussian multiplication to the free induction decay gave a linewidth at half height of 0.05 Hz for the signal of C-13, so that any J(F,C) coupling larger than this value should have led to a splitting of this signal. Figure 1 demonstrates the resolution achieved and shows the ^{13}C signals of C-11–C-16 in **2F**. It is worth mentioning that the magnitude of the ^{19}F,^{13}C couplings in the non-fluorinated ring does not decrease monotonously with increasing distance of the carbon atoms from the fluorine. Most notably, the *pseudopara*-carbon, C-12, which is most distant from F shows a larger J(F,C) value than C-11 to C-14 and C-16, which are all closer to F. This suggests that these relatively small couplings are (at least to a large degree) transmitted through 'bonds,' probably through the interacting π electrons of the parallel benzene rings.

Takemura and Mori[29] also considered the possibility of through-space ^{19}F coupling to H-15 but could not prove such coupling because of the complexity of their spectrum at the ^{1}H NMR observation frequency of 100 MHz. Later, Nikanorov *et al.*[30] reported this ^{19}F,^{1}H coupling constant to be 2.8 Hz but also failed to observe J(F,C-15). We determined J(F,H-15) to be 3.1 Hz, and the slope of the C-15/H-15 cross peak in the ^{13}C,^{1}H-HETCOR spectrum shows that the through-space J(F,C-15) and J(F,H-15) coupling constants are of the same sign. Two more relative signs, ^{n}J(F,C) to ^{n+1}J(F,H), follow from the ^{13}C,^{1}H-HETCOR spectrum, viz. ^{2}J(F,C-5)/^{3}J(F,H-5) > 0 and ^{3}J(F,C-8)/^{4}J(F,H-8) > 0. Not surprisingly, both agree with those in fluorobenzene,[31] i.e. ^{2}J(F,C), ^{3}J(F,C), ^{3}J(F,H) and ^{4}J(F,H) are all positive. The ^{1}H NMR data are also included in Table 1. This table also contains the ^{1}H and ^{13}C SCS values, i.e. the differences between the chemical shifts of **2F** and the chemical shifts of the corresponding nuclei of the parent compound **2H**. These are used below to help distinguish between the structures of the isomeric difluoro compounds, $\mathbf{2F_2}$.

Monofluorodithia[3.3]paracyclophane, 3F

The assignment of the ^{1}H and ^{13}C NMR signals of the aromatic rings and their connected CH_2 groups in the dithia[3.3]paracyclophane **3F** are obtained from ^{1}H,^{1}H-COSY, ^{13}C,^{1}H-HETCOR and ^{13}C,^{1}H-COLOC spectra. The orientation of the protons of the two rings relative to each other, which is important with respect to through-space spin–spin coupling, is clarified by a ^{1}H,^{1}H-COSY spectrum optimized for small long-range couplings and by ^{1}H{^{1}H} NOE difference experiments as follows. The ^{1}H signals at $\delta = 4.11$ and 3.45 belong to the geminal protons at C-3 in the *syn*- and *anti*-orientation, respectively, relative to the fluoro substituent. In the ^{1}H,^{1}H-COSY-LR spectrum one observes cross peaks of these signals with those of the protons at C-1 from four-bond coupling across the sulphur atom, and crosspeaks between the signals of the protons at C-1 and their respective benzylic *syn*-oriented aromatic

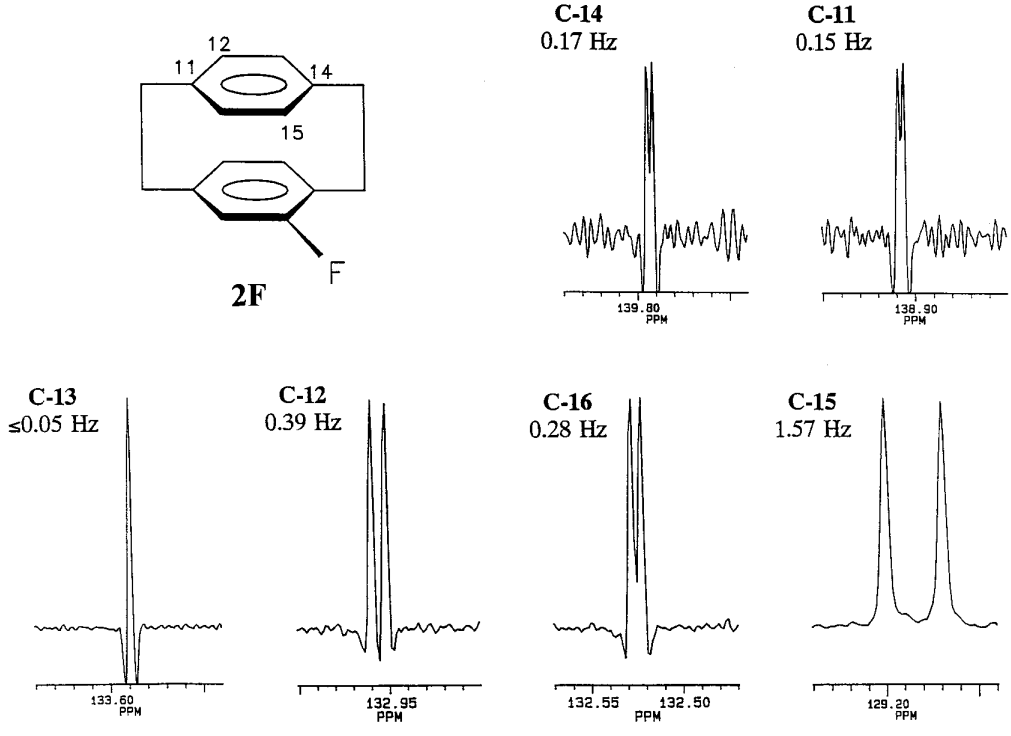

Figure 1. Expansions of the ^{13}C NMR spectrum of **2F** showing ^{19}F,^{13}C spin–spin coupling for the signals of C-11, C-12, C-14, C-15 and C-16 but not for the signal of C-13.

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ortho-protons. This clarifies all assignments with the exception of the two similar chemical shifts of the protons at C-10, which are not of relevance for the problem under study. The relative orientation of the two *p*-xylylene spin systems follows from an NOE observed for H-6 ($\delta = 6.50$) when the resonance of H-18 ($\delta = 6.89$) is saturated. The spectral parameters of **3F** are given in Table 2 together with the SCS values of the aromatic protons and of all ^{13}C nuclei relative to **3H** [**3H**: $\delta_H = 6.85$ (H_{ar}); $\delta_C = 135.5$ (C-4), 129.5 (C-5), 38.3 (C-1)].

A number of through-space couplings to ^{19}F are visible in the ^{13}C NMR spectrum of **3F**, viz. at the signals of C-16 (0.19 Hz), C-18 (0.09 Hz) and C-17 (0.66 Hz). The last carbon atom is *pseudogeminal* with respect to the substituent and has a smaller distance from the fluorine than its neighbours. The decrease of *J*(F,C-17) in **3F** relative to *J*(F,C-15) in **2F** corresponds to the increased non-bonding F···C distance in **3F** with its three-membered bridges compared with **2F** which has two-membered bridges. Similarly, the through-space *J*(F,H-17) coupling of 1.3 Hz in **3F** is more than halved relative to its counterpart, *J*(F,H-15) = 3.1 Hz, in **2F**.

Isomeric difluoro[2.2]paracyclophanes, $2F_2$

As mentioned above, the four diastereomers of $\mathbf{2F_2}$ were not separated and the spectra of their mixture had to be analysed. The ^{19}F spectrum shows the presence of four compounds. Signal intensities in the order from high to low frequencies are approximately 3:2:2:1. These resonances are called α, β, γ, δ in the order mentioned to facilitate the description of the assignment procedure (see below). A standard $^1H,^1H$-COSY and a $^1H,^1H$-COSY-LR spectrum (Fig. 2) help to sort out the proton signals belonging to a common molecule. The aromatic part of the $^1H,^1H$-COSY-LR spectrum is shown in Fig. 2(a). The four isomers of $\mathbf{2F_2}$ can be divided into two

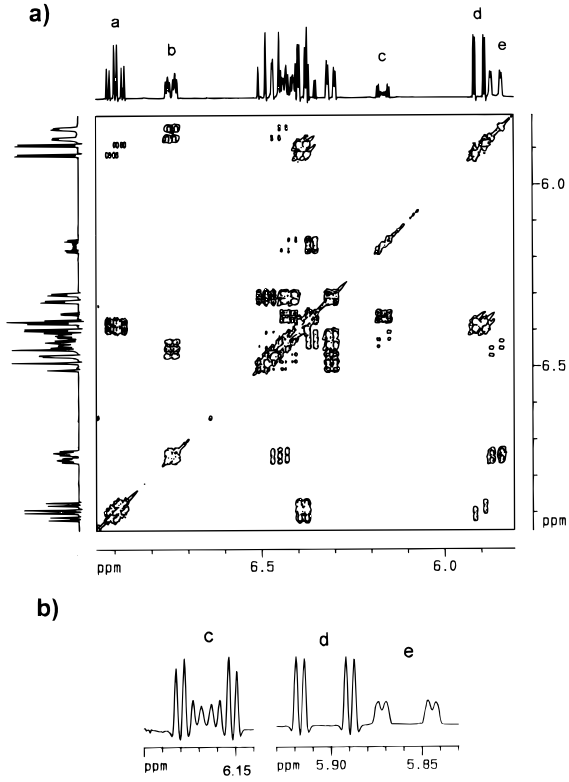

Figure 2. (a) Two-dimensional H,H-COSY-LR spectrum (400 MHz; solvent $CDCl_3$; aromatic spectral region only) of the isomer mixture $\mathbf{2F_2}$. Assignment of labelled signals: H-8 in ψm-$\mathbf{2F_2}$ (signal a), H-7 in ψp-$\mathbf{2F_2}$ (signal b), H-5 in ψg-$\mathbf{2F_2}$ (signal c), H-5 in ψm-$\mathbf{2F_2}$ (signal d), H-5 in ψp-$\mathbf{2F_2}$ (signa e). (b) Expansions of the 5-H multiplets of ψg- (signal c), ψm- (signal d) and ψp-$\mathbf{2F_2}$ (signal e) showing different degrees of second-order effects.

groups according to the symmetry of their bridge proton spin systems.[32] Both the ψo- and the ψp-isomers display one ABCD spectrum for their two bridges, i.e. the bridges have one spin system with four different

Table 2. ^{13}C and ^1H NMR data (δ, ppm and *J*, Hz) for compound 3F

Carbon	δ_C	$\Delta\delta_C$[a]	*J*(F,C)	Carbon	δ_C	$\Delta\delta_C$	*J*(F,C)
1	37.9	−0.4	⩽0.30	10	37.9	−0.4	1.86
3	29.8	−8.5	3.35	12	38.4	0.1	⩽0.30
4	122.8	−12.7	14.36	13	135.5	0.0	⩽0.15
5	159.2	29.7	244.47	14	129.8	0.3	∼0.1
6	116.8	−12.8	23.11	15	129.7	0.2	⩽0.26
7	138.4	2.9	7.57	16	135.4	−0.1	0.19
8	125.2	−4.3	3.09	17	128.0	−1.6	0.66
9	131.7	2.1	4.41	18	129.5	0.0	0.09
Proton[b]	**δ_H**	**$\Delta\delta_H$[a]**	***J*(F,H)**	**Proton**	**δ_H**	**$\Delta\delta_H$**	***J*(F,H)**
1[c]	3.81/3.83			10	3.75/3.77		
3	3.45/4.11			12	3.80/3.80		
6	6.50	−0.35	11.0	14	6.93	0.08	
8	6.69	−0.16		15	7.02	0.17	
9	6.96	0.11	7.9	17	6.97	0.12	1.3
				18	6.89	0.04	

[a] Obtained by subtracting the chemical shifts of **3H** from those of **3F** and rounding the result to one (^{13}C) or two (^1H) decimal places.
[b] ^2J(H,H): (–)14.9 (1,1), (–)14.8 (3,3), (–)15.3 (10,10); ^3J(H,H): 7.8–8.0 Hz; ^4J(H,H): 1.7–2.0 Hz (*meta* couplings); ^5J(H,H): 0.6 Hz (*para* couplings in non-fluorinated ring).
[c] For protons attached to C-1, C-3, C-10 and C-12, the chemical shift mentioned first refers to the *anti*-proton with respect to the fluorine substituent.

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chemical shifts, as opposed to the ψg- and ψm-isomers which have two spin systems (AA′XX′ and BB′CC′) with two different chemical shifts each. These different situations are easily distinguished from the number of cross peaks in the aliphatic part of the ^{1}H,^{1}H-COSY spectrum (not shown).

The isomers within a group can be discriminated by comparing their experimental ^{1}H and ^{13}C chemical shifts with the shifts predicted from increment calculations using the SCS values in **2F** and assuming additivity. As shown in Table 3, the agreement is generally acceptable, better than 0.1 ppm for the ^{1}H shifts and better than 0.9 ppm for ^{13}C, with the exception of ψg-**2F$_2$** where the interaction between the substituents entails deviations from additivity of up to 0.25 ppm in the ^{1}H (H-5/16) and of up to 4.9 ppm (C-4/15) in the ^{13}C spectrum. Another notable exception from SCS additivity is the deviation of 1.5 ppm for C-7/15 in ψp-**2F$_2$**. For all isomers the alternate configurational assignment (i.e. taking ψg for ψm and taking ψo for ψp) would result in very much larger values of $\Sigma|\delta_{exp} - \delta_{calc}| = \Sigma|SCS|$ in both the ^{13}C and the ^{1}H spectra and would be clearly inappropriate.

A further way to distinguish the ψg- and the ψm-isomers of **2F$_2$** makes use of the second-order effects in the ^{1}H NMR signals of the former. The two fluorine atoms in ψg-**2F$_2$** are very close to each other and undergo significant mutual through-space spin–spin coupling (13.7 Hz, see below). This makes the aromatic protons the AA′BB′CC′ part of an AA′BB′CC′XX′ spin

Table 3. ^{13}C and ^{1}H NMR data (δ, ppm and *J*, Hz) for the isomers 2F$_2$

Position	δ_C (exp.)	δ_C (calc.)	ΣJ(F,C)[a]	δ_H (exp.)	δ_H (calc.)
ψg-**2F$_2$**:					
1, 2	28.4	28.6	3.2 or 0.0	3.53 (*syn*)	
				2.75 (*anti*)	
3, 14	125.4	126.0	~18		
4, 15	162.1	157.2	−246.9/+0.4 (*J*)		
5, 16	120.9	121.7	23.0	6.17	5.92
6, 11	142.1	142.1	7.6		
7, 12	128.8	127.9	2.9	6.36	6.42
8, 13	135.5	136.0	5.8	6.42	6.37
9, 10	35.0	34.4	0.9 or 0.0	~3.04/~3.00	
ψo-**2F$_2$**:					
1, 9	33.6	33.3	2.7 or 0.3	~3.00/~3.00	
2, 10	29.7	29.6	?[b]	3.36 (*syn*)	
				2.65 (*anti*)	
3, 11	125.2	125.1	17.9		
4, 16	161.3	160.6	245.8 or 245.5		
5, 15	118.2	118.3	24.4	6.43	6.34
6, 14	143.4	143.0	7.4		
7, 13	128.3	128.5	3.1	6.31	6.30
8, 12	135.7	135.3	6.4	6.49	6.49
ψm-**2F$_2$**:					
1, 2	29.0	28.6	1.7 or 0.5	3.28 (*syn*)	
				2.78 (*anti*)	
3, 14	126.2	126.0	18.0		
4, 13	161.3	161.7	246.1		
5, 12	121.3	122.1	22.5 or 21.5	5.90	5.93
6, 11	142.2	142.1	7.4 or 7.0		
7, 16	127.7	127.5	3.0	6.39	6.41
8, 15	131.6	131.5	8.0 or 5.0	6.90[c]	6.90
9, 10	34.4	34.4	2.6 or 1.2	2.99/2.94	
ψp-**2F$_2$**:					
1, 9	33.4	33.3	2.7 or 0.0	3.05/2.97	
2, 10	29.6	29.6	⩽0.3	3.41 (*syn*)	
				2.67 (*anti*)	
3, 11	125.3	125.1	17.6		
4, 12	161.4	161.0	246.0 or 244.9		
5, 13	122.4	122.8	22.2 or 23.1	5.86	5.81
6, 14	142.7	143.0	7.2		
7, 15	125.6	124.1	4.2	6.74[d]	6.83
8, 16	134.8	134.9	6.5	6.45	6.48

[a] When four lines of approximately equal height or triplets are observed for the X parts of the ABX spectra, the two possibilities for the sums $|J(F,C)+J(F',C)|$ are given.
[b] Not unequivocal.
[c] J(F-4,H-15) = 3.2 Hz.
[d] J(F-4,H-15) = 2.5 Hz.

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system and second-order effects should be most pronounced for protons coupled to fluorine, i.e. for H-5 and H-8. The signals of 5-H in ψg-**2F$_2$** and ψm-**2F$_2$** appear as a complex multiplet and a first-order doublet of doublets, respectively. The signal of 5-H in ψp-**2F$_2$** is an intermediate case and appears as a broadened doublet of doublets [Fig. 2(b)].

Once the proton chemical shifts were assigned, the identification of the fluorine NMR signals was achieved by a two-dimensional ^{19}F,^{1}H-HETCOR spectrum and, redundantly, by selectively proton-decoupled fluorine spectra. The relevant ^{19}F,^{1}H coupling constants in the **2F$_2$**-isomers are ^{3}J(F,H) ~ 11 Hz and ^{4}J(F,H) ~ 7 Hz. When the ^{19}F,^{1}H-HETCOR experiment was optimized for J(F,H) = 9 Hz, cross peaks were observed between each fluorine chemical shift and the chemical shifts of the *ortho*- (H-5) and the *meta*-proton (H-8), (cf. Fig. 3). The resulting ^{19}F assignments in the order of increasing shielding are ψm (signal α), ψo (signal β), ψp (signal γ), and ψg (signal δ) (see Table 4). To obtain the J(F,F) values for the **2F$_2$**-isomers, the ^{13}C satellites in the ^{19}F{^{1}H} spectrum of the isomeric mixture were inspected. These satellites are the AB parts of ABX spin systems (X-part: ^{13}C), from which the magnitude of J(A, B) can be read off directly. As expected, J(F,F) is largest for the *pseudogeminal* isomer, ψg-**2F$_2$**, viz. 13.7 Hz. This value has already contributed to a data set that we used to derive a quantitative relationship between the magnitude of through-space ^{19}F,^{19}F-coupling constants and non-bonded F,F distances.[4] The J(F,F) value in ψo-**2F$_2$** is very much smaller than in the ψg-isomer, only 0.6 Hz. No resolvable ^{19}F,^{19}F coupling is observed in the ^{13}C satellites of the ^{19}F resonance of ψm-**2F$_2$**. In view of the experimental linewidth of 0.1 Hz, J(F,F) in the *pseudometa*-isomer may be taken to be smaller than this value. Surprisingly, in ψp-**2F$_2$** which possesses the largest F,F distance of the isomers, J(F,F) amounts to 2.8 Hz and thus surpasses the values of the ψo- and ψm-isomers. Hence this is not a through-space coupling. Rather, as for the analogous J(F,C) coupling mentioned above, the coupling information must be propagated through the chemical bonding system, probably by way of the inter-ring π–π electron interaction because the pathway along the eight classical chemical bonds between the fluorine substituents at C-4 and C-12 is certainly not favourable enough to allow a 2.8 Hz coupling.

Table 4. ^{19}F NMR data (δ, ppm and J, Hz) for compounds 2F and 3F and of the isomers 2F$_2$ and 3F$_2$

Compound	δ_F	J(F,F)
2F	−113.0	
3F	−119.3	
ψg-**2F$_2$**	−117.5 (δ)	13.7
ψo-**2F$_2$**	−113.2 (β)	0.6
ψm-**2F$_2$**	−111.6 (α)	⩽0.1
ψp-**2F$_2$**	−113.3 (γ)	2.8
ψg-**3F$_2$**	−120.2 (δ)	7.2
ψo-**3F$_2$**	-119.2_6 (β)	
ψm-**3F$_2$**	−117.3 (α)	
ψp-**3F$_2$**	-119.3_4 (γ)	

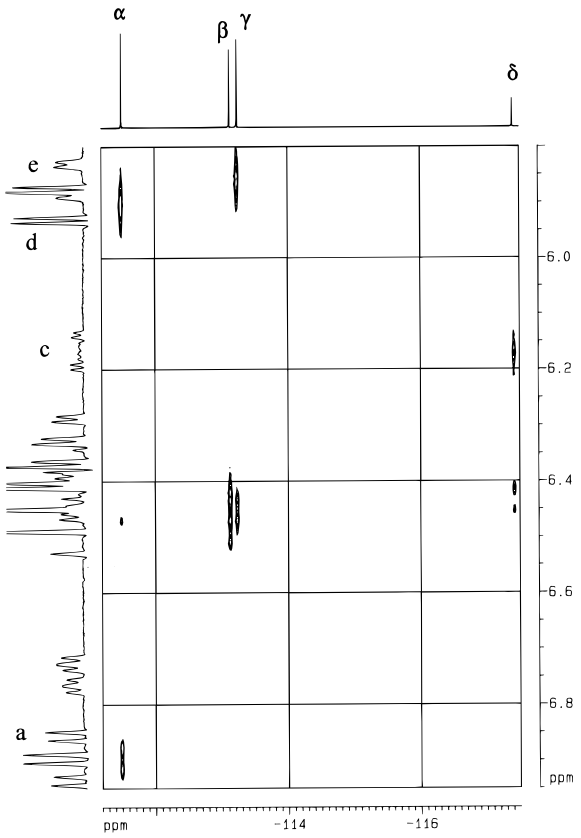
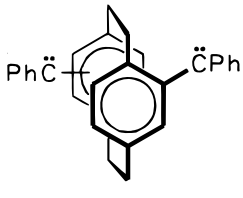


Figure 3. Two-dimensional F,H-HETCOR spectrum of the isomer mixture **2F$_2$** [188 MHz for ^{19}F, horizontal dimension; 200 MHz for ^{1}H, vertical dimension; solvent CDCl$_3$; optimized for J(F,H)=9 Hz]. Signals α, β, γ, and δ correspond to the fluorine in ψm-, ψo-, ψp- and ψg-**2F$_2$**, respectively.

Interestingly, the present pattern of interring ^{19}F,^{19}F couplings in ψo-, ψm- and ψp-**2F$_2$** has some parallel in the results of Izuoka *et al.*[33] for the series of biscarbenes **7**. In their ESR studies of three isomers of **7**, they found a high-spin (quintet) ground state for the ψo- and ψp-isomers of **7** and a low-spin (singlet) ground state for ψm-**7**, and Yamaguchi *et al.*[34] have successfully applied MO theory to the calculation of effective exchange integrals for such cyclophane-type carbene dimers.

Two-dimensional ^{13}C,^{1}H-HETCOR and -COLOC spectra completed the assignment of the NMR signals, but because of severe signal overlap the multiplet patterns of the bridge protons could not be analysed and the ^{1}H chemical shifts had to be taken from the ^{13}C,^{1}H-HETCOR spectrum. The presence of F,F spin–spin coupling in the ψg-, ψp- and ψo-isomers makes their ^{13}C NMR signals multiplets, viz. X parts of ABX or (nearly) AA′X spin systems, from which only the sum of the coupling constants, $|J(F_A,{}^{13}C) + J(F_B,{}^{13}C)|$, can be extracted. In the case of four-line multiplets it may also be uncertain whether the distance between the outer or the inner lines corresponds to this sum. Similarly, in



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triplet-like multiplets the sum may correspond to the spacing of the outer lines or be zero. As J(F,F) is close to zero in the ψm-isomer, its J(F,C) coupling constants can be directly read off the ^{13}C spectrum. Finally, similarly to **2F**, through-space coupling between the fluorine nucleus in ψm-**2F$_2$** and its *pseudogeminal* carbon atom and proton is observed. With values of 1.5 and 3.2 Hz, respectively, these coupling constants have almost the same size as in **2F**. According to the slope of the cross peak in the C,H-HETCOR spectrum, these coupling constants have the same sign.

Isomeric difluorodithia[3.3]paracyclophanes, 3F$_2$

For the interpretation of the ^{1}H,^{13}C (Table 5) and ^{19}F (Table 4) NMR spectra of the four isomeric difluorodithia[3.3]paracyclophanes, **3F$_2$**, the same techniques as for the difluoro[2.2]paracyclophanes were used. The assignment of the sets of signals to the indidual isomers, however, relies mostly on predicted ^{1}H and ^{13}C NMR chemical shifts from the SCS values derived for **3F**. Only for the ψg-isomer was a through-space ^{19}F,^{19}F coupling constant observed [J(F,F) = 7.2 Hz], whereas the ψo-, the ψm- and the ψp-isomers exhibit small through-space couplings between the fluorine nuclei and the *pseudogeminal* carbon atom: J(F-5, C-17) = 0.7, $\geqslant$0.3 and 0.5 Hz, respectively. Owing to the conformational flexibility of the CH_2SCH_2 bridges, these ^{19}F,^{19}F and ^{19}F,^{13}C coupling constants are averaged values over four conformers. Low-temperature experiments to observe the individual conformers separately were unsuccessful because of the low solubility of the compounds at temperatures below 213 K.

Table 5. ^{13}C and ^{1}H NMR data (δ, ppm and J, Hz) for the isomers 3F$_2$

Position	δ_C (exp.)	δ_C (calc.)	J(F,C)[a]	δ_H (exp.)	δ_H (calc.)	J[b]
ψg-**3F$_2$**:						
1, 3	29.3	29.4	3.8 or 1.1 (ΣJ)	4.25 (*syn*) 3.43 (*anti*)		15.5
4, 16	122.5	122.7	14.6 (ΣJ)			
5, 17	160.0	157.7	245.7 or 244.9 (ΣJ)			
6, 18	116.2	116.8	23.4 (ΣJ)	6.64	6.54	
7, 13	138.2	138.4	7.5 (ΣJ)			
8, 14	125.4	125.5	3.2 (ΣJ)	6.72	6.77	
9, 15	131.7	131.9	4.2 (ΣJ)	7.08	7.13	~6.5 J(F,H)
10, 12	38.0	38.0	1.8 (ΣJ)	3.77 (*syn*+*anti*)		
ψo-**3F$_2$**:						
1, 10	37.5	37.5	1.8	3.77 (*syn*+*anti*)		
3, 12	29.9	29.9	3.9	4.11 (*syn*) 3.46 (*anti*)		14.8
4, 13	122.6	122.9	14.2			
5, 18	159.4	159.2	245.1			
6, 17	115.4	115.2	23.1, 0.7	6.67	6.62	
7, 16	138.2	138.3	7.6			
8, 15	125.4	125.4	3.2	6.83	6.86	8.0, 1.8
9, 14	131.9	132.0	4.4	7.01	7.04	
ψm-**3F$_2$**:						
1, 3	30.9	29.4	2.5	3.99 (*syn*) 3.58 (*anti*)		14.9
4, 16	122.7	122.7	14.1			
5, 15	159.7	159.4	246.1			
6, 14	116.8	117.1	22.5	6.65	6.58	
7, 13	138.4	138.4	7.6			
8, 18	125.8	125.2	3.2	6.70	6.73	
9, 17	130.4	130.1	4.7, ~0.3	7.07	7.08	~7.6 J(F,H)
10, 12	37.9	38.0	1.8	3.77 (*syn*+*anti*)		
ψp-**3F$_2$**:						
1, 10	37.4	37.5	1.8	3.82/3.75		15.5
3, 12	30.0	29.9	3.4	4.14 (*syn*) 3.45 (*anti*)		14.6
4, 13	123.1	122.9	14.6			
5, 14	160.1	159.5	244.6			
6, 15	116.5	117.0	23.3	6.67	6.67	
7, 16	138.3	138.3	7.6			
8, 17	124.1	123.7	3.0, 0.5	6.80	6.81	7.8
9, 18	131.5	131.7	4.4	6.99	7.00	

[a] Only the sums |J(F,C)+J(F′,C)| are available for ψg-**3F$_2$**.
[b] J(H,H) values unless stated otherwise.

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The ^{13}C signals of the ψg-isomer can also be distinguished from those of the other isomers by their second-order nature due to the non-zero $^{19}F,^{19}F$ coupling constant.

CONCLUSIONS

We have shown that a 1:1:1:1 mixture of the four isomeric *ar,ar'*-difluoro-2,11-dithia[3.3]paracyclophanes $\mathbf{3F_2}$, by conversion into the bissulphones and subsequent pyrolysis, yields the corresponding *ar,ar'*-difluoro[2.2]paracyclophanes $\mathbf{2F_2}$ in a ratio of approximately 3:2:2:1 ($\psi m:\psi o:\psi p:\psi g$). The ^{13}C, ^{1}H and ^{19}F NMR spectra of the isomeric mixture were assigned without separation of the products. Large through-space J(F,F) coupling constants were observed for the *pseudogeminal* isomers of $\mathbf{3F_2}$ (7.2 Hz) and $\mathbf{2F_2}$ (13.7 Hz). The surprisingly large J(F,F) coupling of 2.8 Hz in ψp-$\mathbf{2F_2}$ is thought to be transmitted by a π–π electron interaction between the parallel aromatic rings.

Acknowledgements

We thank Professor W. Grahn for a gift of **2F** and the Fonds der Chemischen Industrie, Frankfurt am Main, for partial support of this work.

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