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^{1}H, ^{13}C and ^{19}F NMR study of 8-fluoro- and 8,12-difluoro[2.2]metaparacyclophane and of 9-fluoro- and 9,14-difluoro-2,11-dithia[3.3]metaparacyclophane†

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ABSTRACT: The ^{1}H, ^{13}C and ^{19}F NMR spectra of 9,14-difluoro-2,11-dithia[3.3]metaparacyclophane, $\mathbf{3F_2}$, and its 9-monofluoro derivative, **3F**, and of 8,12-difluoro[2.2]metaparacyclophane, $\mathbf{2F_2}$, and its 8-monofluoro derivative, **2F**, were experimentally assigned as fully as possible. Two-dimensional shift correlation techniques (H,H-COSY, C,H- and F,H-HETCOR) were applied and experimental ^{1}H and ^{13}C chemical shifts were compared with those predicted by assuming additivity of substituent chemical shifts (SCS). The difluoro compounds $\mathbf{2F_2}$ and $\mathbf{3F_2}$ occur as conformers with *syn*- and *anti*-orientations of the fluorine substituents. The ^{19}F signals of $\mathbf{3F_2}$ undergo coalescence near 398 K (at 188 MHz) from which the barrier to *syn*/*anti*-interconversion is estimated as $\Delta G^{\ddagger} = 77$ kJ mol^{-1}. The shorter bridges in $\mathbf{2F_2}$ increase $\Delta G^{\ddagger}$ to a lower limit of 89 kJ mol^{-1}. A number of through-space *J*(F,C) and *J*(F,H) couplings were observed. The small magnitudes of the *J*(F,F) couplings in $\mathbf{2F_2}$ and $\mathbf{3F_2}$ (0.4–1.9 Hz) do not allow their unambiguous classification as through-space interactions.

KEYWORDS: NMR; ^{1}H NMR; ^{13}C NMR; ^{19}F NMR; cyclophanes, metaparacyclophanes; long-range coupling; conformational barrier

INTRODUCTION

In a recent paper,[1] we derived an equation that describes the F–F distance (d_{FF}) dependence of scalar through-space[2–4] ^{19}F,^{19}F spin–spin coupling constants:

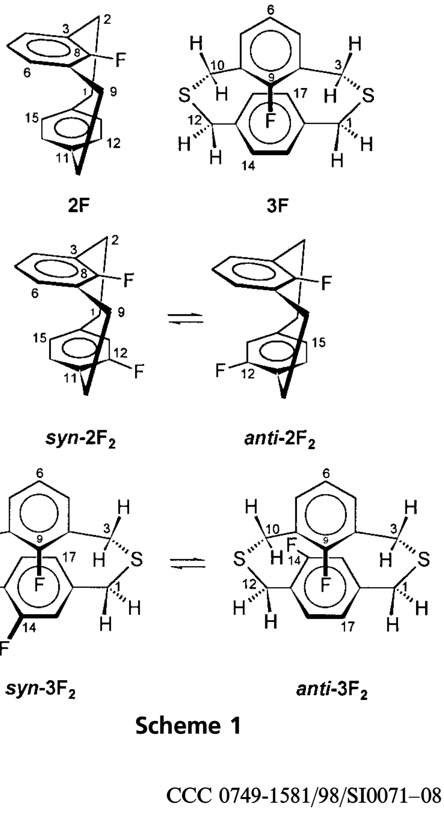
$$J(\mathrm{F,F})[\mathrm{Hz}] = 275\,000 \exp(-0.03211 d_{\mathrm{FF}}\,[\mathrm{pm}]). \quad (1)$$

The data leading to the parameters of Eqn (1) were obtained from difluorinated *syn*-metacyclophanes[5] and paracyclophanes.[6] Because of their particular geometry with the aromatic rings inclined towards each other, the *syn*-metacyclophanes allowed us to realize short non-bonding F–F distances of 242–278 pm whereas larger distances of 300–318 pm occur in the paracyclophanes studied. In this context, we now describe the investigations of difluoro[2.2]- and difluorodithia[3.3]metaparacyclophanes ($\mathbf{2F_2}$ and $\mathbf{3F_2}$, respectively; Scheme 1) carrying one fluorine each at the *para*-bridged ring and between the bridges at the *meta*-bridged ring. For these metaparacyclophanes, slightly larger F–F distances were computed than for the corresponding paracyclophanes. Hence smaller values of through-space *J*(F,F) coupling constants were expected. This would extend the range of the *J*(F,F) *vs.* d_{FF} data pairs and therefore, possibly, the range of non-bonding F–F distances for which Eqn (1) is valid. For the sake of comparison with the difluorometaparacyclophanes, the monofluoro compounds, **2F** and **3F**, with the fluorine at the *meta*-bridged ring were also analysed.

EXPERIMENTAL

Spectra

NMR spectra were recorded at *ca.* 296 K on a Bruker AM-400 spectrometer at 400.1 MHz (^{1}H) and 100.6



Scheme 1

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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 ^1H spectra, to $CDCl_3$ ($\delta = 77.05$) in the ^{13}C spectra and to $\Xi = 94.094056$ 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 ^1H decoupling. For precise determinations of F,C and F,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 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.[7] The high-temperature ^{19}F measurements were performed using a Bruker BVT-1000 variable-temperature unit. The temperature display was calibrated by means of the ^1H chemical shift difference between the CH_2 and OH protons of an 80% ethylene glycol solution in hexadeuteriodimethyl sulfoxide.[8] The spectrum of the calibration sample was measured using the decoupler coils of the ^{19}F probehead. NOE difference spectra[9] 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,[10] depending on the selectivity required.

H,H-COSY[11] experiments and their variants optimized for small long-range couplings (H,H-COSY-LR[12]) 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. C,H-HETCOR spectra[13,14] were run with suppression of H,H coupling in the F_1 dimension.[15,16] 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 C,H-COLOC experiments[17] 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. F,H correlation experiments[18] were carried out with fluorine detection and without suppression of H,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 **$3F_2$** and to 64 and 32 ms, respectively, for **$2F_2$**. 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. Iterative analyses of spin systems were carried out with the NUMMRIT[19] program for Bruker X32 workstations. Electron impact mass spectra were recorded on a Finnigan MAT 8430 mass spectrometer at 70 eV. High-resolution mass determinations were done by peak matching at a resolution of 10000. UV spectra were recorded on a Hewlett-Packard model 8452 diode array spectrometer and infrared spectra on a Nicolet 320 FT-IR spectrometer (KBr pellets). Molecular mechanics computations were carried out using Allinger's program MM2(91).[20] The lacking torsional parameters V_1, V_2 and V_3 for the fragment $C(sp^3)—C(sp^2)—C(sp^2)—F$ were set to 0.0, 15.0 and 0.0 kcal mol^{-1}, respectively.[5]

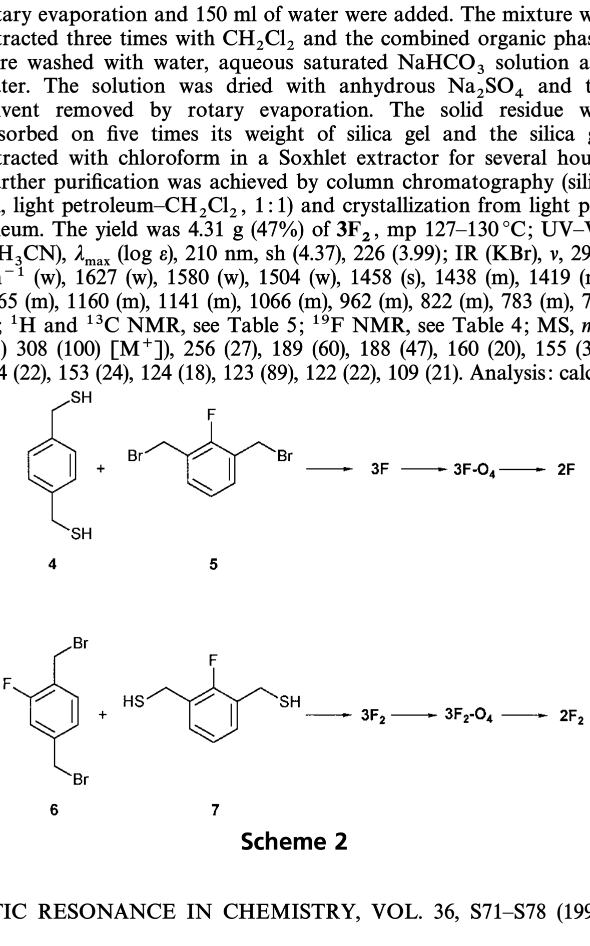
Syntheses

The title compounds were obtained by the reactions depicted in Scheme 2.

9-Fluoro-2,11-dithia[3.3]metaparacyclophane (3F). This known compound[21,22] was prepared[22] from dithiol **4**[23] and dibromide **5**.[24] ^1H and ^{13}C NMR, see Table 2; ^{19}F NMR, see Table 4.

8-Fluoro[2.2]metaparacyclophane (2F). This is also a known compound[21,22] which was obtained in 62% yield (based on converted starting material) by pyrolyzing **$3F\text{-}O_4$**, the *S,S,S′,S′*-tetraoxide[21] of **3F**. A double oven was used with the temperature of the pyrolysis zone set to 550 °C and the temperature of the evaporation zone first to 260 and later to 300 °C. Vögtle[21] reported a yield of 13% (pyrolysis temperature 360 °C). ^1H and ^{13}C NMR, see Table 1; ^{19}F NMR, see Table 4.

9,14-Difluoro-2,11-dithia[3.3]metaparacyclophane ($3F_2$). The preparation followed loosely that described for 2,11-dithia[3.3]metaparacyclophane.[22] A solution of 8.46 g (30.0 mmol) of **6**[6] and 5.65 g (30.0 mmol) of **7** in 2 l of toluene was deoxygenated ('degassed') by bubbling nitrogen through it. Over a period of 24 h it was then slowly added dropwise to a 'degassed' boiling solution of 8.4 g (150 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 solution was dried with anhydrous Na_2SO_4 and the solvent removed by rotary evaporation. The solid residue was adsorbed on five times its weight of silica gel and the silica gel extracted with chloroform in a Soxhlet extractor for several hours. Further purification was achieved by column chromatography (silica gel, light petroleum–CH_2Cl_2, 1:1) and crystallization from light petroleum. The yield was 4.31 g (47%) of **$3F_2$**, mp 127–130 °C; UV–Vis (CH_3CN), λ_{max} (log ε), 210 nm, sh (4.37), 226 (3.99); IR (KBr), ν, 2922 cm^{-1} (w), 1627 (w), 1580 (w), 1504 (w), 1458 (s), 1438 (m), 1419 (m), 1265 (m), 1160 (m), 1141 (m), 1066 (m), 962 (m), 822 (m), 783 (m), 740 (s); ^1H and ^{13}C NMR, see Table 5; ^{19}F NMR, see Table 4; MS, *m/z* (%) 308 (100) [M^+]), 256 (27), 189 (60), 188 (47), 160 (20), 155 (30), 154 (22), 153 (24), 124 (18), 123 (89), 122 (22), 109 (21). Analysis: calcu-



Scheme 2

lated for $C_{16}H_{14}F_2S_2$, C 62.31, H 4.58, S 20.79; found, C 62.16, H 4.23, S 20.48%.

9,14-Difluoro-2,11-dithia[3.3]metaparacyclophane-*S,S,S′,S′*-tetraoxide ($3F_2$-O_4). A 1.50 g (4.9 mmol) amount of **$3F_2$** was stirred for 3 days at room temperature with 20 ml of 50% hydrogen peroxide and 123 ml of glacial acetic acid. The precipitate formed was filtered off, washed with diethyl ether and dried under vacuum to yield 1.60 g (88%) of **$3F_2$-O_4**, m. p. >300 °C. UV–Vis (CH_3CN), λ_{max} (log ε), 200 nm, sh (4.58), 212 (4.25), 224 (4.05), 272 (3.34); IR (KBr), ν, 3049 cm^{-1} (w), 3007 (w), 2980 (w), 2918 (w), 1585 (w), 1508 (w), 1471 (m), 1438 (w), 1413 (w), 1325 (m), 1302 (m), 1265 (m), 1251 (m), 1205 (w), 1173 (w), 1115 (s), 1035 (w), 964 (w), 873 (w), 755 (w), 549 (w), 466 (w); NMR data were not obtained because of low solubility; MS, *m/z* (%) 292 (4), 244 (41) $[M^+ - 2\ SO_2]$, 224 (12), 170 (10), 122 (100) $[C_8H_7F]$. Analysis: calculated for $C_{16}H_{14}F_2O_4S_2$, C 51.60, H 3.79, S 17.22; found, C 51.48, H 3.80, S 17.53%.

8,12-Difluoro[2.2]metaparacyclophane ($2F_2$). A 400 mg (1.1 mmol) amount of **$3F_2$-O_4** was pyrolyzed in an apparatus after Haenel and Staab[25] under a nitrogen atmosphere of 5 Pa at a temperature of 550 °C in the pyrolysis oven and of 260 °C (initially, then raised to 270 °C) in the evaporation oven. The condensate was purified by column chromatography (silica gel, CH_2Cl_2–light petroleum, 1:1) and crystallization from CH_2Cl_2–MeOH. Yield, 108 mg (41%) of **$2F_2$**, m.p. 145 °C; ^1H and ^{13}C NMR, see Table 3; ^{19}F NMR, see Table 4; UV/Vis (CH_3CN), λ_{max} (log ε), 206 nm, sh (4.07), 222, sh (3.56), 230 (3.39), 236 (3.30), 244 (3.17), 280 (2.52); IR (KBr), ν, 3055 cm^{-1} (w), 3020 (w), 2935 (s), 2861 (m), 1566 (m), 1494 (m), 1455 (s), 1441 (s), 1417 (s), 1245 (s), 1195 (s), 1169 (m), 1097 (m), 1064 (m), 873 (w), 815 (m), 777 (s), 737 (m), 720 (w), 617 (w); MS, *m/z* (%) 244 (78) $[M^+]$, 229 (13), 224 (14), 198 (18), 122 (100) $[M^+ - C_8H_7F]$, 96 (15). Analysis: calculated for $C_{16}H_{14}F_2$, C 78.67, H 5.78; found, C 78.80, H 5.87%.

(4-Mercaptomethylphenyl)methanethiol (4).[23] ^1H NMR, $\delta = 7.27$ (s, 4 H, H-ar), 3.72 [d, $^3J(H,H) = 7.4$ Hz, 4 H, CH_2], 1.75 (t, 2 H, SH); ^{13}C NMR, $\delta = 140.0$ (s, C-1,4), 128.4 (d, C-2,3,5,6), 28.6 (t, CH_2).

1,3-Bis(bromomethyl)-2-fluorobenzene (5).[24] ^1H NMR, $\delta = 7.36$ [t, $^3J(F,H) = 7.6$ Hz, $^3J(H,H) = 7.4$ Hz, 2 H, H-4,6], 7.12 (t, 1 H, H-5), 4.52 [d, $^4J(F,H) = 1.1$ Hz, CH_2]; ^{13}C NMR, $\delta = 158.8$ [s, $J(F,C) = 254.1$ Hz, C-2], 131.7 [d, $J(F,C) = 3.6$ Hz, C-4,6], 125.8 [s, $J(F,C) = 14.6$ Hz, C-1,3], 124.7 [d, $J(F,C) = 4.6$ Hz, C-5], 25.2 [t, $J(F,C) = 5.3$ Hz, C-2]; ^{19}F NMR, $\delta = -121.5$.

(2-Fluoro-3-mercaptomethylphenyl)methanethiol (7).[26] ^{19}F NMR, $\delta = -124.4$.

RESULTS AND DISCUSSION

8-Fluoro[2.2]metaparacyclophane (2F)

The signals of the *meta*-bridged ring of **2F** were identified by the magnitudes of the $^{19}F,^{13}C$ coupling constants and by their intensities (C-4,6 *vs.* C-5). The signals of the proton-bearing carbon atoms in the *para*-bridged ring were assigned through a $^{13}C,^1H$-HETCOR spectrum, based on the strong shielding of H-15,16 ($\delta_H = 5.92$) relative to their counterparts H-12,13 ($\delta_H = 7.17$). The shielding of H-15,16 is due to the step-like conformation of the molecule which exposes only these protons to the ring current of the *meta*-bridged ring, *cf.* formula **2F** in Scheme 1. The HETCOR spectrum also served to assign the signals of the bridge carbon atoms after the bridge proton signals had been assigned from the H-1_{syn}/H-13 and H-2_{anti}/H-4 cross peaks in the COSY-LR spectrum which reflect the fact that a cisoid benzylic arrangement, e.g. H-1_{syn}/H-13, leads to stronger cross peaks than a transoid one, e.g. H-1_{syn}/H-15. (The descriptors *syn* and *anti* refer to the orientation of the geminal protons with respect to the fluorine substituent.) We have made use of this fact for assignment purposes several times before.[27,28] The bridge proton assignments were confirmed by the following NOEs (irradiated → enhanced resonances): H-13 → H-1_{syn}, H-2_{syn}; H-4 → H-1_{anti}, H-2_{anti}. The pairing of the geminal protons was also evident from the HETCOR spectrum. Table 1 summarizes the ^{13}C and ^1H NMR data for **2F**. The ^{13}C assignments are in accord with the earlier findings of Takemura and Mori[29] and the chemical shifts agree within 0.1 ppm (note the different numbering scheme of the *para*-bridged ring in Ref. 29). Our $J(^{19}F,^{13}C)$ values are, however, more accurate because the previous data suffer from having been recorded at the coarse digital resolution of 1.25 Hz per data point. In the present study, all ^{13}C signals but one showed ^{19}F coupling albeit rather small (<1 Hz) for the bridge carbons and for C-15,16. Only the resonance of C-11,14 is not split and $J(^{19}F,^{13}C)$ was estimated to be $\leqslant 0.1$ Hz from the half-height linewidth. The couplings $J(^{19}F,^{13}C$-12,13) of 3.7 Hz and $J(^{19}F,^1H$-12,13) of 2.1 Hz are best classified as through-space couplings because the geometry and electronic nature of the pathway between the interacting nuclei are far from being ideal to transmit through-bond couplings of this magnitude. The slope of the C-12,13/H-12,13 HETCOR cross-peak is positive, showing that $J(^{19}F,^{13}C)$ and $J(^{19}F,^1H)$ have like signs, as is the case for the corresponding 4-fluoro[2.2]paracyclophane (**4F22PC**).[6] Relative to the

Table 1. ^{13}C and ^1H NMR data of compound **2F**

Carbon	δ_C	J(F,C) (Hz)	Carbon	δ_C	J(F,C) (Hz)
1,10	37.4	0.9	8	161.4	246.4
2,9	27.9	0.8	11,14	137.2	⩽0.1
3,7	129.0	18.5	12,13	130.6	3.7
4,6	128.2	4.7	15,16	127.0	0.2
5	123.1	4.0			

Proton	δ_H		Proton	δ_H	J(F,H) (Hz)
1,10[a]	3.19/2.49		5	6.80	
2,9	2.78/2.44		12,13	7.17[b]	2.1
4,6	6.73		15,16	5.92	

[a] Shifts given in the order *syn, anti* with respect to the fluorine at C-8.

[b] $J_{12,15} + J_{12,16} = 2.2$ Hz.

latter compound, **2F** shows a larger through-space $J(^{19}F,^{13}C)$ value (3.7 *vs.* 1.6 Hz), which could be due to the decreased non-bonding F–C-distance, which amounts to 280 pm in **2F** and 326 pm in **4F22PC**, according to MM2(91) force field computations.[20] The through-space $J(^{19}F,^{1}H)$ value, on the other hand, is smaller in **2F** (2.1 Hz) than in **4F22PC** (3.1 Hz) although the non-bonding F–H distances are similar: 280 pm in **2F** and 289 pm in **4F22PC**. These distances may therefore not be the only determining factors.

The different ^{13}C and ^{1}H chemical shifts for the opposite sides of the *para*-bridged ring in **2F** show that there is no internal rotation of either this ring or the *meta*-bridged ring on the NMR chemical shift time-scale at room temperature. Such rotation would represent a site exchange of positions 12,13 with 15,16. Vögtle[21] has shown that, at 60 MHz, coalescence of the ^{1}H NMR signals does not take place up to 190 °C and, hence, the rotational barrier ($\Delta G^{\ddagger}$) exceeds 95 kJ mol^{-1}. He found $\Delta G^{\ddagger}(140\,°C) = 84.5 \pm 1.3$ kJ mol^{-1} for the parent [2.2]metaparacyclophane whereas Hefelfinger and Cram[30] reported $\Delta G^{\ddagger}(146\,°C) = 86.2 \pm 1.3$ kJ mol^{-1}. The latter authors showed by the optical stability of a derivative that the kinetic process observed is the rotation of the *meta*-bridged ring.

9-Fluoro-2,11-dithia[3.3]metaparacyclophane (3F)

A rough description of the ^{1}H NMR spectrum of **3F** has been given by Boekelheide *et al.*[22]. They also studied the temperature dependence of the ^{1}H spectrum and determined a $\Delta G^{\ddagger}$ value of 76.1 kJ mol^{-1} (at 93 °C) for the dynamic process taking place (*meta*-ring rotation, see below). This barrier is substantially lower than in **2F** because the increased length of the bridges decreases the strain energy of the transition state. The results of our analysis of the ^{1}H and ^{13}C NMR spectra are given in Table 2. Again, the signal assignments in the ^{13}C spectrum were deduced from the magnitudes of the $^{19}F,^{13}C$ coupling constants, from signal intensities, from the information in the DEPT-135 spectrum and from HETCOR correlations. COLOC cross peaks between the carbon signals of the *para*-bridged ring and the signals of the less shielded geminal proton pair served to distinguish between the two kinds of CH_2 groups. It was not possible to assign the protons within the geminal pairs individually by NOE measurements because polarization/saturation transfer[31] between them took place at room temperature. Thus, irradiation of the H-17 resonance ($\delta = 6.57$) led also to saturation of H-14 and gave strong NOEs at $\delta = 3.88$ and 3.75. Irradiation of any methylene proton resonance caused also saturation of its geminal partner. This indicates that (at least) *meta*-ring rotation occurs sufficiently fast on the T_1 relaxation time-scale at room temperature and causes site exchanges of the protons within the geminal pairs. Rotation of the symmetrical *para*-ring by itself does not exchange the CH_2 proton shifts. *Meta*- and, possibly, *para*-ring rotation must also be the reason for some residual line broadening of the C-14,15 and C-17,18 resonances which prevents the detection of any ^{19}F coupling smaller than 0.7 Hz to C-17,18. The coupling of F-9 to C-14 is, again, considered to be transmitted mainly through space. It amounts to 2.7 Hz, somewhat smaller than J(F-8,C-12) in **2F** and in line with the larger interring distance in **3F** compared with **2F**. The larger distance is also reflected in the smaller chemical shift differences in **3F** between C-14,15 and C-17,18 (0.9 ppm) and between H-14,15 and H-17, 18 (0.50 ppm) relative to **2F** where the analogous differences δ(C-12,13) − δ(C-15,16) and δ(H-12,13) − δ(H-15, 16) are 3.6 and 1.25 ppm, respectively. The inter-ring distance in **3F** is also too large for a through-space coupling to be observed between F-9 and H-14,15.

8,12-Difluoro[2.2]metaparacyclophane ($2F_2$)

The difluoro[2.2]metaparacyclophane $\mathbf{2F_2}$ was found to exist as two stable rotamers with *syn*- and *anti*-oriented

Table 2. ^{13}C and ^{1}H NMR data of compound **3F**

Carbon	δ_C	J(F,C) (Hz)	Carbon	δ_C	J(F,C) (Hz)
1,12	36.9	$\leqslant 0.2$	9	155.4	245.7
3,10	26.4	3.7	13,16	135.2	0.2
4,8	127.6	16.1	14,15	129.3[a]	2.7
5,7	129.8	4.1	17,18	128.4[a]	$\leqslant 0.7$
6	123.5	3.9			
Proton	δ_H	J(H,H) (Hz)	**Proton**	δ_H	J(H,H) (Hz)
1,12[b]	3.88/3.75	13.2 (^2J)	6	6.92	~0.4 [^5J(F,H)]
3,10[b]	3.63/3.37	15.5 (^2J)	14,15	7.07	$N = 2.1$[c]
5,7	7.07	~7.6 (^3J), ~6.9 [^4J(F,H)]	17,18	6.57	

[a] Broadened signals due to exchange.

[b] *Anti*/*syn* relationship relative to the fluorine substituent not implied.

[c] $N = J_{14,17} + J_{14,18}$

fluorine substituents, respectively, in approximately equal proportions. This was most clearly seen in the ^{1}H-decoupled ^{19}F spectrum, which contained two pairs of doublets, one with $J(^{19}F,^{19}F) = 1.87$ Hz and the other with 0.42 Hz (see Table 4). In order to assign the fluorine signals, the ^{1}H NMR spectrum was first assigned (Table 3) and ^{19}F,^{1}H spin coupling correlations were then derived from a ^{19}F,^{1}H-HETCOR experiment. Taking the ^{1}H chemical shifts of the 8-fluoro compound, **2F**, (Table 1) and the chemical shift changes (substituent chemical shifts, SCS) which fluorine causes in the ^{1}H spectrum of benzene,[32] one predicts that the *syn*-conformer should have two proton shifts for the *para*-bridged ring near $\delta = 5.8$ and one near $\delta = 6.8$ whereas in the *anti*-conformer two *para*-ring protons should absorb near $\delta = 7.0$–7.1 and one near $\delta = 5.7$. Inspection of the experimental ^{1}H chemical shift values leaves no doubt as to the assignment of the conformers, (see Table 3).

A ^{19}F,^{1}H-HETCOR experiment optimized for $J(^{19}F,^{1}H) = 7.8$ Hz, approximately the average of the *ortho*- and *meta*-^{19}F,^{1}H coupling constants, helped to assign the chemical shifts of the fluorine nuclei in the *para*-bridged rings of the two conformers. The fluorines in the *meta*-bridged rings were then assigned from the F,F coupling constants and the proton shifts in the same

Table 3. ^{13}C and ^{1}H NMR data of ***syn***- and ***anti***-**2F$_2$**

	syn-2F$_2$		*anti*-2F$_2$	
Carbon	δ_C	J(F,C) (Hz)	δ_C	J(F,C) (Hz)
1	37.1	1.7, 0.7	36.0	2.0, 1.0
2	27.9	0.9, 0.6	28.3	0.9, 0.6
3	128.6	17.6, $\leqslant$0.2	126.7	18.4, 0.7
4	128.3[a]	4.6, $\leqslant$0.2	128.1	4.7, 0.4
5	123.1	4.0, $\leqslant$0.2	123.6	4.2, 0.7
6	128.1[a]	4.6, $\leqslant$0.2	129.2	4.5, 1.6
7	129.3	18.5, $\leqslant$0.2	128.7	18.4, 0.6
8	161.5	245.6, $\leqslant$0.2	161.2	246.8, 0.6
9	25.7	2.0, 1.3	27.7	1.0, 1.0
10	32.6	1.6, 0.8	29.6	0.9, 0.9
11	122.9	18.6, 0.5	124.1	17.3, $\leqslant$0.2
12	163.5	247.3, 3.0	160.3	244.7, $\leqslant$0.2
13	119.2	23.1, 4.3	116.5	24.2, 0.4
14	140.7	7.4, 0.7	140.7	7.6, $\leqslant$0.2
15	123.7	2.5, $\leqslant$0.2	127.1	3.8, 2.8
16	128.9	6.6, 0.5	132.5	4.9, 3.5
Proton	δ_H	J (Hz)	δ_H	J (Hz)
1*syn*	3.15		3.09	
1*anti*	2.48		2.35	13.5 (^{2}J) 10.9 ($^{3}J_{trans}$) 7.3 ($^{3}J_{cis}$) 1.2 [J(F,H)]
2*syn*	2.83		2.83	
2*anti*	2.46		2.49	
4	6.76[a]		6.80	
5	6.78		6.87	
6	6.74[a]		6.85	
9*syn*	3.05		2.79	
9*anti*	2.43		2.50	
10*syn*	3.46	12.6 (^{2}J) 7.3 ($^{3}J_{cis}$)	2.84	
10*anti*	2.27	11.1 ($^{3}J_{trans}$) 7.3 ($^{3}J_{cis}$)	3.09	
13	6.88	11.4 [^{3}J(F,H)] 4.1 [^{n}J(F-8,H)] 1.8 (^{4}J)	5.76	10.2 [^{3}J(F,H)] 1.7 (^{4}J)
15	5.74	7.9 (^{3}J)	7.01	7.8 (^{3}J) 1.9 [^{n}J(F-8,H)]
16	5.87	7.9 [^{4}J(F,H)]	7.14	7.7 [^{4}J(F,H)] 2.4 [^{n}J(F-8,H)]

[a] Assignments are interchangeable.

rings from the F,H-HETCOR and from a H,H-COSY spectrum. Another H,H-COSY spectrum optimized for small coupling constants served to assign the bridge protons in the manner described for **2F**. Finally, the ^{13}C signals of both rotamers were identified by inspecting the cross peaks in C,H-HETCOR and -COLOC spectra. The resulting ^{13}C and ^{1}H assignments are given in Table 3 and the ^{19}F chemical shifts and F,F coupling constants in Table 4.

The potential ^{19}F,^{13}C through-space couplings and the $J(^{19}F,^{19}F)$ values in the conformers of **2F$_2$** are worthy of comment. Although there are observable F,C-couplings in ***syn*-2F$_2$** between F-8 and both C-12 (3.0 Hz) and C-13 (4.3 Hz), which presumably obey a through-space mechanism, a coupling in the opposite direction, i.e. from F-12 to C-8, is not observed. Most likely, the reason for this behaviour lies in the geometry of the molecule. According to our MM2 computations and also to an x-ray diffraction study of the parent molecule,[33] the rings are shifted relative to each other in such a way that the F—C bond at the *meta*-bridged ring lies over the centre of the *para*-bridged ring. This leads to relatively short non-bonding distances F-8 ⋯ C-12 (279 pm, MM2) and F-8 ⋯ C-13 (276 pm) but to a substantially larger distance F-12 ⋯ C-8 (376 pm), in line with the vanishing coupling between the latter nuclei. An analogous situation prevails in ***anti*-2F$_2$** where the shorter distances, F-8 ⋯ C-15 (279 pm) and F-8 ⋯ C-16 (277 pm), give larger F,C-couplings (3.8 and 3.5 Hz, respectively) whereas only small couplings are observed (0.4–1.6 Hz) between F-12 and the distant carbons 4, 5 and 6. Through-space couplings were also found from F-8 to H-15 (1.9 Hz) and H-16 (2.4 Hz). As evidenced by the C,H-HETCOR cross peaks, they have the same sign as J(F-8,C-15) and J(F-8,C-16). Lastly, the F,F-coupling constant is 1.87 Hz in the *syn*- and only 0.42 Hz in the *anti*-conformer. The corresponding F–F distances are computed to be 302 and 489 pm. Looked at superficially, these data may appear to be in line with a through-space F,F-coupling mechanism because of their decrease with distance. However, Eqn (1) which is solely based on *bona fide* F,F through-space coupling constants, would predict a much larger F,F-coupling constant in ***syn*-2F$_2$**, viz. 16.9 Hz for the non-bonding F–F distance of 302 pm estimated by the molecular mechanics method.

High temperature $^{19}F\{^{1}H\}$ NMR measurements using $Cl_2CDCDCl_2$ as the solvent were carried out in an attempt to determine the energy barrier to interconversion of the *syn*- and *anti*-conformers of **2F$_2$**. No indication of commencing signal coalescence or even broadening was observed up to 141 °C (5 °C below the boiling point of the solvent) and the coalescence temperature was estimated to lie well over 150 °C. From this and the smaller of the two chemical shift differences (43.3 Hz in tetrachloroethane-d_2 at 141 °C) between the exchanging fluorine nuclei, $\Delta G^{\ddagger}(150\,°C)$ was calculated to be at least 89 kJ mol^{-1}. Unfortunately, as for both **2F** and **2F$_2$** only lower limits of the rotational barriers could be determined, it is not clear whether the additional fluorine at the *para*-bridged ring in **2F$_2$** causes an increase of the barrier relative to **2F**; see below, however, for a comparison of **3F** and **3F$_2$**.

Table 4. ^{19}F NMR data of compounds **2F** and **3F** and of the isomers of **2F$_2$** and **3F$_2$**

Compound	δ_F	J(F,F) (Hz)	J(F,C)* (Hz)
2F	−105.7		
3F	−117.1		
syn-**2F$_2$**	−110.3 (F-8)	1.87	
	−120.3 (F-12)		
anti-**2F$_2$**	−105.7 (F-8)	0.42	
	−120.4 (F-12)		
syn-**3F$_2$**	−118.9 (F-9)	0.49	244.7
	−120.1 (F-14)		245.3
anti-**3F$_2$**	−117.1 (F-9)	0.66	245.3
	−116.1 (F-14)		249.8

* From the ^{13}C satellites.

9,14-Difluoro-2,11-dithia[3.3]metaparacyclophane (3F$_2$)

At room temperature, this compound also shows two sets of equally intense NMR signals for two rotamers that differ by *syn*/*anti*-orientation of the fluorine substituents. The identification of the rotamers followed largely the procedure described above for **2F$_2$**, i.e. assignment of the ^{1}H spectrum of the *para*-bridged rings by applying the SCS values of a fluorine substituent to the ^{1}H shifts of **3F** followed by a F,H-HETCOR experiment to assign the ^{19}F chemical shifts and H,H-COSY plus H,H-COSY-LR experiments to analyse the rest of the ^{1}H spectrum as well as C,H-HETCOR and -COLOC for the ^{13}C spectrum. Additionally, the $^{1}J(^{19}F,^{13}C)$ values extracted from the ^{13}C spectrum and from the ^{13}C satellites in the ^{19}F spectrum proved the correct assignment of the ^{19}F shifts to the four fluorine atoms in both rotamers of **3F$_2$**. The ^{19}F results are given in Table 4 and the ^{1}H and ^{13}C results in Table 5.

In analogy with **3F**, substantial through-space F,C-coupling constants are found between F-9 and C-14 and C-15 in the *syn*-rotamer and between F-9 and C-17 and C-18 in the *anti*-rotamer. As in **3F**, the non-bonding inter-ring F–H-distances are already too large for through-space F,H-couplings to be observable. Likewise, the F,F-couplings are very small, viz. 0.49 Hz in ***syn*-3F$_2$** and 0.7 Hz in ***anti*- 3F$_2$**. This 'wrong' order and the small magnitude of 0.5 Hz, compared with a value of 6.9 Hz predicted by Eqn (1) with an F–F-distance of 330 pm for $J(^{19}F,^{19}F)$ in ***syn*-3F$_2$**, speak against a through-space mechanism for this coupling. Thus, the fluorinated dithia[3.3]- and [2.2]metaparacyclophanes behave equally in this respect.

In the variable-temperature ^{19}F NMR spectra of **3F$_2$**, the 'inner two' of the four ^{19}F signals (for F-9 in the *syn*- and *anti*-rotamers) showed coalescence at 125 ± 3 °C and the 'outer' signals (for F-14) at a some-

Table 5. ^{13}C and ^{1}H NMR data of *syn*- and *anti*-$3F_2$

	syn-$3F_2$		*anti*-$3F_2$	
Carbon	δ_C	J(F,C) (Hz)	δ_C	J(F,C) (Hz)
1	36.5	1.6	36.8	1.9
3	26.5	3.6	26.9	3.6
4	127.9^a	16.2	127.2^b	15.9, $\geqslant 0.3^c$
5	129.6	4.0	129.8	4.0
6	123.5	3.9	123.6	4.0, 0.2
7	129.8	4.0	130.1	4.3
8	127.5^a	16.1	126.7^b	15.9, $\geqslant 0.2^c$
9	155.4	244.8	155.1	245.7
10	26.4	4.1	26.0	3.6
12	27.5	4.0	30.5	2.0
13	121.4	13.3	123.7	15.8
14	160.0	245.4, 2.2	160.1	249.9
15	117.1	23.5, 3.0	114.9	21.7
16	137.8	7.5, $\geqslant 0.3^c$	138.9	7.7, $\geqslant 0.3^c$
17	124.3	3.3	125.3	2.8, 2.8
18	130.5	3.6	130.8	5.0, 2.4
Proton	δ_H	J(H,H) (Hz)	δ_H	J(H,H) (Hz)
1*syn*	3.83	13.0 (^2J)	3.88	13.5 (^2J)
1*anti*	3.72		3.69	
3*syn*	3.68	15.7 (^2J)	3.67	15.5 (^2J)
3*anti*	3.41		3.41	
5	7.05	7.7 (^3J)	7.12	7.7 (^3J)
6	6.93	7.7 (^3J)	6.98	7.7 (^3J)
7	7.10		7.20	
10*syn*	3.69	16.5 (^2J)	3.68	15.7 (^2J)
10*anti*	3.35		3.37	
12*syn*	4.40	13.5 (^2J)	3.79	12.9 (^2J)
12*anti*	3.34		3.83	
15	6.90	10.2 [^3J(F,H)] 1.8 (^4J)	6.26	11.1 (^3J(F,H)] 1.8 (^4J)
17	6.36	8.0 (^3J)	6.91	7.7 (^3J)
18	6.57	7.9 [^4J(F,H)]	7.09	7.7 [^4J(F,H)]

^{a,b} Identical marks indicate interchangeable assignments.
^{c} Incompletely resolved splitting.

what higher temperature (in $Cl_2CDCDCl_2$). The higher coalescence temperature could not be determined exactly because the averaged shift of the F-14 signals is close to the averaged shift of the F-9 resonances. With a shift difference extrapolated to the coalescence temperature of 306 ± 12 Hz, a $\Delta G^{\ddagger}$ value of 77.0 ± 0.6 kJ mol^{-1} was calculated in close agreement with Boekelheide *et al.*'s value[22] for **3F** (76.2 kJ mol^{-1}). Hence, the additional fluorine substituent at the *para*-bridged ring does not significantly increase the barrier to internal rotation. This appears reasonable as molecular models show that the C-14–F-14 moiety is hardly involved when the tip of the *meta*- bridged ring rotates through the interior of the molecule.

CONCLUSIONS

A number of medium-sized interring ^{19}F,^{13}C couplings have been observed in the fluorinated [2.2]metaparacyclophanes, **2F** and **2F$_2$**, and 2,11-dithia[3.3]metaparacyclophanes, **3F** and **3F$_2$**. According to their size and the relative spatial arrangement of the carbon and fluorine nuclei involved, these couplings are thought to obey mainly a ‘through-space’ mechanism. The same is true for some ^{19}F,^{1}H couplings, but only in the [2.2]metaparacyclophanes. Such couplings could not be observed in the dithia[3.3]metaparacyclophanes because of the larger non-bonding F–H-distances.

The difluoro compounds **2F$_2$** and **3F$_2$** exist as *syn*/*anti* conformers which are long-lived on the NMR timescale at room temperature. The barrier to interconversion in **3F$_2$** is practically identical with that in the monofluoro compound **3F**, whereas the barrier in **2F$_2$** is too high to be determined by coalescence experiments. ^{19}F,^{19}F-couplings are observed in the two conformers of both **2F$_2$** and **3F$_2$**. However, these couplings are much smaller than expected for a prevailing through-space mechanism. This can be judged by applying Eqn (1) to the non-bonding F–F-distances that result from molecular mechanics computations. Although the F–F-distances in ***syn*-2F$_2$** (302 pm) and in the pseudogeminal difluoro[2.2]paracyclophane[6] (300 pm) are calculated to be very similar, the ^{19}F,^{19}F-coupling constants differ substantially and amount to 1.87 and 13.7 Hz, respectively. The inapplicability of Eqn (1) to the $J(^{19}\mathrm{F},^{19}\mathrm{F})$ values in the metaparacyclophanes may be due to the different geometrical arrangement of the C—F bonds in the compounds studied here compared to the difluoro[*n.n*]meta- and -paracyclophanes ($n = 2$, 3) from which the equation was derived. Formally, the aromatic rings in **2F$_2$** and **3F$_2$** are twisted relative to each other by 30° about an axis joining their midpoints, whereas no such large twist is present in the meta- and paracyclophanes. This could indicate that factors other than the non-bonding distance may contribute to determining the magnitude of through-space coupling constants.

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