

Difluoro[2.2]paracyclophanes Characterization by ^1H , ^{13}C and ^{19}F NMR

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Abstract

The four isomers of difluoro[2.2]paracyclophane are uniquely identified on the basis of their ^1H , ^{13}C and ^{19}F NMR spectra. $^{13}\text{C}/^{12}\text{C}$ isotope effects on the ^{19}F chemical shifts were measured and a small transannular effect was detected. © 1998 Elsevier Science S.A. All rights reserved.

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1. Results and discussion

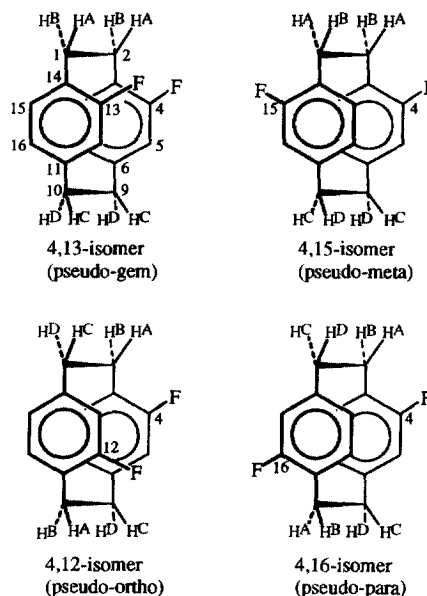
The four isomers of difluoro[2.2]paracyclophane, of which the 4,12- and 4,15-isomers are chiral, were synthesized as described previously [1]. HPLC-separated fractions were used for the preparation of all NMR samples and the purity of these fractions was most conveniently monitored by ^{19}F NMR. Samples of the 4,13-isomer and of the 4,12-isomer were free of other isomers. There was overlapping of HPLC peaks for the 4,15- and 4,16-isomers, but repeated cycles of injection and collection increased the concentration of each isomer to ~70% and allowed an unambiguous assignment of NMR peaks.

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Table 1
 ^1H NMR chemical shifts for difluoro[2.2]paracyclophanes

Isomer	H5	H7	H8	H ^A	H ^B	H ^C	H ^D
4,13-isomer	6.15	6.37	6.43	2.75	3.47	3.02	3.02
4,15-isomer	5.92	6.39	6.87*	2.77	3.25	2.97	2.97
4,12-isomer	6.38*	6.32	6.50	2.67	3.32	2.98	2.98
4,16-isomer	5.87	6.73*	6.46	2.7	3.37	3.0	3.0

*: Indicates the presence of a fluorine substituent on the directly opposite benzene ring position (pseudo-gem relationship).



The ^1H , ^{13}C and ^{19}F NMR data of the four isomers of difluoro[2.2]paracyclophane are summarized in Tables 1, 2 and 3 and the chemical shifts are shown schematically in Fig. 1. The assignment of NMR peaks and the unique identification of each isomer is relatively straightforward once the intra- and inter-ring effects of fluorine substituents are taken into account. Of particular importance is the pseudo-gem

Table 2
 ^{13}C NMR chemical shifts of difluoro[2.2]paracyclophanes

Isomer	C3	C4	C5	C6	C7	C8	C2	C9
4,13-isomer	125.4	162.1*	121.0	142.1	128.8	135.5	28.4	35.0
4,15-isomer	126.2	161.3	121.3	142.2	127.7	131.7*	29.1	34.4
4,12-isomer	125.2	161.3	118.2*	143.4	128.3	135.8	29.7	33.6
4,16-isomer	125.3	161.4	122.4	142.7	125.6*	134.8	29.7	33.4

*: Indicates the presence of a fluorine substituent on the directly opposite benzene ring position (pseudo-gem relationship).

Table 3
 ^{19}F NMR chemical shifts, coupling constants and fluorine isotope shifts, $\Delta\text{F}(^{13}\text{C}/^{12}\text{C})$, for difluoro[2.2]paracyclophanes

Isomer	δF (ppm)	$J(\text{F,F})$ (Hz)	$^1J(\text{C4,F})$ (Hz)	$^2J(\text{C3,F})$ (ppb)	$^2J(\text{C5,F})$	$^1\Delta\text{F}(\text{C4})^a$	$^2\Delta\text{F}(\text{C3})^a$	$^2\Delta\text{F}(\text{C5})^a$
4,13-isomer	-118.1*	13.63*	247.95*	17.55	23.00	-78*		
4,15-isomer	-112.3	0.36	245.94	18.00	21.96	-83	-22	-21
4,12-isomer	-114.0	0.69	245.72	17.90	22.73*	-81	-22	-20*
4,16-isomer	-113.8	2.76	245.55	18.04	22.68	-82		-21

^aFluorine isotope shifts of ^{12}C and ^{13}C compounds. A negative sign implies increased shielding as a result of substitution with the heavier isotope, e.g., $\Delta^{19}\text{F}(^{13}\text{C4}/^{12}\text{C4}) = \delta^{19}\text{F}(^{13}\text{C4}) - \delta^{19}\text{F}(^{12}\text{C4})$.

*: Indicates the presence of a fluorine substituent on the directly opposite benzene ring position (pseudo-gem relationship).

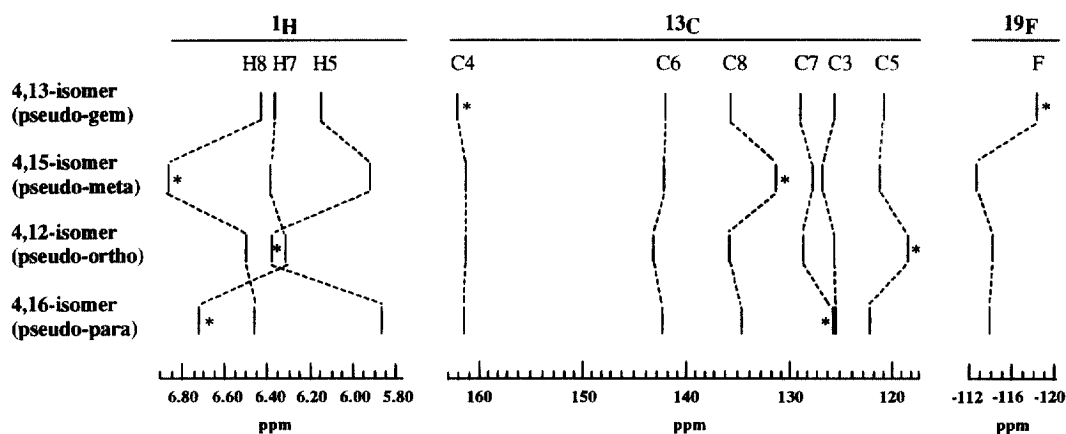


Fig. 1. Summary of NMR chemical shifts of four isomers of difluoro[2.2]paracyclophane. Data are taken from Tables 1, 2 and 3. An asterisk indicates the presence of a fluorine substituent on the directly opposite benzene ring position (pseudo-gem relationship).

relationship, in which a fluorine is on the directly opposite benzene ring position, and an asterisk is used in Tables 1, 2, 3 and Fig. 1 to highlight this pseudo-gem relationship.

The assignments of NMR spectra are in agreement with those of other substituted[2.2]paracyclophanes. For example, the ^1H chemical shift trend of H5 (5.87 ppm), H7 (6.73) and H8 (6.46) in the 4,16-isomer is nearly identical, except for a small upfield displacement of 0.18–0.21 ppm, to that of H5 (5.69), H7 (6.52) and H8 (6.26) in pseudo-*p*-dihydroxy[2.2]paracyclophane [2]. Similarly, H5 (6.38), H7 (6.32) and H8 (6.50) in the 4,12-isomer are nearly identical, except for an upfield displacement of 0.10–0.24 ppm, with H5 (6.28), H7 (6.08) and H8 (6.36) in pseudo-*o*-dihydroxy[2.2]paracyclophane [2]. The downfield ethano bridge protons H^A at 2.67–2.77 ppm (Table 1) are adjacent to a ring fluorine, analogous to the downfield peak δH 2.98 in polyfluoroaryl[2.2]paracyclophanes which is assigned to

ethano protons adjacent to the fluorinated ring, whereas peaks at δH 3.07 are assigned to ethano protons adjacent to the non-fluorinated ring [3]. A pronounced downfield shift is found for δC4 in all four isomers, i.e., δC4 161.3–162.1 ppm (Fig. 1 and Table 2), and a similar effect is found in 4-fluoro[2.2]paracyclophane, i.e., δC4 161.1 [4].

Slightly larger coupling, $^1J(\text{CF})$ 247.95 Hz, is found for the 4,13-isomer (pseudo-gem fluorine) than for the other isomers, 245.55–245.94 Hz (Table 2). The largest fluorine–fluorine coupling, $J(\text{FF})$ 13.62 Hz, is also found for the 4,13-isomer, with significantly smaller couplings in the other isomers, 0.36 to 2.78 Hz (Table 2). Ernst et al. [5] and Ernst and Ibrom [6] have established a correlation in fluorocyclophanes between $J(\text{FF})$ and the F,F internuclear distance [5,6].

Additional peaks are found in the high resolution ^{19}F NMR spectra which are assigned to ^{13}C isotopomers (Table 2). The

carbon $^{12}\text{C}/^{13}\text{C}$ isotope effect of C4 on $\delta^{19}\text{F}$ is -78 ppb for the 4,13-isomer (pseudo-gem), and the isotope effect is slightly larger for the other isomers, -81 to -83 ppb. The isotope effect due to C3 and C5 is less and varies between -20 and -22 ppb in the 4,15-, 4,12- and 4,16-isomers, and the slightly lower value of -20 ppb is associated with a pseudo-gem fluorine. A negative sign implies increased shielding for the heavier isotopomer.

2. Experimental

NMR spectra were recorded on a Bruker AM300 spectrometer at 300.1 (^1H), 282.4 (^{19}F), and 75.47 (^{13}C) MHz, with the use of CHCl_3 (7.24 ppm w.r.t to TMS), C_6F_6 (-162.9 ppm w.r.t. to CFCl_3), and CDCl_3 (77.0 ppm w.r.t. to TMS), respectively, as internal references. Chemical shifts

and coupling constants are given in Tables 1, 2 and 3, and a summary of chemical shifts is shown in Fig. 1.

The synthesis of isomers of difluoro[2.2]paracyclophane, and the manual collection of HPLC fractions for the preparation of NMR samples was carried out as described previously [1].

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