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A FLUORINE NMR DATABASE

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SUMMARY

We have established a fluorine chemical shift database for compounds with the empirical formula C_xF_y. Each record contains the compound's name, literature reference, empirical formula, functional group information, and a nine digit location code and chemical shift for each resonance. The database has over 500 compounds and 3000 chemical shifts. We can ask questions both about compounds as a whole or individual fluorines. Some structures in the literature are inconsistent with the reported nmr parameters. Chemical shift assignments which were not possible earlier can now be made because of the correlations developed in this work.

INTRODUCTION

Fluorine-19 nmr is a powerful analytical method and is recognized as an essential tool in the elucidation of the structure of fluorine-containing compounds. The potential value of the information obtained from a 19-F nmr spectrum is reflected in the number of published tables of 19-F nmr data.[1-3]

Examination of these tables reveals that they are organized on the basis of functional group, i.e., all resonances of a particular functional group (e.g. CF_3) are placed together and then further subdivided by empirical formula or neighboring functional groups. Although this makes it relatively easy to determine the expected range of chemical shift values for a given functional group, it is time-consuming to use these tables to piece together the entire spectrum for a compound with several different types of fluorine. Moreover, it is almost impossible to identify the set of functional groups that might have given rise to an observed 19-F nmr resonance.

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There are no published 19-F nmr tables organized on the basis of chemical shifts, i.e., all chemical shifts listed in numerical order followed by identification of the functional group and specific compound being examined. And yet this is one common way 19-F nmr spectral problems are posed: Which compound (or set of compounds) could possibly give rise to a spectrum with resonances at x, y, and z ppm?

Since the earliest days of nmr, there have been attempts to find correlations between chemical shifts and structural elements. These efforts have been successful with carbon[4] and proton[5] nmr. For fluorine nmr, parameters have been found to fit restricted sets[6,7] of compounds, but the general problem remains unsolved.

Because we perceived a need for a fast and efficient method of answering these and other types of spectral questions, we have assembled a computer-accessible database of 19-F nmr parameters of the perfluorocarbons. In this way, the various types of 19-F nmr data in the database can be accessed in different ways, depending more on the nature of the information desired, and less on the way in which the data is organized.

Although it would be enormously helpful to have all the world's nmr data available in this form, that is not feasible at the present time. Even to assemble all of the 19-F nmr data would require a major commitment of time and resources. We have chosen, therefore, to limit our initial database to neutral perfluorocarbon compounds, C_xF_y. All unmarked bonds to any structure are assumed to be to fluorine. Other workers have also seen the need for searchable fluorine nmr databases. Both carbon-13[8] and fluorine-19[9] spectra have been assembled and are available in machine readable form. The fluorine nmr database [9] has more compounds, a broader selection of compounds, more information about the compounds and their spectra, but is not exhaustive in any one category as is ours in the domain of perfluorocarbons.

This paper describes how the fluorine nmr data were assembled and what information is included for each compound. Examples are given to illustrate the range of questions that can be answered and the insights that can be gained from statistical analysis of this data. The results should be considered less an exercise in computer science than a tool which working synthetic chemists can use to help identify the compounds they prepare.

Gathering the 19-F NMR Data

A combination of manual and computer-assisted retrieval methods was used to search the chemical literature for references to 19-F nmr data for perfluorocarbons, C_xF_y. Chemical Abstracts Formula Indices, 1957-1966, were used to find data published prior to 1967. Because of the computer search strategy employed, Chemical Abstracts Formula Indices, 1967-1981, were also used to search for spectra of selected compounds with fewer than seven fluorine atoms.

The search strategy constructed for CAS Online® was carried out in two stages. First, a substructure search was done in the registry file (Reg File) to retrieve all compounds which contain seven or more fluorine atoms and no atoms other than C, H or F.* Second, the bibliographic file (CA File) was searched for 'preparations' for the 968 compounds retrieved from the Registry File. Over 724 non-patent references were retrieved from the CA File, most of which were searched manually for the desired nmr information. In addition, cross-references were checked when appropriate to find references that were not retrieved by the strategy outlined above. This strategy has some weaknesses, e.g., a 'pure' nmr study of previously known compounds will not be uncovered by this search method. However, the compounds found were sufficiently numerous and diverse in nature to allow the construction of a useful database.

Data Selection

Our 19-F nmr database is chemical-shift oriented; no coupling constants are included. In part this is because the high dispersion of 19-F nmr generally allows structure assignment on the basis of chemical shift information alone. More importantly, full analysis of 19-F nmr spectra is available only for the simplest of molecules; the phrase 'multiplet' occurs regularly in the literature.

We have chosen to include essentially all reasonable chemical shift information that we could find. Even if only one or a few isolated resonances were assigned in a spectrum, those chemical shifts are included. Attempts were made to complete the assignments of spectra where

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*A more sophisticated strategy could have eliminated many of the partially fluorinated hydrocarbons which were retrieved. However, we hope to incorporate this 'extra' data into a database for compounds at a later date.

the shifts were given but not assigned. On the other hand, reports of ‘multiplet between 100-200 ppm’ are completely useless for our purposes.

In some cases, several spectra of the same compound are included in the database. If we remeasured an nmr spectrum of a compound whose spectrum is already in the database, our own shifts are included. For some compounds which we repeatedly encountered, each spectrum is included to illustrate the variability of chemical shifts even under high dilution, constant solvent conditions.

All chemical shifts are reported in ppm upfield from $CFCl_3$; other standards were converted when necessary. Since in general, solvent and concentration effects cannot be corrected for, this information was not stored, but simply increases the variance of the data.

Fields of Definition

Our database is stored on a VAX-cluster within the program Datatrieve®. For transportability the entire database can be printed as an ASCII file. The structure of the database is:

```
DEFINE RECORD FS1 USING
01      FLUORINE.
        03          NAME PIC X(35).
        03          FORMULA QUERY_NAME FORM.
                    06       C PIC 9(2) EDIT_STRING IS Z9.
                    06       F PIC 9(2) EDIT_STRING IS Z9.
        03          REFERENCE QUERY_NAME REF.
                    06       JOURNAL PIC X(5).
                    06       VOL PIC X(3).
                    06       PAGE PIC 9(4) EDIT_STRING IS ZZZ9.
                    06       YEAR PIC 9(2).
        03          COMMENTS QUERY_NAME COM PIC X(10).
        03          NUMBER_FS QUERY_NAME NOF PIC 9(2).
        03          FS OCCURS 1 TO 30 TIMES DEPENDING ON
                    NUMBER_FS.
                    04       EACH_FS QUERY_NAME FL.
                    06       LOC PIC 9(9).
                    06       LOCX REDEFINES LOC.
                             07      BF PIC 9(1).
                             07      GF3 PIC 9(1).
                             07      GF2 PIC 9(1).
                             07      GF1 PIC 9(1).
                             07      GFO PIC 9(1).
                             07      DF3 PIC 9(1).
                             07      DF2 PIC 9(1).
                             07      DF1 PIC 9(1).
                             07      DFO PIC 9(1).
                    06       DELTA PIC 999V9 EDIT_STRING IS ZZ9.9
```

Thirty-five characters are reserved for the name of the compound. Hydrocarbon nomenclature is used; perfluoro is assumed. Common fragments (ethyl, methyl, phenyl, etc.) are abbreviated (ET, ME, PH, etc.) to accommodate as much of the chemical name as possible in the space allotted to this field.

Two spaces each are reserved for the number of Carbons and Fluorines. The combined field can be accessed as FORMula. The JOURNAL name is abbreviated to five characters.

Ten spaces are reserved for single-letter 'COMments' chosen from the list in Table 1. The comments apply to the structure as a whole, not to any one resonance. The numbers in parentheses refer to the number of occurrences of each comment. By using the proper Boolean expression, for example, all compounds with six-membered rings, an endocyclic diene, and no aromatic ring can be isolated.

'NOF' refers to the number of locations and shifts to be included for the compound. In the absence of ambiguous assignments, this is the number of resonances observed.

The location code can be parsed in either of two ways. First, it is a nine-digit entity which can be used to retrieve all fluorines which match it exactly. Second, each of the nine digits representing BF, GF_3...DF_0 can be individually searched. BF is the number of beta fluorines, i.e. the number of other fluorines attached to the same carbon as a given fluorine. Thus BF is two for each of the fluorines of a CF_3 group, one for the fluorines of a $-CF_2-$ group and zero for the fluorine of a $\geqslant$C-F group. GF3 is the number of gamma CF_3 groups, i.e. the number of CF_3 groups attached to the same carbon as a given fluorine. Similarly, GF_2, GF_1 and GF_0 refer to the number of $-CF_2-$, $\geqslant$CF and $\geqslant$C- groups, respectively, attached to the same carbon as a given fluorine. DF_3, DF_2, DF_1 and DF_0 refer to the number of $-CF_3$, $-CF_2-$, $\geqslant$CF and $\geqslant$C- groups, respectively, attached to carbons one bond away from the carbon to which a given fluorine is attached.

A persistent problem in databases of this kind is how to handle ambiguous assignments. For example, the assignment of two distinct CF_3 resonances to their corresponding chemically non-equivalent CF_3 groups may not be certain. In such cases, we have placed four entries in the database. Two entries have the precise location codes for the two CF_3 groups and a 999 designator for the chemical shift indicating the ambiguity. The other two entries have the precise chemical shifts and a 9 in the positions of the location code which differ for the two resonances.

TABLE 1

Comment codes[a]

A	Acetylene (14)	1	1,1-Disubstituted Olefin (53)
B	Bicyclic (87)	2	
C		3	Cyclopropyl (33)
D	Diene (81)	4	Cyclobutyl (116)
E	Entgegen Olefin (42)	5	Cyclopentyl (85)
F		6	Cyclohexyl (138)
G		7	Cycloheptyl (13)
H		8	Cyclooctyl (8)
I	Trisubstituted Olefin (121)	9	
J		0	
K	Alkane (59)	?	Questionable data
L			
M			
N	Endo Olefin (14)		
O	Olefin (389)		
P	Polycyclic (64)		
Q	Tetrasubstituted Olefin (97)		
R	Aromatic (150)		
S	Spiro (2)		
T	Terminal Olefin (27)		
U	Cumulene (12)		
V			
W			
X	Exocyclic Olefin (34)		
Y			
Z	Zuzammen Olefin (119)		

[a] The numbers in parentheses refer to the number of occurrences in the database.

If to within the five-atom shell location code the two CF_3 groups code the same, then to this database there is no ambiguity.

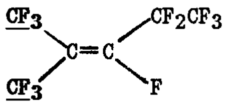
Models

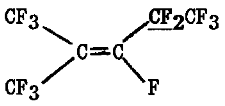
19-F nmr chemical shifts cannot be modelled by simply enumerating the number of alpha, beta and gamma carbons. Parameters analogous to those derived for carbon nmr[4] and fluorine nmr of lightly fluorinated systems[10] could not be found. Because both carbon and fluorine are heavy atoms, both need to be considered for their effects on chemical shifts.

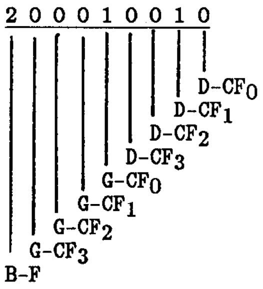
A system based on the number of alpha, beta and gamma carbons and alpha, beta and gamma fluorines (six terms) is still inadequate because it does not distinguish (one CF_2 group plus one quaternary carbon, $>C-\underline{CF}-CF_2$) from (two CF groups, $>CF-\underline{CF}-CF<$) on either side of the fluorine of interest.

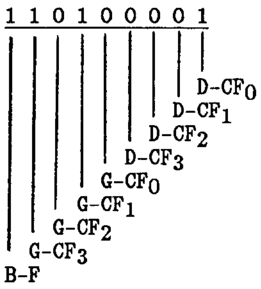
The model we chose includes nine parameters. First is the number of beta fluorines, that is the number of fluorines on the same carbon as the fluorine of interest. Next are the number of gamma and delta CF_3, CF_2, CF_1 and CF_0 groups.

The structural code for two of the fluorines in the 2-methyl-2-pentene are developed below.









This formulation still has limitations. It does not distinguish conformations, cis-trans, or exo-endo geometrical effects. The interior CF_2 groups of linear chains are not differentiated from those in rings.

The two fluorines on C-7 of F-norbornene differ by 19 ppm,[11] yet have the same location code. Two terminal fluorines of $=CF_2$ groups differ by an average of 15 ppm, yet also have identical location codes. Para fluorines in aromatics vary according to electronic effects, yet these are not accommodated by our coding system. The effects of solvent, concentration, temperature and external referencing all combine to produce scatter of the same order as some of the effects we try to measure.

The database represents a compromise between complete structural information, and ease of entry and speed of searching.

Statistics

Having described the construction of this database and the types of the information in each record, we would now like to give some examples of how this data can be manipulated and what insights can be gained from this analysis.

The distribution of the compounds present is not random. Figure 1 shows a plot of the carbon number of the compounds in the database vs. the number of examples. Those present reflect the interests of the synthetic community and the thermodynamics and kinetics of perfluorocarbon chemistry.

Most, but not all, of the smaller carbon content compounds are present. We did not find spectra for some very simple compounds such as difluoroacetylene, F-2,2-dimethyl butane, and F-2,2-dimethylpentane. The majority of the compounds in the database are between C-6 and C-12 with a notable minimum at C-11. Even numbers seem over-represented relative to odd. Aromatic compounds are more heavily represented in the higher carbon numbers than the aliphatics. Dewar benzenes are overrepresented.

By selecting from the beta fluorine field, we can determine that of the 2500* completely assigned chemical shifts there are 1029 CF,

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*This database is a living document, and as new compounds are added the statistics change. The analyses presented were done at different times with different numbers of compounds present. Hopefully, general conclusions will be insensitive to new additions.

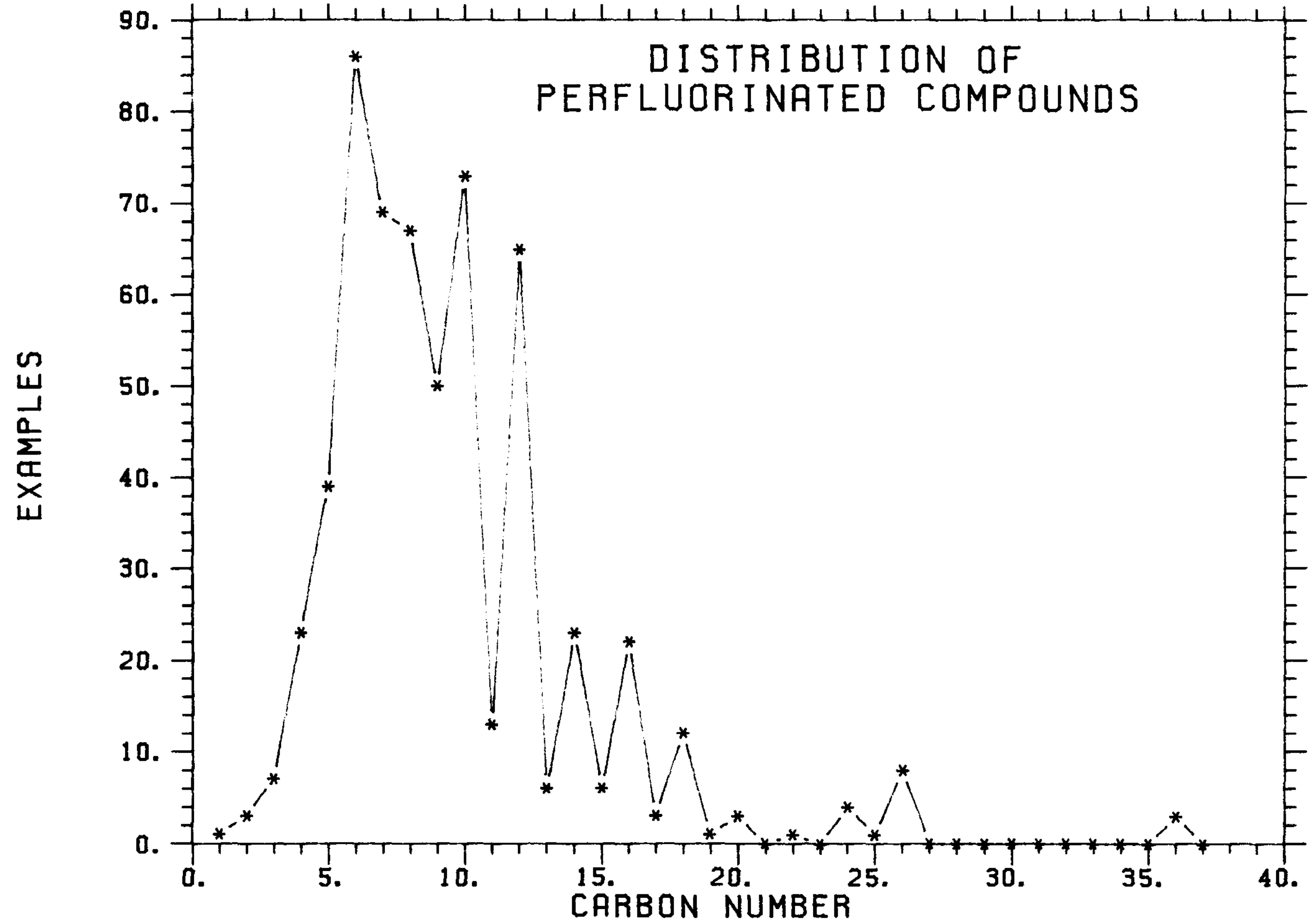


Fig. 1. Number of Examples _vs_. Carbon Number.

809 CF_2, 661 CF_3 and one CF_4. By summing the number of gamma substituents, we can determine the hybridization of the carbon to which the fluorine is attached. The fluorines are attached to 1623 sp^3 carbons, 956 sp^2 carbons and 2 sp carbons. Combining these two sorts, we can divide the CF_2 groups into 149 from terminal olefins (73 cis/trans pairs of $=CF_2$ resonances, two reports of $(CF_3)_2C=CF_2$ and one C_2F_4) and 695 aliphatic $-CF_2-$ groups. The CF groups include 807 =CF- and 238 >CF- groups. It is not possible to further subdivide the =CF- resonances into olefinic and aromatic with our coding system.

Of the 257 CF_3 groups attached to sp^3 carbon, 13 are $(CF_3)_3C$, 78 are $(CF_3)_2CF$, 65 are CF_3CF_2 and 1 is CF_3CF_3. Of the CF_3 groups with no adjacent fluorines, 13 are on an sp carbon, 27 are on an sp^2 carbon and 16 are adjacent to a quaternary sp^3 center.

Figure 2 shows a plot of the number of resonances in a 10 ppm range <u>vs</u>. the center of the range. Each of the three basic fluorine types, sp, sp^2, sp^3 is plotted separately. Although the ranges overlap at the low field end, the highest field resonance of the three classes are distinctly separated at 234, 158 and 89 ppm, respectively. The data for sp carbon shifts are clearly not normally distributed, and represent many different populations which must be considered separately.

Correlations of Local Environment with Shifts

We will first consider correlations of single resonances with structural features. Table 2 contains information about environments of CF_3 groups.

CF_3 GROUPS. The chemical shifts of CF_3 groups attached to sp^3 carbons are most sensitive to the environment of the beta carbon. Each replacement of fluorine by a carbon substituent causes a downfield shift of the gamma CF_3 group by about 10 ppm. CF_3 groups attached to olefinic carbons also show this same 10 ppm downfield shift. The effect of changes at the delta position is comparable to the noise in the data. The shift of CF_3 next to a CF seems characteristic of the number of gamma fluorine atoms independent of whether the carbon has sp^2 or sp^3 hybridization.

Aromatic CF_3 groups occur at lower field than olefinic CF_3. The shift is only slightly sensitive to the ortho substituents. CF_3 on acetylenic carbons in general are at the lowest field, but the range overlaps aromatic CF_3.

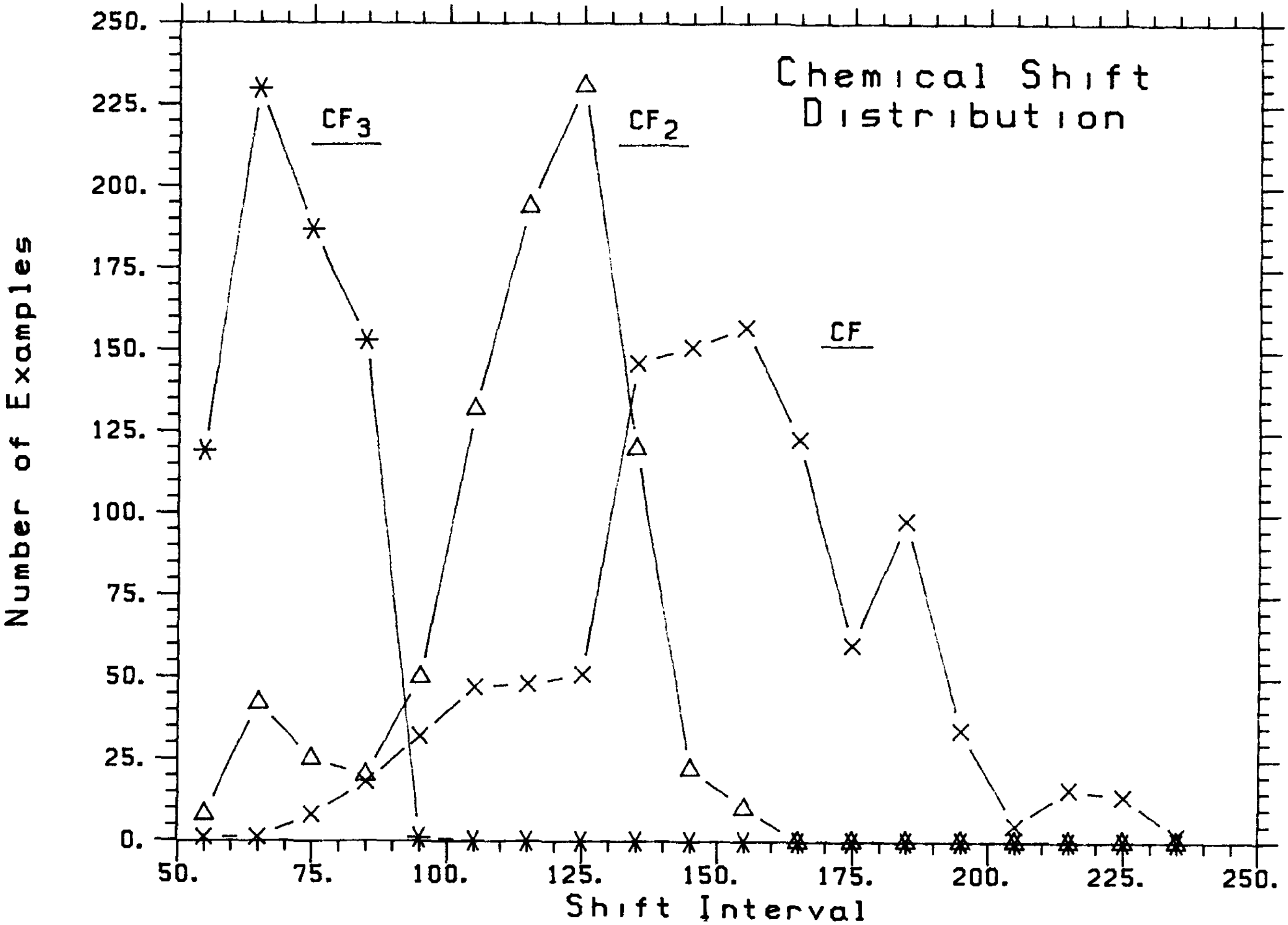


Fig. 2. Number of Examples of Each Hybridization *vs.* Chemical Shift.

TABLE 2

Chemical shifts of selected CF_3 environments

Structure	Examples	Average Shift	Std Dev
$\underline{CF_3}CF_3$	2	89	1
$\underline{CF_3}CF_2R_f$	172	83	4
$\underline{CF_3}CFR_{f2}$	142	73	3
$\underline{CF_3}CR_{f3}$	70	63	5
$\underline{CF_3}CF{=}CF_2$	2	70	1
$\underline{CF_3}CF{=}CFR_f$	44	70	3
$\underline{CF_3}CF{=}CR_{f2}$	27	69	4
$\underline{CF_3}C(R_f){=}CF_2$	63	62	3
$\underline{CF_3}C(R_f){=}CFR_f$	91	60	4
$\underline{CF_3}C(R_f){=}CR_{f2}$	111	61	4
Aromatic $\underline{CF_3}$			
2,6-F	27	57	1
$2\text{-}R_f$,6-F	17	57	2
$2,6\text{-}R_{f2}$	6	54	1
$\underline{CF_3}C{\equiv}C$	14	55	4

TABLE 3

Chemical shifts of selected CF_2 groups

Structure	Examples	Average Shift	Std Dev
$CF_3\underline{CF_2}$	166	118	11
$R_fCF_2\underline{CF_2}$	475	123	10
$R_{f2}CF\underline{CF_2}$	303	121	12
$R_{f3}C\underline{CF_2}$	148	111	12
$CF_3CF_2\underline{CF_2}CF_3$	1	129	-
$CF_3CF_2\underline{CF_2}CF_2R_f$	26	127	2
$CF_3CF_2\underline{CF_2}CFR_{f2}$	18	128	3
$CF_3CF_2\underline{CF_2}CR_{f3}$	15	123	6
$CF_3\underline{CF_2}CF=$	20	122	3
$CF_3\underline{CF_2}C(R_f)=$	41	108	10

$\underline{CF_2 \text{ GROUPS}}$. The chemical shifts of some CF_2 groups as a function of their environment are given in Table 3. The environment on only one side of a CF_2 group is insufficient to determine its chemical shift. If the CF_2 is flanked by one CF_3 group, then the structure on the other side is sufficient to determine the chemical shift. As was found for CF_3 groups, each replacement of fluorine by a carbon substituent moves the CF_2 resonance downfield.

CF_2 groups adjacent to an olefinic carbon respond in the same way as their CF_3 counterparts; replacement of a beta F by R causes approximately a 10 ppm downfield shift.

TABLE 4

Chemical shifts of CF_2 groups in carbocycles

Ring Size	Shift
3^a	151
4^a	138
5	133
6	133^b
7	124
8	120
open	123-125

[a] Different code, but included for comparison

[b] Axial = 142, Equatorial = 124

The codes for CF_2 groups in saturated rings are 102000200 independent of ring size. Yet the chemical shifts are sensitive to ring size as shown in Table 4. The chemical shift does not approach that of internal CF_2s of linear chains until the seven membered ring. The equatorial fluorine of cyclohexane is in an environment very much like that of linear chains, but the axial, more crowded, environment has a very different shift. Conformation is important in determining chemical shift.

Of the CF_2 groups alpha to sp^2 carbons in cyclic monoolefins only cyclopropene has an anomalously high shift as shown in Table 5. The =CF fluorines show the inverse effect with cyclopropene at the lowest field.

The chemical shifts of the vinyl fluorines in open chain compounds cannot be determined by considering the geometrically constrained rings to be good models for the cis isomers.

Table 6 shows the average CF_2 chemical shift on an sp^3 carbon as a function of the two adjacent groups.

The chemical shift range for each functionality is quite large. Cyclopropyl CF_2's are at the high end, while CF_2's between two sp^2 carbons are at the low end. Nevertheless, the regression equation

TABLE 5

Chemical shifts of cyclic monoolefins

Ring Size	=CF	CF_2
3	97	145
4	122	118
5	150	118
6	146	118
7	141	114
c-3-heptene[a]	134	118
t-3-heptene[a]	155	121

[a] Averages of the two non-equivalent resonances

TABLE 6

Chemical shifts of $CF_i\underline{CF_2}CF_j$ as a function of their immediate environment

CF_i i	CF_j j	Number of Examples	Shift	Std Dev
3	3	1	131	0
3	2	59	126	4
2	2	150	131	6
3	1	31	118	10
2	1	57	124	9
1	1	57	120	16
3	0	10	102	10
2	0	150	112	8
1	0	49	109	16
0	0	25	106	22

$$\text{shift} = 118.9 + 10.1*\sum_{j} CF_{ij} - 3.6*\sum_{j} CF_{ij}^2 + 3.3*\prod_{ij}(CF_{ij})$$

where F_{ij} represents the number of i fluorines on the jth carbon, (j = 1, 2) can be derived to fit these average shifts. Three parameters account for 98% of the variance of the average shifts. The CF_1 or CF_0 parameters do not vary according to whether the substituent is on an sp^2 or an sp^3 carbon. The chemical shift seems sensitive to the number of adjacent fluorines, but not to the remaining number of bonds to carbon. The population of i = j = 0 compounds is distinctly bimodal.

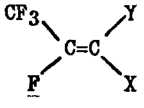
An attempt to find a similar regression expression for the 150 $CF_2\underline{CF_2}CF_2$ groups involving delta parameters failed. The shift range of ± 6 ppm is similar to the errors of an individual measurement.

$\underline{CF_1}$ GROUPS. Table 7 contains the average chemical shifts for sp^3 CF_1 groups as a function of the three adjacent types of CF_i groups. A regression analysis of only those -CF< groups with at least two adjacent CF_3s gave the equation

$$\text{shift} = 159.2 + 15.1*CF_k - 3.7*(CF_k)**2$$

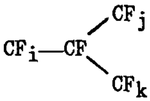
which accounted for 90% of the variance. An attempt to correlate all the -CF< chemical shifts failed. There were simply too many types of resonances and not enough data to give a representative sample of each. Special cases such as bridgehead Dewar benzenes and norbornanes dominated many of the structural types.

Table 8 contains some further relationships between local environment and CF chemical shifts. The last entry in Table 8 is a composite of many different structural types and is expanded further in Table 9.



In some, but not all, cases fluorines on mono-olefins have different chemical shifts than dienes. Z-olefins are at lower field than the corresponding E-olefins. There is not enough data of the various structural types for a regression analysis.

TABLE 7

Chemical shifts of  $CF_i\text{—}CF(CF_j)(CF_k)$ Groups as a Function of

Their Immediate Environment

CF$_i$ i	CF$_j$ j	CF$_k$ k	Number of Examples	Shift	Std Dev
3	3	3	3	189	0
3	3	2	11	183	2
3	3	1	19	182	6
3	3	0	42	172	10
3	2	2	13	189	11
3	2	1	16	188	14
3	2	0	15	175	8
3	1	1	6	181	13
3	1	0	4	174	1
3	0	0	2	154	0
2	2	2	15	206	19
2	2	1	20	195	16
2	2	0	25	183	20
2	1	0	12	191	28
2	1	1	20	182	23
2	0	0	1	158	0
1	1	1	12	180	19
1	0	0	3	197	1
0	0	0	3	180	20

TABLE 8

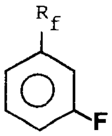
Chemical shifts of selected CF groups

Structure	Examples	Average Shift	Std Dev
$(CF_3)_2\underline{CF}-$	71	177	10
$(CF_3)\underline{CF}<$	52	183	13
$(CF_3)\underline{CF}=$	68	130	32

Aromatic Correlations

We have already discussed CF_3 groups attached to aromatic rings; now we discuss the fluorines directly bonded to these rings. First let us consider the average shifts for some common environments as shown in Table 10.

The meta and para shifts of monosubstituted compounds fall in quite narrow ranges, though the ortho shifts do not. Steric effects do play a role. Location codes for the 3-position of monosubstituted compounds, and the 4-position of 1,2-disubstituted compounds are the same, but the shifts are quite different. The electronic effect of a substituent in the para position is quite large, but is unaccounted for in our coding scheme.



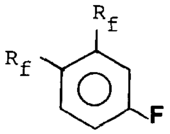


TABLE 9

Chemical shifts of some $CF_3\underline{CF}=CXY$ groups

Structure		Examples	Average Shift	Std Dev
X	Y			
F	F	1	192	
F	CF_3	1	143	
CF_3	F	1	161	
F	CF_2	2	141	4.8
CF_2	F	11	160.3	1.4
F	CF_1	6	138.7	3.0
CF_1	F	6	157.4	3.5
F	CF_0	4	146.0	2.2
CF_0	F	3	158.9	0.1
CF_3	CF_3	1	100.3	
CF_3	CF_2	1	96.3	
CF_3	CF_1	1	87.8	
CF_1	CF_1	1	90.0	
CF_3	CF_0	10[a]	103.3	2.3
CF_3	CF_0	4[b]	75.3	0.6
CF_2	CF_2	0		
CF_2	CF_1	3[b]	81.0	1.8
CF_2	CF_0	1	70.4	
CF_1	CF_1	3	79.9	1.7
CF_1	CF_0	1[a]	100.5	
CF_0	CF_0	3[a]	104.4	3[a]

[a] Dienes; mixed Z/E

[b] Monoenes; mixed Z/E

TABLE 10

Chemical shifts of selected aromatic fluorines

Nine Digit Location Code	Number of Examples	Average Shift	Std Dev
Para[a] 000200020	78	149	2
Meta[b] 000200011	72	161	1
Meta[c] 000200011	75	148	4
Ortho			
000111020	10	136	6
000110120	5	138	1
000110021	87	138	5
000110030	10	136	2

[a] Does not include C_6F_6;

[b] Monosubstituted;

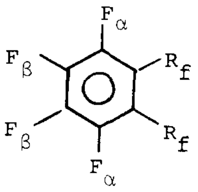
[c] 4- of 1,2-disubstituted compounds

TABLE 11

Aromatic chemical shifts of selected ortho disubstituted tetrafluorobenzenes

Compound	Shifts	
	F-Alpha	F-Beta
F-o-Xylene	132	146
F-Tetralin	136	145
F-1,4-Dihydronaphthalene	137	148
F-Naphthalene	146	155

The same effect is seen in the compounds given in Table 11. Although the steric effects are similar, only electronic effects can explain the similar change of both the alpha and beta locations as the second aromatic ring of naphthalene is formed.



Although all of the methylbenzenes have not been reported, we used the compounds available to construct a regression equation giving the chemical shift as a function of the substituent position.

Shift = 160.6 - 24.7 * (#ortho) - 12.4 * (#para)

The meta parameter was not statistically significant, and this equation accounts for 98% of the variance observed. (N = 13)

<u>Correlations of Chemical Shifts Among Fluorines in a Single Compound</u>

Next we consider some correlations among resonances in the same compound. As a prototypical question, we can ask if there is any relationship between the two chemical shifts of the terminal CF_2s of a $R_fCF=\underline{CF}2$ group. Trifluorovinyl groups have a characteristic set of three resonances. The $=CF_2$ group is a pair of resonances separated by an average of 15 ppm centered at 100 ppm. The X and Y coordinates in Fig. 3 represent these two chemical shifts. Indeed, there is a good linear correlation between the two shifts.

A more probing analysis asks if there is any further correlation with the internal fluorine of a $\underline{CF}=CF_2$ group. The letters in Figure 3 represent the chemical shifts of the internal fluorine. There is a correlation among simple olefins, but conjugated olefins such as butadiene and styrene do not fit.

Initial attempts to find correlations between the shifts of CF_3 and CF_2 groups in C_2F_5 groups were unsuccessful. However when the data was separated according to the substitution of the carbon attached to the ethyl group, some patterns emerged. Each environment has its own slightly different correlation, although much of this difference may be an artifact. Different investigators specialized in the different classes, and measurement errors may be comparable to the correlations being sought. For rather narrowly defined sets of compounds, correlation coefficients between the CF_3 and the CF_2 resonances were typically in the 0.8 - 0.9 range.

The CF_3 and CF resonances of isopropyl groups showed similar patterns. The chemical shift correlations currently available are not sufficient to pair these neighboring types of fluorines. Double resonance experiments can be used to assign these pairs unambiguously.

Applications

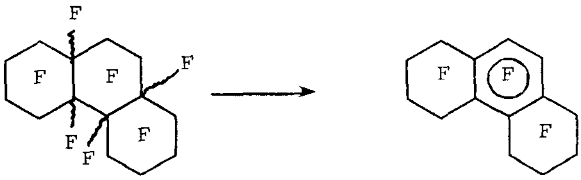
In the discussion above, we have presented a broad but superficial sampling of the kinds of information which can be retrieved from this database as a whole. In this section, a few examples will be given to illustrate some specific applications of this database. They will be divided to show the applicability to structure assignments and resonance assignments.

EXAMPLE 1. The database can be used to match a set of chemical shifts to a previously reported compound. Hill[12] reported the dimerization of HFP to an unsaturated 2-methylpentane. Although the structure presented is isomer A, the nmr presented is that of isomer B. The chemistry is also more consistent with isomer B.

$(CF_3)_2CFCF{=}CFCF_3$ $\qquad$ $(CF_3)_2C{=}CFCF_2CF_3$

A $\qquad$ **B**

EXAMPLE 2. Defluorination of a commercial sample[13] of 'perfluoro(tetradecahydrophenanthrene)' gave a mixture of products. The F-19 nmr database was used to identify both the major product, octadecafluorophenanthrene, and a totally unexpected minor product, octadecafluoroanthracene. No more highly defluorinated products with either ring structure were present. When the carbon skeleton rearrangement occurred, either during the fluorination or the defluorination, is not presently known.



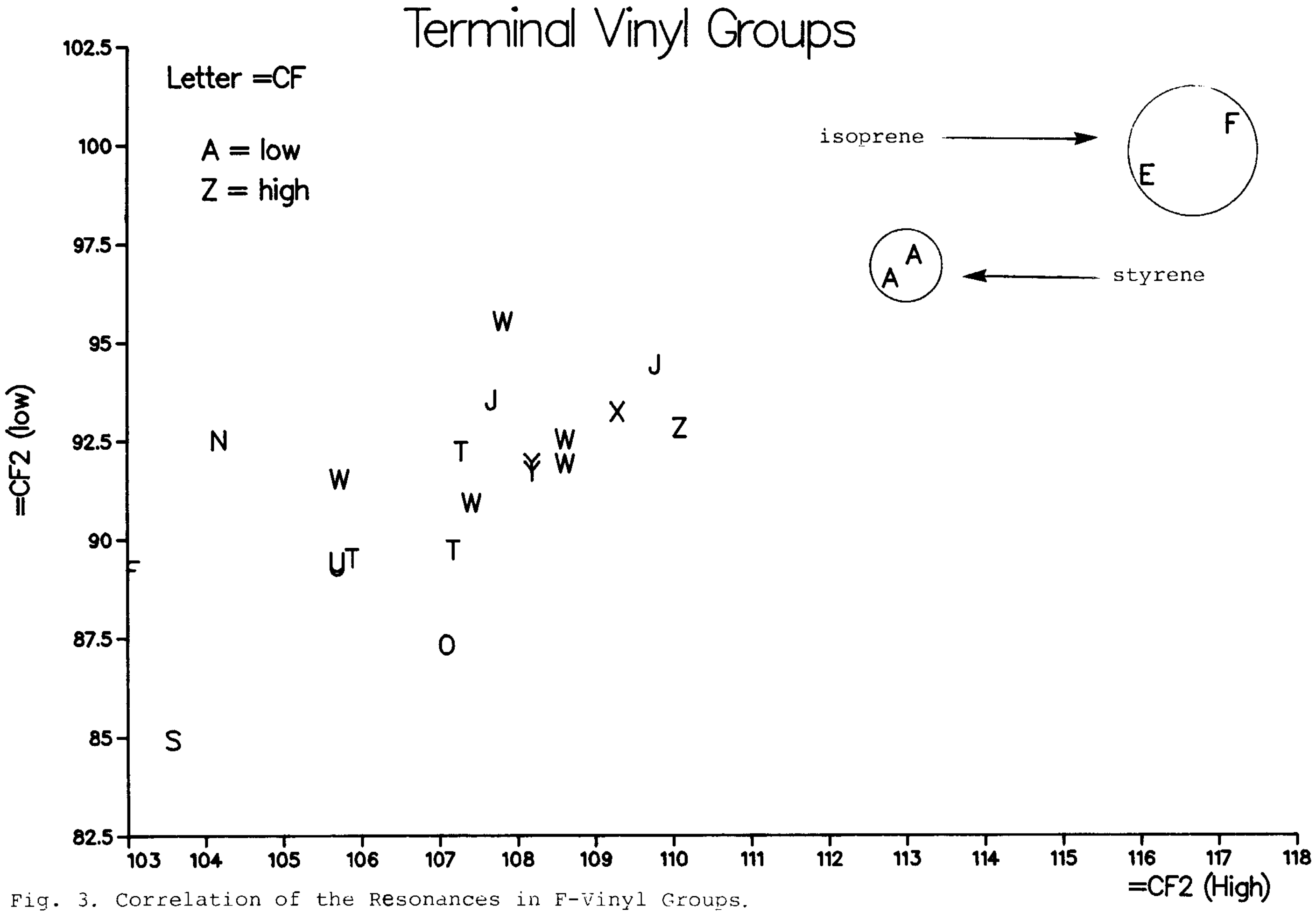
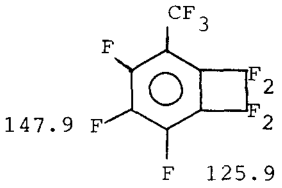


Fig. 3. Correlation of the Resonances in F-Vinyl Groups.

EXAMPLE 3. The stereochemistries of *cis* and *trans* F-2- and 3-heptenes were reassigned by combining chemical shift and coupling constant information. An equilibrium mixture of the heptenes gave rise to a spectrum with 28 resonances. These resonances could be divided into four groups of 7 resonances each by the relative intensities of the signals. The CF=CF fluorine AB patterns were resolved at 300 MHz, and the geometries of the internal heptenes were found to be the reverse of that previously reported [14]. The value of the fluorine-fluorine coupling constant allows unambiguous assignment of the stereochemistry of fluoro-olefin compounds. J_{F-F} is 30 Hz across a cis olefin and over 100 Hz in a trans olefin. Unfortunately, as the two sides of an olefin become more and more alike, the chemical shift difference between the two fluorines decreases. At lower magnetic fields the AX patterns becomes first AB, and then degenerate to accidentally equivalent A_2 from which the coupling constant cannot be extracted. Once the chemical shifts of a few cis/trans pairs have been reliably established, others may be made by analogy, providing both isomers are available.

EXAMPLE 4. In other compounds, resonances which were not assigned originally can now be assigned on the basis of the correlations developed in this work. For example, the indicated aromatic fluorines of F-1-methylbenzocyclobutene were not originally assigned [15]. Given the large number of ring fused benzenes in the database, we can easily assign the alpha and beta fluorines to their respective resonances as shown below.



Eventually it may be possible to create a single database, and perhaps an expert system sitting on top of it, to handle all nmr data. Presently this appears to be too difficult a mountain to climb. For the time being, separate facilities for individual nuclei and classes of compounds seem to divide the problem into manageable chunks. Obvious extensions of this work include hydrofluorocarbons, chlorofluorohydrocarbons, or oxygen containing fluorocarbons.

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