Nuclear Magnetic Resonance of Aromatic Heterocyclics

I. The Proton and ${}^{19}F$ Spectra of 2- and 3-Fluorothiophene

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The ${}^1H$ and ${}^{19}F$ magnetic resonance spectra of 2- and 3-fluoro-thiophene have been analyzed. The H—F spin coupling constants are (in Hz): $J_{2F-3} = 1.62$, $J_{2F-4} = 3.07$, $J_{2F-5} = 3.10$, $J_{3F-2} = 1.08$, $J_{3F-4} = -0.81$, $J_{3F-5} = 3.30$. Except for J_{3F-4} they are all of the same sign as the H—H spin coupling constants. The shift of the fluorine resonance of 2-fluorothiophene is 28.30 ppm and that of 3-fluorothiophene 32.05 ppm downfield from hexafluorobenzene. An isotope shift of the fluorine resonance of 2-fluorothiophene due to ${}^{34}S$ was observed, and is 0.014 ppm. The ${}^{13}C—{}^{19}F$ spin coupling constants are 285 and 256 Hz in 2- and 3-fluorothiophene, respectively.

In earlier investigations a detailed study of the proton magnetic resonance spectra of thiophene and a large number of substituted thiophenes was undertaken.[1-5] The intervals for the different coupling constants and their signs have been determined. The relation between chemical shifts and substituent effects was studied and a qualitative relation between the properties of a substituent in the 2-position and the 5-hydrogen shifts was obtained. The much larger effects of substituents on the fluorine shifts and the good correlation obtained between such shifts and Hammett substituent constants (σ-values) makes a study of the fluorine resonance spectra of substituted fluorothiophenes attractive. The substituent shifts thus obtained could then be used to obtain σ-values for these substituents when attached to the thiophene ring, and perhaps be useful for the prediction of chemical reactivity data. An increased knowledge of the magnitudes and signs of the H—F and F—F spin-spin coupling constants in aromatic systems such as thiophene

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could contribute to a better understanding of the relative importance of the different mechanisms which contribute to these couplings.

In the present paper the analysis of the proton and fluorine magnetic resonance spectra of 2- and 3-fluorothiophene is given. In a following paper the spectra of the four difluorothiophenes, one trifluorothiophene and some other derivatives will be discussed.

MATERIALS

2-Fluorothiophene was first prepared in low yield by the reaction of 2-bromothiophene with SbF_5.[6] The route to fluorothiophenes was, however, opened by Schuetz et al.,[7] who found that 2-thienyllithium and 5-methyl-2-thienyllithium, which are obtained by metalation of thiophene and 2-methyl-thiophene with butyllithium, reacted with perchloryl fluoride to yield 2-fluorothiophene and 2-fluoro-5-methylthiophene. It has earlier been demonstrated that substituted thienyllithium derivatives are easily available from the metalation reaction or by halogen-metal interconversion with substituted bromothiophenes.[8] The reaction of these lithium derivatives with various reagents is a convenient method for the preparation of different disubstituted thiophenes.

3-Fluorothiophene was obtained by halogen-metal interconversion between 3-bromothiophene and ethyllithium * at −50°C followed by the reaction with perchloryl fluoride. Both 2- and 3-fluorothiophene could be separated from thiophene by means of preparative gas-chromatography. The fluorothiophenes were difficult to analyze for carbon and hydrogen. However, analytical gas-chromatography and mass spectrometry[9] as well as proton and ^{19}F magnetic resonance spectra indicated that sufficiently pure compounds had been obtained.

It has also been found that the reaction of thienyllithium derivatives and perchloryl fluoride is of general preparative usefulness for the preparation of fluorothiophenes and a large number of these compounds, which will be described in the following papers, have been synthesized.

RESULTS

3-Fluorothiophene. The proton part of the magnetic resonance spectrum of 3-fluorothiophene in a 45 % benzene solution is shown in Fig. 1a. It is the ABC-part of an ABCX spectrum, where the fluorine resonance is denoted the X part. By use of the "effective Larmor frequency" approach[10] it is easily seen that this ABC part is a superposition of two ABC (three-spin) subspectra with effective chemical shifts:

$$\nu_A{}^{\pm} = \nu_A \pm 1/2\ J_{AX} \qquad \nu_B{}^{\pm} = \nu_B \pm 1/2\ J_{BX} \qquad \nu_C{}^{\pm} = \nu_C \pm 1/2\ J_{CX} \qquad (1)$$

As seen from Fig. 1a the proton part is not strongly coupled and there is no overlapping of lines from different protons. With positive signs for

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* In order to avoid separation problems ethyllithium was used instead of butyllithium.
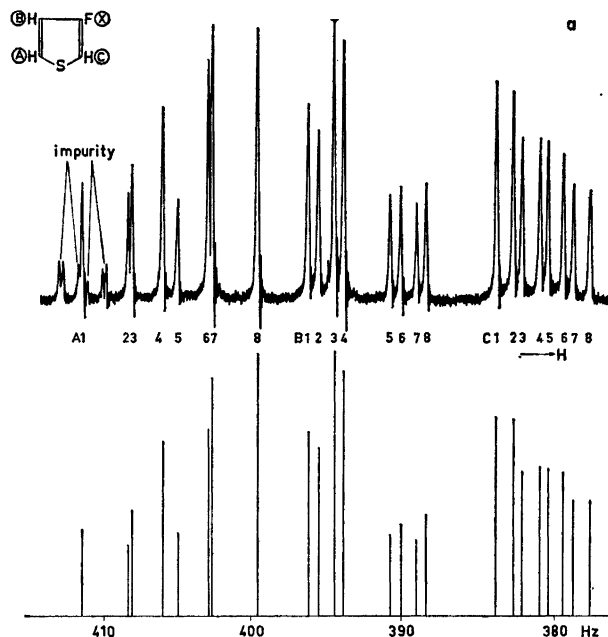
Fig. 1a. The single resonance proton spectrum at 60.000 MHz of 3-fluorothiophene in a 46 % benzene solution. The upper part shows the experimental spectrum and the calculated spectrum is given below. The frequency scale is given with respect to TMS as internal reference. In the experimental spectrum there are also some peaks from an impurity, probably thiophene itself.
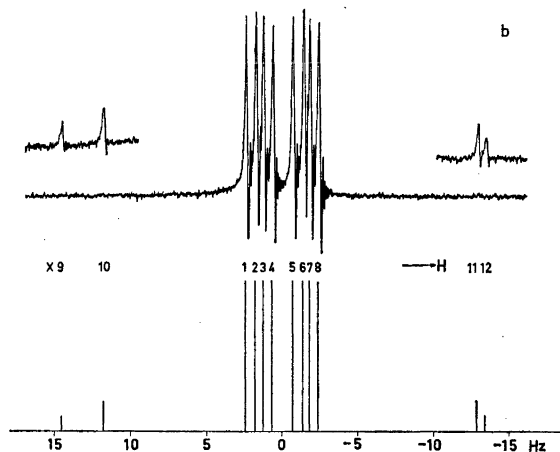
Fig. 1b. The fluorine resonance spectrum at 56.444 MHz of the same compound as in Fig. 1a. The four weak lines (X9,X10,X11,X12) are recorded with both higher rf. field and higher amplification than the eight strong lines (X1—X8). In the theoretical spectrum these four lines are depicted with thirty times larger amplitude factor than the middle band.

the proton-proton couplings [1,2,11-14] there are two sets of energy level diagrams for the two ABC spin systems that give theoretical spectra that agree with the experimental one. From the single resonance spectrum it is not possible to distinguish between the two cases where the spin couplings between the fluorine and the protons in the 4- and 5-positions are of opposite signs, *i.e.* it is not possible to get the sign of J_{3F-2} relative to those of J_{3F-4} and J_{3F-5}. The reason for this is that the 2-proton is not coupled strongly enough to the other two protons. By some tickling [15] experiments (one is shown in Fig. 2) in the ABC part it was, however, possible to choose the correct sign combina-
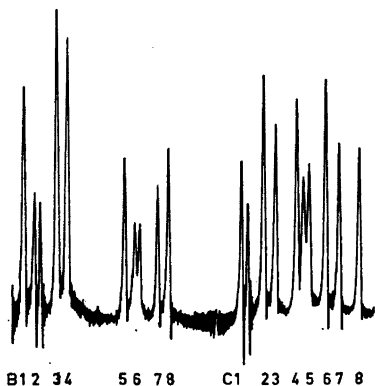

B1 2 34   5 6 78   C1 23 45 67 8

Fig. 2. Double resonance (tickling) spectrum of the ABC-part of 3-fluorothiophene at 56.444 MHz with the second rf. field H_2 at resonance on line A1. The A-lines are not shown. The lines B2 and C1 appear to be regressively connected with A1 whereas B6 and C5 appear to be progressively connected with A1 (*cf.* the energy level diagram in Fig. 3). This experiment alone shows that all the proton-proton couplings carry the same sign and that J_{3F-4} is of opposite sign to J_{3F-2} and J_{3F-5}.
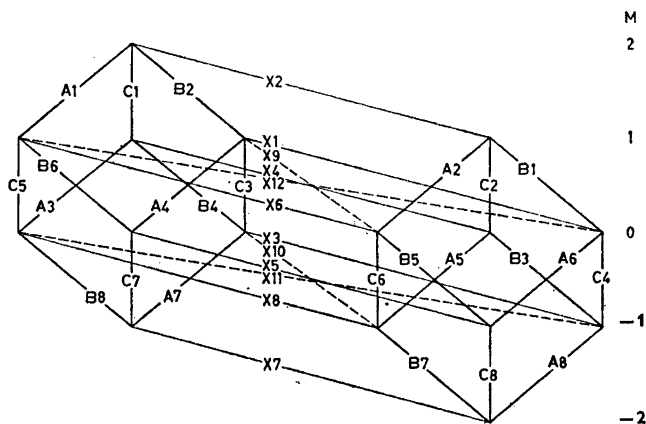

Fig. 3. Energy levels and transitions of the ABCX spin system of 3-fluorothiophene. The diagram may be visualized as a combination of two cubes tilted so as to have three corners in the same plane. Each cube belongs to one definite spin state of nucleus X and form the energy level diagram for one ABC sub spin system. (In the text the two cubes are called one set of energy level diagrams for the two ABC sub spin systems). Each corner of the cube corresponds to one energy level and each cube edge corresponds to an A, B, or C transition. The X transitions are represented by lines joining the two cubes. The lines are numbered according to Figs. 1a and 1b. The four visible combination transitions of the X part are indicated by dashed lines between the two cubes.

Table 1. Chemical shifts ^{a,c} and proton-proton spin couplings in 2-fluorothiophene and 3-fluorothiophene.

Compound	Solvent	Conc. Wt %	Shifts ^{a} (in Hz)				Proton-proton spin couplings (in Hz)				
			ν_2	ν_3	ν_4	ν_5	ortho		meta		
							J_{34}	J_{45}	J_{24}	J_{35}	J_{25}
2-Fluorothiophene	benzene	50	1583.28	348.19 ^{b}	358.31 ^{b}	350.07 ^{b}	3.89	6.02		1.69	
	cyclohexane	41	1587.93	354.83	367.78	361.78	3.88	6.01		1.68	
	cyclohexane	5	1595.97	356.14	369.65	364.01	3.85	5.93		1.68	
3-Fluorothiophene	benzene	46	358.42 ^{b}	1813.34	369.54 ^{b}	380.71 ^{b}		5.38	1.52		3.50
	cyclohexane	77	366.30	1817.91	375.72	390.72		5.36	1.54		3.48
	cyclohexane	22	366.81	1810.39	376.85	393.91		5.33	1.54		3.47
	cyclohexane	6	367.41	1808.30	377.77	395.15		5.36	1.50		3.46

^{a} The proton shifts are given at 56.444 MHz relative to TMS as internal reference and the fluorine shifts are given relative to hexa-fluorobenzene as internal reference.

^{b} These shifts have been measured at 60.000 MHz and recalculated to 56.444 MHz.

^{c} In order to compare the substituent shifts of the protons with other monosubstituted thiophenes, the δ-values at infinite dilution relative to cyclohexane (measured to -1.44 ppm) are calculated to be (in ppm):

2-fluorothiophene: $\nu_3 = -4.88$ $\nu_4 = -5.12$ $\nu_5 = -5.02$
3-fluorothiophene: $\nu_2 = -5.07$ $\nu_4 = -5.25$ $\nu_5 = -5.57$

tion and construct appropriate energy level diagrams (see Fig. 3, where the energy level diagram for the whole ABCX spin system is shown). From the tickling experiments it is evident that J_{3F-4} is of opposite sign to J_{3F-2} and J_{3F-5} and, as previously shown, all the proton-proton couplings carry the same sign.[1,2,11]

With a least squares fit program the shifts and spin coupling constants which give the best fit to the experimental proton spectrum could be calculated. As seen from relation (1), the difference between the effective shifts of the two ABC spectra then gives the absolute values of the proton-fluorine couplings.

The fluorine spectrum of 3-fluorothiophene is shown in Fig. 1b. The eight strong lines at first appear to be symmetrically situated around ν_X, but nevertheless with an accuracy better than ± 0.03 Hz in the measured frequencies of the experimental lines, a slight asymmetry around ν_X is observed. This asymmetry is, however, more pronounced in the combination lines, in the outer flanks of the spectrum, four of which have intensities large enough to be detected. (0.006 and 0.003 if the strongest of the eight lines has an intensity normalized to 1, all at the same rf. field and at negligible saturation). The sense of the asymmetry depends on the signs of the proton-fluorine couplings relative to that of the proton-proton couplings. With a change in the signs of all the proton-fluorine couplings the spectrum will be reflected in ν_X and therefore also the asymmetry. The asymmetry in the experimental ^{19}F spectrum of 3-fluorothiophene is consistent with positive signs for J_{3F-2} and J_{3F-5} and negative sign for J_{3F-4}.

The shifts and coupling constants with their relative signs are given in Tables 1 and 2. The assignment of the three proton bands to the protons in 3-fluorothiophene is based on the known magnitudes of proton-proton spin couplings in thiophenes:[3] $J_{45} > J_{25} > J_{24}$.

Table 2. Fluorine-proton spin couplings in 2-fluorothiophene and 3-fluorothiophene (in Hz).

Compound	Solvent	Conc. Wt. %	J_{2F-3}	ortho J_{3F-2}	J_{3F-4}	meta J_{2F-4}	J_{3F-5}	J_{2F-5}
2-Fluorothiophene	benzene	50	1.62			3.07		3.10
	cyclohexane	41	1.54			3.07		3.08
	cyclohexane	5	1.43			2.95		2.87
3-Fluorothiophene	benzene	46		1.08	−0.81		3.30	
	cyclohexane	77		1.06	−0.84		3.23	
	cyclohexane	22		0.94	−0.88		3.17	
	cyclohexane	6		0.92	−0.88		3.16	

With an experimental uncertainty of at most ± 0.03 Hz in the observed resonance frequencies, the proton-proton and proton-fluorine couplings are given with an accuracy better than ± 0.06 Hz. A complete ABCX spectrum calculated with these parameters gives an X part that agrees very well with the experimental fluorine spectrum.

During the measurements of the dependence of the fluorine resonance shift on concentration in cyclohexane it was discovered that the apparent
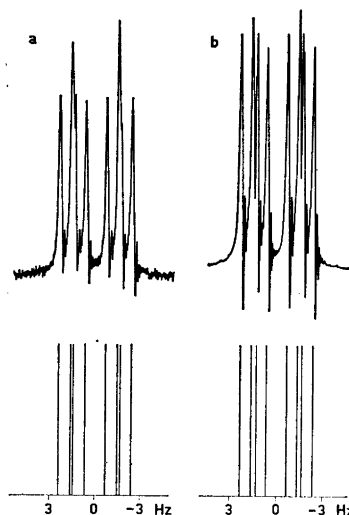
Fig. 4. The fluorine resonance of 3-fluoro-
thiophene in a) a 22 % cyclohexane and
b) a 77 % cyclohexane solution.

asymmetry in the part of the fluorine spectrum with the strong lines is increased
by dilution (here the weak lines on each side of the central band have too
low intensity to be detected). A complete analysis of the whole ABCX spec-
trum at three different concentrations in cyclohexane was therefore performed.
The fluorine spectra at the concentrations 77 % and 22 % are shown in Fig. 4.
At first it was thought that the asymmetry arose because of a decrease in the
shift differences between the protons. Recordings of the proton spectrum,
however, showed that the shifts had actually increased on dilution, especially
that between H5 and the other protons. A comparison of the proton-fluorine
couplings in the three solutions shows that the more pronounced asymmetry
obtained at the lower concentrations is due to the fact that J_{3F-4} and J_{3F-2}
here are nearly equal in magnitude. The coupling J_{3F-2} has decreased 0.14
Hz due to dilution whereas J_{3F-4} has increased slightly in magnitude (0.04
Hz) as given in Table 2. The near equality makes some of the splittings smaller
in the fluorine spectrum and a small asymmetry becomes therefore more
evident (see Fig. 4).

The shift of the fluorine resonance in cyclohexane extrapolated to infinite
dilution is 32.05 $\pm$ 0.02 ppm on the low field side of hexafluorobenzene.

The $^{13}C-^{19}F$ coupling was measured from the ^{13}C satellite spectrum of the
fluorine resonance in the benzene solution and is 256 $\pm$ 1 Hz. The isotope
shift is 5.0 Hz = 0.089 ppm. The $^{19}F-^{13}C(^{12}C)$ isotope shift calculated from
the linear relationship between $^{13}C-^{19}F$ couplings and isotope shifts [16] for
sp^2 hybridized carbon is 0.090 ppm.

2-Fluorothiophene. The proton resonance spectrum of 2-fluorothiophene in
50 % benzene solution is shown in Fig. 5a. As in the 3-fluorothiophene case
we preferred to interpret the ABC part by use of subspectral analysis. As
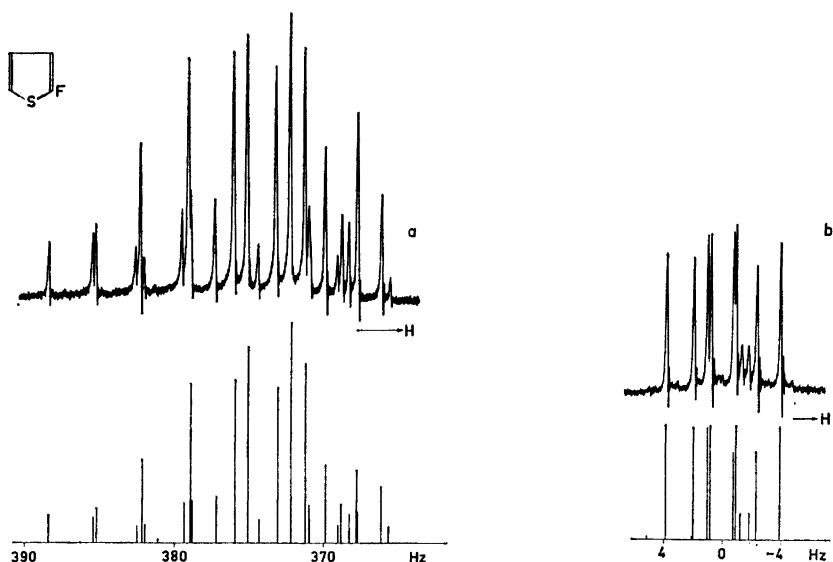the ABC part is strongly coupled, it was not immediately possible to con-

Fig. 5. a. The proton resonance spectrum at 60.000 MHz of 2-fluorothiophene in a 50 %
benzene solution. The upper part shows the experimental spectrum and the spectrum
calculated with the parameters in Tables 1 and 2 is given below. b. The fluorine resonance
spectrum of the same sample as in Fig. 5a. The calculated spectrum is shown with eight
strong lines and four combination lines of finite intensity. In the experimental spectrum
is it possible to see (in four cases) some of the ^{34}S-2-fluorothiophene satellite lines on the
high field side of the ordinary ^{32}S-2-fluorothiophene lines.

struct the appropriate energy level diagrams for the two ABC sub spin systems.
By performing a series of tickling [15] experiments it was, however, possible
to pick out transitions with an energy level in common and together with the
rule of repeated spacings [17] and the intensities of the lines it was then not too
difficult to construct the correct energy level diagrams. From the energy level
diagrams it is inferred that all the proton-fluorine couplings carry the same
sign and, as found earlier,[1,2] that the proton-proton couplings are all of the
same sign. Using the same procedure as in the 3-fluorothiophene case the
parameters given in Tables 1 and 2 were obtained. The assignment of the
resonance frequencies ν_A, ν_B, and ν_C to the three protons is also here done by
means of the known magnitudes of the proton-proton couplings.[3]

   With the parameters obtained, a theoretical X part spectrum could be
calculated and compared with the experimental fluorine spectrum. As seen
from Fig. 5b, the spectrum is not symmetrical about the center ν_X. The asym-
metry shown indicates that the proton-fluorine couplings are of the same sign
as the proton-proton couplings and therefore probably positive in absolute
sign.[1,2,11-14] The calculated X part agrees well with the experimental spectrum.
The deviations in the eight strong lines are at most 0.02 Hz. The deviation
in the combination lines is in one case as large as 0.08 Hz, probably due to the

Fig. 6. The fluorine resonance spectrum of 2-fluorothiophene in a 40 % cyclohexane solution. As this spectrum is simpler than that in Fig. 5b all the eight [34]S satellite lines are clearly visible on the high field side of the stronger lines.
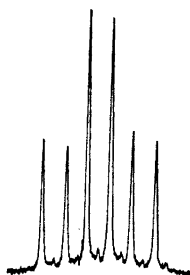
fact that these lines have not been measured very accurately. The average deviation between the 36 calculated and measured transitions of the total ABCX spin system is 0.024 Hz, which is within the experimental uncertainty ($\pm$ 0.03 Hz except for a few lines). The proton-proton and proton-fluorine couplings are given with an accuracy of $\pm$ 0.03 Hz and $\pm$ 0.05 Hz, respectively.*

The spectrum of this compound has also been studied at different concentrations in cyclohexane. The result of the analysis of the ABCX spectrum at two concentrations is given in Tables 1 and 2. The proton-proton couplings agree well with those of the benzene solution except J_{45} which has decreased by 0.09 Hz. As seen from Table 2 the proton-fluorine couplings vary with concentration outside the experimental uncertainty. There is also some evidence that the proton-fluorine couplings (*cf.* J_{2F-3}) vary with solvent, but no extensive study of these couplings in different solvents was performed at this point.

The fluorine spectrum in the cyclohexane solutions is simple and consist of six strong lines (*cf.* Fig. 6). It was not possible from this spectrum to obtain the sign of the proton-fluorine couplings relative to that of the proton-proton couplings. The shift of the fluorine resonance in cyclohexane extrapolated to infinite dilution is 28.30 $\pm$ 0.02 ppm.

In addition to the ordinary fluorine spectrum in the cyclohexane solutions small peaks appear on the high field side of each of the strong lines (see Fig. 6). These peaks have an intensity about 4 % of the strong lines and form another fluorine spectrum, a satellite spectrum, shifted 0.81 Hz upfield from the ordinary spectrum. The possibility that these lines may be spinning sidebands can be ruled out as they do not move when the spinning speed is changed and they are not symmetrical around the stronger lines. It has been concluded that this is an isotope effect on the chemical shift [18]and that the satellite spectrum is that of the naturally present (4 %) [34]S-2-fluorothiophene. The absence of such a satellite spectrum in the spectrum of 3-fluorothiophene. the intensity of the satellite spectrum, and the magnitude of the isotope

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* The spectra of 3- and 2-fluorothiophene have also been analyzed by a least squares fit of all the 36 measured lines. In each case shifts and coupling constants were obtained that agree very well within the experimental uncertainty with our ABCX subspectral analysis. The proton part of 2-fluorothiophene has also been recorded at 100 MHz. The coupling constants obtained agree well with the 60 MHz analysis.

shift exclude the possibility that the satellite spectrum is that of ^{13}C-2-fluoro-thiophene. The isotope shift ^{19}F-C-$^{34}S(^{32}S)$ is therefore (0.014 ± 0.001) ppm. In the fluorine spectrum of 2-fluorothiophene in the benzene solution the effect of the isotope shift is not very evident owing to the complexity of the spectrum but is nevertheless visible here also.

The ^{13}C-^{19}F coupling as measured from the ^{13}C satellite spectrum of the fluorine resonance in the benzene solution is 285 ± 1 Hz and the isotope shift ^{19}F-$^{13}C(^{12}C)$ is 5.8 Hz = 0.103 ppm. The isotope shift calculated from the linear relation [16] between the ^{13}C-^{19}F coupling and the isotope shift is 0.105 ppm.

DISCUSSION

The chemical shifts of the hydrogens of 2-fluorothiophene in dilute cyclo-hexane solution relative to those of the α-proton $(-5.72$ ppm$)$ [4] and β-proton $(-5.53$ ppm$)$ [4] of thiophene are thus $\delta_3 = 0.65$ ppm, $\delta_4 = 0.41$ ppm, and $\delta_5 = 0.70$ ppm. The corresponding values for the hydrogens of 3-fluorothiophene are $\delta_2 = 0.65$ ppm, $\delta_4 = 0.28$ ppm, and $\delta_5 = 0.15$ ppm.

The upfield shifts of the hydrogens of 2-fluorothiophene show the charac-teristic alternating pattern observed for $-I + M$-2-substituted thiophenes. The shift of the 5-hydrogen is of the same magnitude as that observed in 2-methoxythiophene (0.82 ppm). Normally in $-I + M$-substituted thiophenes such as 2-methoxy- and 2-aminothiophene, the upfield shift of the 3-hydrogen resonance is larger than that of the 5-hydrogen, but in 2-fluorothiophene these shifts are reversed, most probably due to the much stronger $-I$-effect of the fluorine than of the other substituents.

The shifts of the hydrogen resonances of 3-fluorothiophene also show the expected pattern for a $-I + M$-3-substituted thiophene. Possible reasons for the larger upfield shift of the 2-hydrogen resonance as compared to that of the 4-hydrogen resonance have been discussed earlier.[4]

An estimate of the shift of the protons caused by the magnetic anisotropy of the fluorine atom was made in a manner similar to that described in Ref. 4. A magnetic anisotropy of $\Delta \chi = -8 \times 10^{-30}$ cm^3/atom gave diamagnetic contributions to the shifts of the protons in 2- and 3-fluorothiophene, which are at most 0.05 ppm and will therefore not change the discussion above.

It is interesting to note that while in the proton magnetic resonance spectra of thiophene the 2-hydrogen resonance occurs at lower field than that of the 3-hydrogen,[4] the 2-fluorine is more shielded than the 3-fluorine in 2-and 3-fluorothiophene, respectively.

Similar inversion between proton and fluorine shifts was also observed when naphthalene was compared with α- and β-fluoronaphthalene.[19,20] Prosser and Goodman [21] have, using an idea by Karplus and Das,[22] given the following equation which relates chemical shifts in conjugated compounds with π-electron densities on the fluorine atom and the bonded carbon atom and with C$-$F bond order

$$\delta = 488 \, \Delta E^{-1}[11.9 \, \Delta q \, (F_z) + 3.9 \, \Delta p \, (C_zF_z) + 0.1 \, \Delta q \, (C_z)] \qquad (2)$$

This equation gave good agreement for *para* substituted fluorobenzenes [23] and it has also been used by Boden *et al.* in substituted perfluorobenzenes.[24] In addition they also introduced a term for the chemical shift from intra-molecular electric field contributions.

Table 3. Bond orders and π-electron densities:
1. calculated with parameters according to Refs. 25 and 26.
2. calculated with parameters according to Refs. 25 and 24 adjusted to the ω-method.

	2-Fluorothiophene		3-Fluorothiophene	
	1	2	1	2
$q(C_z)$	1.0101	0.9880	1.0378	1.0240
$q(F_z)$	1.9836	1.9308	1.9865	1.9462
$p(C_zF_z)$	0.1269	0.2633	0.1136	0.2279

A modified ω-method [25] was used to calculate the π-electron densities and bond orders of 2- and 3-fluorothiophene.

Using $\alpha_C = \alpha$, $\alpha_S = \alpha + \beta$, $\beta_{CC} = 0.75\,\beta$, and $\beta_{CS} = 0.4\,\beta$ (parameter set 3 Ref. 25) together with $\alpha_F = \alpha + 3\beta$ and $\beta_{CF} = 0.5\beta$ (derived from those of Streitwieser [26]) the charge densities and bond orders given in Table 3 were obtained. Formula (2) then gave a larger screening of the 2-fluorine: $\delta = 7.12/\Delta E$ ppm ($\Delta E > 0$, in eV).

However, in order to obtain the correct order for the *para* fluorine shift of perfluorochlorobenzene, Boden *et al.*[24] found it necessary to change the fluorine parameters of Streiwieser [26] to $\alpha_F = \alpha + 2\beta$ and $\beta_{CF} = \beta$. With these parameters, adjusted to the ω-method by changing β_{CF} to 0.75β, we obtained the reverse order of shift $\delta = -23.8/\Delta E$ ppm (see also Table 3), *i.e.* a smaller screening of the 2-fluorine as compared to that of the 3-fluorine. It is obvious that the calculated shifts are very sensitive to the parameters used. It can in addition not be excluded that the different molecular environments of 2- and 3-fluorothiophene (field effects from the hydrogens and the sulphur) also make contributions to the chemical shift. We hope that an application of the formula of Prosser and Goodman to 5-substituted 2-fluoro-thiophenes will help us to find a consistent set of parameters.

Muller and Carr,[27] who have studied the spin-spin coupling constants between ^{19}F and directly bonded ^{13}C nuclei, found that these coupling constants increased with decreased shielding. They suggested that the degree of C—F double bond character is the most important single parameter influencing both the chemical shift and the C—F coupling constants, while the $C^+—F^-$ ionic character is quantitatively less important. They also suggested that when the *s*-character of the carbon orbital of the C—F bond is increased the C—F coupling is reduced. It is interesting to note that the C—F coupling for 3-fluorothiophene (256 Hz) is smaller than that of 2-fluorothiophene (285 Hz) although the fluorine resonance of the former compound occurs at lowest field. Whereas the chemical shifts do not follow the order of C—F double

bond character in the two fluorothiophenes, the magnitude of the C—F coupling does.

Isotope shifts due to sulphur isotopes have earlier been observed by Gillespie and Quail [28] in compounds where fluorine is directly bonded to sulphur in compounds such as SF_6 and SOF_2. The isotope shift varied between 0.033 and 0.053 ppm. For SF_6 the isotope shift due to the presence of ^{33}S (natural occurrence 0.74 %) was also observed.[28] As this isotope has spin 3/2 these authors could also obtain $J_{^{33}S-F}$ from the satellite spectrum. We have made no attempt to observe the satellite spectrum from ^{33}S. To our knowledge the ^{34}S isotope shift in 2-fluorothiophene of 0.014 ppm is the first isotope shift observed for a fluorine not directly bonded to sulphur. As there is no detectable ^{34}S isotope shift of the fluorine resonance of 3-fluorothiophene, the ^{34}S shift of the 2-fluorine resonance is of great help in identifying fluorine resonances in difluorothiophenes such as 2,3- and 2,4-difluorothiophenes and will be discussed in a following paper.

The proton-proton couplings in 3-fluorothiophene are close to the couplings found in 3-nitrothiophene.[2] The value of J_{25} is the largest found in 3-substituted thiophenes. The proton-proton couplings in 2-fluorothiophene are all among the largest found in 2-monosubstituted thiophenes.

The magnitude of the "*ortho*" H—F couplings in the two thiophenes studied here is surprisingly small and it is also a little unexpected that J_{3F-4} and J_{3F-2} are of opposite signs. Vicinal H—F couplings of similar magnitude have been observed for the *cis* H—F coupling in some fluoroethylenes.[29,30] The magnitude of these "*ortho*" couplings is, however, considerably smaller than the *ortho* H—F coupling in fluorobenzenes (6.2—10.4 Hz).[31-36] The "*meta*" couplings J_{2F-4} and J_{3F-5} are larger than the "*ortho*" couplings, but they are only about half the magnitude of the *meta* H—F couplings in fluorobenzenes (4.3—8.3 Hz).[31-36] The coupling J_{2F-5} is also larger than the "*ortho*" couplings and is larger in magnitude than the *para* coupling in fluorobenzenes (—1.3 to —2.7 Hz).[31-35] *

All the proton-fluorine couplings except J_{3F-4} in these two fluorothiophenes are of the same sign as the proton-proton couplings and therefore assumed to be positive in absolute sign.[1,2,11-14] A more detailed discussion of the H—F coupling constants will be given in subsequent papers.

EXPERIMENTAL

The NMR spectra were obtained using a Varian Associates HA-60 spectrometer. The two proton resonance spectra shown in Figs. 1a and 5a were recorded at 60.000 MHz whereas all other spectra were obtained at 56.444 MHz. The spectra were recorded in the frequency sweep mode.

In the fluorine resonance experiments, the resonance from hexafluorobenzene was used as internal reference and as lock signal for the internal stabilization, and the lock frequency was produced by a Muirhead D-890-A decade oscillator.

The resonance peaks were measured by counting the inverse sweep frequency (or the difference between the sweep frequency and the lock frequency) on a Hewlett-Packard frequency counter model 3734 A. In these measurements the frequency was

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* The *para* H—F coupling has been found to be of opposite sign to the *ortho* and *meta* H—F couplings in fluorobenzenes.

swept to exact resonance of the peak to be counted; this was done for the two sweep directions and a mean value was taken.

In the tickling experiments the second weak rf. field was obtained by amplitude modulation of the magnetic field. The modulation frequency was produced by a Philips oscillator PP6050.

The least squares fit calculations and the calculations of theoretical ABCX spectra were performed on a CD 3600 computer.

2-Fluorothiophene. In a nitrogen swept wide neck reaction vessel with a five socket flat flange lid, fitted with a stirrer, a thermometer, nitrogen inlet, perchloryl fluoride inlet, and a reflux condenser protected with a calcium chloride tube was placed 1000 ml of 1.1 N ethereal ethyllithium solution. 70 g (0.85 mole) of thiophene in 100 ml of anhydrous ether was added at such a rate that gentle reflux was maintained. The mixture was then refluxed for 20 min, cooled to $-15°C$ and perchloryl fluoride bubbled into the reaction mixture at a moderate rate, while the temperature was kept at $-15°C$. When 20 % excess of perchloryl fluoride had been bubbled into the solution, the cooling bath was removed and nitrogen was bubbled through for 60 min. The reaction mixture was poured into saturated sodium carbonate solution, the organic layer separated and washed once with soda solution. Most of the ether was distilled off and the residue steam-distilled. The distillate was extracted with ether, dried and fractionated through an efficient column. 37 g of a fraction, b.p. $65-80°C$ was obtained. GLC analyses on a 2 m × 1/8" column packed with apiezon L (20 %) on Chromosorb P (60—80 mesh) using a Perkin-Elmer F 11 Gas Chromatograph indicated this fraction to consist of 86 % of 2-fluorothiophene and 14 % of thiophene. Preparative gas-chromatography on a 2.7 m × 3/8" column packed with apiezon M grease (20 %) on Chromosorb A (45—60 mesh) using a Perkin-Elmer F 21 preparative Gas Chromatograph yielded pure 2-fluorothiophene, b.p. 76°C/760 mm Hg. For mass spectrum see Ref. 9.

3-Fluorothiophene. In the same apparatus as described above 750 ml of 1.21 N ethyllithium was cooled to $-50°C$ and 127 g (0.78 mole) of 3-bromothiophene [37] in 100 ml of anhydrous ether was added in a slow stream. The temperature was allowed to rise to $-30°C$, perchloryl fluoride was bubbled in, and the mixture worked up as described. 30 g of a fraction, b.p. $80-83°C$, was obtained. VPC analyses as described above for the 2-isomer gave only one peak. However, on a 2.7 m × 3/8" column packed with 20 % polyethyleneglycol on Chromosorb A (45—60 mesh) using a Perkin-Elmer F 21 preparative Gas Chromotograph thiophene and 3-fluorothiophene separated clearly and indicated the mixture to consist of 77 % of 3-fluorothiophene and 23 % of thiophene. The retention times for thiophene and 3-fluorothiophene were 23 min and 31 min, respectively, at a column temperature of 70°C. Pure 3-fluorothiophene, b.p. 87°C/760 mm Hg was thus obtained. For mass spectrum see Ref. 9.

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