

Long-range ^{13}C — ^{19}F NMR spin-spin coupling in some α -trifluoromethyl-substituted polychloropyridines

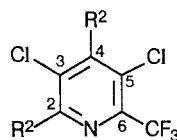
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High resolution ^{13}C NMR spectra of a series of α -trifluoromethyl-substituted polychloropyridines were studied. Long-range ^{13}C — ^{19}F NMR spin-spin coupling through four and five bonds involving carbon atoms of the pyridine ring and the fluorine atom of the CF_3 group was found.

Key words: ^{13}C NMR, long-range ^{13}C — ^{19}F NMR spin-spin coupling constants, α -trifluoromethyl-substituted polychloropyridines.

Polysubstituted pyridines containing trifluoromethyl groups exhibit biological activity.¹ Identification of such compounds by ^{13}C NMR is a rather complicated problem, because literature data on the effects of substituents on chemical shifts (CS) of carbon atoms of the pyridine ring are scarce.^{2,3} Studying ^{13}C — ^1H and ^{13}C — ^{19}F spin-spin coupling (SSC) can considerably help determine the structure of new compounds. The ^{13}C — ^{19}F SSC between fluorine nuclei of the CF_3 group and carbon through one and two bonds in various organic solvents have been studied in several works.⁴ However, there are no publications devoted to long-range ^{13}C — ^{19}F SSC of trifluoromethylpyridines. We decided that the long-range ^{13}C — ^{19}F NMR spin-spin coupling in α -trifluoromethyl-substituted polychloropyridines **1**—**4** was a reason for detailed study of these compounds by ^{13}C NMR.



- 1:** $\text{R}^2 = \text{R}^4 = \text{Cl}$
2: $\text{R}^2 = \text{Cl}$; $\text{R}^4 = \text{SH}$
3: $\text{R}^2 = \text{Cl}$; $\text{R}^4 = \text{SMe}$
4: $\text{R}^2 = \text{H}$; $\text{R}^4 = \text{SCSNMe}_2$

^{13}C NMR chemical shifts and absolute values of ^{13}C — ^{19}F and ^{13}C — ^1H SSC of the compounds studied are presented in Table 1. CS were assigned on the basis of the literature data on ^{13}C NMR spectra of polychloropyridines,^{2,5,6} taking into account ^{13}C — ^1H SSC of carbon nuclei of the pyridine ring. The considerable value of $^2J_{(\text{C}(6),\text{CF}_3)}$ observed in the spectra of **1**—**4** (see Table 1) allows one to distinguish the C(6) atom from the other carbon atoms. None of the spectra of **1**—**4** exhibit ^{13}C — ^{19}F SSC involving the C(5) atom, which

Table 1. Values of CS of ^{13}C NMR (δ) and ^{13}C — ^1H and ^{13}C — ^{19}F SSC (J/Hz) of compounds **1**—**4**

Compound	CS, SSC	C(2)	C(3)	C(4)	C(5)	C(6)	CF_3	Other groups
1	δ_{C}	147.45	134.16	145.86	128.00	142.56	119.77	—
	$J_{\text{C,F}}$	0.9	0.8	—	—	36.3	276.1	—
2	δ_{C}	146.34	129.89	150.77	125.80	141.41	119.94	—
	$J_{\text{C,F}}$	—	0.7	—	—	35.6	275.9	—
	$J_{\text{C,H}}$	—	6.0	3.2	6.5	—	—	—
3	δ_{C}	147.22	137.93	151.42	133.13	142.06	120.08	Me:18.31
	$J_{\text{C,F}}$	1.1	0.9	—	—	35.2	275.8	—
	$J_{\text{C,H}}$	—	—	4.0	—	—	—	—
4	δ_{C}	146.45	143.58	142.13	137.32	143.86	120.70	Me:42.50, 45.29; C=S:188.16
	$J_{\text{C,F}}$	0.9	—	1.1	—	35.2	275.4	—
	$J_{\text{C,H}}$	192.9	0.8	5.5	1.8	10.8	—	—

is in accordance with the known tendency of the J_{CF} value to decrease as the electron density on the carbon nucleus increases.⁷ The signals from C(2) and C(4) of compound **4** after narrowing of the lines (LB = -0.6 Hz) are quartets both in the spectrum with complete proton decoupling and in the proton-coupled spectrum.

Effects of substitution of the chlorine atom by the CF_3 group in compounds **1**–**4** (Table 2) were calculated on the basis of the data obtained, taking into account CS of the corresponding polychloropyridines.^{2,5} This substitution results in the downfield shift of C(3) (3.8–7.2 ppm), in the upfield shift of C(6) (-3.0–4.2 ppm), and exerts almost no effect on CS of C(2), C(4), and C(5) atoms. The positive effect of substitution of the CF_3 group on CS of C(3) atom confirms the conclusion about the similar effects of substituents at *para*-equivalent positions of α -substituted pyridines³ and benzenes.⁸ Comparative analysis of increments of CS for other geometrically equivalent carbon atoms [$\text{C}_{\text{Py}}/\text{C}_{\text{Ph}}$] is difficult due to the considerable effect of the nitrogen atom of the pyridine ring,³ the chlorine atom at the *ortho*-position,⁹ and strong polarization effects of the CF_3 group on the distribution of π -electron density in aromatic systems.¹⁰

Experimental

^1H and ^{13}C NMR spectra of compounds **1**–**4** (50–100 mg mL^{-1}) in CDCl_3 were recorded on a Bruker AC-200 instrument with a working frequency of 200.13 MHz and 50.33 MHz, respectively, at room temperature in 5-mm tubes, and TMS was used as the internal standard. Standard POWGATE and GATADEC subprograms (64k, width of the spectrum 12000 Hz) were used for recording ^{13}C NMR spectra. ^{13}C – ^1H and ^{13}C – ^{19}F SSCC were measured after increasing the number of points to 128k with a final digital resolution of 0.18 Hz.

The syntheses of compounds **1**–**4** have been described previously.^{5,6} Compound **2** (see Ref. 11) was prepared by the reaction between compound **1** (4.28 g, 0.015 mol) and freshly prepared sodium hydrosulfide (1.76 g) in 60 % yield. M.p. 76–77 °C.

2-Methylthio-3,4,5-trichloro-6-trifluoromethylpyridine (3) was obtained by the reaction between compound **1** (2.85 g, 0.01 mol) and sodium methanethiolate (0.77 g, 0.011 mol) at room temperature and was isolated by column chromatography on silica gel (a hexane–benzene (6 : 1) mixture was used as

Table 2. Effects of substitution by the CF_3 group (ppm) in compounds **1**–**4**

Position	Atom	1	2	3	4	$\text{C}_6\text{H}_5\text{CF}_3^*$
<i>ipso</i> -	C(6)	-3.6	-4.2	-4.0	-3.0	-3.8
<i>ortho</i> -	C(5)	-1.7	-0.3	0.2	-0.9	-3.6
<i>meta</i> -	C(2)	+1.3	+0.7	+1.2	+1.1	-1.1
	C(4)	+1.2	+1.0	+1.2	-0.1	-1.1
<i>para</i> -	C(3)	+4.5	+3.8	+5.0	+7.2	+5.1

Note. + designates a downfield shift. * Calculated on the basis of literature data⁸: $\Delta\delta_{\text{C}} = \delta_{\text{C}}(\text{PhCF}_3) - \delta_{\text{C}}(\text{PhCl})$.

the eluent). We obtained 2 g of the product (67 % yield). M.p. 47–49 °C. ^1H NMR, δ : 2.57 (Me).

References

1. Y. Kobayashi and I. Kumadaki, *J. Chem. Soc., Perkin Trans. 1*, 1980, 661; M. Tordeux, B. Langlois, and C. Wakselman, *J. Chem. Soc., Perkin Trans. 1*, 1990, 2293; M. A. McClinton and D. A. McClinton, *Tetrahedron*, 1992, **48**, 6555; A. Mukherjee, S. A. M. Duggan, and W. C. Agosta, *J. Org. Chem.*, 1994, **59**, 178.
2. B. Iddon, A. G. Mack, H. Suschitzky, J. A. Taylor, and B. J. Wakefield, *J. Chem. Soc., Perkin Trans. 1*, 1980, 1370.
3. I. B. Cook, *Aust. J. Chem.*, 1989, **42**, 1493.
4. J. W. Emsley, J. Feeney, and L. H. Sutcliffe, *High Resolution Nuclear Magnetic Resonance Spectroscopy*, Pergamon Press, Oxford, 1966, 2.
5. A. M. Sipyagin, S. V. Pal'tsun, A. V. Piyuk, N. N. Sveshnikov, V. I. Kozlovskii, and Z. G. Aliev, *Zh. Org. Khim.*, 1993, **29**, 1872 [*J. Org. Chem.*, 1993, **29** (Engl. Transl.)].
6. A. M. Sipyagin and B. V. Kunshenko, *Khim. Geterotsikl. Soedin.*, 1994, 657 [*Chem. Heterocycl. Compd.*, 1994 (Engl. Transl.)].
7. E. Breitmaier and W. Voelter, *Carbon-13 NMR Spectroscopy*, Weinheim–New York, 1987, 160.
8. D. F. Ewing, *Org. Magn. Reson.*, 1979, **9**, 499.
9. R. D. Chambers, R. S. Matthews, W. Kenneth, R. Musgrave, and P. G. Urben, *Org. Magn. Reson.*, 1980, **13**, 363.
10. J. M. Fernandez, R. G. Enriquez, W. F. Reynolds, and M. Yu, *Magn. Reson. Chem.*, 1994, **32**, 178.
11. F. E. Torba, USA Pat. 3787420; *Chem. Abstr.*, 1974, **80**, 82674m.

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