^{19}F NMR spectroscopy of polyhalonaphthalenes. Part IV. Halex reactions of polychloroquinolines

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Abstract

Nucleophilic fluoride dechlorination of four starting materials (5,6,7,8-tetrachloro-, 3,5,6,7,8-pentachloro-, 4,7-dichloro-, 2,3,4,5,6,7,8-heptachloro-quinoline) led to the preparation of thirteen new polychloropolyfluoroquinolines via reaction with caesium fluoride in DMSO at 100°C. The product from the perchloroquinoline was an inseparable mixture of $C_9Cl_{7-n}F_nN$ where n is 1–3. These products were studied in the NMR tube. © 1998 Elsevier Science S.A. All rights reserved.

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1. Introduction

So far, in this series, the nucleophilic fluoride dechlorination [1,2] of octachloronaphthalene has been studied and it led to the identification of eighteen new compounds in complicated mixtures via ^{19}F NMR spectroscopy. In the previous note [3], the use of both intra- and inter-ring ^{19}F SCSs (substituent chemical shifts) were investigated by an application to the heterolog, 2,4-dichloropentafluoroquinoline. The SCSs proved accurate and the predictions acceptable. Early work on these Halex reactions with potassium fluoride in sulpholane at 200°C was reported by Fuller [4] in 1965 while Chambers et al. [5] reported the synthesis of heptafluoroquinoline and heptafluoroisoquinoline with KF in sulpholane in 1966. Such reactions in polyhalocompounds are 'nonselective' although this study shows that these reactions are more predictable than previously believed. Similarly, fluorine reactions can be non-specific but Hutchinson and Sandford [6] recently noted that the such exothermic reactions can now be controlled and could be described as selective.

Clark and Nightingale [7] have investigated the use of the dihydrate of methylhexamethyltetramine fluoride for fluorodenitration in chlorocyanonitrobenzenes. There are still significant drawbacks with the known sources of fluoride ions, notably poor solubility, poor activity and difficult to dry. Their reagent was insoluble when dry but the dihydrate still selectively denitrated.

Here, the partially fluorinated compounds are investigated, as a further application of the ^{19}F SCSs and following the solution-state methodology of the previous articles. The products of Halex reactions with CsF in aprotic dry DMSO at 100°C were identified in an NMR tube. Presumably, the fluoride ion in solution will be exchanging readily at 100°C and exist in a bath of receptor sites, mostly the caesium cationic sites.

1.1. Experimental

Compounds are numbered as they appear in this article with IUPAC systematic ring numbering. ^{19}F NMR spectra were measured on a Bruker AC250 at 235.36 MHz, both in dry DMSO and d-chloroform, referenced to $CFCl_3$ in $CDCl_3$. Reactions (10 mg of a compound and 50 mg caesium fluoride, an excess) were followed for 96 h at 100°C in 1 cm^3 of dry aprotic DMSO. Samples were cooled to 22°C for spectroscopic measurement.

The systematic names for 1–17 are as follows:

1	5,6,7,8-tetrachloroquinoline
2	5,6,8-trichloro-7-fluoroquinoline
3	6,7,8-trichloro-5-fluoroquinoline
4	6,8-dichloro-5,7-difluoroquinoline
5	5,8-dichloro-6,7-difluoroquinoline
6	3,5,6,7,8-pentachloroquinoline
7	3,5,6,8-tetrachloro-7-fluoroquinoline
8	3,6,7,8-tetrachloro-5-fluoroquinoline
9	3,6,8-trichloro-5,7-difluoroquinoline
10	3,5,8-trichloro-6,7-difluoroquinoline

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11	4,7-dichloroquinoline
12	4-chloro-7-fluoroquinoline
13	2,3,4,5,6,7,8-heptachloroquinoline
14	3,4,5,6,7,8-hexachloro-2-fluoroquinoline
15	2,3,5,6,7,8-hexachloro-4-fluoroquinoline
16	3,5,6,7,8-pentachloro-2,4-difluoroquinoline
17	2,3,6,7,8-pentachloro-4,5-difluoroquinoline

1.2. Assignment of ^{19}F spectra

1.2.1. The reaction of 5,6,7,8-tetrachloroquinoline{1} with caesium fluoride in DMSO at 100°C

The ^{19}F shifts from run A are summarised in Table 1. Two products were visible after 20 minutes at 100°C and assigned to the 7-position product (− 106.78 ppm) {2} and 5-position product (− 118.22 ppm) {3}: because the peaks were approximately 50/50 it was erroneously thought to be the disubstituted compound. In subsequent spectra, two peaks appeared 4 ppm down-frequency (as found in polychloro-polyfluorobenzenes in sulpholane) which could be attributed to 6,8-dichloro-5,7-difluoroquinoline {4}. In the following predictions, the first column lists the known shifts for 6,8-dichloro-5,7-difluoronaphthalene [8] and the second column lists the substituent chemical shifts from the hypothetical nitrogen insertion method (i.e., NIMs). Such changes from heptafluoroquinoline [9] are outlined in Table 2.

cpd {4}   F5   − 122.2 − 1.5 = − 123.7 ppm   cf. exptl − 122.03 ppm
          F7   − 114.3 + 1.4 = − 112.9 ppm   cf. exptl − 111.28 ppm

where the predictions are much better than the next calculation

F8   − 122.2 − 3.2 = − 125.4 ppm   cf. exptl − 122.03 ppm
F6   − 114.3 − 2.2 = − 116.5 ppm   cf. exptl − 111.28 ppm

After 4 days at 100°C, an unexpected disubstituted product {5} (− 129.06 and − 132.06 ppm) was visible. The 21 Hz coupling eliminates the para combination from the four possible structures (3 ortho and 1 para). Given that ortho coupling constants are 21 (±1) Hz, it seems unlikely that we have produced p-fluorines. Furthermore, using the additive SCSs, disubstitution F5 + F6 or F7 + F8 would require peaks at − 140 ppm. The remaining favoured possibility for compound {5} is to be F6 + F7:

F6   exptl − 132.46 ppm
F7   − 106.8 − 22.0 = − 128.8   exptl − 129.06 ppm

Here the ortho-SCS for chlorine to fluorine at position 7 is − 22.2 ppm very close to the value above from Hogben and Graham [10]. A value of − 18 ppm was found in our previous study [2] of polychloropolyfluoronaphthalenes. In agreement with the previous shifts in heptafluoroquinoline, the peak for F6 is down-frequency of F7 by 3.6 ppm cf 3.4 ppm here.

Table 1
Summary of shifts in reaction A

DMSO	CDCl₃
− 106.78 F7 {2}	− 105.51 ppm
− 111.28 F7 {4}	− 109.57
− 118.22 F5 {3}	− 119.28
− 119.74 weak	− 120.35 w
− 122.03 F5 {4}	− 122.57
− 129.06 F7 {5}	− 128.26
− 132.46 F6 {5}	− 131.84

Table 2
Nitrogen insertion method SCSs in ppm [a]

Position	In CDCl₃	In DMSO
F2	+ 81.87	
F3	− 6.65	
F4	+ 21.35	
F5	− 0.50	− 1.5
F6	− 0.1	− 2.2
F7	+ 0.47	+ 1.4
F8	− 2.53	− 3.2

[a] Real experimental differences, i.e., the difference in ^{19}F NMR shifts of octafluoronaphthalene and heptafluoroquinoline measured as a mixture in CDCl₃ or dry DMSO. The shifts for octafluoronaphthalene in CDCl₃ were − 145.59 and − 154.05 ppm with respect to internal CFCl₃; the assignment for heptafluoroquinoline was reported in 1976.

Table 3
Summary of shifts in reaction B

In DMSO	In CDCl₃
− 105.83 F7 {7}*	− 104.5 ppm
− 107.26	− 106.7
− 109.74 F7 {9}	− 108.3 ppm/J = 2
− 109.94	
− 116.76	Disappeared?
− 120.29 F5 {8}*	− 119.01 ppm
− 120.34	
− 122.98 F5 {9}	− 122.26 J = 2 Hz
− 123.01	− 123.7/J_HF = 10 Hz
− 127.96 F7 {10}	− 127.27/J = 21.2 Hz
− 129.80 F6 {10}	− 129.24/J = 21.2 Hz

1.2.2. The reaction of 3,5,6,7,8-pentachloroquinoline{6} with caesium fluoride in DMSO at 100°C

The starting material appeared 97% pure by proton NMR. The reaction progressed quite smoothly, quickly and showed many products after 4 hours. Broad peaks at − 80 ppm and − 103 ppm were attributable to fluoride ions and a typical spectrum could be described as follows in Table 3.

After 30 min, the starred peaks were visible and were assigned to the mono-substituted products {7} and {8}.

By the same reasoning as above, the peaks at − 122 ppm and − 109 ppm indicate the 5,7-meta difluoro-compound {9}.

Another difluoro compound {10} shows an AX system
− 127.96 and − 129.80 ppm in DMSO with $J = 21.2$ Hz and
its structure and assignment again follows compound {5}.

Predictions for {10}: F6 − 132.4 + 1.7 = − 130.7 exptl − 129.80 ppm
                       F7 − 129.0 + 0.9 = − 128.1 exptl − 127.96 ppm

In this prediction, the first column of data are the shifts
from compound {5} above. The small SCS adjustment were
measured by Adcock et al. [11] in dihalonaphthalenes,
changing the sign in this case, when 'hypothetically' substi-
tuting a hydrogen atom at position 3 with chlorine. These
SCSs were found to be in agreement with SCSs in Kobrina
et al. [12]; horizontally opposed position + 1.8 ppm and the
diametrically opposed value of + 0.4 ppm. These predictions
increase our confidence in the assignment of {9} and {10}.
Furthermore, the *ortho* SCS for Cl to F is again − 22.2 ppm,
in agreement with the value above.

The chlorine in the carbocyclic ring proved more reactive
than the 'isolated' chlorine at C3 in the heterocyclic ring.

1.2.3. The reaction of 4,7-dichloroquinoline{11} with caesium fluoride in DMSO at 100°C and 140°C

Exchange was not expected. Isolated single halides around
an aromatic are reluctant to exchange without adjacent hal-
ides or groups. Here, only one non-fluoride peak was found:
− 112.63 ppm. Further attempts to fully react this material at
350C in a autoclave, failed. The structure was either 12A and
12B which had the following NIMS predictions:

12A   F7   − 115.3 + 1.4 = − 114.0 ppm
12B   F4   − 123.8 + 21.3 = − 102.5 ppm

The shift values for the monofluoronaphthalenes are those
from Singh et al. [13] while the NIMs are the differences
between the shifts of heptafluoroquinoline and octafluoro-
naphthalene (Table 1).

Mass spectroscopy showed this compound to be C_9H_5ClF.
The peak at − 112.63 ppm showed splittings of 10.0 Hz.
8.4 Hz and 1.2 Hz favoring structure 12A.

1.2.4. The reaction of 2,3,4,5,6,7,8-heptachloro-quinoline{13} with caesium fluoride in DMSO at 100°C

The starting material appeared pure by proton NMR. The
reaction progressed quite smoothly, quickly and showed
many products after 1 h. A typical if complicated spectrum
could be described as follows in Table 4.

After 30 min, the starred peaks dominated the spectrum
and were assigned to the mono-substituted products {14} and
{15} with 2,4-meta difluoro-compound {16}. The sharp
peaks at − 102 and − 116 ppm were obviously the 4,5
difluorinated compound where the F,F coupling is 70.5 Hz
cf 59.2 Hz in octafluoronaphthalene [14,15].

The peri-SCS (Cl to F) is 7.6 ppm for F4 and 9.0 ppm for
F5, close to a value of + 7 ppm in part 1 [1].

Table 4
Summary of shifts in reaction D

in DMSO
− 59.00* F2 {14}
− 63.62 F2 {16}
− 67.42 F2
− 67.91 F2
− 94.42* F4 {15}
− 98.75 F4 {16}
− 102.00 F4 $J = 70.5$ {17}
− 107.29 F5
− 114.24
− 115.36 F5 $J = 63.5$
− 116.38 F5 $J = 70.5$ {17}
− 117.41

Competitive reactions in a NMR tube can be studied if the
compounds are simple. Attempting a competitive exchange
using 2,3,4,5,6,7,8-heptachloroquinoline{13} and, say,
hexachlorobenzene is difficult because the product peaks will
appear in the same narrow limited zone of the fluorine spec-
trum. For {13}, the nucleophilic sequence of attack or the
general pattern of attack found here is:

2 = 4 > 5 = 7 > 6 > 3 = 8
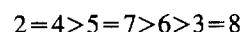
not quite the reverse of the electrophilic order of reactivity
[16]:

5 > 8 = 6 > 3 > 7 ≫ 2 > 4
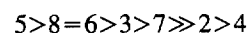
References

[1] R.S. Matthews, J. Fluorine Chemistry 48 (1990) 7 Part I.
[2] R.S. Matthews, J. Fluorine Chemistry 50 (1990) 381 Part II.
[3] R.S. Matthews, J. Fluorine Chemistry 55 (1992) 163 Part III.
[4] G. Fuller, J. Chem. Soc. (1965) 6264.
[5] R.D. Chambers, M. Hole, W.K.R. Musgrave, R.A. Storey, B. Iddon, J. Chem. Soc. C (1966) 2331.
[6] J. Hutchinson, G. Sandford, Topics in Current Chemistry 193 (1997) 1.
[7] J.H. Clark, D.J. Nightingale, J. Fluorine Chemistry 78 (1996) 91.
[8] G.W. Gribble, D.J. Keavy, E.R. Olson, I.D. Rae, A. Staffa, T.E. Herr, M.B. Ferraro, R.H. Contreras, Magn. Reson. Chem. 29 (1991) 422.
[9] R.S. Matthews, Org. Magn. Res. 8 (1976) 240.
[10] M.G. Hogben, W.A.G. Graham, J. Am. Chem. Soc. (1969) 283.
[11] W. Adcock, J. Alste, S.Q.A. Rizvi, M. Aurangzeb, J. Am. Chem. Soc. 98 (1976) 1701.
[12] L.S. Kobrina, V.D. Shteingarts, L.N. Shchegoleva, Isv. Sib.Otd. Akad. Nauk. 1 (1974) 68.
[13] S. Singh, D.D. Desmarteau, S.S. Zuberi, M. Witz, H.-N. Huang, J. Am. Chem. Soc. 109 (1987) 7194.
[14] L. Cassidei, A. DellAtti, O. Sciacovelli, Spec. Lett. 12 (1979) 365.
[15] L. Cassidei, O. Sciacovelli, L. Forlani, Spec. Acta 38A (1982) 755.
[16] G. Jones, Heterocyclic Compounds, Vol. 32, Wiley, 1977, p. 42.