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PREPARATION OF HEXAFLUORO-1,8- and -2,7-NAPHTHYRIDINE

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SUMMARY

Hexachloro-1,8- and -2,7-naphthyridine have been prepared from 2,7-dichloro-1,8-naphthyridine and 1,3,6,8-tetrachloro-2,7-naphthyridine respectively. From these products and their starting materials a series of partially and totally fluorine substituted compounds have been derived.

INTRODUCTION

Fluorine substitution in aromatic molecules usually affects π and σ electronic levels to a different extent. This phenomenon, the "perfluoro-effect"[1], is a valuable tool in the analysis of photoelectronspectra. In the case of symmetrical diaza aromatic molecules, partial and total fluorine substitution may sometimes be used to determine the symmetry of molecular orbitals that correspond with the two "lone pair" energy levels[2].
Thus fluorinated hetero-aromatic molecules deserve attention.

RESULTS AND DISCUSSION

The hexafluorodiazanaphthalenes with both nitrogen atoms in one ring, have been prepared by Chambers et al.[3-6] by direct conversion of the chlorine derivative with dry KF. The same procedure applied to hexachloro-1,8-naphtyridine (1) and its 2,7-isomer (5), was not successful.

(1) did not react at all below its melting point (273°C) and above this temperature (1) or its products, decomposed.

At temperatures up to 280°C (5) was converted to a tetrafluorodichloro-product (6). Extension of the reaction time or raising of the temperature caused excessive decomposition and only traces of the desired hexafluoro-2,7-naphthyridine (8) were observed.

The alternatives were to carry out the reactions in a solvent (sulpholan) or to use a more powerful fluorinating agent (e.g. CsF). Both (1) and (5) reacted with KF in sulpholan to yield the corresponding hexafluoro products.

However, owing to its extreme sensitivity to moisture, (8) could not be isolated from the reaction mixture. Finally a mixture of 4-chloro-1,3,5,6,8-pentafluoro-2,7-naphthyridine (7) and (8) was obtained by heating (6) with dry CsF in a sealed glass capsule at 200°C during one week. Extension of the reaction time did not improve the results.

The mixture of (7) and (8) was separated by G.L.C. on preparative scale.

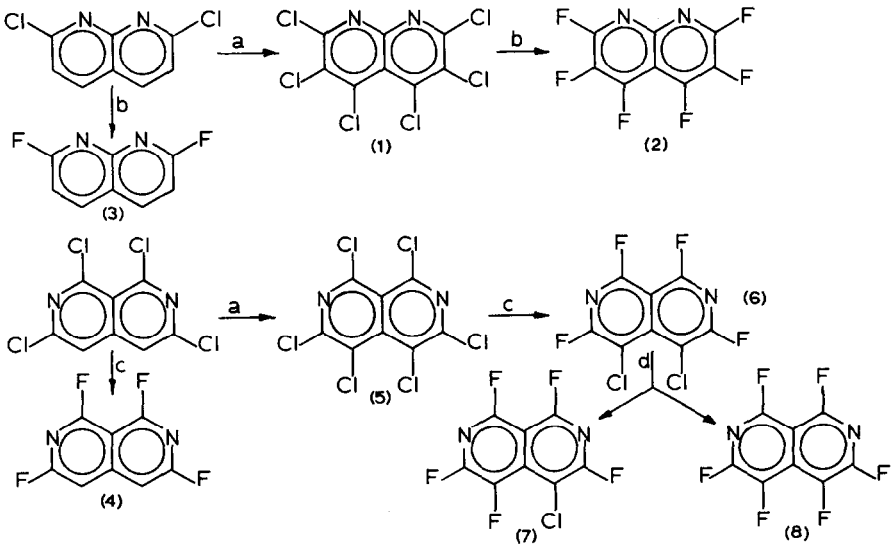
The ^{19}F N.M.R. spectrum of 1,3,6,8-tetrafluoro-2,7-naphthyridine (4) showed absorption at -93,5 and -108,8 p.p.m. (shifts are relative to hexafluorobenzene, see "Experimental"). It is known[7-9] that absorption peaks from fluorine ortho to nitrogen in ^{19}F spectra, are broadened due to incomplete ^{14}N

quadrupolar relaxation. Both absorptions of (4) show this broadening. The spectrum of (8) showed three absorptions (-6,9, - 72,9 and - 105 p.p.m.). Two signals were broadened and one signal (at - 6,9 p.p.m.) showed well resolved fine structure. The ^{19}F spectrum of (6) showed two absorptions, both broadened as in the spectrum of (4). This indicates (6) to be 4,5-dichloro-1,3,6,8-tetrafluoro-2,7-naphthyridine.

Similar broadening is observed in one of the resonance signals (at -31,6 p.p.m.) of hexafluoro-1,8-naphthyridine (2), whereas the other two signals (at -1,3 and -38,9 p.p.m.) showed well resolved narrow fine structure.

EXPERIMENTAL

IR spectra have been recorded on a Perkin Elmer 257; molecular weights have been determined on a C.E.C. 21.110B mass spectrometer; ^{19}F N.M.R. spectra have been measured on a Varian XL 100



Reagents: a,$AlCl_3/Cl_2$;b,KF-sulpholan; c,KF; d,CsF.

spectrometer, using hexafluorobenzene as an internal reference (solvent deutero-acetone, downfield shifts are quoted as negative) melting points have been determined with a Mettler FP 1 melting point apparatus. Sulpholan has been dried over molecular sieves and distilled in vacuo. KF and CsF have been dried in vacuo at 130°C. All manipulations regarding the filling of the glass-capsules took place in a glove-box with a moisture level below 40 p.p.m. Fluorine analyses were carried out under supervision of Mr. W.J. Buis at the analytical Department of the Institute of Organic chemistry T.N.O., Utrecht, The Netherlands.

Hexachloro-1,8-naphthyridine (1)

A synthetical route to (1) has been mentioned in a German Patent[10]. This synthesis is time consuming and not well suited for small scale preparations. Therefore an alternative path was tried.

2,7-dichloro-1,8-naphthyridine[12] (4 g), $AlCl_3$ (4 g) and chlorine (14 ~ 16 g) were sealed in a glass capsule[11] of 100 ml capacity and placed in a protecting autoclave. This autoclave was heated to 280°C for 3 hours. After cooling, the capsule was broken inside the autoclave and vented. The solid yellow product was added to ice water (250 ml), filtered and washed on the filter with 50 ml benzene. The residue was recrystallized from chlorobenzene (charcoal) to give 5,6 g (82,7%) (1) as pale yellow needles. M.p. 271,6 - 273°C (lit.[10]: 272 - 273°C). The mass and I.R. spectra were identical to those of the product derived by the other route.*

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* Dr. G. Beck (Bayer-Leverkusen) was so kind to send an analytical sample of (1) for comparison.

Hexafluoro-1,8-naphthyridine (2)

(1) (4,5 g), KF (25 g) and sulpholan (50 g) were heated at 200°C for 17 hours. The dark slurry was poured into 250 ml ice-water, filtered at the pump and the residue washed with another 50 ml ice-water. The residual brown solid was dissolved in 150 ml acetone and dried. After evaporation of the solvent the residue was sublimed (50°C, 0,1 Torr) to give 1,3 g of a white solid. G.L.C. and mass spectroscopy showed a product composition of (2): 81%; $C_8ClF_5N_2$: 11% and $C_8Cl_2F_4N_2$: 8%. Yield of $C_8F_6N_2$ (based on (1)): 32,5%.

The mixture was recrystallized twice from benzene to give pure (G.L.C.) (2). M.p. 164,9 - 166°C. (Found: C, 40,29; F, 48,13 and N, 11,83%; mol.wt.238. $C_8F_6N_2$ requires C, 40,3; F, 47,9 and N, 11,8%; mol.wt.238).

^{19}F N.M.R. showed absorption at -1,3; -38,9 and -91,6 p.p.m.

ν_{max} (KBr) 1665, 1605, 1485, 1448, 1415, 1385, 1350, 1228, 1195, 1090, 1073 (w), 1040, 830, 784, 772, 740, 725 (w), 692 and 625 (w) cm^{-1}.

2,7-difluoro-1,8-naphthyridine (3)

2,7-dichloro-1,8-naphthyridine[12] (5 g), KF (10 g) and sulpholan (70 g) were stirred during 24 hours at 180 - 185°C. The resulting brown mixture was poured into 250 cc water. After filtration the solid was resuspended in 100 ml water and again filtered at the pump. The brown solid was sublimed at 120°C, 0,1 Torr. to yield 2,1 g of pure (3) (50,4%). M.p. 215,4 - 216,8°C. (Found: C, 57,78; H, 2,52; F, 23,12 and N, 16,84%; mol.wt.166. Calculated for $C_8H_4F_2N_2$: C, 57,83; H, 2,41; F, 22,89 and N, 16,87%; mol.wt.166)

^{19}F N.M.R. showed absorption at -106,3 p.p.m.

ν_{max} (KBr) 3070, 3025, 1625, 1600, 1570, 1495, 1445, 1328, 1312, 1265, 1213, 1135 (w), 1035 (w), 1008 (w), 846, 807, 794 and 685 cm^{-1}.

1,3,6,8-tetrafluoro-2,7-naphthyridine (4)

1,3,6,8-tetrachloro-2,7-naphthyridine[13] (5 g) and KF (50 g) were heated in a sealed glass capsule at 270°C for 5 hours. The contents of the capsule were pumped out into a cold trap and resublimed to give 2,4 g (63,7%) of pure (4). M.p. 58 - 59,6°C. (Found: C, 47,61; H, 0,96; F, 37,30 and N, 13,88%; mol.wt. 202. Calculated for $C_8H_2F_4N_2$: C, 47,52; H, 0,99; F, 36,63 and N, 13,86%; mol.wt. 202).

^{19}F N.M.R. showed absorption at -93,5 and -108,8 p.p.m.

ν_{max} (KBr) 3080, 1638, 1578, 1403, 1355, 1300, 1250, 1222, 1145, 1108, 1095, 1035 (w), 987, 820, 792 (w), 774, 720 and 626 (w) cm^{-1}.

Hexachloro-2,7-naphthyridine (5)

Synthetical route similar to that of (1). 1,3,6,8-tetrachloro-2,7-naphthyridine (8 g), $AlCl_3$ (4 g) and chlorine (14 - 16 g) were heated at 220°C for 3 hours. The dark product was added to ice-water (250 ml), whereupon the lumps desintegrated into a yellow powder. The product was filtered, dissolved in acetone (100 ml) and reprecipitated by adding 300 ml of water. Yield 8,1 g (80,5%). M.p. 144,8 - 146,7. (Found: C, 28,51; Cl, 62,72 and N, 8,32%; mol.wt. 334. $C_8Cl_6N_2$ requires C, 28,48; Cl, 63,2 and N, 8,31%; mol.wt. 334).

ν_{max} (KBr) 1510, 1395 (w), 1365 (w), 1346, 1338, 1275, 1225, 1133, 1032, 902, 778 (w), 690 and 660 cm^{-1}.

4,5-dichloro-1,3,6,8-tetrafluoro-2,7-naphthyridine (6)

(5) (10 g) and KF (50 g) were heated at 260°C for 17 hours. At 100°C volatile products were pumped into a cold trap. The white product was recrystallized twice from benzene (colourless needles) and sublimed (40°C, 0,05 Torr). Yield 5,2 g of (6) (64,7%). M.p. 102,3 - 104 °C. (Found: C, 35,56; Cl, 26,15; F, 27,78 and N, 10,44%; mol.wt.2711. Calculated for $C_8Cl_2F_4N_2$: C, 35,42; Cl, 26,20; F, 27,74 and N, 10,33%; mol.wt.271). ^{19}F N.M.R. showed absorption at -97,0 and -108,2 p.p.m. ν_{max} (KBR) 1615, 1595, 1572, 1423, 1390, 1310, 1068, 830, 798, 790 and 742 (w) cm^{-1}.

4-chloro-1,3,5,6,8-pentafluoro-2,7-naphthyridine (7) and *hexafluoro-2,7-naphthyridine* (8)

5 g of (6) and CsF (50 g) were mixed and transferred to a glass capsule. KF (ca 40 g) was added to fill the capsule completely. The mixture was heated at 200°C for one week. 3,2 g of a white solid were obtained by pumping the volatile components into a cold trap. G.L.C. proved this product to be composed of 51% (7), 45% (8) and 4% decomposition products. Based on the amount of (6) used, the yields of (7) and (8) were 34,8 and 33% respectively. Separation of (7) and (8) was effected by G.L.C. on preparative scale (column 2 m; 20% SE - 30).

Analytical data for (7): M.p. 41,3 - 43°C. (Found: C, 37,85; Cl, 14,07; F, 37,37 and N, 11,04%; mol.wt.254. $C_8ClF_5N_2$ requires C, 37,80; Cl, 13,98; F, 37,40 and N, 11,02%; mol.wt.254). ν_{max} (KBr) 1635, 1595, 1505, 1430, 1390, 1340, 1245 (w), 1140 (w), 1085 (w), 900, 815, 790, 762 (w) and 708 (w) cm^{-1}.

Analytical data for (8): M.p. 61,4 - 62,8°C. (Found: C, 40,48; F, 48,17 and N, 1170%; mol.wt.238. $C_8F_6N_2$ requires: C, 40,34; F, 47,90 and N, 11,76%; mol.wt.238).

^{19}F N.M.R. showed absorption at - 6,9, -72,9 and -105 p.p.m.

ν_{max} (KBr) 1645, 1590, 1535, 1460, 1445, 1415, 1395, 1370, 1255 (w), 1208, 1118 (w), 930, 872, 786, 728, 707 (w) and 662 (w) cm^{-1}.

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