Journal of Fluorine Chemistry, 12 (1978) 159–166

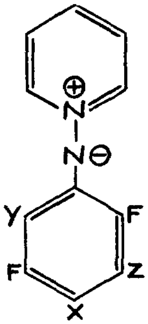
Received: January 23, 1978

SHORT COMMUNICATION

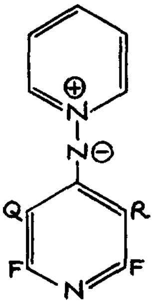
Fluorocarbon Derivatives of Nitrogen. Part II [1]. Synthesis of Fluorinated N-Aryl and N-Heteroaryliminopyridinium Ylides

R.E. BANKS* and S.M. HITCHEN

Chemistry Department, the University of Manchester
Institute of Science and Technology, Manchester M60 1QD
(Great Britain)



(I) X = Y = Z = F
(II) X = CN, Y = Z = F
(III) X = F, Y = CN, Z = OMe



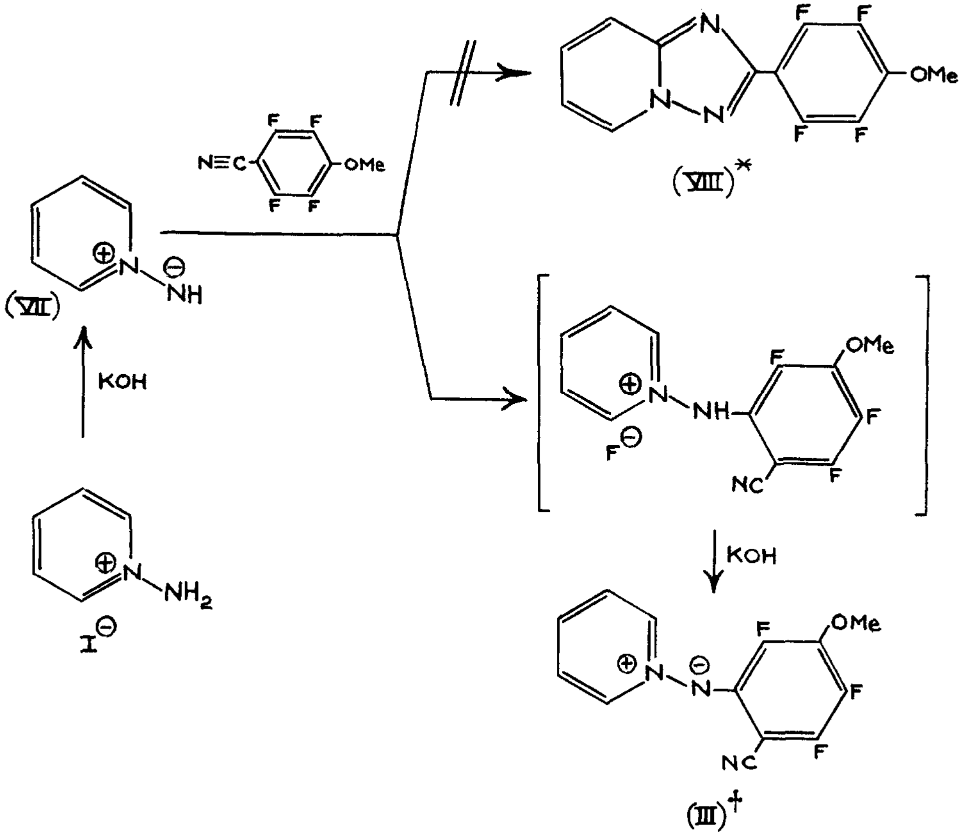
(IV) Q = R = F
(V) Q = F, R = Cl
(VI) Q = R = Cl

The isolable iminopyridinium ylides (I)-(VI) have been prepared by treating hexafluorobenzene,

---

[*] To whom enquiries should be addressed.

pentafluorobenzonitrile, tetrafluoro-4-methoxybenzonitrile, pentafluoropyridine, 3-chlorotetrafluoropyridine, and 3,5-dichlorotrifluoropyridine, respectively, with N-iminopyridinium ylide (VII) under basic conditions. This work stemmed from a study of fluorinated indolizines [2], and in particular from an attempt to synthesise the 3-azaindolizine (VIII) through utilization of the dipolarophilic potential of the cyano function of tetrafluoro-4-methoxybenzonitrile [3] (see the Scheme).



SCHEME

*None detected (t.l.c.). † Crude yield 84%.

Formation of the indolizine was thwarted by the ease with which N-iminopyridinium ylide displaced fluorine from the nitrile, the final product being the new N-aryliminopyridinium ylide (III) - an outcome which prompted us to establish the generality of this reaction in the polyfluoroaromatic field [4].

EXPERIMENTAL

N.m.r. spectroscopy

N.m.r. spectra were obtained with a Perkin-Elmer R32 instrument operating at 84.6 MHz (^{19}F) or 90 MHz (^{1}H). Chemical shifts to high field of reference signals are designated negative.

Starting materials

N-Aminopyridinium iodide (NAPI) [5], pentafluorobenzonitrile [6], tetrafluoro-4-methoxybenzonitrile [7], and pentafluoro-, 3-chlorotetrafluoro-, and 3,5-dichlorodifluoro-pyridine [8] were synthesised according to published procedures. Hexafluorobenzene was purchased [Fluorochem Ltd.].

Generation of N-iminopyridinium ylide

Deep blue, or purplish blue, solutions of N-iminopyridinium ylide (NIPY) were prepared immediately prior to use by treating corresponding solutions of N-aminopyridinium iodide (NAPI) with an excess of base [9]. The solutions were used as prepared; thus, when anhydrous potassium carbonate was employed as the base, no attempt was made to remove the solid material.

Reactions of fluorinated aromatics with N-iminopyridinium ylide

(a) Hexafluorobenzene

A solution of hexafluorobenzene (2.00 g, 10.8 mmole) in DMF (10 cm^3) was added to NIPY [ex NAPI (2.22 g, 10.0 mmole) + K_2CO_3 (3 g) in DMF (10 cm^3) (stirred for 15 min at 20 °C)] in the same solvent. The greenish black mixture was stirred for 48 h then filtered; the filtrate, plus DMF (5 x 5 cm^3) used to wash the precipitate, was poured into water (75 cm^3), and the greenish-brown material which precipitated was purified by column chromatography (40 x 2.5 cm silica gel eluted with Me_2CO) followed by recrystallization [Me_2CO-H_2O (60:40 v/v)], to provide N-(pentafluorophenyl)iminopyridinium ylide (nc) (1.49 g, 5.73 mmole, 57%) [Found: C, 50.6; H, 1.7; F, 36.4; N, 10.8%; M (mass spec.), 260. $C_{11}H_5F_5N_2$ requires C, 50.8; H, 1.9; F, 36.5; N, 10.8%; M, 260] as golden yellow plates, m.p. 156-157 °C (decomp.), $\lambda_{max.}$ (mull) 1500 cm^{-1} (C_6F_5 nucleus), δ_F [ca. 30% soln. in $(CD_3)_2SO$ at 70 °C; ext. CF_3CO_2H] -75.0 (2-,6-F), -88.5 (3-,5-F), and -98.9 (4-F) p.p.m. (rel.int. 2:2:1), δ_H (same soln.; ext. 1,4-$Cl_2C_6H_4$) +0.1 (3-,4-,5-H) and +0.95 (2-,6-H) p.p.m. (rel.int. 3:2), and m/e 260 ($M^{+\cdot}$, 40%), 181 ($C_6F_5N^{+\cdot}$, 18%), and 79 ($C_5H_5N^{+\cdot}$, 100%).

(b) Pentafluorobenzonitrile

A solution of pentafluorobenzonitrile (0.605 g, 3.13 mmole) in ethanol (5 cm^3) was added to NIPY [ex NAPI (0.80 g, 3.60 mmole) + K_2CO_3 (2 g) in EtOH (20 cm^3)] in the same solvent. The yellow mixture was stirred for 2 days then filtered; the filtrate, plus ethanol (2 x 10 cm^3) used to wash the precipitate, was evaporated and the residue (shown by t.l.c. to contain only one tractable product) was purified by a combination of column chromatography (40 x 2.5 cm alumina eluted with Me_2CO) and recrystallization (using aqueous ethanol) to provide N-(4-cyanotetrafluorophenyl)iminopyridinium ylide (nc) (0.13 g, 0.48 mmole, 16%) [Found: C, 54.0; H, 1.8; F, 28.5; N, 15.4%; M (mass spect.), 267. $C_{12}H_5F_4N_3$ requires C, 53.9; H, 1.9; F, 28.5; N, 15.7%; M, 267] as yellowish green needles, m.p. 235-237 (decomp.), $\lambda_{max.}$ (mull) 2232 (C≡N str.) µm, δ_F (*ca.* 40% soln. in CF_3CO_2H; ext. CF_3CO_2H) -53.8 (3-,5-F) and -74.0 (2-,6-F) p.p.m. (rel.int. 1:1), δ_H (same soln.; ext. 1,4-$Cl_2C_6H_4$) +1.0 (3-,5-H), +1.53 (4-H), and +1.83 (2-,6-H) p.p.m. (rel.int. 2:1:2), and *m/e* 267 ($M^{+\cdot}$, 93%), 188 ($NCC_6F_4N^{+\cdot}$, 4%), and 79 ($C_5H_5N^{+\cdot}$, 100%).

(c) Tetrafluoro-4-methoxybenzonitrile

A yellow precipitate appeared immediately when a solution of tetrafluoro-4-methoxybenzonitrile (0.135 g, 0.659 mmole) in ethanol was added to NIPY [*ex* NAPI (o.16 g, 0.72 mmole) + 2M-KOH aq.(1.0 cm^3, 2.0 mmole)] in aqueous potassium hydroxide. The mixture was stirred for 1 h then poured into water (50 cm^3); recrystallization (aqueous ethanol) of the solid product (0.154 g; one t.l.c. spot) gave *N*-(2-cyano-3,4,6-trifluoro-5-methoxyphenyl)-iminopyridinium ylide (n.c.) (0.145 g, 0.520 mmole, 79%) as yellow needles, m.p. 192-193 °C (decomp.). This product possessed the same spectral characteristics [$\lambda_{max.}$(mull) 2220 (C≡N str.) µm, δ_F (*ca.* 40% soln. in CF_3CO_2H; ext. CF_3CO_2H) -54.3 (3-F), -65.2 (6-F), and -73.7 (4-F) p.p.m. (rel.int. 1:1:1), and δ_H (same soln.; ext. 1,4-$Cl_2C_6H_4$) +0.98 (3-,5-H), +1.47 (4-H), +1.80 (2-,6-H), and -2.96 (OCH_3) p.p.m. (rel.int. 2:1:2:3)] as a sample [Found: C, 55.6; H, 2.6; F, 20.6; N, 14.9. $C_{13}H_8F_3N_3O$ requires C, 55.9; H, 2.9; F, 20.4; N, 15.05%] obtained in 33% yield (after recrystallization) using a NAPI : KOH molar ratio of only 1:1.5.

(d) Pentafluoropyridine

A solution of pentafluoropyridine (1.72 g, 10.2 mmole) in ethanol (10 cm^3) was added to NIPY [*ex* NAPI (2.22 g, 10.0 mmole) + K_2CO_3 (3 g) in EtOH (80 cm^3) (stirred for 15 min at 20 °C)]. The mixture was stirred overnight, then filtered; the precipitate was washed with water (20 cm^3), dried *in vacuo* over P_2O_5, and recrystallized from aqueous ethanol to give *N*-(2,3,5,6-tetrafluoro-4-pyridyl)iminopyridinium ylide (nc) (1.75 g, 7.22 mmole, 72%) [Found: C, 49.3; H, 1.9; F, 31.2; N, 17.4%; *M* (mass spec.), 243. $C_{10}H_5F_4N_3$ requires C, 49.4; H, 2.1; F, 31.3; N, 17.3%; *M*, 243] as pale yellow needles, m.p. 231-232.5 °C (decomp.), $\lambda_{max.}$ (mull) 1475 cm^{-1} (C_5F_4N nucleus), δ_F [40% soln. in $(CD_3)_2SO$ at 70 °C; ext. CF_3CO_2H] -20.4 (2-,6-F) and -84.8 (3-,5-F) p.p.m. (rel.int. 1:1), δ_H (same soln. at 120 °C; ext. 1,4-$Cl_2C_6H_4$) +0.3 to +0.8 (3-,4-,5-H) and +1.43 (2-,6-H) p.p.m. (rel.int. 3:2), and *m/e* 243 ($M^{+\cdot}$, 96%), 164 ($C_5F_4N_2^{+\cdot}$, 1%), and 79 ($C_5H_5N^{+\cdot}$, 100%).

(e) 3-Chlorotetrafluoropyridine

Experiment (d) was repeated with 3-chlorotetrafluoropyridine (2.0 g, 10.8 mmole) in place of pentafluoropyridine. The product was *N*-(3-chloro-2,5,6-trifluoro-4-pyridyl)iminopyridinium ylide (nc) (1.78 g, 6.86 mmole, 69%) [Found: C, 46.0; H, 2.1; F, 21.5; N, 16.2%; *M* (mass spec.) 259.5. $C_{10}H_5ClF_3N_3$ requires C, 46.2; H, 1.9; F, 22.0; N, 16.2%; *m*, 259.5], isolated as yellow needles, m.p. 213-215 °C (decomp.) (recrystallized from aqueous ethanol), δ_F [*ca.* 20% soln. in $(CD_3)_2SO$ at 70 °C; ext. CF_3CO_2H] -2.0 (2-F), -19.5 (6-F), and -88.5 (5-F) p.p.m. (rel.int. 1:1:1), δ_H (same soln. at 70 °C; ext. 1,4-$Cl_2C_6H_4$) +0.3 to +0.8 (3-,4-,5-H) and +1.4 (2-,6-H) p.p.m. (rel.int. 3:2), and *m/e* 261 [$M(^{37}Cl)^{+\cdot}$, 20%], 259 [$M(^{35}Cl)^{+\cdot}$, 60%], and 79 ($C_5H_5N^{+\cdot}$, 100%).

(f) 3,5-Dichlorotrifluoropyridine

Experiment (d) was repeated with 3,5-dichlorotrifluoropyridine (2.1 g, 11.5 mmole) in place of pentafluoropyridine. The product (recrystallized from aqueous acetone) was N-(3,5-dichloro-2,6-difluoro-4-pyridyl)iminopyridinium ylide (nc) (2.5 g, 9.1 mmole, 91%), isolated as lemon yellow crystals [Found: C, 43.7; H, 1.8; Cl, 25.7; F, 14.0; N, 15.4%; M (mass spec.), 276. $C_{10}H_5Cl_2F_2N_3$ requires C, 43.5; H, 1.8; Cl, 25.7; F, 13.8; N, 15.2%; M, 276], m.p. 235-237 °C (decomp.), δ_F [ca. 30% soln. in $(CD_3)_2SO$ at 110 °C; ext. CF_3CO_2H] +1.3 (br. s)(2-,6-F) p.p.m., δ_H (same soln. at 110 °C; ext. 1,4-$Cl_2C_6H_4$) +0.3 to +0.8 (3-,4-,5-H) and +1.2 (2-,6-H) p.p.m. (rel.int. 3:2), and m/e 279 [$M^{+\cdot}$ ($^{37}Cl_2$), 7%], 277 [$M^{+\cdot}$ ($^{37}Cl^{35}Cl$), 43%], 275 [$M^{+\cdot}$ ($^{35}Cl_2$), 65%], and 79 ($C_5H_5N^{+\cdot}$, 100%).

The award of an SRC Studentship to S.M.H. is gratefully acknowledged.

REFERENCES

1 Part I, R.E. Banks and C. Oppenheim, J.Fluorine Chem., 12 (1978), 27.

2 R.E. Banks and S.M. Hitchen, work in progress.

3 For a recent review of the synthesis of 3-azaindolizines, see T. Uchida and K. Matsumoto, Synthesis, (1976) 209.

4 In the hydrocarbon field, it has been known for some time [T. Okamoto, S. Hayashi, H. Horikiri, and M. Hirobe, Yakugaku Zasshi, 91 (1971), 210] that N-iminopyridinium ylide (prepared in situ from N-aminopyridinium chloride or iodide and NaOEt/EtOH) attacks activated (in the S_NAr sense) aryl and heteroaryl monohalides [e.g., 2,4-$(NO_2)_2C_6H_3Cl$, 2-bromopyridine, 4-chloroquinoline-N-oxide] to provide the corresponding N-substituted iminopyridinium ylides.

5 R.Gösl and A. Meuwsen, Org. Synth., 43 (1963), 1.

6 J.M. Birchall, R.N. Haszeldine, and M.E. Jones, J.Chem.Soc. (C), (1971), 1341.

7 J.M. Birchall, R.N. Haszeldine, and M.E. Jones, J.Chem.Soc. (C), (1971),1343.

8 R.E. Banks, R.N. Haszeldine, J.V. Latham, and I.M. Young, J.Chem.Soc., (1965) 594.

9 See, for example, T. Okamoto, M. Hirobe, Y. Tamai, and E. Yabe, Chem.Pharm.Bull., **14** (1966), 506 (2*M*-KOH/EtOH); T. Okamoto, M. Hirobe, and T. Yamazaki, *ibid.*, p. 512 (K_2CO_3/DMF); T. Sasaki, K. Kanematsu, and A. Kakehi, J.Org.Chem., **37** (1972), 3106 (K_2CO_3/EtOH); and A. Kakehi and S. Ito, *ibid.*, **39** (1974) 1542 (K_2CO_3/$CHCl_3$). For a recent review of heteroaromatic *N*-imines, see H.-J. Timpe, Adv. Heterocyclic Chem., **17** (1974), 213.