

and the ether was decanted. This residue was dissolved in 2 drops of water. The ultraviolet absorption spectrum in water (max. at 262.5 μ , min. at 230 μ) corresponded to that of a 1- β -D-aldopentofuranosyluracil. Electrophoresis (Whatman 3MM paper, borate buffer, 0.07 *M*, pH 9.2, 800 v., 2.5 hr.) revealed only one spot of high intensity under ultraviolet light. Its anodic migration was 3.5 cm., which corresponded to that of a test sample of 1- β -D-arabinofuranosyluracil (XVI) of anodic

migration, 3.5 cm. No absorption was found which corresponded to that of a test sample of 1- β -D-xylofuranosyluracil (anodic migration 13.5 cm.).

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Synthesis of Pyridines from Butadiene and Cyanogen-Like Molecules

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Experiments are described using a series of "cyanogen-like" molecules, *i.e.*, $\text{CF}_3\text{CF}_2\text{CN}$, $\text{CF}_3\text{CF}_2\text{CF}_2\text{CN}$, CF_2ClCN , and CFCl_2CN , as the dienophiles for the synthesis of new pyridines from 1,3-butadiene. The gas phase reaction proceeds smoothly at moderately high temperatures (350–450°) and atmospheric pressures. Pyridinic products are formed in very nearly 100% yields based on the nitrile having fluorine as the only substituent.

The formation of 2-perfluoromethylpyridine through the addition of perfluoroacetonitrile and butadiene and the reaction kinetics of this cyclization reaction in the homogeneous gas phase have been reported.^{1b,c} As with cyanogen, the addition reaction proceeds^{1d} at moderately high temperatures (350–400°) at atmospheric pressures in the homogeneous gas phase. The present work reports the results for experiments with related "cyanogen-like" molecules as dienophiles [*e.g.*, $\text{CF}_3\text{CF}_2\text{CN}$, $\text{CF}_3(\text{CF}_2)_2\text{CN}$, CF_2ClCN , and CFCl_2CN] in this new pyridinic synthesis.

Experimental

Chemicals.—Butadiene, 99.0% purity, b.p. –3.0° (Matheson Co., C.P. grade), was degassed three times (–195°) prior to use. The nitriles, CF_3CN , b.p. –60°; $\text{CF}_3\text{CF}_2\text{CN}$, b.p. –35°; $\text{CF}_3(\text{CF}_2)_2\text{CN}$, b.p. –5°; CF_2ClCN , b.p. –18.3°; and CCl_2FCN , b.p. 35°, each obtained in 98% purity (Peninsular ChemResearch Inc., Columbia Organic Chemicals Co.), were similarly treated.

Apparatus and Procedure.—The continuous flow assembly, previously described,^{1d} was modified to take a large reaction vessel (5 l.). The latter was pretreated with an 8-hr. oxygen "sweep" (100 cc./min.) at 500°, prior to each experiment. The whole assembly was flushed with an inert gas (dry nitrogen, 2 hr., 100 cc./min.) after the oxygen pretreatment and prior to an experiment; on completion of each run a similar nitrogen "chase" was used to recover the materials remaining in the system. Gaseous reactants were monitored by precision Manostat flowmeters (Model No. FM 1043 B). A continuous feed injection assembly was used for liquid reactants (*e.g.*, CCl_2FCN). This consisted of a 50-cc. Perfektum syringe, gear driven at a constant rate (0.16 mole/hr.) through a Borg 3-phase motor (30 r.p.m.) and micrometer screw.

Table I summarizes the experimental conditions, material balances, conversions of reactants per pass, and yields of pyridinic products. Deviation of the over-all material balance (Table I) from 100% is attributed to experimental losses due to transfer steps in the crude product analysis (weighings, low temperature fractionations). The composition of the distillate was quantitatively established by vapor phase chromatography using 550-silicone and di-*n*-decyl phthalate columns. The refractive indices and boiling points for the three new pyridinic products together with the values for 2-perfluoroalkylpyridine are as follows: (1) 2-pentafluoroethylpyridine, n_D^{25} 1.3949, b.p. 151°; (2) 2-heptafluoro-*n*-propylpyridine, n_D^{25} 1.3814, b.p. 162°; (3) 2-difluoromonochloromethylpyridine, n_D^{25} 1.4646, b.p. 162°.

(1)(a) Union Carbide Fellow in Chemistry, 1962–1963; (b) G. J. Janz, J. M. S. Jarvie, and W. E. Fitzgerald, *J. Am. Chem. Soc.* **78**, 978 (1956); (c) G. J. Janz and J. M. S. Jarvie, *J. Phys. Chem.* **60**, 1430 (1956); (d) G. J. Janz and M. A. DeCrescente, *J. Org. Chem.* **23**, 765 (1958).

TABLE I

SYNTHESIS OF 2-PERHALOALKYLPYRIDINES				
Run conditions	CF_3CN	$\text{CF}_3\text{CF}_2\text{CN}$	$\text{CF}_3\text{CF}_2\text{CF}_2\text{CN}$	CF_2ClCN
Contact time, hr.	0.44	0.46	0.49	0.38
Total time, min.	125	107	120	115
Temperature, °C. ($\pm 3^\circ$)	400	400	400	400
Butadiene, moles	0.19	0.17	0.19	0.31
RCN, moles	0.24	0.18	0.17	0.19
Material Recovery, wt. %	98	92	92	100
Conversions per single pass, mole %				
Butadiene	71	54	89	59
RCN	45	33	22	31
Yields of pyridinic product, mole %				
A ^a	79	62	22	4
B ^b	99	97	97	12

^a Yield of pyridinic based on converted diene. ^b Yield of pyridinic based on converted nitrile.

The physical constants for 2-methylpyridine (n_D^{25} 1.4155, b.p. 143°) agreed with those previously reported.^{1b}

Both 3-vinylcyclohexene-1 and styrene were confirmed as by-products but were not quantitatively assessed. An azeotrope (b.p. ~124°) containing 0.32 mole % of 2-trifluoromethylpyridine and 0.68 mole % of 3-vinylcyclohexene-1 was found to be present in the crude resulting from the reaction between CF_3CN and butadiene at 400°. No azeotropes were detected in the experiments with the other nitriles.

The experiments with CFCl_2CN and 1,3-butadiene were less successful than for CF_2ClCN (Table I). The pyrolysis and side reactions were very extensive. While separation of the pyridinic product in trace amounts appeared possible, these experiments were not taken any further.

Results

Confirmation of the pyridinic products was through infrared and mass spectra, n.m.r. analysis, and microelemental combustion analysis for nitrogen. The results were as follows.

Infrared Spectra.—All spectra were gained with a Perkin-Elmer Model 21 double beam recording spectrophotometer having sodium chloride optics. A cell thickness of 0.025 mm. was used.

2-Trifluoromethylpyridine.—The infrared spectrum was in exact agreement with that reported in detail in the earlier communication^{1b} in which the structure was confirmed through a vibrational assignment and by microelemental analyses.

2-Pentafluoroethylpyridine.—The infrared frequencies (cm^{-1}) and intensities are 3040 (m), 2565 (vw), 1977 (vw), 1761 (vw), 1595 (s), 1475 (m), 1442 (s), 1333 (s), 1303 (vs), 1213 (s), 1199 (s), 1192 (s), 1157 (s), 1112 (vs), 1086 (s), 1047 (s), 995 (s), 982 (vs), 964 (m), 853 (vw), 850 (vw), 822 (vw), 786 (vs), 761 (vs), 745 (vs), 726 (vw), 693 (vw), 669 (w).

2-Heptafluoropropylpyridine.—The infrared frequencies (cm^{-1}) and intensities are 3080 (m), 2950 (vw), 2750 (vw), 2085 (vw), 1982 (vw), 1794 (vw), 1600 (s), 1535 (vw), 1474 (m), 1444 (s), 1423 (vw), 1404 (vw), 1351 (vs), 1304 (m), 1290 (s), 1223 (s), 1208 (s), 1181 (s), 1157 (w), 1120 (s), 1098 (m), 1084 (m), 1057 (s), 1038 (s), 996 (s), 967 (m), 937 (vs), 904 (s), 891 (s), 857 (w), 843 (w), 822 (w), 814 (vw), 784 (s), 753 (m), 747 (s), 728 (w), 712 (vw), 704 (s), 692 (s), 675 (m), 651 (m).

2-Difluorochloromethylpyridine.—The infrared frequencies (cm^{-1}) and intensities are 3460 (w), 3080 (m), 2945 (w), 2530 (w), 2220 (w), 2000 (w), 1967 (w), 1934 (vw), 1895 (w), 1870 (w), 1795 (vw), 1747 (vw), 1685 (w), 1641 (w), 1613 (m), 1594 (vs), 1582 (m), 1473 (s), 1439 (vs), 1397 (m), 1291 (vs), 1237 (s), 1152 (vs), 1127 (vs), 1082 (vs), 1067 (vs), 1042 (vs), 993 (vs), 982 (w), 924 (vs), 894 (s), 841 (m), 782 (vs), 744 (vs), 709 (vs), 668 (vw).

Vibrational Assignment.—The infrared frequencies which are generally used to characterize pyridines were reported by Cannon and Sutherland² as 3020, 1600–1590, 1500 (s) or lower, near 1200 (s), 1100–1000 (s), 900–650 cm^{-1} (two strong bands). More specifically, the infrared spectra of pyridine³ and 2-methylpyridine⁴ show 1596, 1474, 1445, 1043, and 995 cm^{-1} to be characteristic of the ring vibrations. The observed frequencies at 3040, 1595, 1475, 1442, 1213, 1086, 1047, 995, 786, 745 cm^{-1} for 2-pentafluoroethylpyridine; 3080, 1600, 1474, 1444, 1223, 1098, 1038, 996, 784, 747 cm^{-1} for 2-heptafluoropropylpyridine; and 3080, 1594, 1473, 1439, 1237, 1082, 1042, 993, 782, 744 cm^{-1} for 2-difluorochloromethylpyridine are in close agreement with these characteristic pyridinic ring assignments. The corresponding vibrations in 2-trifluoromethylpyridine are at 3040, 1596, 1474, 1445, 1250, 1100, 1043, 999, 795, 745 cm^{-1} .

The spectra for twenty-one aromatic compounds containing trifluoromethyl substituents have been studied by Randle and Whiffen⁵ to gain the characteristic frequencies. The fundamental symmetrical and antisymmetrical stretching frequencies of the CF_3 group were thus assigned as 1321 (± 9), 1179 (± 7), and 1140 (± 9) cm^{-1} , respectively. Inspection of the observed spectra shows that the bands at 1333, 1192, 1157, and 1351, 1208, 1157 cm^{-1} for the 2-pentafluoroethyl- and 2-heptafluoropropylpyridines, respectively, may be assigned to the CF_3 group accordingly.

An investigation⁶ of a series of benzotrifluorides established the assignment of a CF_2 deformation frequency at 658–665 cm^{-1} . In 2-pentafluoroethyl-, 2-heptafluoropropyl-, and 2-difluorochloromethylpyridines, the frequencies at 669, 651, and 668 cm^{-1} may be accordingly assigned.

Investigations by Risgin and Taylor⁷ of a series of pentafluoroethyl halides established that 1125 ± 10 and 1181 cm^{-1} are characteristic of the symmetrical CF_2 stretch and antisymmetrical stretch. The observed frequencies at 1112, 1199; 1120, 1181; and 1127, 1152 in the spectra of pentafluoroethyl-, heptafluoropropyl- and difluorochloromethylpyridines, respectively, correspond closely to these values and are assigned accordingly.

Risgin and Taylor⁷ also confirmed that, in the side chain, the symmetrical C–C stretch is at $755 \pm 8 \text{ cm}^{-1}$ and the antisymmetrical CF_2 deformation is at $698 \pm 10 \text{ cm}^{-1}$. In 2-pentafluoroethylpyridine and 2-heptafluoropropylpyridine these frequencies are found at 761, 693, and 753 cm^{-1} , respectively.

The CF_2Cl group stretching frequency has been established at 982 cm^{-1} .⁷ It also is found to be present at 982 cm^{-1} in difluorochloromethylpyridine.

A series of chlorofluoroethanes have been investigated by Thompson and Temple.⁸ The C–Cl stretching vibration thus was characterized at 783 cm^{-1} . This mode is present in 2-difluorochloromethylpyridine at 782 cm^{-1} .

Mass Spectra and Assignments.—Mass spectra of 2-pentafluoroethylpyridine and 2-heptafluoropropylpyridine were gained with a Consolidated Electrodynamics Model 212-60 mass spectrometer. The ionizing potential and current were set at 70 v. and 15 amp., respectively. Both pyridines were degassed five times prior to these analyses. The results and assignments are in Tables II and III.

Mass peaks 77, 78, and 79 readily characterize pyridine. The large amounts of CF_2^+ (50) fragmentation relative to CF_3^+ (69) give strong support for the straight-chain character of the perfluoroalkyl side chain in 2-heptafluoropropylpyridine. The great ease of fragmentation at a C–C bond relative to a C–F bond would predict the CF_3^+ mass peak to be much larger than the CF_2^+ mass peak if the perfluoroalkyl side chain were branched. The close correspondence of these peaks, and the relatively small amounts of CF^+ (31) are additional support for the structures advanced from the infrared spectral assignments.

N.m.r.—Fluorine and proton n.m.r. spectra for the 2-tri-, penta- and heptafluoropyridines, measured elsewhere⁹ with the samples from this laboratory, confirm a pyridinic structure and the position and structure of the side chains in accord with the preceding studies.

Microelemental analyses¹⁰ were as follows: 2-trifluoromethylpyridine, see ref. 1c; 2-pentafluoroethylpyridine, N, 7.11 (found: N, 6.88); 2-heptafluoropropylpyridine, N, 5.67 (found: N, 5.40).

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(10) Geller Microanalytical Laboratories, Charleston, W. Va.

TABLE II
PEAK ASSIGNMENTS FOR THE MASS SPECTRA OF
2-PENTAFLUOROETHYLPIRIDINE

Mass no.	Relative intensity	Assignment
12	0.60	C ⁺
13	3.90	CH ⁺
14	12.33	N ⁺
19	0.34	F ⁺
24	0.89	C ₂ ⁺
26	51.11	CN ⁺ , C ₂ H ₂ ⁺
27	26.67	CHN ⁺
31	0.67	CF ⁺
38	53.33	C ₃ H ₂ ⁺
39	0.74	C ₂ HN ⁺ ; C ₃ H ₃ ⁺
40	37.8	C ₃ H ₄ ⁺ ; C ₂ H ₂ N ⁺
50	43.3	CF ₂ ⁺
52	14.3	C ₃ H ₂ N ⁺ , C ₄ H ₄ ⁺
53	100	C ₃ H ₃ N ⁺
57	44.4	C ₂ NF ⁺ ; C ₃ H ₂ F ⁺
62	3.90	C ₂ F ₂ ⁺
63	0.60	C ₂ HF ₂ ⁺
64	8.4	C ₄ H ₂ N ⁺
65	32.8	C ₄ H ₂ N ⁺
66	24.7	C ₄ H ₄ N ⁺
68	9.56	C ₄ HF ⁺
69	2.22	CF ₃ ⁺ , C ₄ H ₂ F ⁺
76	18.8	C ₂ NF ₂ ⁺
77	81.1	C ₅ H ₃ N ⁺
78	61.7	C ₅ H ₄ N ⁺
79	26.1	C ₅ H ₅ N ⁺ , C ₅ F ⁺
95	0.28	C ₅ H ₄ F ⁺
100	0.48	C ₂ F ₄ ⁺
119	0.51	C ₂ F ₅ ⁺
128	73.9	C ₆ H ₄ NF ₂ ⁺
178	6.33	C ₇ H ₄ NF ₄ ⁺
197	50.0	C ₇ H ₄ NF ₆ ⁺

Discussion

The microelemental results and the infrared, mass, and n.m.r. spectra results confirm the formation of 2-pentafluoroethylpyridine and 2-heptafluoropropylpyridine in the butadiene nitrile addition reaction when perfluoroethyl- and heptafluoropropyl cyanides, respectively, are used as dienophiles. The predicted product from the difluorochloromethyl cyanide-butadiene reaction is 2-difluorochloromethylpyridine by analogy with the preceding. The vibrational assignment of the infrared spectrum (above) is in accord with this viewpoint and gives additional support. The yields in this synthesis were inadequate for the additional work (n.m.r., microelemental analyses, and mass spectra) as required for more rigorous confirmation of structure.

It is apparent (Table I) that, with the exception of the chlorofluoronitriles, the pyridinic product is quantitatively formed (almost 100% yields) based on the reacted nitrile. The lower yields relative to the diene reflect the attrition of the diene through competing processes.

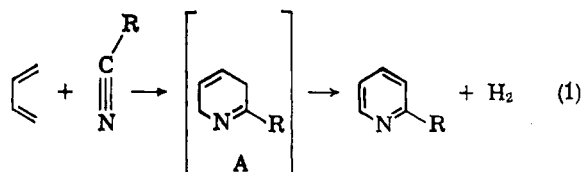
The formation of pyridinic products by the high temperature addition-cyclization reaction has been characterized kinetically^{1c} as a Diels-Alder process in which the (C≡N) bond is the dienophile.

The reactivity of CF₃CN as a "cyanogen-like" dienophile in this synthesis has been attributed^{1b} to the pronounced electrophilic properties of the perfluoromethyl group in proximity to the C≡N bond.

TABLE III
PEAK ASSIGNMENTS FOR THE MASS SPECTRA OF
2-HEPTAFLUOROPROPYLPYRIDINE

Mass no.	Relative intensity	Assignment
12	0.158	C ⁺
13	0.303	CH ⁺
14	0.702	N ⁺
19	0.193	F ⁺
24	0.539	C ₂ ⁺
26	0.114	CN ⁺ , C ₂ H ₂ ⁺
27	12.72	CHN ⁺
31	0.092	CF ⁺
38	34.60	C ₃ H ₂ ⁺
39	4.47	C ₃ H ₃ , C ₂ HN ⁺
40	2.67	C ₂ H ₂ N ⁺ ; C ₃ H ₄ ⁺
50	43.64	CF ₂ ⁺
52	10.75	C ₄ H ₄ ⁺ ; C ₃ H ₂ N ⁺
53	57.89	C ₃ NH ₃ ⁺
62	3.68	C ₂ F ₂ ⁺
63	1.71	C ₂ HF ₂ ⁺
64	6.71	C ₄ H ₂ N ⁺
65	21.1	C ₄ H ₂ N ⁺
66	16.45	C ₄ H ₄ N ⁺
68	12.94	C ₄ HF ⁺
69	1.32	CF ₃ ⁺ , C ₄ H ₂ F ⁺
76	14.04	C ₂ NF ₂ ⁺
77	80.92	C ₅ H ₃ N ⁺
78	42.11	C ₅ H ₄ N ⁺
95	0.09	C ₅ H ₄ F ⁺
100	1.32	C ₂ F ₄ ⁺
119	2.24	C ₂ F ₅ ⁺
125	1.54	C ₃ HF ₄ ⁺
128	100	C ₆ H ₄ NF ₂
150	2.28	C ₃ F ₆ ⁺
169	1.18	C ₃ F ₇ ⁺
178	0.145	C ₇ NH ₄ F ₄ ⁺
228	1.51	C ₈ H ₄ NF ₆ ⁺
247	9.87	C ₈ H ₄ NF ₇ ⁺

The marked change in electrophilic properties of the CF₃ group through replacement of one fluorine by chlorine is strikingly shown in its effect on the decreased yields (Table I) and decreased thermal stability of CF₂ClCN.



The perhaloalkylpyridine synthesis (eq. 1) differs from most conventional Diels-Alder processes since the primary adduct is a dihydrocyclic structure (A), rather than a tetrahydrocyclic system. The inherent thermodynamic instability of the dihydro aromatics at 400° relative to the fully aromatized systems¹¹ undoubtedly accounts for the observed direct formation of the fully aromatized pyridinic products in the present studies.

This work is being extended to evaluate the reaction kinetics; the relative reactivity of the perfluoroalkane nitriles by competitive experiments also is being investigated and will be reported at a later date.

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