A Synthesis of 2-Substituted Tetrafluoropyridines

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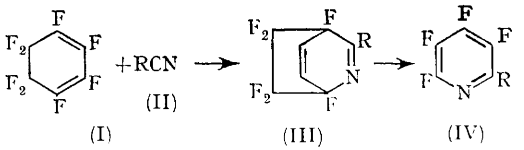
ALTHOUGH 4-substituted tetrafluoropyridines can easily be synthesised from pentafluoropyridine,[1] 2- and 3-substituted tetrafluoropyridines are not readily available. In the course of our research into the Diels–Alder reactions of polyfluorocyclohexa-1,3-dienes[2] we have found that the addition of alkynes to perfluorocyclohexa-1,3-diene (I) and pyrolysis of the 1,4,5,6,7,7,8,8-octafluorobicyclo-[2,2,3]octa-2,5-dienes so formed gave 1,2-disubstituted tetrafluorobenzenes in good yields.

We now report an analogous synthesis of 2-substituted tetrafluoropyridines (IV), using nitriles (II) as dienophiles.



The reaction was carried out by heating (I) and [II; R = CF_3, Br, C_6F_5, $(CF_2)_3CN$] in Pyrex ampoules containing dipentene as a free-radical inhibitor. Reactions condition and yields of [III; R = Br, $(CF_2)_3CN$] and [IV; R = CF_3, Br, C_6F_5, $(CF_2)_3CN$, $(CF_2)_3C_5F_4N$] are shown in Table 1. Yields quoted are after separation from product mixtures by g.l.c. The molecular formulae of the products were determined from the accurate masses of the highest peaks in the mass spectra. The structures of compounds (IV) were unambiguously assigned from their ^{19}F n.m.r. spectra (Table 2). Only one of these compounds, (IV; R = CF_3), has been prepared previously[3] and our data are in agreement with those reported. Both adducts [III; R = Br, or $(CF_2)_3CN$] showed two absorptions in the double-bond region of the i.r. spectrum [R = Br, 1765 and 1615; R = $(CF_2)_3CN$, 1775 and 1660 cm.$^{-1}$], their ^{19}F n.m.r. spectra were consistent with the structures assigned, and pyrolysis under vacuum of (III; R = Br) gave (IV; R = Br) in 43% yield.

TABLE 1

Nitrile (II)	Mole ratio (I) : (II)	Temp.	Time (hr.)	Yield % (III)	Yield % (IV)
R = CF_3	1:1	400°	16	–	40
Br	1:3	400	15	–	40
Br	2:3	380	12	9	18
C_6F_5	1:1	390	64	–	4
$(CF_2)_3CN$	1:2	350	16	4	1
$(CF_2)_3CN$	1:2	350	64	–	10†

† Together with perfluoro-1,3-bis-2,2′-pyridylpropane, 10%.

TABLE 2

Compound R	Chemical shifts F(3)	F(4)	F(5)	F(6)	F–F Coupling constants $J_{3,4}$	$J_{3,5}$	$J_{3,6}$	$J_{4,6}$	$J_{4,6}$	$J_{5,6}$	Conc. in CCl_4 (vol. %)	Reference C_6F_6
CF_3	–21·4	–28·0	–13·5	–82·0	17·7	10·1	28·1	17·0	19·8	24·1	100	ext.
Br	–7·5	–29·3	–33·2	–82·6	17·2	4·6	22·7	18·2	17·0	25·6	100	ext.
C_6F_5	–8·2	–24·7	*ca.* –22·7	–81·7	17·2	4·7	24·9	17·4	17·8	25·4	30	int.
$(CF_2)_3CN$	–23·4	–28·0	–14·0	–83·2	17·8	—	26·4	17·8	18·8	24·3	50	int.
$(CF_2)_3C_5F_4N$	–23·4	–26·8	–12·4	–82·3	18·2	—	27·4	18·2	18·6	24·2	20	int.

Acetonitrile and benzonitrile did not react under these conditions; presumably the success of this reaction is dependent on a strongly electronegative group attached to the nitrile.

(*Received, August* 26, 1968, *Com.* 1162.)

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[3] (a) R. E. Banks, J. E. Burgess, and R. N. Haszeldine, *J. Chem. Soc.*, 1965, 2720; (b) J. Lee and K. G. Orrell, *ibid.*, 1965, 582.