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PRELIMINARY NOTE

Preparation of Fluoroalkenes from Fluoroacetonitrile

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SUMMARY

A fluorocyanophosphate prepared from fluoroacetronitrile at low temperat reacts with aromatic aldehydes in a modified Wittig procedure to give fluorocyanoalkenes in moderate yield.

Medicinal and biological science exerts an increasing demand for fluorinated organic material [1]. Biologically active molecules containing a vinylic fluorine atom are currently of special interest [2-5], but synthetic methods are limited for their preparation.

The main synthetic methods for the preparation of vinylic fluorides are based on the work of Burton and Thenappan [6] who have greatly explored the use of fluoro Wittig reagents, and on the work of Machleidt and Wessendorf [7] who developed a fluorophosphonate reagent from bromofluoroacetate. Schwartz and Lee developed an alternative method based on the fluorination of vinyl lithium compounds[8].

These combined methods furnish vinyl fluorides in which the accompanying terminal atom is a proton, halogen, or ester function.

X=H, CO_2Et, Halogen

In an attempt to further expand the use of Wittig reagents in the preparation of terminal vinylic fluorine compounds, we sought to develop a phosphonate reagent from fluoroacetonitrile which is readily available, and to easily manipulate the terminal nitrile function through conventional chemistry.

We found that reaction of the anion from fluoroacetonitrile at -78°C with diethylchlorophosphate followed by addition of an aromatic aldehyde produces fluorocyanoalkenes in 45-82% yield as shown in Table I. In a

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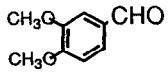
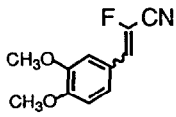
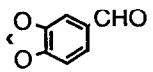
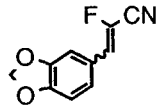
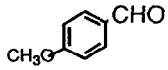
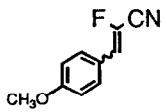
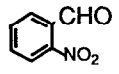
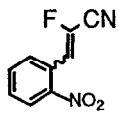
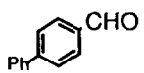
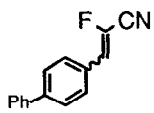
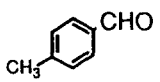
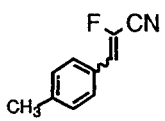
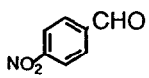
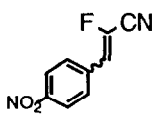
TABLE I

Starting Material	Product	ø ^{19}F ($J_{H,F}$)[a] Z	ø ^{19}F ($J_{H,F}$)[a] E	Z/E[b]	Yield[c] %
		-50.1 (40)	-51.1 (20)	0.5/1	46
		-45.2 (40)	-46.4 (21)	4/1	45
		-49.1 (41)	-50.2 (20)	1/1	52
		-44.3 (37)	-41.0 (26)	1.6/1	62
		-46.0 (44)	-46.8 (20)	3/1	82
		-47.8 (43)	-48.4 (20)	3/1	51
		-39.8 (37)	-39.3 (20)	2/1	45

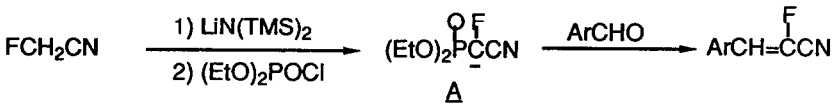
[a] Chemical shifts are reported upfield from trifluoroacetic acid (ø 0.0 ppm). Coupling constants are in Hertz. F and H are trans in the Z isomer.

[b] Isomer ratios are determined from F NMR peak integration.

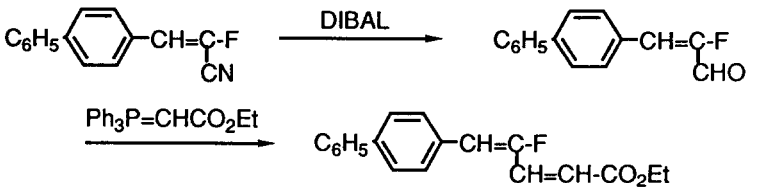
[c] Yields are for pure products isolated by flash chromatography.

typical procedure $LiN(TMS)_2$ was prepared from 2.2 mmol of $HN(TMS)_2$ and 2.2 mmol of n-BuLi in hexane at -78°C. After 5 mn a mixture of aryl-aldehyde (2 mmol) and diethylchlorophosphate (2 mmol) in 2 ml of dry THF was added rapidly. The mixture was allowed to come to room temperature during 1 hour and then heated at reflux for 30 mn. The product was isolated after extraction (EtOAc) and washing (NaCl solution) followed by flash chromatography.

The reaction presumably proceeds through intermediate A in the phosphonate modification of the Wittig reaction. The intermediate A however could not be detected and did not react with aliphatic aldehydes. Instead the aliphatic aldehydes produced complex mixtures from aldol-type reactions. Unsuccessful aliphatic aldehydes were: phenylacetaldehyde, phenylproponaldehyde, isobutylaldehyde, cyclohexancarboxaldehyde.



The cyano function of the fluorocyano alkene from 4-formylbiphenyl was reduced to the aldehyde and further condensed in a Wittig reaction to form the fluorodiene as shown below. Aldehyde ^{19}F NMR ($CDCl_3$ vs TFA) - δ-39.2, -39.4, -39.6, -39.9 (doublet of doublets). Fluorodiene ^{19}F NMR δ-41 -42.2, -42.5 (doublet of doublets). The conversions serve to indicate the synthetic utility possible with the fluorocyanoalkenes.



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