Journal of Fluorine Chemistry, *49* (1990) 147–150

Received October 30, 1989, accepted March 19, 1990

PRELIMINARY NOTE

Preparation of Fluoroalkenes from Fluoroacetonitrile

TIMOTHY B. PATRICK* and SOURENA NADJI

Chemistry Department, Southern Illinois University
Edwardsville, Illinois 62026 (USA)

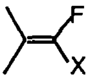
SUMMARY

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.



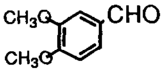
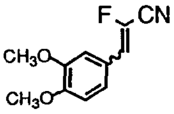
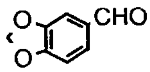
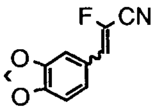
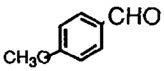
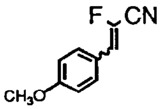
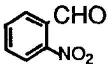
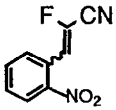
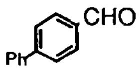
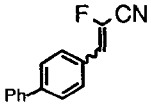
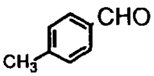
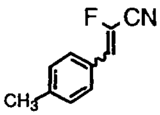
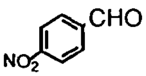
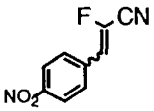
X=H, CO_2Et, Halogen

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

0022-1139/90/$3.50

TABLE I

Starting Material	Product	ø ^{19}F ($J_{H,F}$)[a]		Z/E[b]	Yield[c]
		Z	E		%
		-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

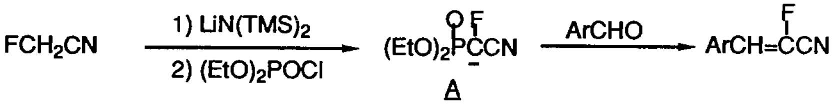
[a] Chemical shifts are reported upfield from trifluoroacetic acid (ø 0.0 ppm). Coupling constants are in Hertz. F and H are <u>trans</u> in the Z isomer.

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

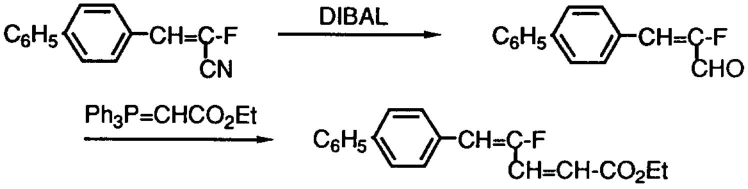
[c] Yields are for pure products isolated by flash chromatography.

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 arylaldehyde (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.



This study was funded by the Petroleum Research Fund, administered by the American Chemical Society.

1 R. Filler and Y. Kobayashi, *Biomedical Aspects of Fluorine Chemistry* Elsevier, Amsterdam, 1982; R. Filler (ed.); *Biochemistry Involving* Carbon-Fluorine Bonds: ACS Symposium Series 28, American Chemical Society, Washington, DC 1982.

2 J.T. Welch, *Tetrahedron*, *43* (1987) 3123.

3 A.E. Asato, H. Matsumoto, M. Denny and R.S.H. Liu, J. Am. Chem. Soc., 100 (1978) 5957.

4 S.W. Djuric, R.B. Garland, L.N. Nysted, R. Pappo, G. Plume and L. Swenton, J. Org. Chem.,52 (1987) 9728.

5 M.A. Findeis and G.M. Whitesides, J. Org. Chem.,52 (1987) 2838.

6 D.J. Burton and A. Thenappan, Tetrahedron Lett., 30 (1989) 3641 and references cited therein.

7 H. Machleidt and R. Wessendorf, Annalen, 679 (1964) 20; H. Machleidt and G. Strehlke, Ibid., 681 (1965) 21.

8 S.H. Lee and J. Schwartz, J. Am. Chem. Soc., 108 (1986) 2445.