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2,2-DIFLUORO-1-PHENOXYVINYLLITHIUM: A NEW REAGENT FOR THE PREPARATION OF 2-PHENOXY-2-ALKENOIC ACIDS FROM CARBONYL COMPOUNDS[1)]

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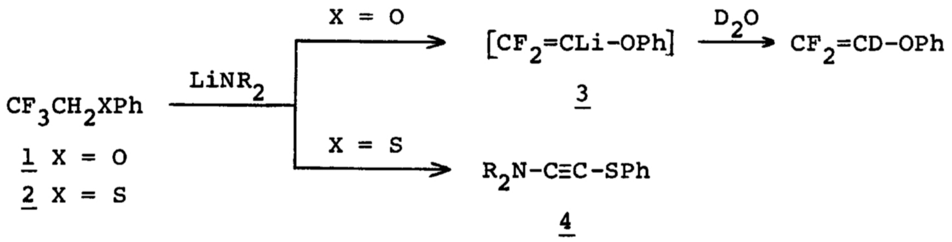
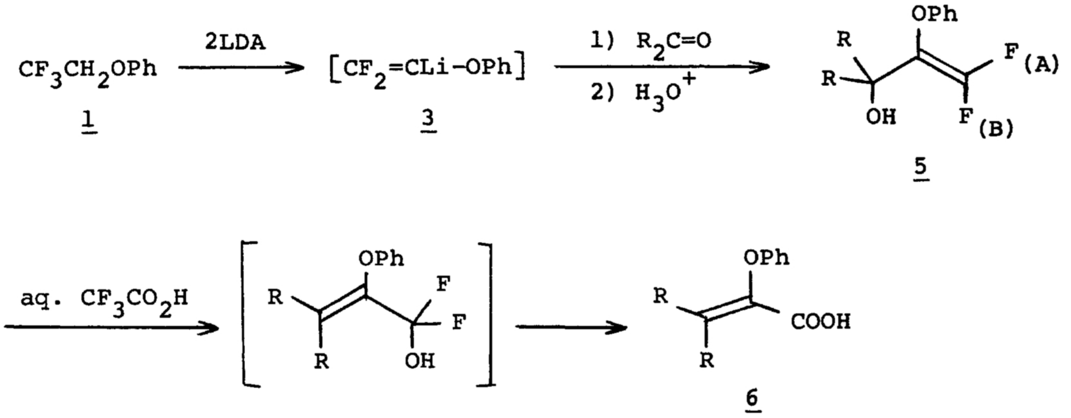
The title reagent 3, readily generated *in situ* from the reaction of 2,2,2-trifluoroethoxybenzene (1) with lithium diisopropylamide, was found to be useful for the preparation of 2-phenoxy-2-alkenoic acids (6) from various carbonyl compounds *via* facile acid hydrolysis of the initially formed difluorovinylcarbinols (5).

There has been considerable interest in the reactions involving carbanions stabilized by β-fluorine atoms in organofluorine chemistry.[2)] In our previous papers,[3)] we reported the formation of the difluorovinyllithium (3) by the reaction of 2,2,2-trifluoroethoxybenzene (1) with lithium dialkylamides; this is in contrast to the formation of thioynamines (4) with 2,2,2-trifluoroethylthiobenzene (2).



As a part of continuing investigation of organofluorine reagents in organic synthesis, we now wish to demonstrate the synthetic potentiality of the title reagent 3 which provides a new method for the preparation of 2-phenoxy-2-alkenoic acids (6)[4)] from the reaction of 3 with carbonyl compounds followed by acid hydrolysis of the initially formed difluorovinylcarbinols (5) (Scheme 1). The complete scheme is therefore a two-step operation requiring no isolation of intermediates. The procedure is operationally simpler and more versatile than the conventional ones.[5)]

Scheme 1

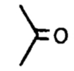
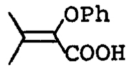
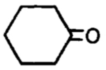
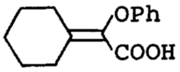
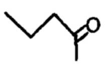
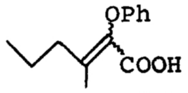
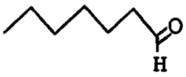
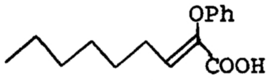
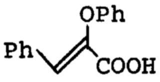
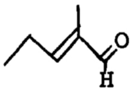
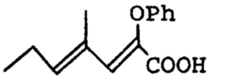


Treatment of 1 with 2 equiv. of lithium diisopropylamide (LDA) in tetrahydrofuran at -60°C for 30 min resulted in the formation of the vinyllithium 3 in essentially quantitative yield.[6)] The lithium salt 3 was then treated with carbonyl compounds at -50∿0°C for 3 h followed by quenching (saturated aqueuos ammonium chloride) to give the corresponding alcohol 5 in good yields (Table 1). Treatment of 5 with 5% aqueous trifluoroacetic acid at 100°C for 3 h followed by usual work-up afforded the desired 2-phenoxy-2-alkenoic acids (6) in good yields (Table 1). Some physical data for 5 and 6 are summarized in Table 2.

The following features of the present method are noteworthy. (1) This procedure is applicable to a variety of carbonyl compounds including α,β-unsaturated aldehydes. (2) The alkenoic acids (6d-f) derived from aldehydes possessed the single geometry, presumably the Z geometry,[7)] while 6c derived from the unsymmetrical ketone was obtained as an E : Z mixture. The stereochemical results of the present method are in contrast to those of the Grell's method[5a)] which is based on the reactions of ethyl diethylphosphonoethoxyacetate with aldehydes. For example, the Wittig-type reaction with benzaldehyde afforded the unsaturated ester (PhCH=C(OEt)CO_2Et) in the E/Z ratio of 1 : 2.

In summary, the utilization of the title reagent 3 permits ready access to 2-phenoxy-2-alkenoic acids (6). Furthermore, the present examples serve to illustrate potential applicability of fluorine-stabilized carbanions in organic synthesis.

Table 1. Preparations of Alkenoic Acids (6)

	Carbonyl Compounds	Yield of 5 (%)a)	Carboxylic Acids 6	Yield of 6 (%)b)	E/Zc)
a		60		76	——
b		70		87	——
c		51		53	4/5
d		62		78	Z only
e	PhCHO	——d)		52a)	(Z only)
f		54		59	(Z only)

a) Yields based on the starting trifluoroethoxybenzene (1).
b) Yields based on the alcohol 5. c) For the stereochemistry, see ref. 7.
d) Alcohol 5e was not isolated.

Table 2. Physical Properties of 5 and 6

	5a)			6		
	Bp/mmHg, °C	^{19}F NMR, ppmb) F(A)	F(B)	Mp (°C) (lit.)	IR(cm^{-1}) (KBr or liq.)	Selected ^{1}H NMR, ppmc)
a	75-77/3	16.7 (d)	24.5 (d)	115-115.5 (118)d)	1690(C=O) 1635(C=C)	1.83(s,3H) 2.23(s,3H)
b	101-103/0.15	16.5 (d)	24.7 (d)	125.5-126.5	1680(C=O) 1620(C=C)	2.3(m,2H) 2.9(m,2H)
c	93-95/3	17.0 (d)	26.0 (d)	oil	1690(C=O) 1630(C=C)	Z;2.17(s,3H),2.1(t,2H) E;1.74(s,3H),2.6(t,2H)
d	111-116/0.05	18.3 (d)	31.0 (d of d)	oil	1700(C=O) 1650(C=C)	2.1(d of t,2H) 6.5(t,1H)
e	oil	18.7 (d)	29.5 (d of d)	181.5-183 (183)e)	1695(C=O) 1635(C=C)	7.1-7.9(m,11H)
f	82-84/0.01	18.7 (d)	30.3 (d of d)	108-110	1695(C=O) 1625(C=C)	1.85(s,3H),5.9(t,1H) 7.10(s,1H)

a) IR and ^{1}H NMR spectra for 5 were consistent with the assigned structures.
b) CF_3CO_2H as external standard, solvent CCl_4.
c) TMS as internal standard, solvent $CDCl_3$. d) Ref. 5c. e) Ref. 5d.

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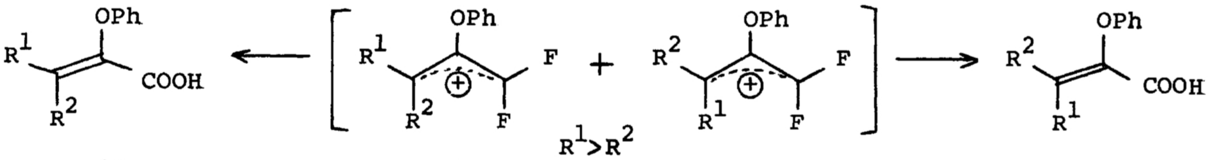
4) For the synthetic usefulness of this particular type of unsaturated carboxylic acids, see R. E. Ireland, R. H. Mueller, and A. K. Willard, J. Am. Chem. Soc., 98, 2668 (1976) and ref. 5a.

5) (a) W. Grell and H. Machleidt, Justus Liebigs Ann. Chem., 699, 53 (1966); (b) L. N. Owen, J. Chem. Soc., 1945, 385; (c) T. Padmanathan and M. U. S. Sultanbawa, ibid., 1963, 4210; (d) Th. Groger and E. Waldmann, Monatsh. Chem., 89, 370 (1958)

6) The lithium salt 3 was also trapped by methyl iodide to give 1,1-difluoro-2-propenyloxybenzene in 94% yield (by ^{19}F NMR assay).

7) While the Z geometry of 6d was established by the nmr analysis, the stereochemistry of 6e and 6f could not be spectroscopically determined. However, the Z geometry is highly probable for 6e and 6f since the product stereochemistry seems to be primarily determined by minimization of steric interactions in the intermediates of hydrolysis, 7E and 7Z. In the case where R^2=H, the R^1 group prefers to be orientated away from the difluoromethylene group resulting in the formation of 6Z. When R^2 is an alkyl group, the situation appears more balanced and E : Z mixtures are formed.



6Z 7Z 7E 6E

For similar stereochemical arguments, see T. Nakai, T. Mimura, and A. Ari-izumi, Tetrahedron Lett., 1977, 2425; B. M. Trost and J. L. Stanton, J. Am. Chem. Soc., 97, 4018 (1975).

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