A Novel One-pot Synthesis of Fluoroenynes

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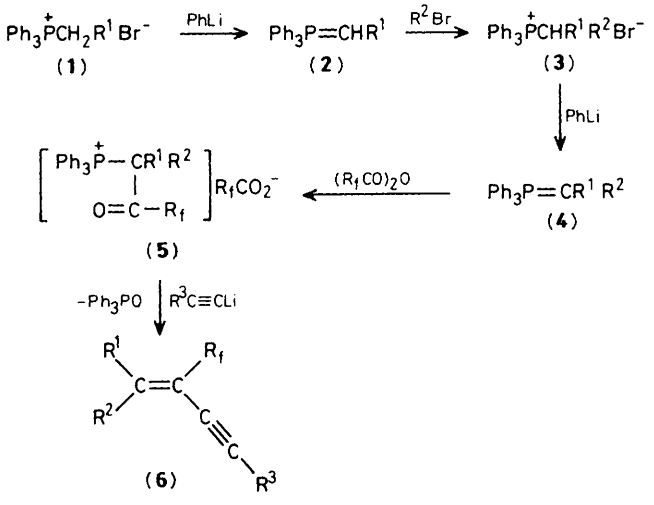
A novel one-pot synthesis of fluoroenynes *via* eliminative nucleophilic addition of β-ketophosphonium salts to acetylide anions is described.

Enynes are important intermediates in synthetic organic chemistry, being essential components in the synthesis of some biologically active compounds[1] and capable of undergoing many useful organic transformations.[2] Therefore reactions leading to the formation of enynes, especially fluoroenynes, have attracted much attention. So far as we know, no reports have appeared in the literature reporting a one-pot synthesis of fluoroenynes. A one-pot synthesis of enynes has been reported previously,[3] but the starting materials, α-chlorocarbonyl compounds, of that synthesis are not readily available.

Table 1. Synthesis of fluoroenynes (**6**).

Compound	R^1	R^2	R_f	R^3	Method[a]	B.p., °C/mmHg	Yield,[b] %	*E*:*Z*[c]
(**6a**)	Me	$PhCH_2$	CF_3	Bu^n	A	100/1	80	83:17
(**6b**)	Me	Pr^n	CF_3	Bu^n	A	92/10	72	60:40
(**6c**)	Me	$CH_2{=}CHCH_2$	CF_3	Bu^n	A	90/10	47	60:40
(**6d**)	Me	Ph	C_2F_5	Ph	B	63—64[d]	44	98:2
(**6e**)	Me	Me	CF_3	Ph	B	75/1	73	
(**6f**)	Me	Me	C_2F_5	Ph	B	82/1	50	
(**6g**)	Me	Me	$n\text{-}C_3F_7$	Ph	B	90/1	43	
(**6h**)	Me	Me	CF_3	Bu^n	B	80/10	50	
(**6i**)	Me	Me	C_2F_5	Bu^n	B	85/10	70	
(**6j**)	$-[CH_2]_4-$		CF_3	Bu^n	B	95/10	61	
(**6k**)	$-[CH_2]_4-$		C_2F_5	Ph	B	95/1	72	

[a] Method A: (**1**) used as starting material; method B: (**3**) used as starting material. [b] Isolated yields. All products exhibited n.m.r., i.r., mass spectroscopic analysis consistent with the assigned structures. [c] The ratios of *E*- and *Z*-isomer are estimated on the basis of n.m.r. data. [d] M.p.



Scheme 1

We have recently described a novel synthesis of tetrasubstituted fluoroalkenes *via* eliminative nucleophilic addition of β-ketophosphonium salts.[4] As an extension of this study, we now report a novel one-pot synthesis of fluoroenynes *via* eliminative nucleophilic addition of β-ketophosphonium salts to an acetylide anion. The reaction sequence is shown in Scheme 1.

In a typical procedure a solution of ethylidenetriphenylphosphorane (**2a**) generated from ethyltriphenylphosphonium bromide (**1a**) (4 mmol) and phenyl-lithium (4 mmol) in diethyl ether (30 ml) is stirred at 20 °C under nitrogen while a diethyl ether solution of a benzyl bromide (4 mmol) is slowly added. After stirring at 20 °C for 0.5 h, a second portion of phenyl-lithium (4 mmol) is added. The mixture is stirred for a further 1 h, cooled to −78 °C, and trifluoroacetic anhydride (*ca.* 3.9 mmol) is slowly added until the characteristic ylidic colour disappears. After this addition and stirring at −78 °C for 1 h, an excess of lithium n-butylacetylide (*ca.* 9 mmol) is added. The mixture is allowed to warm to room temperature and stirred for a further 2 h. The filtrate is collected, diluted with diethyl ether (50 ml), washed with water until neutral, and dried. Evaporation of the solvent gives a residue which is purified by column chromatography on silica gel on elution with light petroleum (b.p. 60—90 °C) to afford product (**6a**). The results are shown in Table 1.

This one-pot synthesis of fluoroenynes is convenient and offers a wide scope, since R^1 and R^2 may be an alkyl, allylic, phenyl, benzylic, or alicyclic group. Thus, this reaction provides a new method for the facile synthesis of the title compounds which should be useful for further elaboration in the synthesis of biologically active compounds.

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