Tetrahedron Letters, Vol.27, No.3, pp 357-360, 1986 0040-4039/86 $3.00 + .00
Printed in Great Britain

AN EFFICIENT SYNTHESIS OF α-*F*-ALKYNYLATED ALCOHOLS BY NEW SILOXANE-FLUORIDE ION CATALYZED REACTION OF 1*H*-*F*-1-ALKENEPHOSPHONATES WITH ALDEHYDES[1]

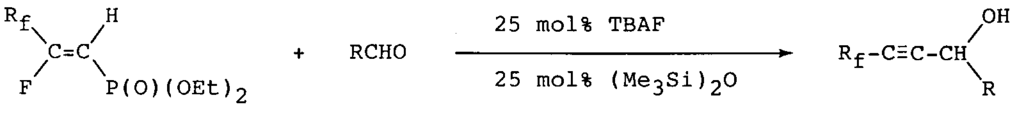
Takashi Ishihara,* Takashige Maekawa, and Teiichi Ando
Department of Industrial Chemistry, Faculty of Engineering,
Kyoto University, Yoshida, Kyoto 606, Japan

Abstract: 1*H*-*F*-1-Alkenephosphonates react smoothly with a variety of aldehydes under the influence of catalytic amounts of hexamethyldisiloxane and tetrabutylammonium fluoride at room temperature to afford the corresponding α-*F*-alkynylated alcohols in good to excellent yields.

Acetylenic alcohols are useful compounds capable of undergoing many organic transformations and hence are employed successfully as key intermediates in the synthesis of natural products including carotenoids,[2] prostaglandins,[3] and steroids.[4] In view of the high versatility of these compounds combined with the recent intensive elaborations[5] for introducing a fluorine or fluoroalkyl substituent into organic molecules, it must be of much value to develop an effective method for the synthesis of fluorine-containing acetylenic alcohols.

In our continuing studies[6] to exploit the synthetic utility of fluorinated alkenephosphonates and related compounds, we have found that various aldehydes can readily be perfluoroalkynylated under very mild conditions with 1*H*-*F*-1-alkenephosphonates accessible[6a] in two steps from *F*-alkanoic acid chlorides.

The reaction described in this communication is a novel reaction of 1*H*-*F*-1-alkenephosphonates with a carbonyl compound promoted by a siloxane-fluoride ion as catalyst, which provides an efficient and simple method for the synthesis of α-*F*-alkynylated alcohols.

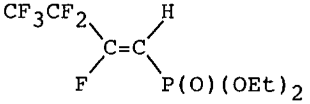
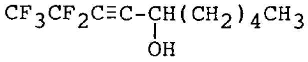
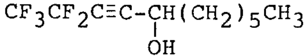
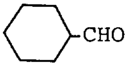
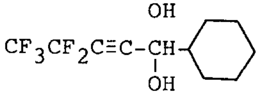
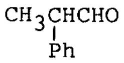
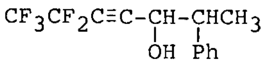
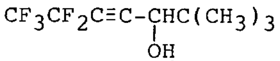
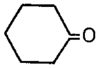
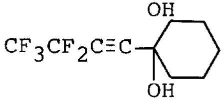
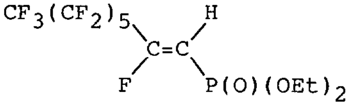
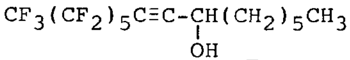
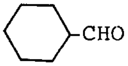
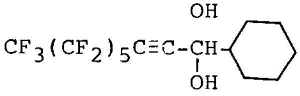
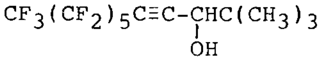
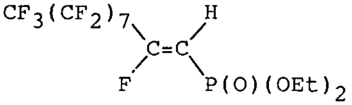
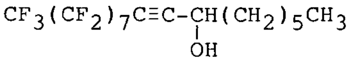
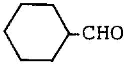
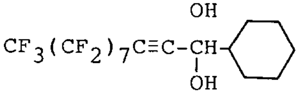
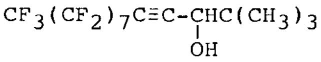
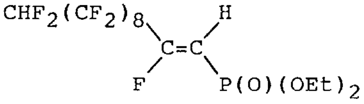
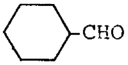
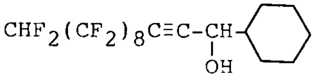


1

2

1*H*-*F*-1-Alkenephosphonates (**1**) were allowed to react with an aldehyde in the presence of catalytic amounts (25 mol% each) of hexamethyldisiloxane and tetrabutylammonium fluoride (TBAF) in tetrahydrofuran (THF) at room temperature, to give the corresponding *F*-alkyl-substituted acetylenic alcohols (**2**)[7] in good to excellent yields. Other organosilanes such as ethoxytrimethylsilane and hexamethyldisilazane could be used in this reaction

Table I. Synthesis of α-F-Alkynylated Alcohols **2**

Phosphonate **1**	Carbonyl compd	Product **2**	Yield %
	$CH_3(CH_2)_4CHO$	 $CF_3CF_2C{\equiv}C\text{-}\underset{OH}{CH}(CH_2)_4CH_3$	74
	$CH_3(CH_2)_5CHO$	 $CF_3CF_2C{\equiv}C\text{-}\underset{OH}{CH}(CH_2)_5CH_3$	75
			86
	 $CH_3\underset{Ph}{CH}CHO$	 $CF_3CF_2C{\equiv}C\text{-}\underset{OH}{CH}\text{-}\underset{Ph}{CH}CH_3$	72[a]
	$(CH_3)_3CCHO$	 $CF_3CF_2C{\equiv}C\text{-}\underset{OH}{CH}C(CH_3)_3$	89
			54[a]
	$CH_3(CH_2)_5CHO$	 $CF_3(CF_2)_5C{\equiv}C\text{-}\underset{OH}{CH}(CH_2)_5CH_3$	81
			82
	$(CH_3)_3CCHO$	 $CF_3(CF_2)_5C{\equiv}C\text{-}\underset{OH}{CH}C(CH_3)_3$	92
	$CH_3(CH_2)_5CHO$	 $CF_3(CF_2)_7C{\equiv}C\text{-}\underset{OH}{CH}(CH_2)_5CH_3$	60
			69
	$(CH_3)_3CCHO$	 $CF_3(CF_2)_7C{\equiv}C\text{-}\underset{OH}{CH}C(CH_3)_3$	71
			67

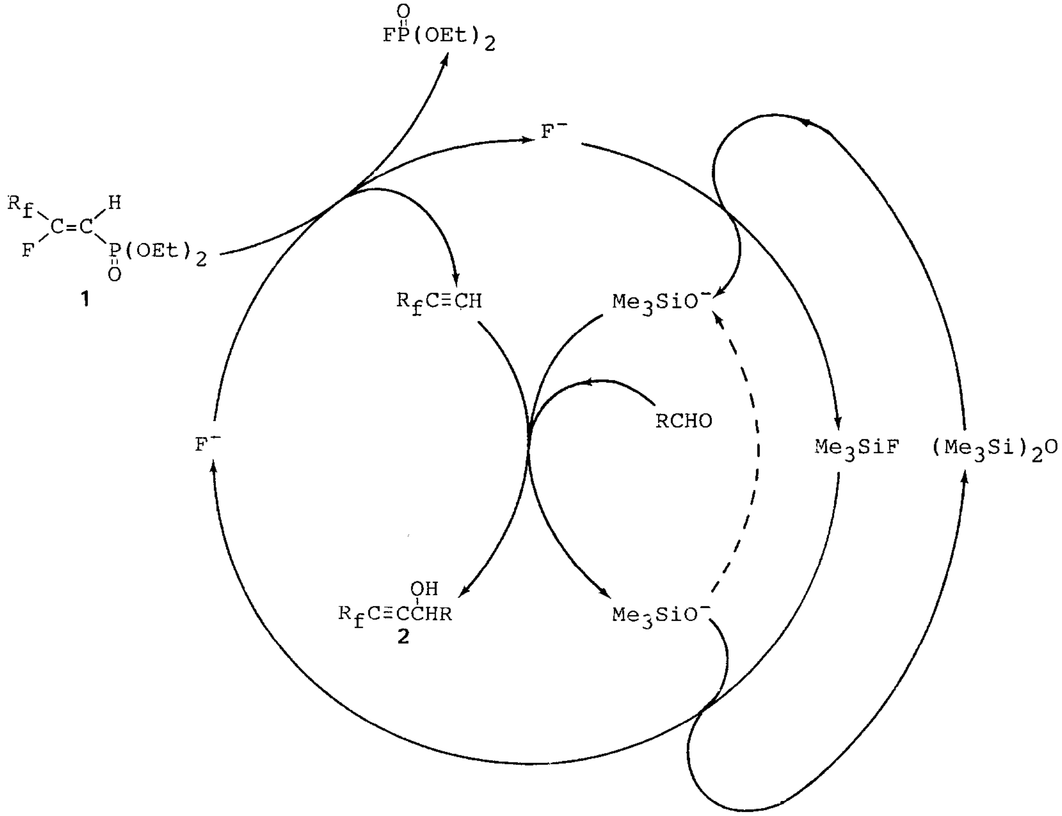
a) An equimolar amount of hexamethyldisiloxane was used.

but the use of hexamethyldisiloxane gave the best results.[8] Out of the sources of fluoride ion examined, i.e., TBAF, cesium fluoride, and potassium fluoride, TBAF was the most efficient for the reaction. THF was better than any other solvents employed such as dichloromethane, diethyl ether, and dimethylformamide. The results of the reaction are summarized in Table I.

A variety of aldehydes underwent the reaction smoothly with the fluoroalkenephosphonate (**1**) to afford high yields of the F-alkynylated alcohols (**2**), while the reaction of ketones such as 3-pentanone, 3-methyl-2-butanone, and acetophenone with **1** occurred reluctantly to form the alcohols **2** in no more than 20% yields, which could not be improved in spite of the amounts of the catalysts and the reaction temperature being varied. The chemoselectivity of the present reaction may be illustrated by the treatment of hexanal with **1** (R_f=F-Et) in the presence of acetophenone, which produced **2** (R_f=F-Et, R=n-C_5H_{11}) selectively in a yield of 74%.

It should be noted that the reaction is catalytically promoted by the action of hexamethyldisiloxane and fluoride ion, whose effective interaction results in the generation of fluorotrimethylsilane and trimethylsiloxide ion during the reaction. The latter species can act as a base[9] for converting F-alkylacetylene, formed in situ from the phosphonate **1** and fluoride ion, to the corresponding acetylide anion. This intermediary acetylide anion reacts with an aldehyde to give the product **2** with the concomitant formation of the siloxide anion, which is either reused as the base or converted into hexamethyldisiloxane, as depicted in the following possible reaction cycle.[10]

Of much significance is that the alkenephosphonates **1** can be employed as a good candidate for perfluoroalkynylation of a carbonyl compound under nearly neutral conditions and in a simple manner, since such reaction gener-



ally requires strong bases and tedeous manipulations.

The general procedure of the reaction is as follows: To a well-stirred solution of hexamethyldisiloxane (0.25 mmol) and TBAF (0.25 mmol, 1M in THF) in anhydrous THF were added dropwise 1*H*-*F*-1-alkenephosphonate **1** (1.0 mmol) and successively an aldehyde (1.0 mmol) at 0°C. The whole mixture was stirred at ambient temperature for 2h. Quenching the reaction with water and extraction with ether, followed by isolation with column chromatography on silica gel gave analytically pure α-*F*-alkynylated alcohols **2**.[7]

References and Notes

1 Presented at the 1984 International Chemical Congress of Pacific Basin Societies, Honolulu, Hawaii, December 1984, Abstract No. 10F14.

2 K.K. Chan, N.C. Cohen, J.P. De Noble, A.C. Specian, Jr., and G. Saucy, J. Org. Chem., **41**, 3497 (1976).

3 J.F. Bagli and T. Bogri, Prostaglandins, **10**, 503 (1975), and references cited therein.

4 W.S. Johnson, R.S. Brinkmeyer, U.M. Kapoor, and T.M. Yarnell, J. Am. Chem. Soc., **99**, 8341 (1977).

5 T. Fuchikami, J. Synth. Org. Chem. Jpn., **42**, 775 (1984); I. Kumadaki, *ibid*., **42**, 786 (1984); K. Bannai and S. Kurozumi, *ibid*., **42**, 794 (1984); H. Yoshioka, C. Takayama, and N. Matsuo, *ibid*., **42**, 809 (1984); Y. Hanzawa, K. Kawagoe, N. Kobayashi, T. Oshima, and Y. Kobayashi, Tetrahedron Lett., **26**, 2877 (1985); Y. Hanzawa, A. Yamada, and Y. Kobayashi, *ibid*., **26**, 2881 (1985).

6 (a) T. Ishihara, T. Maekawa, and T. Ando, Tetrahedron Lett., **24**, 4229 (1983); (b) T. Ishihara, M. Yamana, and T. Ando, *ibid*., **24**, 5657 (1983); (c) T. Ishihara, T. Maekawa, and T. Ando, *ibid*., **25**, 1377 (1984); (d) T. Ishihara, Y. Yamasaki, and T. Ando, *ibid*., **26**, 79 (1985); (e) Y. Yamasaki, T. Maekawa, T. Ishihara, and T. Ando, Chem. Lett., 1387 (1985).

7 All products were fully characterized by their spectroscopic (IR, MS, ^{1}H, ^{19}F and/or ^{31}P NMR) and analytical data.

8 Tertiary amines such as triethylamine and pyridine were much less effective than organosilanes, low yields of **2** being obtained.

9 For the recent reports on the use of an organosilane and fluoride ion as a base, see: J. Boyer, R.J.P. Corriu, R. Perz, and C. Reye, J. Chem. Soc., Chem. Commun., 122 (1981); *Idem*, Tetrahedron, **37**, 2165 (1981); R.J.P. Corriu, R. Perz, and C. Reye, *ibid*., **39**, 999 (1983); R.J.P. Corriu and R. Perz, Tetrahedron Lett., **26**, 1311 (1985); M. Joucla and J. Le Brun, *ibid*., **26**, 3001 (1985), and references cited therein.

10 It was found that treatment of phenylacetylene with pivalaldehyde under similar conditions gave the corresponding acetylenic alcohol in 64% yield.

(Received in Japan 17 October 1985)