

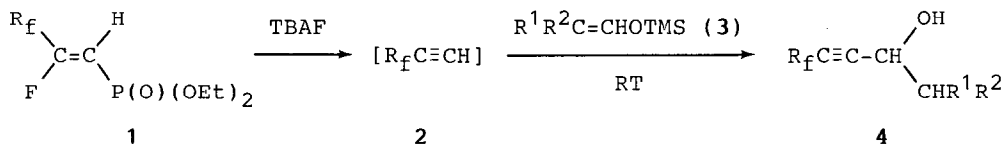
NEW FLUORIDE ION-CATALYZED REACTION OF F-ALKYLACETYLENES WITH SILYL ENOL  
ETHERS. AN EFFICIENT ROUTE TO F-ALKYL-SUBSTITUTED PROPARGYLIC  
ALCOHOLS AND  $\alpha$ -HYDROXY KETONES

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**Abstract:** Treatment of F-alkylacetylenes, generated *in situ* from 1H-F-1-alkenephosphonates, with silyl enol ethers in the presence of a catalytic amount of tetrabutylammonium fluoride gives good yields of F-alkyl-substituted propargyl alcohols or 4-(1H-F-alkylidene)-1,3-dioxolane derivatives, the latter being converted to the corresponding  $\alpha$ -hydroxy ketones.

Propargylic alcohols are one of the valuable intermediates in organic synthesis. The methods commonly employed for preparing such compounds are the alkynylation of aldehydes or ketones by use of metal acetylides.<sup>1</sup> An attractive method using alkynylsilanes and fluoride ion has also been reported very recently.<sup>2</sup>

In the course of our studies on the synthesis and reactions of fluorine-containing acetylenic compounds,<sup>3</sup> we have now found that a fluoride ion-catalyzed reaction of F-alkylacetylenes with various silyl enol ethers affords the corresponding F-alkynylated alcohols or 4-(1H-F-alkylidene)-1,3-dioxolane derivatives in good yields, depending on the reaction conditions. This type of reaction is, to our best knowledge, quite unprecedented and can serve as an effective method generally applicable for the synthesis of F-alkyl-substituted propargylic alcohols and  $\alpha$ -hydroxy ketones.



When F-alkylacetylenes (2),<sup>3</sup> prepared *in situ* from 1H-F-1-alkenephosphonates 1<sup>4</sup> and a catalytic amount of fluoride ion, were allowed to react with a silyl enol ether (3)<sup>5</sup> in tetrahydrofuran (THF) at room temperature, the corresponding F-alkyl-substituted propargyl alcohols (4)<sup>6</sup> were obtained in moderate to good yields. Out of the sources of fluoride ion employed, such as tetrabutylammonium fluoride (TBAF), cesium fluoride (CsF), and potassium fluoride, TBAF was the most efficient for the present reaction. The reaction in diethyl ether, triglyme, or dimethylformamide (DMF) resulted

Table I. Synthesis of F-Alkyl-substituted Propargylic Alcohols **4**

Alkenephosphonate <b>1</b>	Silyl enol ether <sup>a</sup> <b>3</b>	Product <b>4</b>	Yield <sup>b</sup> %
	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>4</sub> CH=CHOTMS <b>3c</b>	CF <sub>3</sub> C≡C-CH(OH)(CH <sub>2</sub> ) <sub>5</sub> CH <sub>3</sub>	34
		CF <sub>3</sub> C≡C-CH(OH)-	45
	CH <sub>3</sub> CH <sub>2</sub> CH=CHOTMS <b>3a</b>	CF <sub>3</sub> CF <sub>2</sub> C≡C-CH(OH)(CH <sub>2</sub> ) <sub>2</sub> CH <sub>3</sub>	67
	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>3</sub> CH=CHOTMS <b>3b</b>	CF <sub>3</sub> CF <sub>2</sub> C≡C-CH(OH)(CH <sub>2</sub> ) <sub>4</sub> CH <sub>3</sub>	67
	<b>3c</b>	CF <sub>3</sub> CF <sub>2</sub> C≡C-CH(OH)(CH <sub>2</sub> ) <sub>5</sub> CH <sub>3</sub>	79
	<b>3d</b>	CF <sub>3</sub> CF <sub>2</sub> C≡C-CH(OH)-	65
	CH <sub>2</sub> =CH-CH=CHOTMS <b>3e</b>	CF <sub>3</sub> CF <sub>2</sub> C≡C-CH(OH)CH=CHCH <sub>3</sub>	28 <sup>c</sup>
		CF <sub>3</sub> CF <sub>2</sub> C≡C-CH(OH)-	60 <sup>d</sup>
	<b>3c</b>	CF <sub>3</sub> (CF <sub>2</sub> ) <sub>5</sub> C≡C-CH(OH)(CH <sub>2</sub> ) <sub>5</sub> CH <sub>3</sub>	81
	<b>3d</b>	CF <sub>3</sub> (CF <sub>2</sub> ) <sub>5</sub> C≡C-CH(OH)-	85
	<b>3c</b>	CF <sub>3</sub> (CF <sub>2</sub> ) <sub>7</sub> C≡C-CH(OH)(CH <sub>2</sub> ) <sub>5</sub> CH <sub>3</sub>	70
	<b>3d</b>	CF <sub>3</sub> (CF <sub>2</sub> ) <sub>7</sub> C≡C-CH(OH)-	71

a) TMS stands for SiMe<sub>3</sub>. b) Purified by column chromatography on silica gel. c) After addition of **3e** at -78°C, the mixture was stirred at the same temperature. d) 25 mol% of TBAF and mixed solvent (THF/DMF=2/1) were used.

either in a quantitative recovery of **1** or in a decreased yield of the product **4**. The use of THF as solvent gave the best results.

The general procedure for the present reaction is as follows: TBAF (1M in THF) (10 mol%) was added to a solution of 1H-F-1-alkenephosphonate **1** in anhydrous THF at 0°C under a nitrogen atmosphere, and the mixture was stirred for 0.5 h at room temperature. To this mixture was added dropwise a silyl enol ether **3** (1.1 equiv) under cooling with an ice bath. After being stirred for 1 h at room temperature, the reaction mixture was treated with water, followed by extraction with ether, drying over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentration in vacuo. The residual oil was chromatographed on silica gel to give analytically pure F-alkylated propargyl alcohol **4**. The results are

Table II. Preparation of 4-(1H-F-Alkylidene)-1,3-dioxolanes 5

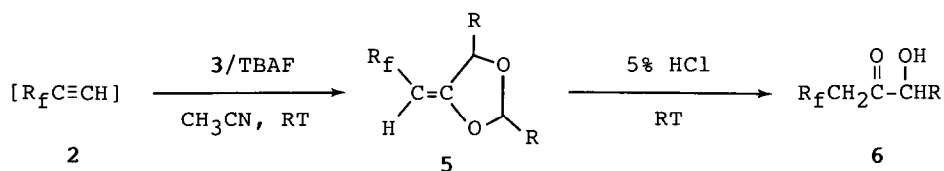
R <sub>f</sub> in 1	Silyl enol ether 3	R in 5 and 6	Yield of 5 <sup>a</sup> %	Yield of 6 <sup>b</sup> %
CF <sub>3</sub>	3a	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>2</sub>	73 <sup>c</sup>	- <sup>d</sup>
	3b	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>4</sub>	73 <sup>c</sup>	99
	3d	cyclo-C <sub>6</sub> H <sub>11</sub>	55 <sup>c</sup>	99
CF <sub>3</sub> CF <sub>2</sub>	3b	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>4</sub>	87	99
	3c	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>5</sub>	72	- <sup>d</sup>
	3d	cyclo-C <sub>6</sub> H <sub>11</sub>	49	99
CF <sub>3</sub> (CF <sub>2</sub> ) <sub>5</sub>	3b	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>4</sub>	41	- <sup>d</sup>

a) Purified by column chromatography. b) Obtained by bulb-to-bulb distillation. The products 6 decomposed on column or thin-layer chromatography. c) 50 mol% of TBAF and 3 equiv of 3 were used. d) Not examined.

summarized in Table I.<sup>7</sup>

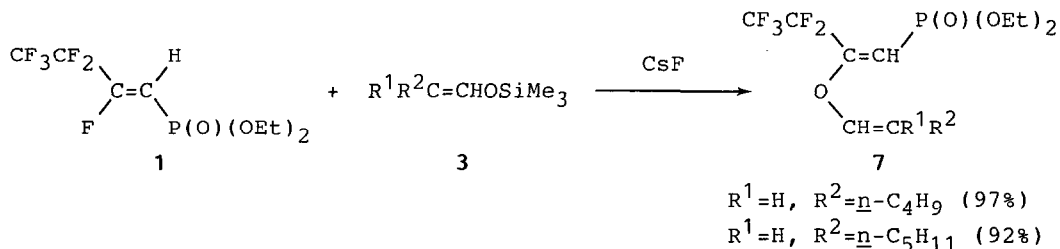
Silyl enol ethers 3 derived from aldehydes readily underwent the reaction with F-alkylacetylene (2) in the presence of TBAF to afford the corresponding acetylenic alcohols 4. The reaction with silyl enol ethers from ketones, however, proceeded reluctantly to give very low yields (not more than 20%) of the desired products, which could not be improved in spite of the reaction conditions being varied. In the case of 1-(trimethylsilyloxy)cyclohexene, the addition of DMF corresponding to a half-volume of the THF used could raise the yield of the product 4 up to 60%.

Interestingly, silyl enol ethers (3) play a dual role in this reaction. Thus, an enolate anion generated from 3 and fluoride ion acts, on one hand, as a base for converting an *in situ* prepared terminal F-alkylacetylene into the corresponding acetylide anion and, on the other hand, as the source of the original carbonyl compound<sup>8</sup> which reacts as an electrophile with the acetylide anion to produce the product 4.<sup>9</sup>



It is noteworthy that the reaction of 2 with 2.5 equivalents of silyl enol ether 3 in acetonitrile (CH<sub>3</sub>CN) gives cyclic compounds, or 4-(1H-F-alkylidene)-1,3-dioxolane derivatives 5,<sup>6,10</sup> in good yields. Some typical results are shown in Table II.<sup>7</sup> The use of CH<sub>3</sub>CN is essential to the formation of 5, though its reason or the reaction mechanism is not clear at present. The products 5 could easily be converted quantitatively<sup>11</sup> into the corresponding F-alkyl-containing α-hydroxy ketones 6.<sup>6</sup>

It has also been found that the change of the mode of addition of silyl enol ethers **3** can cause a quite different reaction, *i.e.*, addition-elimination reaction; the addition of  $\underline{1}\text{H-F-1}$ -alkenephosphonates **1** to a mixture of silyl enol ether **3** (1.1 equiv) and CsF (1.2 equiv) in THF at 0°C, followed by stirring for 2 h at the same temperature and a usual workup, afforded  $\underline{\text{F}}$ -alkylated phosphonates **7**<sup>6</sup> in high yields.



Studies on the application of  $\underline{\text{F}}$ -alkynylated alcohols **4** and of the phosphonates **1** and related compounds to organic synthesis are now in progress.

#### References and Notes

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5. H.O. House, L.J. Czuba, M. Gall, and H.D. Olmstead, *J. Org. Chem.*, **34**, 2324 (1969); R.M. Rubottom and J.M. Gruber, *ibid.*, **42**, 1051 (1977).
6. The spectral (IR, MS, <sup>1</sup>H, <sup>19</sup>F, and/or <sup>31</sup>P NMR) and analytical data pertaining to all compounds were consistent with the assigned structures.
7. Neither phenylacetylene nor 1-octyne underwent the reaction of this type with silyl enol ethers **3** under the same reaction conditions.
8. The aldol reaction between silyl enol ethers and carbonyl compounds in the presence of fluoride ion has recently been reported. See: E. Nakamura, M. Shimizu, I. Kuwajima, J. Sakata, K. Yokoyama, and R. Noyori, *J. Org. Chem.*, **48**, 932 (1983), and references cited therein. Such condensation products were not detected in the present reaction.
9. The reaction of pure **2**<sup>3</sup> with **3** under the same conditions gave comparable results.
10. The products **5** were obtained as a mixture of stereoisomers.
11. Treatment of **5** with 5% HCl in CH<sub>3</sub>CN overnight at room temperature resulted in cleavage of the 1,3-dioxolane ring, giving the products **6**.

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