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Generation of F-Alkyl-substituted Vinyl Thionium Ion Intermediates and Their Reaction with Silyl Enol Ethers. A New Route to δ-F-Alkyl-α,β;γ,δ-unsaturated Carbonyl Compounds

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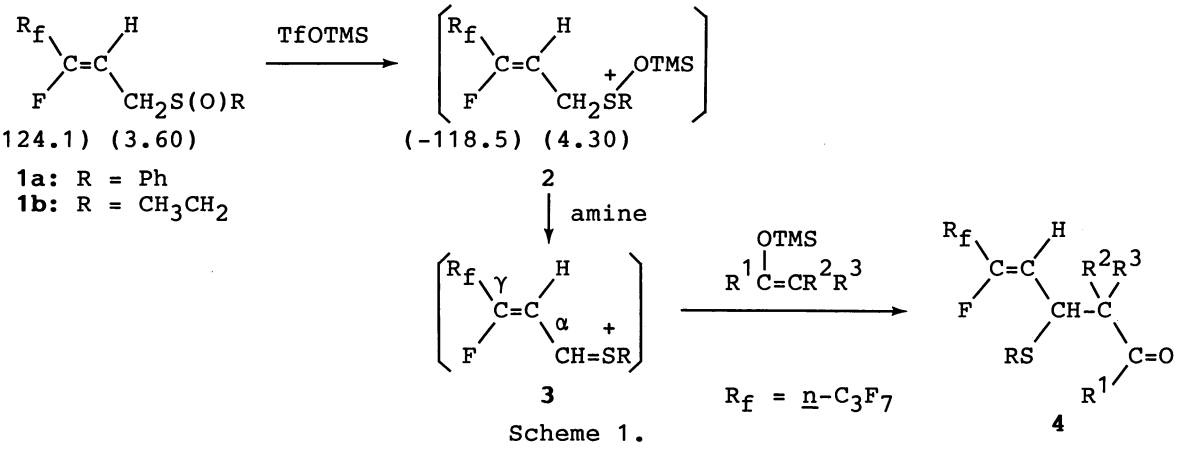
Treatment of 3-F-alkyl-3-fluoro-2-propenyl phenyl or ethyl sulfoxide with trimethylsilyl triflate and a hindered amine produces the corresponding vinyl thionium ion species, which readily reacts with silyl enol ethers to give δ-F-alkylated γ,δ-unsaturated carbonyl compounds. These compounds are converted into δ-F-alkyl-α,β;γ,δ-unsaturated carbonyl compounds in good yields.

Considerable attention has recently been paid to α-thiocarbocation-mediated reactions,[1,2] which become a useful process for the carbon-carbon bond formation and have been exploited in the synthesis of several complex molecules.[3] In contrast, there exist few or no studies directed towards the generation and utilizations of F-alkyl-substituted α-thiocarbocation intermediates,[4] probably due to the problem that such intermediates are difficult to be generated owing to marked electron-withdrawing effect of fluorine substituents on their stability.

This communication discloses that F-alkylated vinyl thionium ion intermediate (**3**) can efficiently be generated by treating sulfoxide (**1**) with trimethylsilyl triflate[5] and a hindered amine at low temperature, and that this intermediate reacts regioselectively with a variety of silyl enol ethers to give the corresponding coupling products (**4**) in good yields.

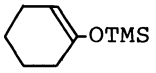
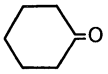


1a: R = Ph
1b: R = CH_3CH_2

Scheme 1.

F-Butylethene[6] (1.2 equiv.) was treated with benzenethiol-K_2CO_3 or ethanethiol-KOH in tetrahydrofuran (THF) at 70-80 °C for 20 h in a sealed tube to give

Table 1. Reaction of Sulfoxides **1** with Silyl Enol Ethers or Allylstannanes

Entry	R	Method[a]	Silyl enol ether or allylstannane	Time / h	Yield/%[b] of **4**
1	Ph	A	$CH_2=C(OTMS)CH_3$	2	86
2	Ph	B		3	39
3	Ph	C	CH_3COCH_3	3	62 (75)
4	CH_3CH_2	C		3	60
5	Ph	A	$CH_2=C(OTMS)(CH_2)_4CH_3$	7	83
6	Ph	C	$CH_3CH_2COCH_2CH_3$	3	74 (89)
7	Ph	A		2.5	63 (85)
8	Ph	A[c]		3	49
9	Ph	A[d]		3.5	(74)
10	Ph	A[e]		20	45 (77)
11	CH_3CH_2	A		3	71
12	Ph	B		6	37
13	Ph	C		2	67
14	Ph	A	$CH_2=C(OTMS)-Ph$	3	64 (88)
15	Ph	C	CH_3COPh	5	85 (87)
16	Ph	C	CH_3CH_2COPh	2	71
17	Ph	C	CH_3CH_2CHO	4	61 (87)
18	Ph	A	$CH_3CH_2CH=CH(OTMS)$	4.5	55 (81)
19	Ph	C	$CH_3CH_2CH_2CHO$	5.5	75 (87)
20	Ph	A	$CH_3CH=C(OTMS)-OCH_3$	6	73
21	Ph	A	$CH_2=CHCH_2-SnBu_3$	6	65 (91)
22	Ph	A	$CH_2=C(CH_3)CH_2-SnBu_3$	6.5	85
23	Ph	A	(E)-$PhCH=CHCH_2-SnBu_3$[f]	10	63 (76)

a) $NEt(i\text{-}Pr)_2$ was used as base, unless otherwise noted. Method A: **1** was added to a mixture of silyl enol ether, TfOTMS, and amine at -78 °C. Method B: TfO-9-BBN was employed as promoter, instead of TfOTMS. Method C: One-pot procedure. See the text. b) The yields refer to pure isolated compounds. The values in parentheses were determined by ^{19}F NMR. c) NEt_3 was used. d) N-Ethylpiperidine was employed. e) HMDS was used. f) Reacted exclusively on the γ carbon.

(Z)-3-F-propyl-3-fluoro-2-propenyl phenyl or ethyl sulfide,[7a] which was oxidized with an equimolar amount of m-chloroperbenzoic acid in CH_2Cl_2 at -40 °C for 2 h to furnish the corresponding sulfoxide (**1a** or **1b**).[7b] When the sulfoxide **1** was

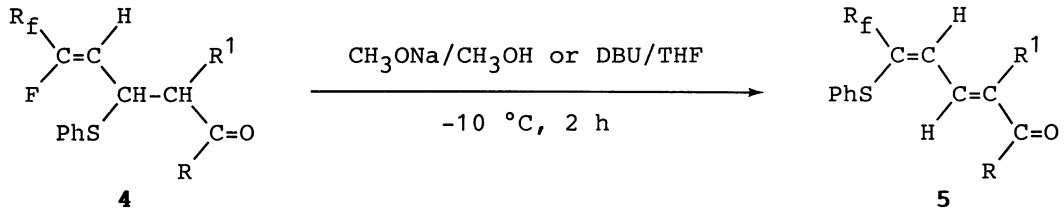
allowed to react with a silyl enol ether (1.5 equiv.) in the presence of trimethylsilyl triflate (TfOTMS) (1.3 equiv.) and an amine (1.3 equiv.) in CH_2Cl_2 under an argon atmosphere at -78 °C for a specified period, the corresponding fluorinated carbonyl compound (**4**)[8] was obtained in good yield (Method A). Out of the amines examined, NEt(i-Pr)$_2$ (Entry 7), NEt_3 (Entry 8), N-ethylpiperidine (Entry 9), or hexamethyldisilazane (HMDS) (Entry 10) was effective for the reaction. 9-Borabicyclo[3.3.1]nonyl triflate (TfO-9-BBN) could also be used as promoter (Method B) in place of TfOTMS, though the yields of products were appreciably reduced (Entries 2 and 12). Other promoters, such as trifluoroacetic anhydride, trimethylsilyl trifluoroacetate, iodotrimethylsilane, and chlorotrimethylsilane, did not effect the expected reaction. The results of the reaction are summarized in Table 1.

The present reaction could be carried out in a one-pot procedure using carbonyl compounds (Method C) as follows. To a CH_2Cl_2 solution of a ketone (1.2 equiv.) and NEt(i-Pr)$_2$ (2.5 equiv.) was added TfOTMS (2.5 equiv.) via a syringe at 0 °C under argon. For the case of an aldehyde is crucial the order of addition of the reagents: An aldehyde (1.5 equiv.) was gradually added to a mixture of TfOTMS (2.8 equiv.) and NEt(i-Pr)$_2$ (2.8 equiv.) at 0 °C.[9] After the mixture was stirred at 0 °C for 10 min and at room temperature for 2 h, a CH_2Cl_2 solution of **1** was dropwise added to it at -78 °C. The whole mixture was stirred at the same temperature for a specified period. A usual workup followed by silica-gel column chromatography afforded analytically pure product **4**[8] in good yield.

It is noteworthy that a variety of silyl enol ethers derived from carbonyl compounds including an ester react exclusively on the α carbon of an intermediately generated thionium ion **3** to lead to the products **4**.

Various allylstannanes[10] were also found to react with **3** under the similar conditions to give the corresponding α-allylated sulfides[8] in high yields (Entries 21-23). The replacement of TfOTMS with TfO-9-BBN in this reaction did not cause the reaction, the starting sulfoxide and allylic stannane being recovered. This fact suggests that TfOTMS plays a critical role in the generation of the intermediate **3** from **1**. ^1H and ^{19}F NMR analyses revealed that adding TfOTMS to a $CDCl_3$ solution of **1** substantially shifted the resonances due to allylic methylene protons and vinylic fluorine to lower fields (Scheme 1). This observation is suggestive of the formation of a sulfonium ion species **2**, as shown in Scheme 1, which may be converted into the intermediate **3** by the action of the amine.

The treatment of above-obtained compound **4** with sodium methoxide in methanol



4 **5**

R = Ph, R^1 = H; 81% (CH_3ONa), 82% (DBU)
R = CH_3, R^1 = H; 66% (CH_3ONa), 65% (DBU)
R = H, R^1 = CH_3CH_2; 76% (DBU)

or 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in THF at -10 °C provided good yield of a single stereoisomer of δ-F-propyl-α,β;γ,δ-unsaturated aldehyde and ketone (5),[8] a class of useful compounds in organic synthesis, whose synthetic application is being pursued.

References

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2) Y. Tamura, H.-D. Choi, H. Maeda, and H. Ishibashi, Tetrahedron Lett., 22, 1343 (1981); T.V. Lee and J.O. Okonkwo, ibid., 24, 323 (1983); I. Fleming and J. Iqbak, ibid., 24, 327 (1983); I.K. Stamos, ibid., 26, 477 (1985); K. Akiba, Y. Takasu, and M. Wada, ibid., 26, 2463 (1985); I.K. Stamos, ibid., 26, 2787 (1985); Y. Kita, O. Tamura, H. Yasuda, F. Itoh, and Y. Tamura, Chem. Pharm. Bull., 33, 4235 (1985); Y. Tamura, T. Yakura, Y. Shirouchi, and J. Haruta, ibid., 34, 1061 (1986); T. Takeda, Y. Kaneko, and T. Fujiwara, Tetrahedron Lett., 27, 3029 (1986); I.K. Stamos, ibid., 27, 6261 (1986); Y. Hashimoto, H. Sugumi, T. Okauchi, and T. Mukaiyama, Chem Lett., 1987, 1691; Y. Hashimoto, H. Sugumi, T. Okauchi, and T. Mukaiyama, ibid., 1987, 1695; T. Takeda, Y. Kaneko, H. Nakagawa, and T. Fujiwara, ibid., 1987, 1963; R. Hunter and C.D. Simon, Tetrahedron Lett., 29, 2257 (1988).

3) P. Magnus, T. Gallagher, P. Brown, and P. Pappalardo, Acc. Chem. Res., 17, 35 (1984); P. Magnus and P. Brown, J. Chem. Soc., Chem. Commun., 1985, 184.

4) Only one report on the electrochemical generation of trifluoromethylated thionium ion intermediate has appeared. See: T. Fuchigami, Y. Nakagawa, and T. Nonaka, Tetrahedron Lett., 27, 3869 (1986).

5) For the use of trialkylsilyl triflate as promoter in Pummerer-like reactions, see: R. Hunter and C.D. Simon, Tetrahedron Lett., 27, 1385 (1986); N. Tokitoh, Y. Igarashi, and W. Ando, ibid., 28, 5903 (1987).

6) Thanks are due to Japan Halon Co. Ltd. for a supply of F-butylethene.

7) a) R = Ph: 76%; bp 87-88 °C (5 mmHg, 1 mmHg = ca. 133.3 Pa); R = CH_3CH_2: 50%; bp 49-52 °C (16 mmHg); b) **1a**: 84%; ^{1}H NMR δ 3.59 (m, 2H), 5.63 (ddd, J=31.0, 8.4, 7.8 Hz, 1H), 7.46 (m, 5H); ^{19}F NMR δ -81.3 (t, J=8.5 Hz, 3F), -118.9 (dq, J=17.7, 8.5 Hz, 2F), -124.2 (m, 1F), -127.7 (d, J=8.5 Hz, 2F). **1b**: 92%; ^{1}H NMR δ 1.33 (t, J=7.3 Hz, 3H), 2.70 (q, J=7.3 Hz, 2H), 3.55 (m, 2H), 5.85 (dt, J=31.4, 8.0 Hz, 1H); ^{19}F NMR δ -81.2 (t, J=8.5 Hz, 3F), -118.9 (dq, J=14.0, 8.5 Hz, 2F), -124.0 (m, 1F), -127.6 (d, J=8.5 Hz, 2F).

8) The spectroscopic and analytical data for all new compounds were fully consistent with the assigned structures including the stereochemistry.

9) For the synthesis of silyl enol ethers from carbonyl compounds and trialkylsilyl triflate, see: H. Emde, D. Domsch, H. Feger, U. Frick, A. Gotz, H.H. Hergott, K. Hofmann, W. Kober, K. Krageloh, T. Oesterle, W. Steppan, W. West, and G. Simchen, Synthesis, 1982, 1.

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