JOC*Article*

1-Trifluoromethylvinylsilane as a $CF_2{=}C^-{-}CH_2^+$ Synthon: Synthesis of Functionalized 1,1-Difluoro-1-alkenes via Isolable 2,2-Difluorovinylsilanes

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Various 1,1-difluoro-1-alkenes such as monosubstituted 1,1-difluoro-1-alkenes, 2-bromo-1,1-difluoro-1-alkenes, and 3,3-difluoroallylic alcohols are synthesized in two simple steps from 1-trifluoromethylvinylsilane: (i) its S_N2' reaction with nucleophiles to construct 2,2-difluorovinylsilanes and (ii) the subsequent substitution of electrophiles for the vinylic silyl group. The combination of these two processes allows a one-pot synthesis of the functionalized 1,1-difluoro-1-alkenes starting from 1-trifluoromethylvinylsilane, which functions as a $CF_2{=}C^-{-}CH_2^+$ synthon.

Introduction

Fluorine-containing molecules are finding increasing utility in various fields such as pharmaceutical and agricultural chemistry and material science.[1] Among these compounds, 1,1-difluoro-1-alkenes are of special interest, due to their diverse utility as building blocks for fluorinated compounds and polymers.[2] The activity of these compounds as new types of enzyme inhibitors[1d,e] and pesticides[3] has also attracted much attention in recent years. Although a number of examples of the preparation of 1,1-difluoro-1-alkenes have been reported,[2,4] the generality of these methods is still limited. The development of general synthetic methods for highly functionalized 1,1-difluoro-1-alkenes remains a challenge of practical importance.

One straightforward route to their synthesis involves the generation and reaction of 2,2-difluorovinylmetals.[4,5] Most reported difluorovinylmetals **1** reactive enough to act as a vinyl anion, however, incorporate an α-position electron-withdrawing group[5] such as an oxygen-containing group,[6] a halogen,[7] a trifluoromethyl group,[8] or an aryl group[9] (Figure 1). These substituents are needed to enhance the thermal stability of **1** against β-elimination of the metal fluoride leading to 1-fluoro-1-alkynes.[5,10,11] Thus, very few reactive 2,2-difluorovinylmetals lacking an α-anion-stabilizing group at the 1-position have been

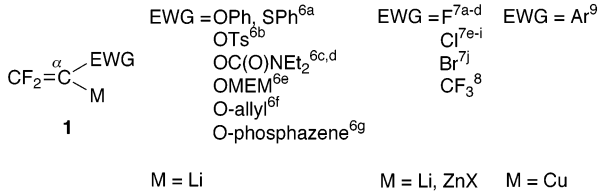

FIGURE 1. *gem*-Difluorovinylmetals stabilized by an α-position electron-withdrawing group.

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(1) (a) Welch, J. T.; Eswarakrishnan, S. *Fluorine in Bioorganic Chemistry*; Wiley: New York, 1991. (b) *Organofluorine Compounds in Medicinal Chemistry and Biochemical Applications*; Filler, R., Kobayashi, Y., Yagupolskii, L. M., Eds.; Elsevier: Amsterdam, The Netherlands, 1993. (c) *Organofluorine Chemistry: Principles and Commercial Applications*; Banks, R. E., Tatlow, J. C., Smart, B. E., Eds; Plenum Press: New York, 1994. (d) *Selective Fluorination in Organic and Bioorganic Chemistry*; ACS Symp. Ser. No. 456; Welch, J. T., Ed.; American Chemical Society: Washington, DC, 1991. (e) *Biomedical Frontiers of Fluorine Chemistry*; ACS Symp. Ser. No. 639; Ojima, I., McCarthy, J. R., Welch, J. T., Eds.; American Chemical Society: Washington, DC, 1996. (f) Resnati, G. *Tetrahedron* **1993**, *49*, 9385.

(2) (a) Tozer, M. J.; Herpin, T. F. *Tetrahedron* **1996**, *52*, 8619. (b) Percy, J. M. *Contemp. Org. Synth.* **1995**, *2*, 251.

(3) (a) Hatano, K.; Nakamoto, Y.; Umeyama, H.; Noritake, T. JP 2001288142, 2001; *Chem. Abstr.* **2001**, *135*, 303602. (b) Fujii, K.; Hatano, K.; Tsutsumiuchi, K.; Nakamoto, Y. JP 2000198769, 2000; *Chem. Abstr.* **2000**, *133*, 89329. (c) Boger, M.; Maienfisch, P.; Pitterna, T. WO 9962866, 1999; *Chem. Abstr.* **2000**, *132*, 22762. (d) Fujii, K.; Hatano, K.; Narita, I.; Sikita, S.; Tanaka, T.; Nakamoto, Y. WO 9952874, 1999; *Chem. Abstr.* **1999**, *131*, 271889.

(4) Ichikawa, J. *J. Fluorine Chem.* **2000**, *105*, 257 and references therein.

(5) For reviews, see: (a) Brisdon, A. K.; Banger, K. K. *J. Fluorine Chem.* **1999**, *100*, 35. (b) Coe, P. L. *J. Fluorine Chem.* **1999**, *100*, 45. (c) Burton, D. J.; Yang, Z.-Y.; Morken, P. A. *Tetrahedron* **1994**, *50*. 2993. (d) Normant, J.-F. *J. Organomet. Chem.* **1990**, *400*, 19.

(6) (a) Nakai, T.; Tanaka, K.; Ishikawa, N. *Chem. Lett.* **1976**, 1263. (b) Tanaka, K.; Nakai, T.; Ishikawa, N. *Tetrahedron Lett.* **1978**, *19*, 4809. (c) Crowly, P. J.; Howarth, W. M.; Owton, W. M.; Percy, J. M.; Stansfield. K. *Tetrahedron Lett.* **1996**, *37*, 5975. (d) Lee, J.; Tsukazaki, M.; Snieckus, V. *Tetrahedron Lett.* **1993**, *34*, 415. (e) Patel, S. T.; Percy, J. M.; Wilkens, R. D. *J. Org. Chem.* **1996**, *61*, 166. (f) Metcalf, B. W.; Jarvi, E. T.; Burkhart, J. P. *Tetrahedron Lett.* **1985**, *26*, 2861. (g) Allcock, H. R.; Suszko, P. R.; Evans, T. L. *Organometallics* **1982**, *1*, 1443.

(7) (a) Burdon, J.; Coe, P. L.; Haslock, I. B.; Powell, R. L. *J. Fluorine Chem.* **1999**, *99*, 127. (b) Banger, K. K.; Brisdon, A. K.; Gupta, A. *Chem. Commun.* **1997**, 139. (c) Burdon, J.; Coe, P. L.; Haslock, I. B.; Powell, R. L. *Chem. Commun.* **1996**, 49. (d) Anilkumar, R.; Burton, D. J. *Tetrahedron Lett.* **2002**, *43*, 2731. (e) Brown, S. J.; Corr, S.; Percy, J. M. *Tetrahedron Lett.* **2000**, *41*, 5269. (f) Bainbridge, J. M.; Brown, S. J.; Ewing, P. N.; Gibson, R. R.; Percy, J. M. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2541. (g) Burdon, J.; Coe, P. L.; Haslock, I. B.; Powell, R. L. *J. Fluorine Chem.* **1997**, 151. (h) Anilkumar, R.; Burton, D. J. *Tetrahedron Lett.* **2002**, *43*, 6979. (i) Shigeoka, T.; Kuwahara, Y.; Watanabe, K.; Sato, K.; Omote, M.; Ando, A.; Kumadaki, I. *J. Fluorine Chem.* **2000**, *103*, 99. (j) Nguyen, B. V.; Burton D. J. *J. Org. Chem.* **1998**, *63*, 1714.

(8) Morken, P. A.; Burton D. J. *J. Org. Chem.* **1993**, *58*, 1167.

(9) Ishihara, T.; Yamana, M.; Ando, T. *Tetrahedron Lett.* **1983**, *24*, 5657.

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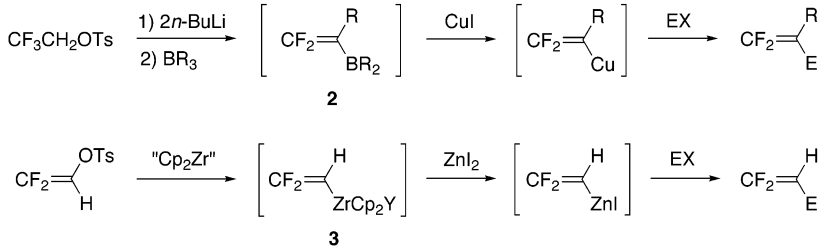
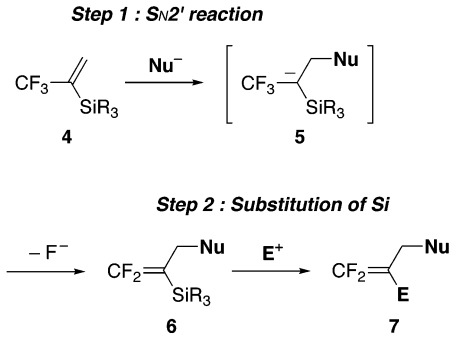
SCHEME 1. Difluoroalkene Synthesis via Nonstabilized 2,2-Difluorovinylmetals



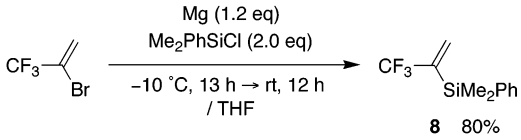
2 **3**

SCHEME 2. Synthetic Strategy toward 1,1-Difluoro-1-alkenes



4 **5** **6** **7**

SCHEME 3. Preparation of Dimethylphenyl(1-trifluoromethylvinyl)silane (8)



8 80%

described. As a solution to this problem, we have already developed thermostable 2,2-difluorovinylboron **2** and -zirconium **3** species to achieve the difluoroalkene synthesis via transmetalation to copper and zinc intermediates, respectively (Scheme 1).[4] Thermostable, unsubstituted 2,2-difluorovinylzinc reagent also has been reported by Burton.[12]

In terms of thermal stability the corresponding silicon species, 2,2-difluorovinylsilanes, also attracted our attention and prompted us to investigate their chemistry. Eventually, we developed the synthetic method for 1,1-difluoro-1-alkenes via 2,2-difluorovinylsilanes, which consists of two steps: the construction and the reaction of difluorovinylsilanes (vide infra). The preliminary results of this approach have been briefly reported in our previous communication, where the first step was treated mainly (Tables 1 and 2) along with a few examples of the second step.[13] Combining the results of the second step (Table 3) and their one-pot reaction (Table 4) with those published earlier by us, we present here a full account of our studies on the synthesis of 1,1-difluoro-1-alkenes starting from 1-trifluoromethylvinylsilane via 2,2-difluorovinylsilanes, which are quite stable, easy to handle, and can be stored under air.

(10) Runge, A.; Sander, W. W. *Tetrahedron Lett*. **1990**, *31*, 5453.

(11) For example, unsubstituted 2,2-difluorovinyllithium should be generated at −110 °C and undergoes a smooth β-elimination even at −80 °C.[5d]

(12) Nguyen, B. V.; Burton, D. J. *J. Org. Chem*. **1997**, *62*, 7758.

(13) Ichikawa, J.; Ishibashi, Y.; Fukui, H. *Tetrahedron Lett.* **2003**, *44*, 707.

Results and Discussion

(a) Synthetic Strategy toward 1,1-Difluoro-1-alkenes. For the synthesis of diverse 1,1-difluoro-1-alkenes, it is necessary to prepare a variety of 2,2-difluorovinylsilanes. Since the carbon substituents at the 1-position of reported 2,2-difluorovinylsilanes are limited to phenyl and triphenylsilylmethyl groups,[14] our investigation started with the development of a widely applicable synthetic route to these compounds.

1-Trifluoromethylvinyl compounds are known to react with nucleophiles in an S_N2' fashion to afford 1,1-difluoro-1-alkenes.[15] The following limitations of this reaction, however, have restricted its applicability: the necessity of (i) an electron-withdrawing group such as a carbonyl or an aryl group on the 2-position of the 3,3,3-trifluoropropene framework and/or (ii) highly reactive nucleophiles such as alkyllithiums. For example, it has been reported that 5-phenyl-2-trifluoromethyl-1-pentene which had an alkyl group on the 2-position reacted with butyllithium to give the corresponding difluoroalkene, while no reaction was observed with phenyllithium.[15d]

We expected that (i) utilizing the α-anion-stabilizing effect of silicon could overcome these drawbacks to support the generation of intermediary anion **5** and therefore to promote the S_N2' reaction[16] and that at the same time (ii) the reaction would provide a solution to the synthesis of 2,2-difluorovinylsilanes desired above. Furthermore, the resulting vinylsilanes **6** would allow in turn the introduction of the second substituent by the replacement of the silyl group.[17] Thus, as depicted in Scheme 2 the sequence of reactions starting from 1-trifluoromethylvinylsilanes **4** could provide a wide variety of 1,1-difluoro-1-alkenes **7** bearing two kinds of substituents (Nu, E). In this sequence, 1-trifluoromethylvinylsilanes **4** function as $CF_2{=}C^-{-}CH_2^+$ synthons.

(b) Synthesis of 1,1-Difluoro-1-alkenes. In the S_N2' reaction of β-silyl allylic ethers, a phenyl group on the

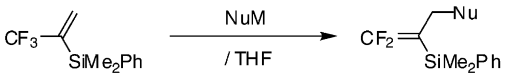
(14) (a) Okano, T.; Ito, K.; Ueda, T.; Muramatsu, H. *J. Fluorine Chem*. **1986**, *32*, 377. (b) Xu, Y.; Jin, F.; Huang, W. *J. Org. Chem*. **1994**, *59*, 2638.

(15) For the S_N2' reaction of 1-trifluoromethylvinyl compounds [$CH_2{=}C(Y)CF_3$], see: Y = CO_2R (CO_2H): (a) Kitazume, T.; Ohnogi, T.; Miyauchi, H.; Yamazaki, T. *J. Org. Chem*. **1989**, *54*, 5630. (b) Fuchikami, T.; Shibata, Y.; Suzuki, Y. *Tetrahedron Lett*. **1986**, *27*, 3173. Y = SPh, SePh: (c) Feiring, A. E. *J. Org. Chem*. **1980**, *45*, 1962. Y = Ph: (d) Bégué, J.-P.; Bonnet-Delpon, D.; Rock, M. H. *J. Chem. Soc., Perkin Trans. 1* **1996**, 1409. Y = H (Me): (e) Hiyama T.; Obayashi, M.; Sawahata, M. *Tetrahedron Lett*. **1983**, *24*, 4113. (f) Kendrick, D. A.; Kolb, M. *J. Fluorine Chem*. **1989**, *45*, 265. (g) Bergstrom, D. E.; Ng, M. W.; Wong, J. J. *J. Org. Chem*. **1983**, *48*, 1902.

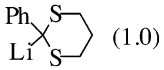
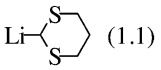
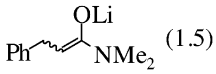
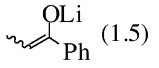
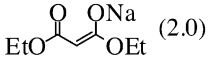
(16) The favorable effect of an α-silyl group in α,β-unsaturated enones on the Michael reaction is well documented. Stork, G.; Ganem, B. *J. Am. Chem. Soc*. **1973**, *95*, 6152.

(17) (a) Weber, W. P. *Silicon Reagents for Organic Synthesis*; Splinger: Berlin, Germany, 1983. (b) Colvin, E. W. *Silicon in Organic Synthesis*; Butterworth: London, UK, 1981.

TABLE 1. S_N2' Reaction of 8 with Nucleophiles

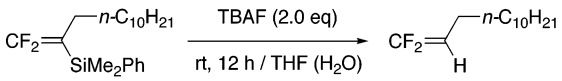


8 9

Entry	NuM (eq)	Conditions	9 / %
1	$LiAlH_4$ (0.5)	0 °C, 5 h	**9a** 88
2	*n*-C_4H_9Li (1.05)	–78 °C, 40 min	**9b** 93
3	*n*-$C_{10}H_{21}Li$ (1.1)	–78 °C, 1 h	**9c** 99
4[a]	PhLi (1.1)	–78 °C, 2.5 h → 0 °C	**9d** 85
5	 (1.0)	–78 °C, 3 h → 0 °C	**9e** 89
6	 (1.1)	–78 °C, 1 h → rt	**9f** 75
7	 (1.5)	–78 °C, 10 min → 0 °C, 15 min	**9g** 85
8	 (1.5)	–78 °C, 30 min → reflux, 8 h	**9h** 59
9	 (2.0)	reflux, 24 h	**9i** 55
10	*i*-Pr_2NLi (1.2)	–78 °C, 1 h → 0 °C, 1 h	**9j** 86
11[b]	*i*-BuNHLi (1.2)	rt, 6 h	**9k** 51

[a] *N*,*N*,*N*′,*N*′-Tetramethylethylenediamine (1.0 equiv) was used. [b] DMF was used as solvent.

SCHEME 4. Protodesilylation of 9c



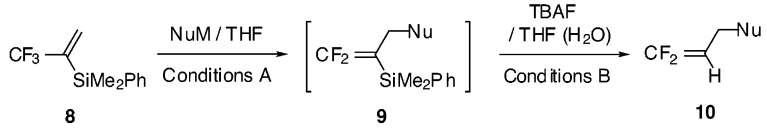
9c **10a** 99%

silicon has been reported to play an important role in raising their reactivity.[18] Taking into consideration its boiling point as well as the S_N2' reactivity, we adopted dimethylphenylsilyl group for **4**. After some attempts, we found that the in situ generated 1-trifluoromethylvinylmagnesium bromide[19] was efficiently trapped with dimethylphenylsilyl chloride to afford **8** in 80% yield (Scheme 3). Thus obtained **8** was stable enough to be stored at room temperature under air for long periods (no less than 6 months), despite a report on the susceptibility to *β*-elimination generating 1,1-difluoroallene.[20]

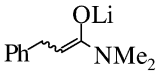
We then investigated the S_N2' reaction of **8** with various nucleophiles. The results are summarized in Table 1. S_N2' products **9** were obtained in excellent yield for $LiAlH_4$ and alkyl- and aryllithiums without overreaction, the substitution of the vinylic fluorines in **9** via addition−elimination process (entries 1−4).[21,22] Acyl anion equivalents, 2-lithio-1,3-dithianes, afforded the

(18) Kishi, N.; Imma, H.; Mikami, K.; Nakai, T. *Synlett* **1992**, 189.
(19) The Grignard reagent was prepared from 2-bromo-3,3,3-trifluoro-1-propene in the presence of an electrophile. Jiang, B.; Wang, Q.-F.; Yang, C.-G.; Xu, M. *Tetrahedron Lett.* **2001**, *42*, 4083.
(20) Drakesmith, F. G.; Stewart, O. J.; Tarrant, P. *J. Org. Chem.* **1968**, *33*, 280.
(21) (a) Smart, B. E. In *Organofluorine Chemistry, Principles and Commercial Applications*; Banks, R. E., Smart, B. E., Tatlow, J. C., Eds.; Plenum: New York, 1994; p 57. (b) Lee, V. J. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: Oxford, UK, 1991; Vol. 4, p 69. (c) Ichikawa, J.; Wada, Y.; Fujiwara, M.; Sakoda, K. *Synthesis* **2002**, 1917 and references therein.
(22) The replacement of the vinylic fluorines in **9b** by *n*-BuLi readily proceeded at −45 °C to give 5-fluoro-6-dimethylphenylsilyl-5-undecene in 93% yield (*E*:*Z* = 12:88). The same reaction of 1,1-difluoro-2-phenyl-1-hexane with *n*-BuLi occurred at −45 °C to afford 5-fluoro-6-phenyl-5-decene in 95% yield (*E*:*Z* = 69:31). These results reveal that the effect of silicon works as favorably as that of the phenyl group in the substitution of the vinylic fluorines. The stereochemistry of the *E* and *Z* isomers was determined by NOESY spectroscopy. See also: (a) Martin, S.; Sauvêtre, R.; Normant, J.-F. *Tetrahedron Lett.* **1983**, *24*, 5615. (b) Huang, X.-h.; He, P.-y.; Shi, G.-q. *J. Org. Chem.* **2000**, *65*, 627.

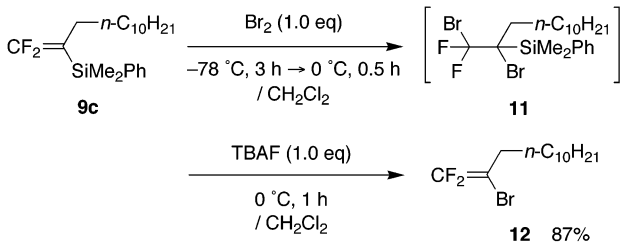
TABLE 2. One-Pot Synthesis of Monosubstituted 1,1-Difluoro-1-alkenes 10



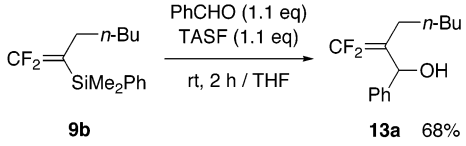
8 9 10

Entry	NuM (eq)	Conditions A	TBAF / eq	Conditions B	**10** / %
1	*n*-$C_{10}H_{21}$Li (1.0)	–78 °C, 25 min	2.0	rt, 4 h	**10a** 82
2	 (1.0)	–78 °C, 1 h	1.1	rt, 2 h	**10b** 80
3	 (1.5)	–78 °C, 30 min	1.1	0 °C, 10 min	**10c** 64

SCHEME 5. Bromodesilylation of 9c



SCHEME 6. Reaction of 9b with Aldehyde



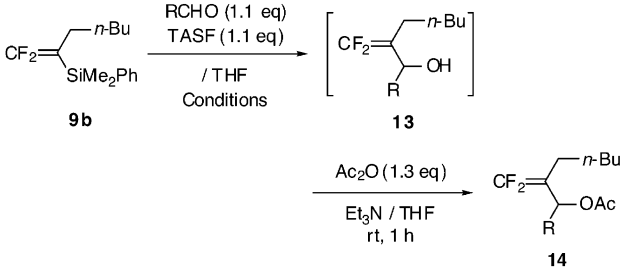
corresponding **9e** and **9f** in high yield (entries 5 and 6). In addition, **8** reacted with ketone, ester, and amide enolates at the carbon α to their carbonyl groups. Although only limited examples have been reported for the S_N2' reaction of 1-trifluoromethylvinyl compounds with ester enolates,[15c,f] **8** reacted not only with amide and ketone enolates (entries 7 and 8) but even with the less reactive malonate anion (entry 9). These results clearly show that **8** is much more reactive than α-(trifluoromethyl)styrene bearing a phenyl group instead of the silyl group.[15d,22] Nitrogen nucleophiles derived from secondary and primary amines also underwent the S_N2' reaction of **8** to give 3,3-difluoroallylamines **9j** and **9k** in 86% and 50% yields, respectively (entries 10 and 11).

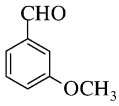
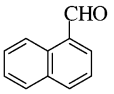
The results of the S_N2' reaction of **8** with various nucleophiles encouraged us to investigate the next step, substitution of the silyl group. It is known that dimethylphenylsilyl−vinylic carbon bonds are cleaved with tetrabutylammonium fluoride (*n*-Bu_4NF, TBAF) under relatively harsh conditions (at 80 °C in DMSO).[23] The removal of the silyl group in **9c**, however, proceeded smoothly even at room temperature on treatment with a moist THF solution of *n*-Bu_4NF,[24] leading to monosubstituted difluoroalkene **10a** in 99% yield (Scheme 4).

(23) Oda, H.; Sato, M.; Morizawa, Y.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1983**, *24*, 2877.

(24) The THF solution of *n*-Bu_4NF (1.0 M) contained water (10 vol %).

TABLE 3. Synthesis of 3,3-Difluoroallylic Acetates 14



Entry	RCHO	Conditions	**13** /%[a]	**14** /%
1	PhCHO	rt, 2 h	**13a** 66	**14a** 63
2		rt, 1.5 h	**13b** 67	**14b** 67
3		rt, 4.5 h	**13c** 70	**14a** 69
4[b]	$Ph(CH_2)_2CHO$	rt, 5 h	**13d** 21	**14d** 19

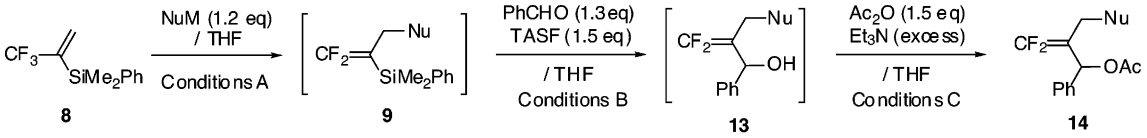
[a] Not isolated. Yield was determined by ^{19}F NMR. [b] 3-Phenylpropanal (1.2 equiv), TASF (1.2 equiv), and acetic anhydride (1.5 equiv) were used.

Next, attempted combination of the S_N2' process and the above-mentioned protodesilylation gave rise to a one-pot synthesis of difluoroalkenes. On treatment of **8** with nucleophiles and then with moist *n*-Bu_4NF, the two processes successively proceeded to yield the corresponding monosubstituted difluoroalkenes **10** (Table 2). This one-pot sequence was successfully applied to the construction of difluoroalkenes bearing functional groups such as 1,3-dithiane and amide moieties (entries 2 and 3).

We also examined the substitution of bromine atom for the vinylic silyl group.[17] When **9c** was treated with bromine, dibromide **11** was obtained in low yield due to its instability.[25] Successive treatment of **9c** with bromine

(25) Sayferth, D.; Wada, T.; Maciel, G. E. *Inorg. Chem.* **1962**, *1*, 232.

TABLE 4. One-Pot Synthesis of 3,3-Difluoroallylic Acetates 14



Entry	NuM	Conditions A	Conditions B	Conditions C	**14** / %
1	*n*-C_4H_9Li	–78 °C, 20 min	rt, 2.5 h	rt, 1 h	**14a** 67
2		–78 °C, 1 h	rt, 2 h	rt, 1 h	**14e** 72
3	*i*-Pr_2NLi	–78 °C, 1 h → 0 °C, 45 min	rt, 5 h	rt, 1.5 h	**14f** 70

and *n*-Bu_4NF without isolation of **11** smoothly effected dibromination and elimination of a silyl bromide to give 2,2-difluorovinyl bromide **12**, a useful building block, in 87% yield (Scheme 5).

Furthermore, C−C bond formation was investigated by utilizing the vinylic silicon.[26] While there are several reports on the fluoride-promoted reaction of vinylsilanes with aldehydes, all of these vinylsilanes have an α-position anion-stabilizing group such as a carbonyl and cyano group,[27] a phenyl group,[23] and a halogen.[28] Despite lack of an anion-stabilizing group, **9b** was treated with benzaldehyde and *n*-Bu_4NF to afford difluoroallylic alcohol **13a** in 22% yield along with 1,1-difluoro-1-heptene (51% yield determined by ^{19}F NMR). The yield of **13a** was improved up to 68% by using tris(diethylamino)sulfonium difluorotrimethylsilycate (TASF)[29] instead of *n*-Bu_4NF (Scheme 6).[30] Since difluoroallylic alcohols **13** were easily hydrolyzed via the allylic cations leading to α,β-unsaturated acids under acidic conditions, we isolated the products as the corresponding acetates **14** (Table 3). Compared to aromatic aldehydes, an aliphatic aldehyde gave the corresponding acetate **14d** in lower yield (entry 4), due to the self-aldol reaction.

The one-pot synthesis of difluoroallylic acetates **14** was accomplished by the combination of the S_N2' process and the reaction with benzaldehyde, followed by acetylation (Table 4). On treatment of **8** with nucleophiles and then benzaldehyde and TASF, followed by Ac_2O and Et_3N, the three-step sequence including two C−C bond formations proceeded readily to yield the desired difluoroallylic acetates **14** in good yield. Thus, this methodology provides a new entry to highly functionalized 1,1-difluoro-1-alkenes.

Conclusion

We have established a new synthetic method for 1,1-difluoro-1-alkenes with the introduction of two kinds of groups in different polarities by utilizing the following properties of the silyl group: (i) Its α-anion-stabilizing effect promotes the S_N2' reaction of 1-trifluoromethylvinylsilane **8** with nucleophiles to construct 2,2-difluorovinylsilanes **9**, and (ii) the subsequent substitution of electrophiles for the silyl group affords monosubstituted 1,1-difluoro-1-alkenes **10**, 2-bromo-1,1-difluoro-1-alkenes **12**, and 3,3-difluoroallylic alcohols **13** or their acetates **14**. In this process, **8** turns out to function as a versatile $CF_2{=}C^-{-}CH_2^+$ synthon, opening an efficient access to functionalized 1,1-difluoro-1-alkenes.

Experimental Section

(2,2-Difluoro-1-methylvinyl)dimethylphenylsilane (9a). To a suspension of lithium aluminum hydride (152 mg, 0.500 mmol) in THF (8 mL) was added **8** (462 mg, 2.00 mmol) in THF (2 mL) over 10 min at −78 °C under argon. After the reaction mixture was stirred at 0 °C for 5 h, the reaction was quenched with MeOH (4 mL) and aqueous HCl (10 mL, 2 M). Organic materials were extracted with Et_2O (10 mL × 3). The combined extracts were washed with brine and then dried over $MgSO_4$. After removal of the solvent under reduced pressure (30 kPa), the residue was purified by PTLC (pentane) to give **9a** (374 mg, 88%) as a colorless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 0.41 (3H, s), 0.42 (3H, s), 1.52 (3H, dd, J_{HF} = 2.3, 2.3 Hz), 7.35−7.38 (3H, m), 7.50−7.52 (2H, m). ^{13}C NMR (126 MHz, $CDCl_3$) δ −2.9, 10.5 (dd, J_{CF} = 6, 6 Hz), 75.7 (dd, J_{CF} = 30, 2 Hz), 127.9, 129.3, 133.7, 137.1, 155.8 (dd, J_{CF} = 305, 281 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 84.3 (1F, d, J_{FF} = 37 Hz), 88.0 (1F, d, J_{FF} = 37 Hz). IR (neat) 1697, 1221, 1090, 812, 775, 731, 698 cm^{-1}. Anal. Calcd for $C_{11}H_{14}F_2Si$: C, 62.23; H, 6.65. Found: C, 62.05; H, 6.71.

1,1-Difluoro-1-tridecene (10a). To a solution of **9c** (177 mg, 0.50 mmol) was added *n*-Bu_4NF (TBAF, 0.44 mL, 1.0 M in THF, 0.44 mmol) at 0 °C under argon. The reaction mixture was stirred for 12 h at room temperature. Phosphate buffer (pH 7) was added to quench the reaction, and organic materials were extracted with Et_2O (10 mL × 3). The combined extracts

(26) Mikami, K.; Wakabayashi, H.; Nakai, T. *J. Org. Chem.* **1991**, *56*, 4337 and references therein.

(27) (a) Matsumoto, K.; Oshima, K.; Utimoto, K. *Chem. Lett.* **1994**, 1211. (b) Sato, Y.; Takeuchi, S. *Synthesis* **1983**, 734. (c) Sato, Y.; Hitomi, K. *J. Chem. Soc., Chem. Commun.* **1983**, 170.

(28) For the reaction of fluorinated vinylsilanes with aldehydes, see: (a) Hanamoto, T.; Harada, S.; Shindo, K.; Kondo, M. *Chem. Commun.* **1999**, 2397. (b) Yudin, A. K.; Prakash, G. K. S.; Deffieux, D.; Bradley, M.; Bau, R.; Olah, G. A. *J. Am. Chem. Soc.* **1997**, *119*, 1572. (c) Fujita, M.; Obayashi, M.; Hiyama, T. *Tetrahedron* **1988**, *44*, 4135. (d) Martin, S.; Sauvêtre, R.; Normant, J.-F. *J. Organomet. Chem.* **1984**, *264*, 155.

(29) Fujita, M.; Hiyama, T. *Org. Synth.* **1990**, *69*, 44.

(30) For reports on the utility of 3,3-difluoroallylic alcohols, see: Patel, S. T.; Percy, J. M.; Wilkens, R. D. *J. Org. Chem.* **1996**, *61*, 166 and references therein.

were washed with brine and dried over $MgSO_4$. After removal of the solvent under reduced pressure (30 kPa), the residue was purified by PTLC (hexane) to give **10a** (106 mg, 99%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (3H, t, J = 7.0 Hz), 1.26−1.35 (17H), 1.96 (2H, br dt, J = 7.9, 7.9 Hz), 4.12 (1H, dtd, J_{FH} = 25.6 Hz, J = 7.9 Hz, J_{FH} = 2.7 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 14.1, 22.1 (d, J_{CF} = 4 Hz), 22.7, 28.9, 29.3, 29.4 (dd, J_{CF} = 2, 2 Hz), 29.4, 29.5, 29.6, 29.6, 31.9, 78.0 (dd, J_{CF} = 21, 21 Hz), 156.2 (dd, J_{CF} = 285, 285 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 69.5 (1F, dd, J_{FF} = 50 Hz, J_{FH} = 26 Hz), 71.9 (1F, d, J_{FF} = 50 Hz). IR (neat) 3725, 2924, 2854, 1747, 914, 744 cm^{-1}. Anal. Calcd for $C_{13}H_{24}F_2$: C, 71.52; H, 11.08. Found: C, 71.31; H, 11.18.

One-pot reaction from 8: To a solution of 1-iododecane (323 mg, 1.20 mmol) in Et_2O (1.2 mL) was added *t*-BuLi (1.70 mL, 1.5 M in pentane, 2.55 mmol) over 5 min at −78 °C under argon. After being stirred at room temperature for 1 h, the reaction mixture was added to a solution of **8** (232 mg, 1.01 mmol) in THF (5 mL) at −78 °C over 5 min. After the reaction mixture was stirred at −78 °C for 20 min, *n*-Bu_4NF (2.00 mL, 1.0 M in THF, 2.00 mmol) was added. The resulting mixture was stirred at room temperature for 4 h. Phosphate buffer (pH 7) was added to quench the reaction, and organic materials were extracted with Et_2O (5 mL × 3). The combined extracts were washed with brine and dried over $MgSO_4$. After removal of the solvent under reduced pressure (30 kPa), the residue was purified by PTLC (hexane) to give **10a** (179 mg, 82%) as a colorless oil.

2-Bromo-1,1-difluoro-1-tridecene (12). To a solution of **9c** (356 mg, 1.01 mmol) in CH_2Cl_2 (8 mL) was added bromine (60 μL, 1.17 mmol) in CH_2Cl_2 (2 mL) at −78 °C over 3 h under argon. After the reaction mixture was stirred at 0 °C for 30 min, *n*-Bu_4NF (1.10 mL, 1.0 M in THF, 1.10 mmol) was added. The mixture was stirred at 0 °C for 1 h, and phosphate buffer (pH 7) was added to quench the reaction. Organic materials were extracted with CH_2Cl_2 (10 mL × 3). The combined extracts were washed with brine and dried over $MgSO_4$. After removal of the solvent under reduced pressure, the residue was purified by PTLC (hexane) to give **12** (262 mg, 87%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (3H, t, J = 7.0 Hz), 1.21−1.32 (17H, m), 1.52 (2H, br t, J = 7.0 Hz), 2.43 (1H, m). ^{13}C NMR (126 MHz, $CDCl_3$) δ 14.0, 22.7, 27.2 (d, J_{CF} = 2 Hz), 28.3, 29.2, 29.4, 29.5, 29.6, 29.6, 30.6, 31.9, 81.2 (dd, J_{CF} = 41, 20 Hz), 153.2 (dd, J_{CF} = 287, 283 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 70.8 (1F, dd, J_{FF} = 44 Hz, J_{HF} = 3 Hz), 77.1 (1F, d, J_{FF} = 44 Hz). IR (neat) 2922, 2852, 1267, 1173, 960, 771 cm^{-1}. Anal. Calcd for $C_{13}H_{23}BrF_2$: C, 52.42; H, 7.74. Found: C, 52.53; H, 7.80.

3,3-Difluoro-2-pentyl-1-phenyl-2-propenyl Acetate (14a). To a solution of **9b** (133 mg, 0.49 mmol) and benzaldehyde (56 μL, 0.55 mmol) in THF (4 mL) was added TASF (0.55 mL, 1.0 M in THF, 0.55 mmol) at room temperature under argon. The reaction mixture was stirred at room temperature for 2 h, and then treated with Et_3N (1 mL) and acetic anhydride (61.3 μL, 0.65 mmol). After the mixture was stirred for 1 h at room temperature, phosphate buffer (pH 7) was added to quench the reaction. Organic materials were extracted with AcOEt (10 mL × 3), and the combined extracts were washed with brine and dried over $MgSO_4$. After removal of the solvent under reduced pressure, the residue was purified by PTLC (hexane-AcOEt 10:1) to give **14a** (88 mg, 63%) as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.82 (3H, t, J = 7.1 Hz), 1.14−1.23 (5H, m), 1.28−1.30 (1H, m), 1.83−1.85 (1H, m), 1.92−1.94 (1H, m), 2.17 (3H, s), 6.63 (1H, br s), 7.28−7.30 (3H, m), 7.34−7.37 (2H, m). ^{13}C NMR (126 MHz, $CDCl_3$) δ 13.9, 22.1, 22.2, 23.4, 28.1, 31.4, 71.9 (d, J_{CF} = 7 Hz), 90.3 (dd, J_{CF} = 19, 12 Hz), 125.6, 127.8, 128.5, 138.1, 154.9 (dd, J_{CF} = 291, 289 Hz), 169.6. ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 70.7 (1F, d, J_{FF} = 42 Hz), 72.5 (1F, d, J_{FF} = 42 Hz). IR (neat) 2956, 2931, 2866, 1747, 1371, 1265, 1227, 1328, 1018 cm^{-1}. Anal. Calcd for $C_{16}H_{20}F_2O_2$: C, 68.07; H, 7.14. Found: C, 68.07; H, 7.22.

One-pot reaction from 8: To a solution of **8** (117 mg, 0.509 mmol) in THF (4 mL) was added *n*-BuLi (0.39 mL, 1.55 M in hexane, 0.60 mmol) at −78 °C under argon. After the reaction mixture was stirred for 20 min, benzaldehyde (66 μL, 0.65 mmol) and TASF (0.75 mL, 1.0 M in THF, 0.75 mmol) were successively added. The reaction mixture was stirred at room temperature for 2.5 h, and then treated with Et_3N (1 mL) and acetic anhydride (71 μL, 0.75 mmol). The mixture was stirred at room temperature for 1 h, and phosphate buffer (pH 7) was added to quench the reaction. Organic materials were extracted with AcOEt (10 mL × 3). The combined extracts were washed with brine and dried over $MgSO_4$. After removal of the solvent under reduced pressure, the residue was purified by PTLC (hexane−AcOEt 10:1) to give **14a** (97 mg, 67%) as a pale yellow oil.

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Supporting Information Available: Experimental procedures and spectroscopic data for **8**, **9b**−**k**, **10b**,**c**, **13a**, and **14b**−**f**. This material is available free of charge via the Internet at http://pubs.acs.org.

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