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Synthetic utility of 2,3,3,3-tetrafluoroprop-1-ene (HFO-1234yf)

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ABSTRACT

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Dedicated to Professor Iwao Ojima for his 70th birthday.

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1. Introduction

2,3,3,-Tetrafluoroprop-1-ene **1a** (HFO-1234yf) has recently been drawing significant attention as the potent fluorinated refrigerant with the global warming potential of only 4, no ozone depleting potential, and a very short atmospheric lifetime of ca. 11 days **[1]**. Moreover, its similar thermophysical performance to widely used HFC-124a at present **[2]** allowed to launch its installation to air-conditioning systems for vehicles on markets and thus, their production in an industrial scale should open a readily available route of this interesting partially fluorinated alkene **1a** whose previous synthetic application was limited mainly to preparation of polymer materials **[3]**. Then, we have started our research for clarification of its reactivity from the synthetic point of view, and found out that **1a** smoothly reacted with alkoxides by the well-known addition–elimination sequence which was reported in detail in this article.

2. Results and discussion

Before starting our synthetic study, computation was performed for the representative seven compounds **1a–g** for comparison of the basic information on frontier orbital energy

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levels and natural charges by using the Gaussian 09W software [4] using the B3LYP/6-311 + + G** level of theory. As described in Table 1, introduction of fluorine atoms to the propene framework was found to give a significant impact. For example, trifluorination at C³ like the case of **1a-e** allowed to significantly decrease the frontier orbital energy levels from the ones of the prototypical counterpart 1g, which should endow clear activation of these molecules toward a variety of nucleophiles. Moreover, the vinylic fluorine atom affected the electronic circumstance around the carbon-carbon double bond on the basis of the so-called $p-\pi$ repulsive interaction [5], rendering the carbon C² possessing this unique atom electropositive (1a and f). The same trend albeit weakly was noticed for the compound **1e** with a methoxy group at the C² position, while bromine in the same halogen family did not indicate such a special feature at all (see, 1c). Combination of these two characteristic information led us to strong anticipation that anionic species would preferentially react with **1a** at the C² site in spite of the already reported $S_N 2'$ type reactions of appropriate nucleophiles to **1b-d** [6,7].

First of all, we have searched adequate types of nucleophiles using such representative reagents as benzyl alcohol, benzylamine, thiophenol, diethyl malonate, and phenol (Entries 1–5 in Table 2). Thus, a solution containing Nu⁻ species generated by simple mixing of nucleophiles (NuH) and bases (1.1 equiv to NuH) in a solvent indicated was transferred to a pressure tight reactor where 1.2 equiv of **1a** was introduced. After 0.5 h reaction at room temperature, it was found out that benzyl alcohol was the only one

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 at its C² position by the reaction of a variety of alkoxides, forming CF₃-containing vinyl ethers in excellent yields.

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2,3,3,3-Tetrafluoroprop-1-ene, known as the environmentally benign fluorinated olefin recently

employed for the car air-conditioning system, was proved to follow the addition-elimination sequence

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Table 1

Representative physical properties of prop-1-enes^a.

$\begin{array}{c} X_3C^3\\ C^2 \equiv C^1\\ Y\\ 1a\ X=Y=F\\ 1b\ X=F,\ Y=H\\ 1b\ X=F,\ Y=Br\\ 1c\ X=F,\ Y=Br\\ 1d\ X=F,\ Y=Me_2PhSi\\ \end{array}$

		Energy level (eV)		Natural charge		
х	Y	НОМО	LUMO	C ¹	C ²	C ³
F	F (1a)	-8.524	-1.324	-0.408	0.318	1.017
F	Н (1b)	-8.661	-1.302	-0.306	-0.287	1.041
F	Br (1c)	-7.908	-1.613	-0.334	-0.210	1.038
F	Me ₂ PhSi (1d)	-7.266	-1.211	-0.285	-0.535	1.054
F	MeO (1e)	-7.333	-0.616	-0.473	0.240	1.043
Н	F (1f)	-7.218	-0.269	-0.480	0.423	-0.639
Н	H (1g)	-7.154	-0.128	-0.391	-0.167	-0.610

^a Computation was carried out by the Gaussian 09W (rev. D.01) software with the B3LYP/6-311++G** level of theory. Natural charge was obtained by the NBO analysis.

Table 2

Investigation of reaction conditions.

NIII I	Baso So	olvent,	CH ₂ =CF(C	F ₃)	CF ₃			
inuir +	0 °C, 0.5 h		Solvent, Temp., Time		Nu [·]			
					2			
Entry	NuH	(Equiv) ^a	Base	(Equiv) ^a	Solvent	Temp. (°C)	Time (h)	Yield ^b (%)
1	PhCH ₂ OH	(0.83)	NaH	(0.92)	THF	rt	0.5	6
2	PhCH ₂ NH	l ₂ (0.83)	n-BuLi	(0.92)	THF	rt	0.5	_c
3	PhSH	(0.83)	NaH	(0.92)	THF	rt	0.5	_c
4	CH ₂ (CO ₂ H	(0.83)	NaH	(0.92)	THF	rt	0.5	_c
5	PhOH	(0.83)	NaH	(0.92)	THF	rt	0.5	_c
6	PhCH ₂ OH	(0.83)	NaH	(0.92)	THF	rt	3	[6]
7	PhCH ₂ OH	(0.83)	NaH	(0.92)	THF	60	2	52
8	PhCH ₂ OH	(0.83)	NaH	(0.92)	DMF	rt	2	56
9	PhCH ₂ OH	(0.83)	NaH	(0.92)	DMF	rt	Overnight	62
10	PhCH ₂ OH	(0.83)	NaH	(0.92)	DMF	60	2	59
11	PhCH ₂ OH	(0.83)	NaH	(0.92)	DMF	100	2	60
12	PhCH ₂ OH	(0.83)	NaH	(0.92)	DMSO	60	2	60
13	PhCH ₂ OH	(1.5)	NaH	(1.65)	DMF	rt	2	85
14	PhCH ₂ OH	(2)	NaH	(2.2)	DMF	rt	2	[99]
15	PhCH ₂ OH	(3)	NaH	(3.3)	DMF	rt	2	98

^a Based on the amount of **1a** (1.0 equiv). Yields were calculated on the basis of NuH (Entries 1–12) and **1a** (Entries 13–15).

^b Yields were determined by ¹⁹F NMR using PhCF₃ as an internal standard, and in the brackets were shown the isolated yields. Yields were calculated on the base of the amount of NuH (Entries 1–12) or **1a** (Entries 13–15).

^c No reaction was observed.

example which actually experienced the addition–elimination type substitution at the C² site of 2,3,3,3-tetrafluoroprop-1-ene **1a** in spite of a rather low yield. MeMgBr and *n*-BuLi were employed as a base instead of NaH in Entry 1, but the resultant metal alkoxides did not work properly (not shown in the Table). Although extension of the reaction period did not give any fruitful result (Entries 6 vs 1), increase of the temperature to 60 °C affected the reaction significantly to produce the desired product **2a** in 52% yield (Entry 7).

The same process under various conditions (solvents, temperature, and time)clarified that irrespective of temperature and time, constant formation of approximately 60% yield of **2a** was observed by employment of either DMF or DMSO as a solvent (Entries 8–12). For obtaining better results, quantity of a nucleophile was increased from 0.83 equiv to 3 equiv (Entries 8 and 13–15), and eventually, the condition shown in Entry 14 was proved to be the best among tested, realizing almost quantitative construction of the desired addition–elimination product **2a**.

Successful determination of the reaction conditions as above allowed us to employ a variety of alcohols for clarification of scope and limitation of the present process whose results were collected in Table 3. Like the case of benzyl alcohol, 1- and 2-phenylethanols, and 3-phenylprop-2-en-1-ol (cinnamyl alcohol) behaved in a similar manner to furnish the corresponding products in more than 80% yields in every instance. Interesting to note is the case of Entry 4 whose product **2d** with the allyl vinyl ether structure applicable for Claisen rearrangement was successfully isolated because of occurrence of this addition–elimination process only at room

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Table 3

Reaction of **1a** with a variety of alkoxides^a.

	NaH, Solvent,	Solvent, rt, 2 h OR				
ROH -	0 °C, 0.5 h					
			2			
Entry	R	(Equiv) ^b	Solvent	Product	Isolated yield (%)	
1	PhCH ₂ -	(2.0)	DMF	2a	99	
2	PhCH(CH ₃)-	(2.0)	DMF	2b	81	
3	PhCH ₂ CH ₂ -	(2.0)	DMF	2c	87	
4	PhCH=CHCH ₂ -	(2.0)	DMF	2d	81	
5	4-CH ₃ O-C ₆ H ₄ -CH ₂ -	(2.0)	DMF	2e	98	
6	$4-H_3C-C_6H_4-CH_2-$	(2.0)	DMF	2f	99	
7	$4-Br-C_{6}H_{4}-CH_{2}-$	(2.0)	DMF	2g	38	
8	$4-O_2N-C_6H_4-CH_2-$	(2.0)	DMF	No reaction		
9	$n - C_6 H_{13} -$	(3.0)	THF:DMF=3:1	2h	36	(Quant) ^c
10	c-C ₆ H ₁₁ -	(3.0)	THF:DMF=3:1	2i	44	(87) ^c
11	4-t-Bu-c-C ₆ H ₁₀ -	(3.0)	THF:DMF=3:1	2j	60	(92) ^c
12	2-HOH ₂ C-C ₆ H ₄ -CH ₂ -	(1.0)	DMF	2k ^d	89	
13	2-HOH ₂ C-C ₆ H ₄ -CH ₂ -	(0.25) ^e	DMF	21 ^f	91	
14	4-HOH ₂ C-C ₆ H ₄ -CH ₂ -	(1.0)	DMF	2m ^g	42	[48] ^h
15	$4-HOH_2C-C_6H_4-CH_2-$	(0.25) ^e	DMF	2m ^g	74	[17] ^h

^a 1.1 equiv of NaH to ROH was employed unless otherwise noted.

^b Equivalent was calculated on the basis of the amount of **1a**.

^c The yields shown in the parenthesis were determined by ¹⁹F NMR.

^d Product **2k** was obtained as the result of selective reaction at the only one of the two OH groups of the substrate.

4.4 equiv of NaH to ROH (2.2 equiv/OH) was employed and yields were calculated on the base of the amount of alcohols.

^f Product **2I** was obtained as the result of selective reaction at the both OH groups of the substrate.

^g Product **2m** was obtained as the result of selective reaction at the both OH groups of the substrate.

^h In the bracket was shown the recovery of $1,4-C_6H_4(CH_2OH)_2$.

temperature. Attachment of a strong electron-withdrawing CF_3 moiety would exceedingly improve the stability of **2d** with the inherently electron-rich vinyl ether part, which rendered chromatographic isolation possible.

p-Substituted benzyl alcohols with electron-donating (Entries 5 and 6) as well as -withdrawing groups (Entries 7 and 8) were tested in this transformation. Almost quantitative conversion was noticed for alcohols with methoxy and methyl groups at the para position, while only 38% yield was attained by 4-bromobenzyl alcohol and the strongly electron-withdrawing 4-nitro substituent completely inhibited the desired reaction which was apparently due to low nucleophilicity of the resultant electron-deficient alkoxide. n- and c-Hexanols were proved to similarly affect the present process with recording excellent yields at the stage of completion of the reaction, while ready loss of products was noticed during workup and chromatographic purification processes due to their relatively high volatility, and close boiling points of products and the excess substrate alcohols rendered their separation by distillation difficult (Entries 9 and 10). This problem was slightly improved by employment of tert-Bu-possessing cyclohexanol with higher boiling point (Entry 11). In these cases, the mixed solvent system of THF:DMF = 3:1 was required because the corresponding alkoxides were insoluble in DMF while this solvent albeit in a small portion was important for attainment of better chemical yields.

Interesting observation was encountered in the case of benzenedimethanols as substrates. Thus, as our expectation, mono- and disubstitution products **2k** and **1** were selectively prepared in excellent yields just by control of the amount of 1,2-benzenedimethanol added, while this was not the case for the corresponding 1,4-dimethanol, leading to formation of disubstituted product **2m** irrespective of the equivalent of the nucleophile. The reason on this clear difference was not clear at present.

 CF_3 -containing vinyl ethers **2** thus obtained were found to possess enough reactivity toward such an electrophile as *N*-bromosuccinimide (NBS), affording the addition products **3a**

or **b** in high yields when the reactions were conducted under reflux in methanol or ethanol, respectively (Scheme 1). These products can be recognized as the acetals from 1-bromo-3,3,3-trifluoroacetone which were, different from the corresponding nonfluorinated counterparts, not easily accessible from the parent ketone. Thus, in spite of ready transformation to the corresponding hemiacetals by attack of an alcohol molecule to the activated carbonyl carbon by the strongly electron-withdrawing CF_3 group, this unique electronic effect significantly retards the elimination of an OH group under the usual acidic conditions. Actually, brominated acetals **3** were unprecedented thus far [8].

Another utilization of the addition–elimination product from **1a** was exemplified by **2d** which, as reported previously [9,10], experienced facile [3,3] sigmatropic rearrangement. The desired conversion proceeded just by stirring **2d** in toluene at room temperature, leading to formation of the ketone **4** in 61% isolated yield (Scheme 2).



Scheme 1. Conversion of 2 to bromotrifluoroacetone acetals.



Scheme 2. Claisen rearrangement of 2d.

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3. Conclusion

As shown above, we have clarified the unique reactivity of 2,3,3,3-tetrafluoroprop-1-ene **1a** toward nucleophiles, and found out that this fluorinated olefin **1a** smoothly and regiospecifically reacted with alkoxides to furnish the corresponding substitution products **2** as a result of addition–elimination sequence at the 2 position. **2** was also proved to experience bromonium ion addition in an alcoholic solvent, leading to successful formation of hitherto unknown acetals which is difficult to be accessible from the parent 1-bromo-3,3,3-trifluoroacetone due to the electroninc effect of the CF₃ group.

4. Experimental

4.1. General

All reactions were carried out under an argon atmosphere in dried glassware with magnetic stirring. Anhydrous THF and CH₂Cl₂ were purchased and were used without further purification. DMF was used after distillation in the presence of NaH. Spherical neutral silica gel (63–210 µm) was employed for column chromatography. ¹H (300.40 MHz), ¹³C (75.45 Hz), and ¹⁹F (282.65 Hz) NMR spectra were recorded in CDCl₃ and chemical shifts were recorded in parts per million (ppm), downfield from internal tetramethylsilane (Me₄Si: δ 0.00, for ¹H and ¹³C) or hexafluorobenzene (C₆F₆: δ -163.00 for ¹⁹F). Data were tabulated in the following order: number of protons, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; b, broad peak), coupling constants in Hertz. Infrared (IR) spectra were reported in wave numbers (cm^{-1}) . High resolution mass spectra were taken on a JEOL JMS-700 MS spectrometer and reported in wave numbers (cm⁻¹). Elemental analyses were conducted on a PerkinElmer2400 Series II CHNS/O System.

4.2. General procedure for the preparation of 2

4.2.1. 2-(Benzyloxy)-3,3,3-trifluoroprop-1-ene (2a)

To a two-necked flask containing 0.576 g of NaH (55% in paraffin, 13.2 mmol) in 15 mL of DMF under an argon atmosphere at 0 °C was slowly added 1.24 mL of benzyl alcohol (12.0 mmol). After 30 min stirring at this temperature, the resultant alkoxide solution was transferred to a pressure tight reactor with 50 mL capacity where 2,3,3,3-tetrafluoroprop-1-ene (HFO-1234yf, 1a) was introduced at room temperature so as to set the inside pressure as 0.3 MPa after evacuation at -100 °C. This method allowed to add approximately 6 mmol of 1a. After stirring for 2 h at room temperature, the crude reaction mixture was poured into a saturated aqueous solution of NH₄Cl (20 mL) and acidified to ca. pH = 6 by 1 M aqueous HCl, and the resultant solution was extracted three times with Et₂O. The combined ethereal layer was dried over anhydrous Na₂SO₄, and removal of the desiccant by filtration and concentration furnished a crude material, which was chromatographed on silica gel using a solution of hexane:Et₂O = 10:1 as an eluent to afford 1.210 g (5.99 mmol) of 2ain quantitative yield. Rf = 0.63 (hexane:AcOEt = 3:1). ¹H NMR δ 4.51 (1*H*, qd, *J* = 1.8, 3.9 Hz), 4.61 (1*H*, d, *J* = 4.2 Hz), 4.89 (2*H*, s), 7.25–7.37 (5H, m). ¹³C NMR δ 70.4, 88.2 (q, J = 3.6 Hz), 119.8 (q, J = 272.9 Hz), 127.3, 127.8, 128.6, 138.0, 150.0 (q, J = 34.5 Hz). ¹⁹F NMR δ –73.78 (s). IR (neat) ν 3067, 3034, 2927, 1658, 1348, 1193, 1160, 1026 cm⁻¹. Anal. Calcd for $C_{10}H_9F_3O$: C, 59.41; H, 4.49. Found: C, 59.44; H, 4.44.

4.2.2. 3,3,3-Trifluoro-2-[(1-phenylethyl)oxy]prop-1-ene (2b)

1.466 g (12.0 mmol) of 1-phenylethanol was employed instead of benzyl alcohol, and the same procedure afforded 1.051 g

(4.86 mmol) of **2b** as a yellow oil in 81% yield. Rf = 0.60 (hexane:AcOEt = 3:1). ¹H NMR δ 1.59 (3*H*, d, *J* = 6.0 Hz), 4.24 (1*H*, qd, *J* = 1.9, 3.9 Hz), 4.74 (1*H*, d, *J* = 4.2 Hz), 5.08 (1*H*, q, *J* = 6.5 Hz), 7.25–7.39 (5*H*, m). ¹³C NMR δ 23.9, 76.9, 89.6 (q, *J* = 3.7 Hz), 123.4 (q, *J* = 267.7 Hz), 125.8, 127.8, 128.7, 141.4, 148.6 (q, *J* = 34.1 Hz). ¹⁹F NMR δ –74.12 (s). IR (neat) ν 3067, 3033, 2935, 1656, 1604, 1385, 1348, 1284, 1161, 1029 cm⁻¹. Anal. Calcd for C₁₁H₁₁F₃O: C, 61.11; H, 5.13. Found: C, 60.66; H, 5.11.

4.2.3. 3,3,3-Trifluoro-2-[(2-phenylethyl)oxy]prop-1-ene (2c)

1.466 g (12.0 mmol) of 2-phenylethanol was employed instead of benzyl alcohol, and the same procedure afforded 1.129 g (5.22 mmol) of **2c** as a yellow oil in 87% yield. Rf = 0.71 (hexane:AcOEt = 3:1). ¹H NMR δ 3.06 (2*H*, t, *J* = 7.1 Hz), 3.97 (2*H*, t, *J* = 7.1 Hz), 4.39 (1*H*, qd, *J* = 1.9, 4.2 Hz), 4.79 (1*H*, d, *J* = 4.2 Hz), 7.21–7.35 (5*H*, m). ¹³C NMR δ 36.0, 69.3, 87.1 (q, *J* = 3.5 Hz), 119.7 (q, *J* = 272.9 Hz), 121.2, 128.3, 128.4, 137.4, 150.2 (q, *J* = 34.4 Hz). ¹⁹F NMR δ -73.78 (s). IR (neat) ν 3066, 3032, 2928, 2856, 1657, 1604, 1349, 1297, 1161, 1030 cm⁻¹. HRMS-FAB (*m*/*z*): [M]⁺ calcd. for C₁₁H₁₁F₃O, 216.0762; found, 216.0726.

4.2.4. 3,3,3-Trifluoro-2-[(*E*)-(3-phenylprop-2-en-1-yl)oxy]prop-1ene (**2d**) [9]

1.55 mL (12.0 mmol) of (*E*)-3-phenylprop-2-en-1-ol was employed instead of benzyl alcohol, and the same procedure afforded 1.102 g (4.83 mmol) of **2d** as a yellow oil in 81% yield. Rf = 0.57 (hexane:AcOEt = 3:1). ¹H NMR δ 4.50 (1H, qd, *J* = 1.8, 3.6 Hz), 4.52 (2H, dd, *J* = 1.4, 5.9 Hz), 4.87 (1H, d, *J* = 4.2 Hz), 6.32 (1H, td, *J* = 5.9, 16.2 Hz), 6.69 (1H, brd, *J* = 15.9 Hz), 7.25–7.37 (5H, m). ¹³C NMR δ 69.2, 87.9 (q, *J* = 3.7 Hz), 119.8 (q, *J* = 272.0 Hz), 126.6, 127.1, 127.3, 127.4, 128.6, 133.9, 150.0 (q, *J* = 34.5 Hz). ¹⁹F NMR δ –73.77 (s).

4.2.5. 3,3,3-Trifluoro-2-[(4-methoxybenzyl)oxy]prop-1-ene (2e)

1.658 g (12.0 mmol) of 4-methoxybenzyl alcohol was employed instead of benzyl alcohol, and the same procedure afforded 1.393 g (6.00 mmol) of **2e** as a colorless oil in quantitative yield. Rf = 0.71 (Hexane:AcOEt = 3:1). ¹H NMR δ 3.81 (3*H*, s), 4.50 (1*H*, qd, *J* = 1.9, 3.9 Hz), 4.81 (2*H*, s), 4.86 (1*H*, d, *J* = 3.9 Hz), 6.89–6.93 (2*H*, m), 7.27–7.31 (2*H*, m). ¹³C NMR δ 55.2, 70.3, 88.0 (q, *J* = 3.7 Hz), 114.0, 119.8 (q, *J* = 272.7 Hz), 127.3, 129.2, 150.1 (q, *J* = 34.5 Hz), 159.7. ¹⁹F NMR δ –73.73 (s). IR (neat) ν 3007, 2939, 1654, 1615, 1587, 1396, 1303, 1029 cm⁻¹. HRMS (ESI–, *m/z*): [M–H]⁻ calcd for C₁₁H₁₀F₃O₂, 231.0631; Found, 231.0636.

4.2.6. 3,3,3-Trifluoro-2-[(4-methylbenzyl)oxy]prop-1-ene (2f)

1.466 g (12.0 mmol) of 4-methylbenzyl alcohol was employed instead of benzyl alcohol, and the same procedure afforded 1.277 g (5.91 mmol) of **2f** as a colorless oil in 99% yield. Rf = 0.74 (hexane:AcOEt = 3:1). ¹H NMR δ 2.36 (3*H*, s), 4.51 (1*H*, qd, J = 1.8, 4.2 Hz), 4.84 (2*H*, s), 4.85 (1*H*, d, J = 3.9 Hz), 7.17–7.25 (4*H*, m). ¹³C NMR δ 21.1, 70.5, 88.1 (q, J = 3.5 Hz), 119.8 (q, J = 272.9 Hz), 127.5, 129.3, 132.2, 138.2, 150.2 (q, J = 34.5 Hz). ¹⁹F NMR δ –73.70 (s). IR (neat) ν 3030, 2926, 2881, 1656, 1519, 1395, 1019 cm⁻¹. HRMS (ESI–, *m/z*): [M–H]⁻ calcd for C₁₁H₁₀F₃O, 215.0682; Found, 215.0686.

4.2.7. 2-[(4-Bromobenzyl)oxy]-3,3,3-trifluoroprop-1-ene (2g)

0.748 g (4.0 mmol) of 4-bromobenzyl alcohol and 0.192 g (55%, 4.4 mmol) of NaH were employed for the reaction with HFO-1234yf (0.1 MPa, ca. 2 mmol), and the same procedure afforded 0.213 g (0.75 mmol) of **2g** as a colorless oil in 38% yield. Rf = 0.57 (hexane:AcOEt = 3:1). ¹H NMR δ 4.45 (1*H*, qd, *J* = 2.0, 4.4 Hz), 4.84 (2*H*, s), 4.89 (1*H*, d, *J* = 3.6 Hz), 7.23–7.25 (2*H*, m), 7.49–7.53 (2*H*, m). ¹³C NMR δ 69.1, 88.4 (q, *J* = 3.7 Hz), 119.7 (q, *J* = 272.7 Hz), 122.2, 128.8, 131.7, 134.2, 149.8 (q, *J* = 34.7 Hz). ¹⁹F NMR δ –73.28

(s). IR (neat) ν 3031, 2933, 1658, 1596, 1464, 1396, 1304, 1158, 1072 cm $^{-1}$. Anal. Calcd for $C_{10}H_8BrF_3O$: C, 42.73; H, 2.87. Found: C, 43.05; H, 3.07.

4.2.8. 2-(Hexyloxy)-3,3,3-trifluoroprop-1-ene (2h)

1.50 mL (12.0 mmol) of *n*-hexanol in a mixed solvent of DMF (15 mL) and THF (5 mL) was reacted with HFO-1234yf under 0.2 MPa pressure (*ca.* 4 mmol), and the same procedure afforded 0.353 g (1.80 mmol) of **2 h** as a colorless oil in 45% yield. Rf = 0.89 (hexane:AcOEt = 3:1). ¹H NMR δ 0.90–1.74 (11H, m), 3.78 (2H, t, *J* = 6.6 Hz), 4.51 (1H, qd, *J* = 1.8, 4.2 Hz), 4.76 (1H, d, *J* = 3.6 Hz). ¹³C NMR δ 13.9, 22.5, 25.5, 28.4, 31.4, 68.8, 86.7 (q, *J* = 3.5 Hz), 119.9 (q, *J* = 273.3 Hz), 150.6 (q, *J* = 34.3 Hz). ¹⁹F NMR δ –74.10 (s). IR (neat) ν 2934, 2861, 2357, 1654, 1468, 1396, 1348, 1265, 1163 cm⁻¹. HRMS (ESI+, *m/z*): [M + H]⁺ calcd for C₉H₁₆F₃O, 197.1153; Found, 197.0787.

4.2.9. 2-(Cyclohexyloxy)-3,3,3-trifluoroprop-1-ene (2i)

1.28 mL (12.0 mmol) of *c*-hexanol was used instead of *n*-hexanol in 4.2.8, and the same procedure afforded 0.344 g (1.77 mmol) of **2i** as a colorless oil in 44% yield. Rf = 0.91 (hexane:AcOEt = 3:1). ¹H NMR δ 1.34–1.45 (6H, m), 1.76–1.91 (4H, m), 4.05 (1H, m), 4.51 (1H, qd, *J* = 1.7, 3.7 Hz), 4.76 (1H, d, *J* = 3.6 Hz). ¹³C NMR δ 23.3, 25.5, 30.6, 76.2, 87.4 (q, *J* = 3.7 Hz), 120.2 (q, *J* = 253.5 Hz), 148.8 (q, *J* = 33.9 Hz). ¹⁹F NMR δ –74.21 (s). IR (neat) ν 2941, 2861, 2367, 1649, 1451, 1387, 1344, 1265, 1160, 1045 cm⁻¹. HRMS (ESI+, *m/z*): [M + H]⁺ calcd for C₉H₁₄F₃O, 195.0997; Found, 195.0993.

4.2.10. 2-[(4-tert-Butylcyclohexyl)oxy]-3,3,3-trifluoroprop-1-ene (**2j**)

1.875 g (12.0 mmol) of 4-*tert*-butylcyclohexanol was used instead of *n*-hexanol in 4.2.8, and the same procedure afforded 0.599 g (2.39 mmol) of **2j** as a colorless oil in 60% yield. Rf = 0.94 (hexane:AcOEt = 3:1). ¹H NMR δ 0.86 (9H, s), 1.06–1.37 (5H, m), 1.85–2.15 (4H, m), 3.98 (1H, m), 4.41 (1H, qd, *J* = 1.7, 3.8 Hz), 4.81 (1H, d, *J* = 3.6 Hz). ¹³C NMR δ 21.2, 25.4, 27.6, 31.3, 47.5, 72.5, 87.4 (q, *J* = 3.3 Hz), 120.0 (q, *J* = 274.2 Hz), 149.0 (q, *J* = 33.7 Hz). ¹⁹F NMR δ –73.92 (s). IR (neat) ν 2950, 2868, 2357, 1650, 1479, 1389, 1350, 1284, 1049, 1028 cm⁻¹. Anal. Calcd for C₁₃H₂₁F₃O: C, 62.38; H, 8.46. Found: C, 62.29; H, 8.35.

4.2.11. 2-[(3,3,3-Trifluoroprop-1-en-2-yl)oxymethyl]benzyl alcohol (**2k**)

0.276 g (2.0 mmol) of 1,2-benzenedimethanol and 0.096 g (55%, 2.2 mmol) of NaH were employed for the reaction with HFO-1234yf (0.1 MPa, *ca.* 2 mmol), and the same procedure afforded 0.413 g (1.78 mmol) of **2k** as a colorless oil in 89% yield. Rf = 0.30 (hexane:AcOEt = 3:1). ¹H NMR δ 1.88 (1*H*, br), 4.62 (1*H*, qd, *J* = 1.9, 3.8 Hz), 4.73 (2*H*, s), 4.92 (1*H*, d, *J* = 3.9 Hz), 4.99 (2*H*, s), 7.32–7.46 (4*H*, m). ¹³C NMR δ 62.7, 68.7, 88.4 (q, *J* = 3.7 Hz), 119.8 (q, *J* = 273.0 Hz), 128.0, 128.6, 128.9, 129.0, 133.0, 139.1, 149.9 (q, *J* = 35.1 Hz). ¹⁹F NMR δ –73.52 (s). IR (neat) ν 3339, 3073, 3031, 2930, 1608, 1455, 1291, 1161, 1029 cm⁻¹. Anal. Calcd for C₁₁H₁₁F₃O₂: C, 56.90; H, 4.77. Found: C, 56.98; H, 4.95.

4.2.12. 1,2-Bis[(3,3,3-trifluoroprop-1-en-2-yl)oxymethyl]benzene (**2l**)

0.207 g (1.5 mmol) of 1,2-benzenedimethanol and 0.288 g (55%, 6.6 mmol) of NaH were employed, and the same procedure afforded 0.447 g (1.37 mmol) of **2l** as a colorless oil in 91% yield. Rf = 0.66 (hexane:AcOEt = 3:1). ¹H NMR δ 4.51 (2H, qd, J = 1.8, 3.9 Hz), 4.61 (2H, d, J = 4.2 Hz), 4.89 (4H, s), 7.25–7.37 (4H, m). ¹³C NMR δ 68.7, 88.4 (q, J = 3.5 Hz), 119.8 (q, J = 272.9 Hz), 129.0, 129.1, 133.1, 149.9 (q, J = 34.7 Hz). ¹⁹F NMR δ –73.64 (s). IR (neat) ν 3073,

3035, 2937, 1659, 1347, 1196, 1157, 1022 cm $^{-1}.$ Anal. Calcd for $C_{14}H_{12}F_6O_2:$ C, 51.54; H, 3.71. Found: C, 51.59; H, 3.79.

4.2.13. 1,4-Bis[(3,3,3-trifluoroprop-1-en-2-yl)oxymethyl]benzene (**2m**)

0.207 g (1.5 mmol) of 1,2-benzenedimethanol and 0.288 g (55%, 6.6 mmol) of NaH were employed, and the same procedure afforded 0.362 g (1.11 mmol) of **2m** as a colorless oil in 74% yield. Rf = 0.54 (hexane:AcOEt = 3:1). mp. 52.4 °C. ¹H NMR δ 4.51 (2*H*, qd, *J* = 1.8, 4.2 Hz), 4.89 (2*H*, d, *J* = 4.2 Hz), 4.90 (4*H*, s), 7.26–7.39 (4*H*, m). ¹³C NMR δ 70.1, 88.3 (q, *J* = 3.5 Hz), 119.8 (q, *J* = 272.9 Hz), 127.6, 135.4, 150.0 (q, *J* = 34.7 Hz).¹⁹ F NMR δ –73.72 (s). IR (KBr) ν 3074, 3041, 2933, 1659, 1347, 1196, 1157, 1022 cm⁻¹. Anal. Calcd for C₁₄H₁₂F₆O₂: C, 51.54; H, 3.71. Found: C, 51.65; H, 3.60.

4.3. General procedure for the preparation of **3a**

4.3.1. 2-(Benzyloxy)-3-bromo-1,1,1-trifluoro-2-methoxypropane (**3a**)

A methanol solution (18 mL) containing N-bromosuccinimide (0.392 g, 2.20 mmol) and 2-benzyloxy-3,3,3-trifluoroprop-1-ene (0.202 g, 1.00 mmol) was refluxed for 3 h under an argon atmosphere. After evaporation of the solvent, the resultant white solid was successively washed with H₂O and Et₂O, and the obtained liquid was extracted with Et₂O three times. The combined ethereal layer was dried over anhydrous Na₂SO₄ and removal of the desiccant by filtration and concentration furnished a crude material, which was chromatographed on silica gel using a solution of hexane:Et₂O = 10:1 as an eluent to afford 0.274 g (0.878 mmol) of **3a** in 88% vield. Rf = 0.71 (hexane:AcOEt = 3:1). ¹H NMR δ 3.50 (3*H*, s), 3.63 (2*H*, s), 4.68 (1*H*, d, *J* = 11.3 Hz), 4.79 (1*H*, d, *J* = 11.1 Hz), 7.31–7.39 (5*H*, m). ¹³C NMR δ 27.8, 51.2 (q, *J* = 1.3 Hz), 65.3 (q, *J* = 1.6 Hz), 97.1 (q, *J* = 29.8 Hz), 120.4 (q, *J* = 291.8 Hz), 127.4, 127.6, 128.5, 136.6. ¹⁹F NMR δ –77.08 (s). IR (neat) ν 3092, 3066, 3034, 2985, 2954, 1608, 1498, 1345, 1029 cm⁻¹. Anal. Calcd for C₁₁H₁₂BrF₃O: C, 42.20; H, 3.86. Found: C, 42.49; H, 3.90.

4.3.2. 2-Benzyloxy-3-bromo-2-ethoxy-1,1,1-trifluoropropane (3b)

By using the same amount of ethanol instead of methanol, 0.2807 g (0.858 mmol) of **3b** was obtained in 86% yield. Rf = 0.74 (hexane:AcOEt = 3:1). ¹H NMR δ 1.28 (3*H*, t, *J* = 7.1 Hz), 3.64 (2*H*, s), 3.73 (1*H*, m), 3.82 (1*H*, qd, *J* = 7.2, 9.3 Hz), 4.68 (1*H*, d, *J* = 11.4 Hz), 4.80 (1*H*, d, *J* = 11.4 Hz), 7.29–7.38 (5*H*, m). ¹³C NMR δ 14.7, 27.3, 59.3 (q, *J* = 1.4 Hz), 65.0 (q, *J* = 1.6 Hz), 96.9 (q, *J* = 28.3 Hz), 120.4 (q, *J* = 292.2 Hz), 126.7, 127.6, 128.6, 136.7. ¹⁹F NMR δ -77.34 (s). IR (neat) ν 3066, 3034, 2983, 2935, 2904, 1610, 1498, 1344, 1029 cm⁻¹. HRMS (ESI+, *m*/*z*): [M + Na]⁺ calcd for C₁₂H₁₄BrF₃O₂Na, 349.0027; Found, 349.0047.

4.4. Preparation of 1,1,1-trifluoro-4-phenylhex-5-en-2-one (4) [10]

0.114 g (0.50 mmol) of 3,3,3-trifluoro-2-[(*E*)-(3-phenylprop-2-en-1-yl)oxy]prop-1-ene in CH₂Cl₂ (5 mL) was added at 0 °C under an argon atmosphere 0.12 mL (1.0 mmol) of BF₃·OEt₂ and stirring was continued for 30 min at this temperature. After addition of H₂O (5 mL), extraction with CH₂Cl₂, drying with anhydrous Na₂SO₄, and concentration furnished a crude material, which was chromatographed on silica gel using a solution of hexane:A-cOEt = 8:1 as an eluent to afford 0.070 g (0.306 mmol) of **4a** in 61%yield. Rf = 0.62 (hexane:AcOEt = 3:1). ¹H NMR δ 3.11 (1*H*, dd, *J* = 6.6, 18.0 Hz), 3.20 (1*H*, dd, *J* = 7.5, 18.0 Hz), 4.01 (1*H*, q, *J* = 7.2 Hz), 5.07 (1*H*, td, *J* = 1.2, 17.1 Hz), 5.12 (1*H*, td, *J* = 1.2, 10.5 Hz), 5.96 (1*H*, ddd, *J* = 6.6, 10.2, 16.8 Hz), 7.25–7.37 (5*H*, m). ¹³C NMR δ 41.7, 43.1, 115.4 (q, *J* = 292.3 Hz), 115.5, 127.0, 127.4, 128.8, 139.1, 141.4, 189.4 (q, *J* = 35.2 Hz). ¹⁹F NMR δ -80.83 (s).

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