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An Effective Preparation of Sulfonyl- or Sulfinyl-Substituted Fluorinated Alkenes and their Stereoselective Addition–Elimination Reactions with Organocuprates

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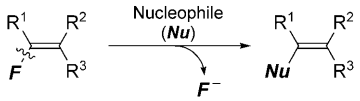
Abstract: Treatment of trifluorovinyl- or pentafluoropropen-1-yl sulfone or sulfoxide, which are easily prepared from commercially available 1,2-dibromofluoroalkanes, with various organocuprates affords substitution or β-reduction products in good to excellent yields through an addition–elimination reaction sequence.

Keywords: addition–elimination reaction · cuprates · dialkylzinc reagents · fluorinated alkenes · Grignard reagents

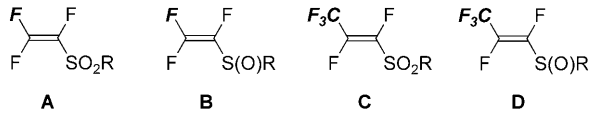
Introduction

Selective C–F bond-cleavage as well as C–F bond-forming reactions have become important transformations in organic chemistry.[1] Recently, new C–C bond-forming reactions involving C–F bond-cleavage have been reported by several groups.[2] Among the synthetic methods that involve C–F bond-cleavage reactions, the addition–elimination reaction of fluorinated alkenes is recognized as one of the most convenient and powerful procedures for the transformation of a C–F bond into other C–X bonds (X = C,[3] O,[4] S,[5] N,[6] and so forth; Scheme 1).



Scheme 1. C–F bond-cleavage during the addition–elimination reaction of fluorinated alkenes.

Fluorine-substituted α,β-unsaturated compounds are suitable substrates for the addition-elimination reaction. We recently reported that fluorinated alkenes that contain an ester group smoothly underwent the addition–elimination reaction, leading to β-substituted fluorinated alkenes in good yields.[3c,d,f] For this study, fluorine-substituted α,β-unsaturated sulfones or -sulfoxides, such as compounds **A**–**D** (Scheme 2) were chosen as substrates. They might be quite



Scheme 2. Fluorine-substituted α,β-unsaturated sulfones and sulfoxides (A–D).

useful and valuable building blocks for the synthesis of a variety of new organofluorine compounds, and applicable in the synthesis of various functional materials. So far, there have been few[7] (for compound **A**) or no published reports (for compounds **B**, **C**, and **D**) concerning their synthetic preparation.

Herein, we describe the convenient and simple preparation of trifluorovinyl compounds **A** and **B** (in three steps, starting from 1,2-dibromotetrafluoroethane) and pentafluoropropen-1-yl compounds **C** and **D** (in two steps starting from 1,2-dibromohexafluoropropane). In addition, we demonstrate the direct transformation of a C–F bond into a C–C bond through an addition–elimination process, by the reaction of trifluorovinyl compounds (**A**, **B**) with organo-

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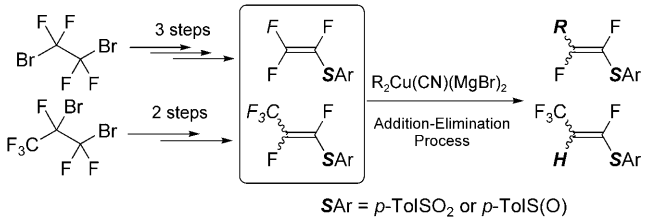
cuprates. We also show that the C–F bond at the β position to the sulfur-containing group of pentafluoropropen-1-yl compounds (**C**, **D**) can be selectively converted into a C–H bond by reaction with a number of organocuprate reagents (Scheme 3).

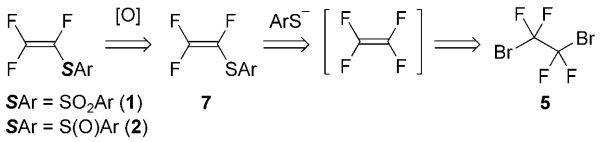


Scheme 3. Synthesis and addition-elimination reactions of polyfluorovinyl compounds.

Results and Discussion

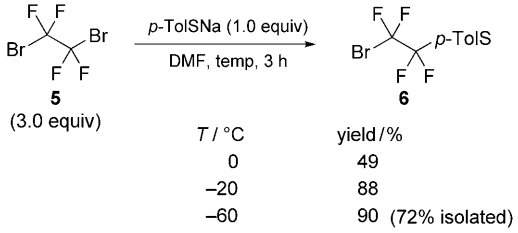
Preparation of Trifluorovinyl and Pentafluoropropen-1-yl Sulfone and Sulfoxide

As shown in Scheme 4, trifluorovinyl sulfone **1** and sulfoxide **2** could be obtained from the oxidation of trifluorovinyl sulfide **7**, which was prepared by an addition–elimination reaction of tetrafluoroethene with an arenethiolate. Tetrafluoroethene could be generated in situ from commercially available 1,2-dibromotetrafluoroethane **5**.[8]



Scheme 4. Retrosynthesis of **1** and **2**.

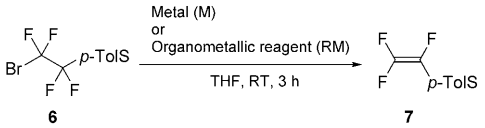
Initially, the generation of tetrafluoroethene from **5**, and the subsequent addition–elimination reaction with arenethiolate were examined. On treatment of **5** with sodium *para*-toluenethiolate in DMF at 0 °C for 3 hours, the desired trifluorovinyl sulfide **7** was not observed at all. Instead, the substitution product **6** was formed in 49 % yield.[9] By changing the reaction temperature from 0 °C to −20 °C or −60 °C, the yield of **6** was improved to 88 % and 90 % yield (72 % isolated), respectively (Scheme 5).



Scheme 5. Reaction of **5** with *para*-toluenethiolate.

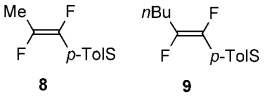
Subsequently, the reaction of **6** with various metals or organometallic reagents was examined in order to obtain the trifluorovinyl sulfide **7**. The results are shown in Table 1.

Table 1. Reductive Br–F elimination by treating with metal or organometallic reagent.



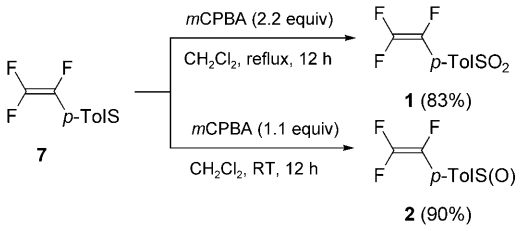
Entry	M/RM	Yield of **7** [%][a]
1	Zn	0
2	Mg	67
3	EtMgBr	62
4[b]	EtMgBr	87 (65)
5[c]	MeLi	0
6[d]	*n*BuLi	0

[a] Determined by ^{19}F NMR spectroscopy. The yield of isolated product is given in parentheses. [b] Carried out at 0 °C. [c] Product **8** (shown below) was obtained in 73 % yield. [d] Product **9** (shown below) was obtained in 73 % yield.



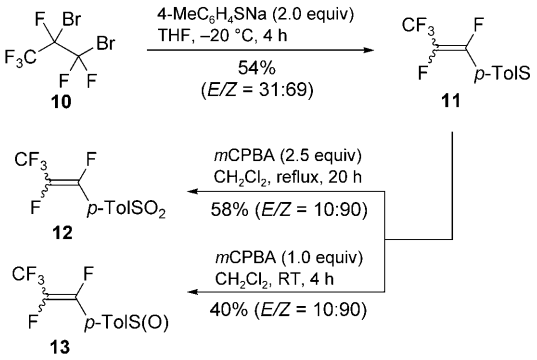
Thus, the treatment of **6** with zinc dust in THF at room temperature for 3 hours did not lead to **7** at all (Table 1, entry 1). On the contrary, the organomagnesium reagent, generated either by direct insertion of **6** with Mg or by Br/Mg exchange with EtMgBr, was found to immediately undergo Br–F elimination, to provide vinyl sulfide **7** in 67 % and 62 % yields, respectively (Table 1, entries 2 and 3). The best result (87 % yield) was obtained by treating **6** with EtMgBr in THF at 0 °C for 3 hours. The reaction was attempted using MeLi or *n*BuLi, but the desired product **7** was not obtained in either case. Instead, the products from successive Br–F elimination/addition–elimination sequences (**8** and **9**) were each formed in 73 % yield (Table 1, entries 5 and 6).

Finally, the trifluorovinyl sulfide **7** was subjected to oxidation with 2.2 equivalents of *meta*-chloroperbenzoic acid (*m*CPBA) in CH_2Cl_2 at reflux for 12 hours, thus affording trifluorovinyl sulfone **1** in 83 % yield. When the oxidation reaction was carried out with 1.1 equivalents of *m*CPBA in CH_2Cl_2 at room temperature for 12 hours, trifluorovinyl sulfoxide **2** was isolated in 90 % yield (Scheme 6).



Scheme 6. Oxidation of **7** to trifluorovinyl sulfone (**1**) and trifluorovinyl sulfoxide (**2**).

Pentafluoropropen-1-yl sulfone (**12**) and sulfoxide (**13**) could also be prepared from 1,2-dibromohexafluoropropane (**10**) in a similar manner, as shown in Scheme 7. Thus, the



Scheme 7. Preparation of pentafluoropropen-1-yl sulfone (**12**) and sulfoxide (**13**) from 1,2-dibromohexafluoropropane (**10**).

treatment of **10** with 2.0 equivalents of sodium *para*-toluenethiolate in THF at −20 °C for 4 hours gave the fluorinated vinyl sulfide **11** in 54% yield as a mixture of *E* and *Z* isomers (*E*/*Z* = 31:69), formed from successive Br−F elimination/addition–elimination reactions. The vinyl sulfide **11** was oxidized with *m*CPBA (2.5 equiv) in CH_2Cl_2 at reflux for 20 hours into fluorinated vinyl sulfone **12** in 58% yield (*E*/*Z* = <10:90) (after isolation by column chromatography on silica gel). The pentafluoropropen-1-yl sulfoxide **13** was isolated in 40% yield (*E*/*Z* = <10:90) from the oxidation of **11** with 1.0 equivalent of *m*CPBA in CH_2Cl_2 at room temperature for 4 hours.

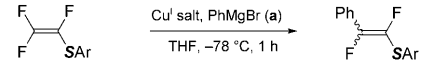
Reaction of Trifluorovinyl Sulfone (1) and Sulfoxide (2) with Organocuprates

With the fluorinated vinyl sulfone **1** or sulfoxide **2** in hand, we studied the reaction of **1** or **2** with organocopper reagents that were derived from Grignard reagents and copper(I) salts; the results are summarized in Table 2.

On treatment of **1** with 1.1 equivalents of PhMgBr (**a**) in the absence of a copper(I) salt in THF at −78 °C for 1 hour, the addition–elimination product **3a** was not obtained at all, and the starting sulfone **1** was recovered in 75% yield (Table 2, entry 1). Organocuprates prepared from CuBr or CuI were obviously not efficient for the addition–elimination reaction (Table 2, entries 2 and 3). Whilst the use of 1.1 equivalents of "lower-ordered" phenyl organocuprate CuCN/PhMgBr (**a**; 1:1) did not lead to a significant improvement (Table 2, entry 4), the "higher-ordered cyanocuprate"[10] CuCN/PhMgBr (1:2) participated well in the addition–elimination reaction, thus providing 2-phenyl-1,2-difluorovinyl sulfone **3a** in 58% yield (Table 2, entry 5). Importantly, high stereoselectivity was observed in the reaction (*E*/*Z* = 9:91). Optimization of the reaction conditions was performed, and the best result was obtained when **1** was reacted with 2.2 equivalents of organocuprate, prepared from 2.2 equivalents of CuCN and 4.4 equivalents of PhMgBr (**a**), in THF at −78 °C for 1 hour (isolated in 80% yield, *E*/*Z* = 2:98; Table 2, entry 6). Trifluorovinyl sulfoxide **2** was also subjected to the addition–elimination reaction with diphenylcyanocuprate, giving 2-phenyl-1,2-difluorovinyl sulfoxide **4a** in good yield with high stereoselectivity (>59% yield, *E*/*Z* = <19:81).

The addition–elimination reactions of **1** with 2.2 equivalents of organocuprates that were derived from various Grignard reagents, were then performed under the optimized reaction conditions (entry 6 in Table 2). The results are shown in Table 3.

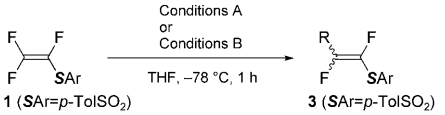
Table 2. Reaction of sulfone **1** or sulfoxide **2** with PhMgBr (**a**) in the presence of copper(I) salt.



Entry	Substrate	Cu^I [equiv]	PhMgBr [equiv]	Yield of **3a** or **4a** [%][a]	*E*/*Z*[a]	Recovered **1** or **2** [%][a]
1	**1**	none	1.1	0	–	75
2		CuBr (1.1)	2.2	0	–	73
3		CuI(1.1)	2.2	6	0:100	50
4		CuCN(1.1)	1.1	0	–	87
5		CuCN(1.1)	2.2	58	9:91	25
6		CuCN(2.2)	4.4	84 (80)	2:98	0
7	**2**	CuCN(1.1)	2.2	67 (50)	19:81	0
8		CuCN(2.2)	4.4	59	15:85	0

[a] Determined by ^{19}F NMR spectroscopy. The yield of isolated product is given in parentheses.

Table 3. Addition–elimination reaction of **1** or **2** with organocuprates derived from various Grignard reagents.



Entry	Substrate	R	Yield of **3** or **4** [%][c]	*E*/*Z*[c]
1	**1**[a]	Ph (**a**)	84 (80)	2:98
2		4-$MeOC_6H_4$ (**b**)	78 (69)	3:97
3		3-$MeOC_6H_4$ (**c**)	95 (89)	2:98
4		2-$MeOC_6H_4$ (**d**)	80 (61)	5:95
5		4-MeC_6H_4 (**e**)	94 (71)	3:97
6		4-$CF_3C_6H_4$ (**f**)	98 (95)	<1:>99
7		*n*Bu (**g**)	89 (88)	43:57
8		*s*Bu (**h**)	70 (58)	4:96
9		*c*-Hex (**i**)	85 (72)	14:86
10		β-Styryl (**j**)	78 (52)	78:22
11	**2**[b]	Ph (**a**)	67 (50)	12:88
12		4-MeC_6H_4 (**e**)	27	22:78
13		*n*Bu (**g**)	44	30:70

[a] Conditions A (entries 1–10): Organocuprates were prepared from 2.2 equiv of CuCN and 4.4 equiv of Grignard reagent. [b] Conditions B (entries 11–13): Organocuprates were prepared from 1.1 equiv of CuCN and 2.2 equiv of Grignard reagent. [c] Determined by ^{19}F NMR spectroscopy. The yield of isolated product is given in parentheses.

As shown in Table 3 (entries 2–6), various aryl Grignard reagents containing either an electron-donating or electron-withdrawing group participated well in the *Z*-selective addition–elimination reaction, thus leading to the products of type **3** in good yields (isolated in 69–95% yields) and high stereoselectivity (*E/Z* = <5:95). When alkyl Grignard reagents such as *n*-butyl- (**g**), *sec*-butyl- (**h**), and cyclohexylmagnesium bromide (**i**) were used, the addition–elimination reaction proceeded smoothly to provide the corresponding β-alkylated products **3g**, **3h**, and **3i** in 89%, 70%, and 85% yields, respectively (Table 3, entries 7–9). However, for the products **3g** and **3i**, the obtained stereoselectivity was low (*E/Z* = 43:57 and 14:86, respectively). The organocuprate derived from β-styrylmagnesium bromide (**j**) was also reactive, but afforded the opposite stereoselectivity (78%, *E/Z* = 78:22). In addition, the reactions of the trifluorovinyl sulfoxide **2** with an organocuprate generated from 4-methylphenyl- (**e**) or *n*-butylmagnesium bromide (**g**) were carried out under the conditions of entry 7 in Table 2. Both Grignard reagents **e** and **g** were efficient nucleophiles for the reaction, but the yield of the products **4**, as well as their stereoselectivity were low (27–44% yield, *E/Z* = <12:88).

Reaction of Pentafluoropropen-1-yl Sulfone (12) or Sulfoxide (13) with Organocuprates

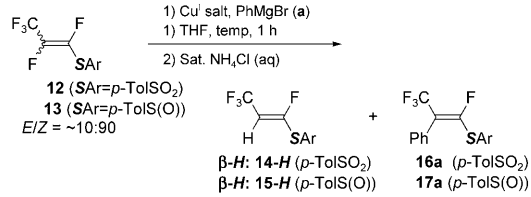
Next, our attention was directed toward the reaction of pentafluoropropen-1-yl sulfone **12** or sulfoxide **13** with various organocuprates. The results of the reactions of **12** or **13** with PhMgBr (**a**) in the presence of copper(I) salts are summarized in Table 4.

The treatment of sulfone **12** with 1.1 equivalent of PhMgBr (**a**) in the absence of a copper(I) salt in THF at −78 °C for 1 hour, followed by work-up (sat. NH_4Cl aq), did not lead to the addition–elimination product **16a**, and the reaction resulted in the quantitative recovery of the starting sulfone **12** (Table 4, entry 1). It was found that the molar ratio of copper(I) salt and Grignard reagent was crucial for the reaction outcome (Table 4, entries 2 and 3). The reaction of **12** with organocuprates derived from 1.1 equivalents of each of CuCN and PhMgBr (**a**) was sluggish, whilst in the presence of an organocuprate derived from 1.1 equivalents of CuCN and 2.2 equivalents of PhMgBr, the reaction proceeded efficiently to give the β-reduction product **14-*H*** in 70% yield after hydrolysis. The use of a higher temperature (−20 °C) did not improve the yield (Table 4, entry 4). When the reaction was performed using 2.2 equivalents of diphenylcyanocuprate in THF at −78 °C for 1 hour, **14-*H*** was obtained in the highest yield (88%). The use of additives (TMSCl or DMSO, 1.0 equiv) did not dramatically influence the reaction, and the formation of the addition–elimination product **16a** was observed in low yield (<20%; Table 4, entries 6 and 7).[11] Interestingly, the reaction in the presence of CuBr or CuI, instead of CuCN, led to the α-reduction product **18** as the major product in 56% or 31% yield, respectively (Table 4, entries 8 and 9). When sulfoxide **13** was used as the substrate, the corresponding addition–elimination product **17a** was produced preferentially, though in moderate yields (41–45%, entries 10 and 11).

Various sorts of Grignard reagent were applied to the reaction using the reaction conditions from Table 4, entry 5 (for **12**) and entry 11 (for **13**). The results are collected in Table 5.

The organocuprates derived from 4-methoxyphenyl- (**b**) or 3-methoxyphenylmagnesium bromide (**c**) also participated successfully in this reaction, affording the β-reduction product **14-*H*** in 43% and 40% yield, along with their corresponding addition–elimination products **16b** and **16c** in 16% and 10% yield, respectively (Table 5, entries 2 and 3). 2-Methoxyphenyl- (**d**), 4-methylphenyl- (**e**), and 4-(trifluoromethyl)phenylmagnesium bromide (**f**) were not effective for the formation of **14-*H***. However, when Grignard reagent **e** or **f** was employed, not only **14-*H*** but also the α-reduction product **18** and/or desulfonylative arylation product **19** were observed (Table 5, entries 4–6). As shown in entries 7 and 10, *n*-butyl- (**g**) or β-styrylmagnesium bromide

Table 4. Reaction of the sulfone **12** or sulfoxide **13** with PhMgBr (**a**) in the presence of copper(I) salt.



Entry	Substrate	Cu^{I} salt [equiv]	PhMgBr [equiv]	*T* [°C]	Yield of **β-*H*** [%][a]	Yield of **16a** or **17a** [%][a]	Recovered **12** or **13** [%][a]
1	**12**	None	1.1	−78	0	0	quant.
2		CuCN(1.1)	1.1	−78	9	0	73
3		CuCN(1.1)	2.2	−78	70	0	24
4		CuCN(1.1)	2.2	−20	62	0	9
5		CuCN(2.2)	4.4	−78	88 (82)	0	trace
6[b]		CuCN(2.2)	4.4	−78	86	trace	trace
7[c]		CuCN(2.2)	4.4	−78	31	20	trace
8[d]		CuBr(2.2)	4.4	−78	trace	0	41
9[d]		CuI(2.2)	4.4	−78	7	0	54
10	**13**	CuCN(1.1)	2.2	−78	12	41	19
11		CuCN(2.2)	4.4	−78	0	45	trace

[a] Determined by ^{19}F NMR spectroscopy. The yield of isolated product is given in parentheses. [b] TMSCl was employed as an additive. [c] DMSO was employed as an additive. [d] In entries 8 and 9, α-reduction product **18** (shown below) was obtained in 56% and 31% yields, respectively.

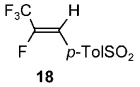


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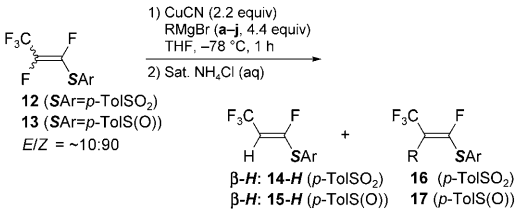
Table 5. Addition-elimination reaction of **12** or **13** with organocuprates derived from various Grignard reagents.



Entry	Substrate	R	Yield of **β-*H*** [%][a]	Yield of **16** or **17** [%][a]	Recovered **12** or **13** [%][a]
1	**12**	Ph (**a**)	88 (82)	0	trace
2[b]		4-$MeOC_6H_4$ (**b**)	43	16	7
3[b]		3-$MeOC_6H_4$ (**c**)	40	10	trace
4		2-$MeOC_6H_4$ (**d**)	2	0	83
5[c]		4-MeC_6H_4 (**e**)	5	trace	28
6[d]		4-$CF_3C_6H_4$ (**f**)	10	trace	30
7		*n*Bu (**g**)	79 (65)	12	trace
8		*s*Bu (**h**)	trace	0	75
9		*c*-Hex (**i**)	10	12	60
10		β-Styryl (**j**)	85 (79)	0	trace
11	**13**	Ph (**a**)	0	45	0
12		4-$MeOC_6H_4$ (**b**)	0	50	0
13		3-$MeOC_6H_4$ (**c**)	0	56	0
14		2-$MeOC_6H_4$ (**d**)	0	0	0
15		4-MeC_6H_4 (**e**)	0	41	0

[a] Determined by ^{19}F NMR spectroscopy. The yield of isolated product is given in parentheses. [b] Trace amounts of **18** and **19** were observed in the reaction mixture. [c] Products **18** and **19** (shown below) were obtained in 5% and 24% yields, respectively. [d] Product **18** was obtained in 48% yield.

(**j**) are good nucleophiles for this reaction, leading to **14-*H*** in 79% or 85% yield, respectively. On the other hand, other aliphatic Grignard reagents **h** and **i** were less successful, and large amounts of the starting sulfone **12** were recovered (Table 5, entries 8 and 9). The reaction of **13** with organocuprates that were generated from various aryl Grignard reagents, such as **a**–**c**, **e**, and **f**, gave their corresponding addition–elimination products **17a–c** and **17e**, in 41–56% yields, respectively (Table 5, entries 11–13 and 15). 2-Methoxyphenylmagnesium bromide (**b**) was found to be unreactive under these conditions.

The results of the reaction between **12** or **13** and various organozinc reagents are tabulated in Table 6. Thus, the reaction of the sulfone **12** with 1.1 equivalents of diethylzinc (**k**) in the absence of a copper(I) salt in THF at −78°C for 1 hour did not provide the corresponding β-reduction product **14-*H*** at all (Table 6, entry 1). CuCN as the catalyst was not efficient in this reaction, although the employment of CuCN·2LiCl[12] (1.1 equiv) was found to give **14-*H*** in 34% yield (Table 6, entries 2 and 3). The best result was obtained when the reaction was performed with 2.2 equivalents of the mixed organocuprate CuCN·2LiCl/**k** (1:2), so that the β-reduction product **14-*H*** was isolated in 85% yield (Table 6, entry 4). Dimethylzinc (**l**), diisopropylzinc (**m**), and diphenylzinc (**n**) investigated under the same reaction conditions (Table 6, entries 5–7). The reaction with organocuprate derived from **l** or **m** proceeded to give the corresponding β-reduction product **14-*H*** in 57% or 35% yield, respectively, together with other side-products, such as the α-reduction product **18** (for the reaction with **l**) and addition–elimination product **16m** (for the reaction with **m**) (Table 6, entries 5 and 6). However, under the same conditions, diphenylzinc (**n**) was not reactive at all (Table 6, entry 7). Similarly, the reaction of the sulfoxide **13** with an organocuprate derived from CuCN·2LiCl and diethylzinc (**k**) in THF at −78°C for 1 hour was examined. It was observed that the amount of organocuprate significantly affected the yield of the β-reduction product **15-*H*** (Table 6, entries 8 and 9). A good yield (80%) was obtained when 2.2 equivalents of organocuprate was used (Table 6, entry 9). Dimethylzinc (**l**) also participates in this process to afford the β-reduction product **15-*H*** in 44% yield after hydrolysis (Table 6, entry 10). However, in that case, the side product of α-reduction (**20**) was also formed in 44% yield. The reaction of **13** with 2.2 equivalents of an organocuprate derived from **m** proceeds readily to give the corresponding β-reduction product **15-*H*** in 93% yield (Table 6, entry 11). Diphenylzinc (**n**) was again not efficient for the addition–elimination reaction, affording in quantitative recovery of the starting sulfoxide **13** (Table 6, entry 12).

Next, we considered the cross-coupling reaction of organocopper intermediates, generated in situ using Method A (for sulfone **12**) or Method B (for sulfoxide **13**), with various electrophiles (Table 7).

When the fluorinated vinyl sulfone **12** was reacted with diphenylcyanocuprate (2.2 equiv), which was prepared from CuCN (2.2 equiv) and PhMgBr (**a**, 4.4 equiv), followed by treatment with I_2 (5.0 equiv) at −78°C for 1 hour, 1,3,3,3-tetrafluoro-2-iodopropen-1-yl sulfone **14** was obtained in 60% yield (Table 7, entry 1). However, carbon electrophiles, such as allyl, methallyl, and crotyl bromide[13] did not afford satisfactory results (Table 7, entries 2–4). In the case of the sulfoxide **13**, a vinylcopper intermediate was formed in the reaction with organocuprate (prepared by mixing CuCN·2LiCl (2.2 equiv) and diethylzinc (**k**, 4.4 equiv). Whilst this organocopper species did not react with I_2 at all, allylic electrophiles afforded some C–C bond formation product (Table 7, entries 5–8). The α-reduction side-product **20** was observed

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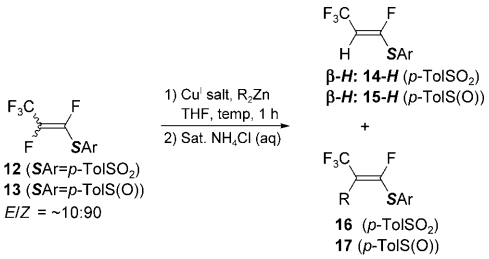
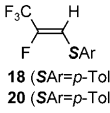
Table 6. Addition–elimination reaction of **12** or **13** with organocuprates derived from various dialkylzinc reagents.



Entry	Substrate	Cu^I salt [equiv]	R_2Zn [equiv]	Yield of **β-*H*** [%][a]	Yield of **16** or **17** [%][a]	Recovered **12** or **13** [%][a]
1	**12**	none	Et_2Zn (**k**;1.1)	0	0	quant.
2		CuCN(1.1)	Et_2Zn(**k**;2.2)	0	0	90
3		CuCN·2LiCl(1.1)	Et_2Zn(**k**;2.2)	34	trace	46
4		CuCN·2LiCl(2.2)	Et_2Zn(**k**;4.4)	quant. (85)	0	0
5[b]		CuCN·2LiCl(2.2)	Me_2Zn (**l**;4.4)	57	trace	0
6		CuCN·2LiCl(2.2)	iPr_2Zn (**m**;4.4)	35	30	0
7		CuCN·2LiCl(2.2)	Ph_2Zn (**n**;4.4)	0	0	quant.
8[c]	**13**	CuCN·2LiCl(1.1)	Et_2Zn (**k**;2.2)	40	0	44
9[c]		CuCN·2LiCl(2.2)	Et_2Zn(**k**;4.4)	80	0	0
10[c]		CuCN·2LiCl(2.2)	Me_2Zn (**l**;4.4)	44	0	5
11		CuCN·2LiCl(2.2)	iPr_2Zn (**m**;4.4)	93 (75)	0	0
12		CuCN·2LiCl(2.2)	Ph_2Zn (**n**;4.4)	0	0	quant.

[a] Determined by ^{19}F NMR spectroscopy. The yield of isolated product is given in parentheses. [b] The α-reduction product **18** (shown below) was obtained in 40% yield. [c] In entries 8–10, the α-reduction product **20** was obtained in 12%, 18%, and 44% yield, respectively.



in all of the reactions involving sulfoxide **13**, in 16–21% yield.

Possible Reaction Mechanism for the Stereoselective Addition–Elimination Reaction of Trifluorovinyl or Pentafluoropropen-1-yl Derivatives with Organocuprates

A possible reaction mechanism for the stereoselective addition–elimination reaction of trifluorovinyl (**1** and **2**) or pentafluoropropen-1-yl derivatives (**12** and **13**) with organocuprates is given in Scheme 8.

The trifluorovinyl derivatives **1** and **2** can react with an organocuprate to generate an intermediate ***Int*-A**, which may exist in two possible conformations: one is where copper and sulfonyl group occupy a *gauche* orientation, and the other is where they are occupied an *anti*-periplanar orientation. In an equilibrium between ***Int*-A(*gauche*)** and ***Int*-A-(*anti*)**, the latter would be favored over ***Int*-A(*gauche*)** owing to steric repulsion between the copper and sulfonyl groups. Then, the elimination of MgBrF from ***Int*-A(*anti*)** takes place preferentially to form ***Int*-B**, followed by rapid reductive elimination of RCu, thus finally providing the (*Z*)-1,2-difluorovinyl derivatives **3** and **4**, respectively. The pentafluoropropen-1-yl derivatives **12** and **13** also undergo nucleophilic *cis*-addition of organocuprate and successive *anti*-elimination of M–F, leading to the corresponding vinylcopper species ***Int*-C**. Such species may be stabilized by the strong electron-withdrawing effect of a CF_3 group.[14] By treatment with various electrophiles (including H_2O), the vinylcopper species ***Int*-C** is converted into the corresponding 1,3,3,3-tetrafluoropropen-1-yl derivatives **14** and **15**, along with the formation of homo-coupling product (R–R). On the other hand, the addition–elimination products **16** and **17** may be formed from reductive elimination of R–CuX through five-membered intermediate ***Int*-D**, in which the coordination of a sulfinyl oxygen to the copper center would facilitate the reductive elimination.

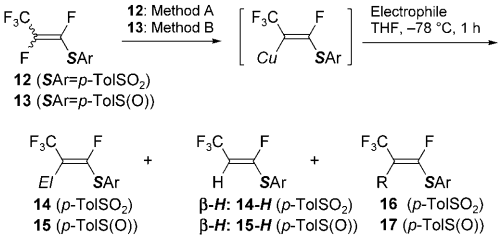
Conclusions

In conclusion, we have achieved the effective preparations of the trifluorovinyl sulfone **1**, sulfoxide **2**, and pentafluoropropen-1-yl derivatives **12** and **13** from commercially available 1,2-dibromo-tetrafluoroethane (**5**) or -hexafluoropropane (**10**). The trifluorovinyl sulfone **1** and sulfoxide **2** can be easily subjected to the addition–elimination reaction with organocuprate reagents that are derived from 1:2 mixtures of CuCN and Grignard reagents, thus leading to the corresponding substitution products **3** and **4** in good to excellent yields and high *Z* selectivity. The reactions of **12** and **13** with organocuprates proceeded smoothly to form relatively stable 1,3,3,3-tetrafluoropropen-1-ylcopper intermediates, which could be converted into 1,3,3,3-tetrafluoropropen-1-yl derivatives **14** and **15** by trapping with various electrophiles. Furthermore, the addition–elimination products **16** and **17** were obtained from the reaction using **13** as a substrate or DMSO as an additive.

Experimental Section

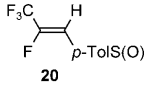
Typical procedure for the reaction of the trifluorovinyl sulfone 1 with PhMgBr (a) in the presence of CuCN: To a suspension of CuCN (0.059 g, 0.66 mmol) in THF (1.0 mL), in a 50 mL three-necked round-bottomed flask equipped with a magnetic stirrer bar, a thermometer, a rubber septum, and an inlet tube for argon, a 0.8 M solution of PhMgBr (**a**, 1.6 mL, 1.3 mmol) in THF was added dropwise at −78 °C. To the resulting solution was slowly added 0.071 g (0.30 mmol) of 1,2,2-trifluorovinyl 4-methylphenyl sulfone (**1**) in THF (2 mL) from a syringe at −78 °C. After stirring for 1 h at −78 °C, the reaction mixture was poured into ice-cooled water (50 mL), followed by extraction with Et_2O

Table 7. Directed cross-coupling of the organocopper intermediate with various electrophiles.



Entry	Substrate	Electrophile	Yield of **14** or **15** [%][c]	Yield of **16** or **17** [%][c]	Yield of **β-H** [%][c]
1	**12**[a]	I_2	60	14	trace
2			7	7	79
3			6	6	73
4			14	5	48
5[d]	**13**[b]	I_2	0	0	68
6[d]			44	0	31
7[d]			47	0	13
8[d]			53	0	8

[a] Method A (entries 1–4): PhMgBr (**a**, 4.4 equiv), CuCN (2.2 equiv), THF, −78 °C, 1 h; [b] Method B (entries 5–8): Et_2Zn (**k**; 4.4 equiv), CuCN·2LiCl (2.2 equiv), THF, −78 °C, 1 h. [c] Determined by ^{19}F NMR spectroscopy. [d] In entries 5–8, the α-reduction product **20** (shown below) was obtained in 20%, 21%, 18%, and 16% yield, respectively.

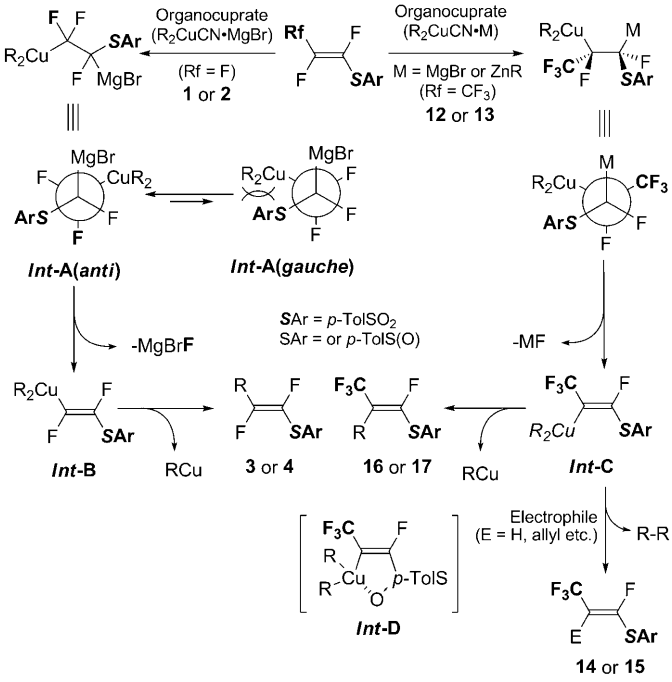


(30 mL×5). The organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. Column chromatography of the residue using hexane/benzene (2:1) yielded 1,2-difluoro-2-phenylethenyl 4-methylphenyl sulfone (**3a**, 0.033 g, 80%).

1,2-Difluoro-2-phenylethenyl 4-methylphenyl sulfone (3a): 80% yield; IR (KBr) 2371, 2345, 1647, 1345, 1158 cm^{-1}; (*Z*)-**3a**: ^1H NMR ($CDCl_3$): $\delta=2.47$ (s, 3H), 7.43 (m, 5H), 7.67 (dd, $J=8.4$, 1.6 Hz, 2H), 7.95 (d, $J=8.4$ Hz, 2H); ^{19}F NMR ($CDCl_3$): $\delta=-154.09$ (d, $J=134.2$ Hz, 1F), −136.04 (d, $J=134.2$ Hz, 1F); (*E*)-**3a**: ^1H NMR ($CDCl_3$): $\delta=2.46$ (s, 3H), 7.36 (dd, $J=8.4$, 1.6 Hz, 2H), 7.54 (m, 5H), 7.73 (d, $J=8.4$ Hz, 2H); ^{19}F NMR ($CDCl_3$): $\delta=-141.28$ (d, $J=4.4$ Hz, 1F), −99.63 (d, $J=4.4$ Hz, 1F); HRMS (FAB) calcd for [M+H] $C_{15}H_{13}F_2O_2S$: 295.0606, found 295.0595.

Typical procedure for the preparation of 1,3,3,3-tetrafluoropropen-1-yl 4-methylphenyl sulfone (14-*H*): A 30 mL two-necked round-bottomed flask equipped with a magnetic stirrer bar, a rubber septum, and an inlet tube for argon was charged with a suspended solution of CuCN (0.059 g, 0.66 mmol) in THF (1 mL). To this solution was slowly added a solution of PhMgBr (**a**, 1.3 mmol) in THF by syringe at −78 °C. The mixture was warmed up to −20 °C and stirred for 15 minutes. Pentafluoropropen-1-yl 4-methylphenyl sulfone (**12**, 0.086 g, 0.3 mmol) was added to the resulting solution by syringe at −78 °C. After being stirred for 1 hour, the reaction mixture was poured into ice-cooled saturated aqueous NH_4Cl (30 mL), followed by extraction with ether (30 mL×5). The organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Column chromatography on silica gel of the residue using hexane/benzene (5:1) yielded pure 1,3,3,3-tetrafluoropropen-1-yl 4-methylphenyl sulfone (**14-*H***, 0.071 g, 82%).

(*E*)-1,3,3,3-Tetrafluoropropen-1-yl 4-methylphenyl sulfone (14-*H*): 82% yield; IR (neat) 3105, 1693, 1594, 1354, 1340, 1262, 1194, 1091 cm^{-1}; ^1H NMR ($CDCl_3$): $\delta=2.50$ (s, 3H), 6.41 (dq, $J=28.0$, 7.1 Hz, 1H), 7.44 (ABq, $J=8.3$ Hz, 2H), 7.85 (ABq, $J=8.3$ Hz, 2H); ^{13}C NMR ($CDCl_3$): $\delta=21.82$, 104.13 (q, $J=37.6$ Hz), 120.58 (q, $J=272.1$ Hz), 129.37, 130.55, 131.83, 147.34, 160.69 (dq, $J=323.1$, 4.8 Hz); ^{19}F NMR ($CDCl_3$): $\delta=-109.98$ (dq, $J=28.0$, 16.9 Hz, 1F), −59.62 (dd, $J=16.9$, 7.1 Hz, 3F); HRMS (FAB) calcd for [M+H] $C_{10}H_9F_4O_2S$: 269.0260, found 269.0255.



Scheme 8. A possible reaction mechanism for the stereoselective addition–elimination reaction of trifluorovinyl (**1** and **2**) or pentafluoropropen-1-yl derivatives (**12** and **13**) with organocuprates.

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