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Preparation of Trifluorovinyl Compounds by Lithium Salt-promoted Monoalkylation of Tetrafluoroethene

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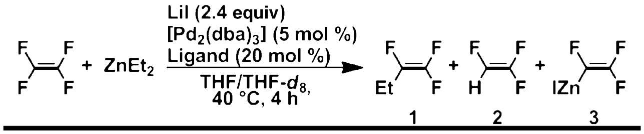
Treatment of tetrafluoroethene (TFE) with diethylzinc in the presence of lithium iodide gave 1,1,2-trifluoro-1-butene in moderate yield. In the absence of lithium iodide, however, the nucleophilic addition of diethylzinc to TFE proceeded very slowly to afford ethyl 1,1,2,2-tetrafluorobutylzinc. The addition of lithium iodide to a solution of ethyl-1,1,2,2-tetrafluorobutylzinc resulted in a smooth transformation into 1,1,2-trifluoro-1-butene. In the presence of lithium chloride, the reaction of TFE with benzyl or allyl Grignard reagents afforded the corresponding monosubstituted products in good to excellent yields.

Trifluorovinyl compounds, in particular trifluorostyrene and its derivatives, have increasingly attracted attention, since they are regarded as a potential monomer for the preparation of polymers with a perfluorinated main chain.[1] However, conventional methods for their preparation thus far have not been fully established. For example, most initial preparation routes of trifluorostyrenes have required multistep reactions.[2,3] The Pd(0)-catalyzed cross-coupling reaction of trifluorovinylzinc or tin reagents emerged in the 1980s as a more direct synthetic method.[2e,4,5] Alternative routes to synthesize α,β,β-trifluorostyrenes via the cross-coupling of chlorotrifluoroethene with arylboronic acids have recently been reported.[6] The usefulness of tetrafluoroethene (TFE) as an ideal starting material for the preparation of organofluorine products developed from its utility as economical bulk organofluorine feedstock. Therefore, we demonstrated a Pd-catalyzed coupling reaction of TFE with aryl zinc compounds to yield α,β,β-trifluorostyrene derivatives.[7] Furthermore, we recently developed a Pd(0)/PR$_3$-catalyzed cross-coupling reaction of fluoroalkenes with arylboronates.[8]

Our next concern was the development of a synthetic method for monoalkylated trifluorovinyl species. However, an initial attempt to apply the use of ZnEt$_2$ to our reaction conditions failed to give the desired 1,1,2-trifluoro-1-butene (**1**). Instead, trifluorovinylzinc iodide (**3**) was obtained in 20% yield with the concomitant generation of ethane and ethene (Table 1, Run 1).[9] As anticipated, the use of tertiary phosphines such as PCy$_3$ and P*n*-Bu$_3$ as the ligand afforded trifluoroethene (**2**) in moderate yield (Runs 2 and 3). These results clearly showed that β-hydride elimination took place in preference to reductive elimination from a (PR$_3$)$_2$Pd(Et)(CF=CF$_2$) intermediate to give **1**. Employing P*t*-Bu$_3$ with a strong σ-donation ability and substantial bulkiness promoted reductive elimination to give the desired product **1**, but the yield (21%) was low, and **3** was obtained concomitantly as the major product in this reaction (Run 4). These results prompted a review of the reaction of TFE with organometallic reagents. Although some groups have already reported such a reaction,[2c,3,10] the selective monoalkylation of TFE still remains unexploited. We herein report a series of reactions using TFE with either ZnEt$_2$ or alkylmagnesium reagents. The use of appropriate additives enabled the selective monoalkylation of TFE in moderate to excellent yields.

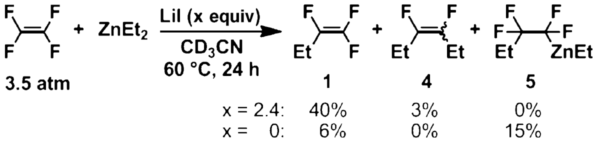
Table 1. Pd(0)-catalyzed coupling reaction of TFE with ZnEt$_2$ in the presence of lithium iodide[a]



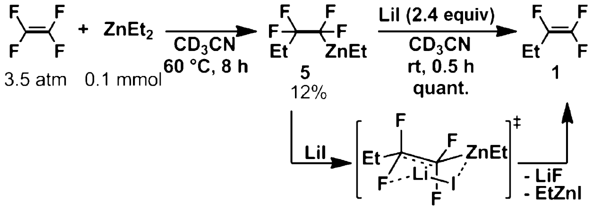
Run	Ligand	Yield/%[b]		
		1	**2**	**3**
1	none	N. D.	N. D.	20
2	PCy$_3$	N. D.	65	9
3	P*n*-Bu$_3$	N. D.	68	4
4	P*t*-Bu$_3$	21	N. D.	31

[a]General conditions: TFE (3.5 atm, >0.30 mmol), ZnEt$_2$ (0.10 mmol), LiI (0.24 mmol), THF/THF-d_8 (0.6 mL, v/v′ = 2/1), PhCF$_3$ (0.10 mmol, as a standard for ^{19}F NMR). [b]Yields were determined by ^{19}F NMR.

In the presence of lithium iodide, the treatment of TFE[11] with diethylzinc in CD$_3$CN at 60 °C for 24 h resulted in the formation of **1** in 40% yield (eq 1). In this reaction, the formation of disubstituted isomers, EtCF=CFEt (**4**), was observed as a minor product. By contrast, NMR observation revealed that the same reaction conducted in the absence of lithium iodide gave a carbozincation product, EtCF$_2$CF$_2$ZnEt (**5**), in 15% yield. The reaction of the adduct **5** generated in situ with lithium iodide in CD$_3$CN at room temperature smoothly underwent the elimination of ethylzinc halide to give **1** in a quantitative yield (eq 2).



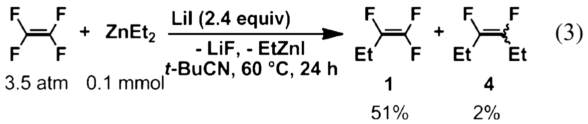
(1)



(2)

These results indicated that lithium iodide promoted the elimination reaction via a putative 6-membered transition state,[12] leading to the conversion of the initial carbozincation product **5** into **1**. Another role of lithium iodide might be rationalized by enhancing the nucleophilicity of diethylzinc as a result of generating an active zincate species such as Li[Et_2ZnI].[13,14]

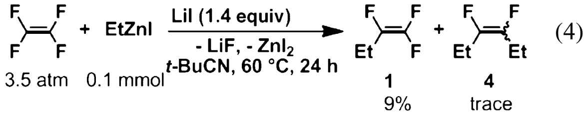
The yield of **1** was improved to 51% under the same reaction conditions with the exception of the employment of *t*-BuCN in the place of MeCN as the reaction solvent (eq 3), because an undesired side reaction involving diethylzinc with MeCN in the presence of lithium iodide, generating ethane as a result of deprotonation of the α-carbon, was suppressed.[15] However, the resultant ethylzinc iodide showed less reactivity toward TFE under the same reaction conditions (eq 4), and therefore, the yield of **1** was improved to approximately 50%.



1 51%

4 2%

(3)

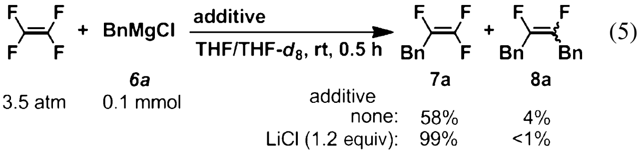


1 9%

4 trace

(4)

We next investigated the reaction of alkylmagnesium reagents with TFE. The reaction of benzylmagnesium chloride (**6a**) with TFE in THF/THF-d_8 at room temperature for 0.5 h led to the formation of (2,3,3-trifluoroallyl)benzene (**7a**) in a moderate yield (eq 5). As reported by Jiang et al.,[2c] formation of the corresponding disubstituted product **8a** was observed. Monitoring of the reaction by means of ^{19}F NMR spectroscopy detected no generation of the carbomagnesiation product. We found that the addition of lithium chloride improved the rate and selectivity of the reaction to give **7a** in a quantitative yield. Lithium chloride might enhance the reactivity of benzylmagnesium chloride as a result of the formation of ate species.[16]



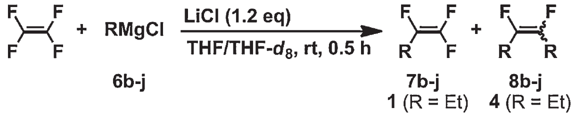
6a 7a 8a

additive	7a	8a
none:	58%	4%
LiCl (1.2 equiv):	99%	<1%

(5)

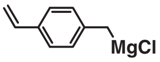
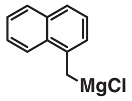
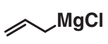
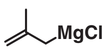
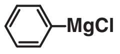
Table 2 shows the scope and limitation of the LiCl-promoted monosubstitution reaction of TFE with respect to various Grignard reagents. The reaction of (4-vinylbenzyl)magnesium chloride (**6b**) with TFE gave the desired product **7b** in an excellent yield (Run 1). The use of (1-naphthylmethyl)magnesium chloride (**6c**) afforded 1,1,2-trifluorovinyl compound **7c** in a moderate yield (Run 2). Both allylmagnesium chloride (**6d**) and 2-methylallylmagnesium chloride (**6e**) allowed a clean formation of 1,1,2-trifluoropentane-1,4-diene derivatives **7d** and **7e** (Runs 3 and 4). Simple alkylmagnesium reagents such as ethylmagnesium chloride (**6f**) retarded the reaction, and **6f** was completely consumed after 18 h to give a complicated mixture that contained **1** in 13% yield (Run 5). In addition, the use of *t*-butylmagnesium chloride (**6g**) afforded the corresponding monosubstituted product **7g** in 22% yield, along with the concomitant formation of a complicated mixture of fluorine-containing molecules (Run 6). Further substrate scope using aryl, vinyl, and alkynyl Grignard reagents was examined. Treatment with phenylmagnesium chloride (**6h**) with TFE in the presence of lithium chloride gave α,β,β-trifluorostyrene (**7h**) as a major product (Run 7). However, a considerable amount of a mixture of difluorostilbenes **8h** was formed, which was consistent with a previous report by Jiang.[2c] A similar tendency to form a substantial quantity of disubstituted product was observed when vinylmagnesium chloride (**6i**) was employed as the substrate, and the yield of 1,1,2-trifluoro-1,3-butadiene (**7i**) was 31% (Run 8). The reaction of ethynylmagnesium chloride (**6j**) for 22 h gave 1,1,2-trifluoro-1-buten-3-yne (**7j**) in 17% yield (Run 9).

Table 2. LiCl-promoted monosubstitution reaction of TFE with RMgCl **6**[a]



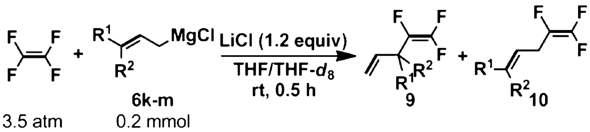
6b-j 7b-j 8b-j

1 (R = Et) 4 (R = Et)

Run	RMgCl (**6b–6j**)		Conv. of **6**/%	Yield/%[b]	
				7b–7j or **1**	**8b–8j** or **4**
1		(**6b**)	100	93 (**7b**) [55]	4 (**8b**)
2		(**6c**)	100	51 (**7c**) [18]	4 (**8c**)
3		(**6d**)	100	>99 (**7d**) [96]	<1 (**8d**)
4		(**6e**)	100	>99 (**7e**) [94]	<1 (**8e**)
5[c]	**EtMgCl**	(**6f**)	100	13 (**1**)	0 (**4**)
6[d]	***t*-BuMgCl**	(**6g**)	100	22 (**7g**)	0 (**8g**)
7[e]		(**6h**)	100	74 (**7h**)	21 (**8h**)
8		(**6i**)	100	31 (**7i**)	39 (**8i**)
9[f]		(**6j**)	100	17 (**7j**)	0 (**8j**)

[a]General conditions: TFE (3.5 atm, >0.30 mmol), **6** (0.10 mmol), LiCl (0.12 mmol), THF/THF-d_8 (0.6 mL, v/v′ = 2/1), $PhCF_3$ (0.10 mmol, as a standard for ^{19}F NMR). [b]Yields were determined by ^{19}F NMR. The values in brackets were of isolated yields. [c]For 18 h. [d]For 48 h. [e]For 27 h. [f]For 22 h.

The reaction of crotylmagnesium chloride (**6k**) with TFE in the presence of lithium chloride resulted in the quantitative formation of a mixture of monoalkylated products (eq 6). In this major product **9k**, a C–C bond was formed at the γ-position of crotylmagnesium chloride. In addition, the use of γ-methylcrotyl Grignard reagent **6l** also gave the γ-substituted product **9l** as a major product. However, when cinnamylmagnesium chloride (**6m**) was used, a C–C bond formation occurred predominantly between the α-position of the cinnamyl group and the trifluorovinyl group to give the corresponding α-substituted product **10m** as a major product, while this reaction was somewhat retarded.



(6)

6k-m

9

10

3.5 atm

0.2 mmol

R^1 = Me, R^2 = H (**6k**)	81% (**9k**)	19% (**10k**)
R^1 = R^2 = Me (**6l**)	67% (**9l**)	33% (**10l**)
R^1 = Ph, R^2 = H (**6m**)	3% (**9m**)	39% (**10m**)

In conclusion, we have demonstrated the selective monosubstitution reaction of TFE with either diethylzinc or alkylmagnesium chloride. The use of suitable lithium salts enhanced both the yield and selectivity of the desired monoalkylated products in both reactions. A lithium iodide-promoted monoethylation reaction employing diethylzinc would involve an addition–elimination mechanism. In addition, the combination of benzyl- and allylmagnesium reagents and lithium chloride gave the corresponding monoalkylated products in excellent yields.

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