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Mechanistic study on a unique S_N2'-type reaction of allylic alcohols with organolithium reagent accelerated by a proximal trifluoromethyl group

Hiromichi Egami [a,b,e], Yoshihiko Usui [a,c], Shintaro Kawamura [a,b,d], Ryo Shimizu [a,c], Sayoko Nagashima [c], Mikiko Sodeoka [a,b,c,d,*]

[a] Synthetic Organic Chemistry Laboratory, RIKEN, 2-1 Hirosawa, Wako, Saitama 351-0198, Japan
[b] Sodeoka Live Cell Chemistry Project, ERATO, Japan Science and Technology Agency, 2-1 Hirosawa, Wako, Saitama 351-0198, Japan
[c] Graduate School of Science and Engineering, Saitama University, 255 Shimo-okubo, Sakura-ku, Saitama 338-8570, Japan
[d] RIKEN Center for Sustainable Resource Science, 2-1 Hirosawa, Wako, Saitama 351-0198, Japan
[e] School of Pharmaceutical Sciences, University of Shizuoka, 52-1 Yada, Suruga-ku, Shizuoka 422-8526, Japan

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ABSTRACT

We previously found that treatment of (*Z*)-trifluoromethylated-2-aryl allylic alcohols with organolithium provided the S_N2'-type product through C–O bond cleavage. Interestingly, no additive was required to enhance the nucleophilicity of the organolithium, and the free hydroxyl group served as a leaving group. The mechanistic studies of the unique transformation indicated that chelation of alkoxide and fluorine of the trifluoromethyl group to the lithium ion play a crucial role in controlling the reactivity and selectivity. Furthermore, theoretical investigation supported this interpretation.

1. Introduction

The S_N2' reaction is a fundamental reaction in organic chemistry, and various types of S_N2' reactions have long been utilized in organic synthesis. In general, an allylic compound bearing a leaving group, such as halide or sulfonate, is used as an electrophile in S_N2' reactions with soft nucleophiles, and transition metal catalysis has recently enabled the use of allylic carboxylates and allylic alcohols in this type of reaction [1]. However, the S_N2' reaction of allylic alcohol with a main group metal reagent, such as organolithium, is difficult without prior activation of the hydroxyl group [2].

On the other hand, addition of an organolithium reagent to alkenes is a well-established reaction known as carbolithiation [3]. Additives such as *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA), *N*,*N*′-dimethylpropyleneurea (DMPU), or a directing group that has a strong coordination ability to the lithium ion are usually required to promote this reaction, except in the case of *tert*-butyllithium [4]. Despite extensive studies on the carbolithiation of alkenes, including allylic alcohols [5], very few examples of S_N2'-type reaction of allylic alcohols are known [6]. Reported examples are restricted to terminal alkene or cyclopent-2-en-1-ol, and TMEDA is required as an additive to enhance the nucleophilicity of the organolithium reagents by dissociating their aggregated state.

There is increasing interest in introducing a trifluoromethyl group into organic frameworks due to its metabolic stability, lipophilicity and electronic character [7], and trifluoromethylation reactions, as well as transformations of trifluoromethylated compounds, have been actively studied [8]. Since carbolithiation exploits the properties of the trifluoromethyl group, trifluoromethyl-substituted alkene

* Corresponding author at: Synthetic Organic Chemistry Laboratory, RIKEN, 2-1 Hirosawa, Wako, Saitama 351-0198, Japan.
E-mail address: sodeoka@riken.jp (M. Sodeoka).

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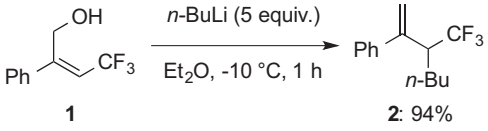
species, such as α-trifluoromethylstyrene, have been investigated as substrates [9]. But, in these cases, the alkyl anion attacks the β-position of the trifluoromethyl group and *gem*-difluoroalkene is generated via elimination of the fluoride ion.

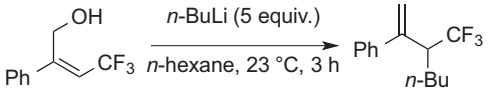
We have been investigating trifluoromethylation reactions and further transformations of the obtained trifluoromethylated compounds [10]. During our work on the trifluoromethylation of allylsilanes [11], we observed a unique transformation: treatment of (*Z*)-trifluoromethylated 2-phenyl allylic alcohol **1** with *n*-butyllithium (*n*-BuLi) provided the S_N2'-type reaction product **2** in excellent yield (Eq. (1)) [11a]. The substrate has a trisubstituted alkene moiety and no additive was required for this reaction. In addition, the hydroxyl group acts as a leaving group, suggesting the generation of Li_2O during the reaction [12]. Herein, we report a mechanistic study on this unique S_N2'-type reaction of trifluoromethylated 2-aryl allylic alcohols with alkyllithium reagent, together with a theoretical investigation of the mechanism.



1 **2**: 94% (1)

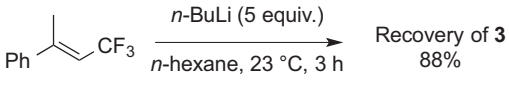
2. Results and discussion

In general, organolithium reagents exhibit various aggregation modes depending upon the conditions; for example, solvents and additives are well known to affect the reactivity of organolithium reagents [13]. Hence, we first examined the solvent effect in this S_N2' reaction using **1** as a substrate in *n*-hexane, which has no ability to coordinate to lithium ion (Eq. (2)). Compound **2** was isolated in 96% yield at ambient temperature, even though the nucleophilicity is expected to be low. This result is inconsistent with previously reported carbolithiations of styrene derivatives and allylic alcohols [4,5]. We anticipated that the reason for this difference might be that the lithium alkoxide moiety generated in situ from substrate **1** works as a directing group. We hypothesized that fluorine of the trifluoromethyl group would coordinate to the lithium ion of lithium alkoxide to fix the conformation of the intermediate [14], providing an energetically favorable carbolithiation pathway via structural activation of the double bond.



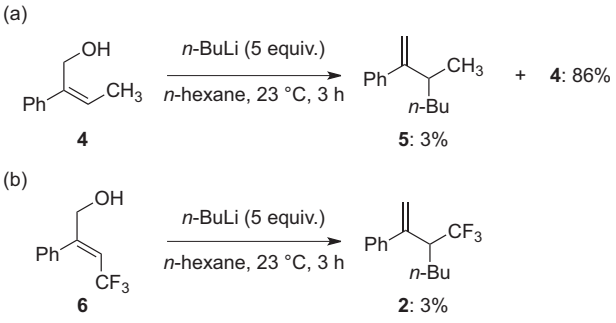
1 **2**: 96% (2)

To test this idea, we chose (*Z*)-α-methyl-β-trifluoromethylstyrene **3** as a substrate (Eq. (3)). No carbolithiated product was detected and the starting material **3** was recovered in 88% yield, suggesting that the hydroxyl group serves not only as a leaving group, but also as a directing group.



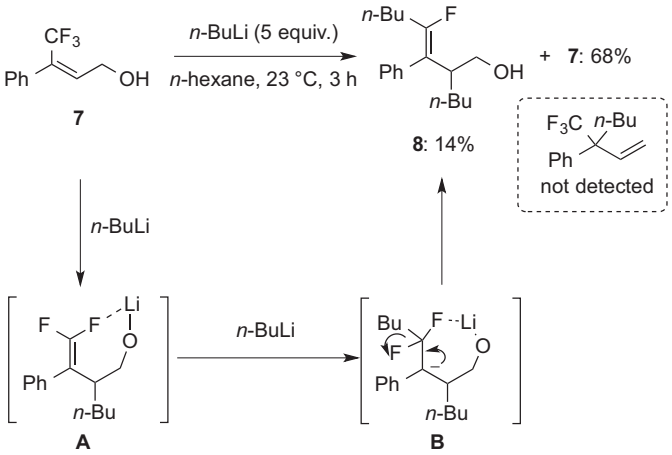
3 (3)

Next, substrates **4** and **6** were treated with *n*-BuLi under the standard conditions in order to examine the influence of the trifluoromethyl group (Scheme 1). The reaction of **4** bearing a methyl group instead of a trifluoromethyl group afforded only 3% yield of alkylated product **5**, and allylic alcohol **4** was recovered in 86% yield (Scheme 1a). This indicates that the trifluoromethyl group profoundly accelerates the S_N2'-type reaction. The trifluoromethyl group was considered to work not only as an electron-withdrawing group, which electronically enhances the reactivity of the substrate, but also as a chelating group [14]. The reaction with (*E*)-isomer **6** afforded a complex mixture, and the desired product **2** was obtained in only 3% yield under the same conditions as used in the reaction of (*Z*)-isomer **1** (Scheme 1b). Thus, we concluded that the trifluoromethyl group plays a crucial role in the reaction by chelating to lithium alkoxide and fixing the conformation of the substrate, and its orientation in (*Z*)-isomer **1** is geometrically more favorable for chelation, compared with that in (*E*)-isomer **6**.

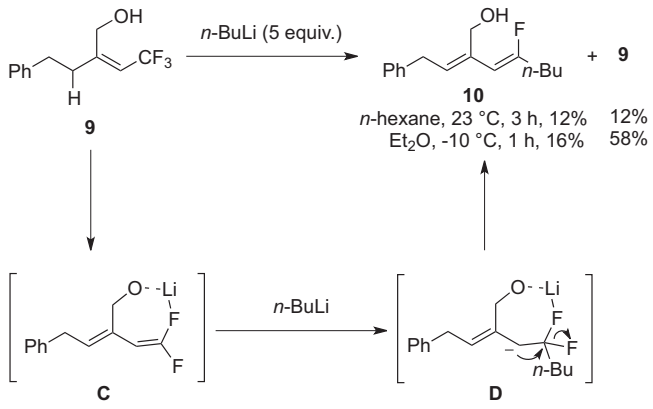


Scheme 1. Effect of the trifluoromethyl group.

We then examined the influence of the aryl group on the substrate. It is well known that styrene derivatives are good substrates for regioselective carbolithiation using the combination of *n*-BuLi and TMEDA, due to the stability of the benzyl anion [4]. Therefore, the regioisomer **7** was used for the reaction (Scheme 2). Here, the hydroxyl group, which was regarded as the leaving group in our S_N2'-type reaction was not eliminated, and substrate **7** was converted to butyl-substituted fluoroalkene **8** in 14% yield. The corresponding S_N2'-type reaction product was not detected. In this particular reaction system, *n*-BuLi appeared to attack the β-position of the trifluoromethyl group instead of the α-position, to provide intermediate **A**. The regioselectivity of this step was explained by a stability of benzylic anion, and a steric effect might participate to some extent in determination the selectivity. The lithium alkoxide form of product **8** could then be generated via addition-elimination of *gem*-difluoroalkene **A**. It is noteworthy that the geometry between the phenyl group and the fluorine atom of product **8** is *trans*. This strongly suggested that the alkoxide and the fluorine atom would both coordinate to the lithium ion.



Scheme 2. Effect of the aryl group.



Scheme 3. Reaction of alkyl substrate **9**.

Substrate **9** bearing a phenethyl group in place of the phenyl group was also used as a substrate to gain further information regarding the influence of the aryl group in this reaction (Scheme 3). However, deprotonation at the allylic position was faster than nucleophilic attack on the vinylic carbon. The resulting intermediate **C** reacted with *n*-BuLi to afford compound **10**, albeit in low

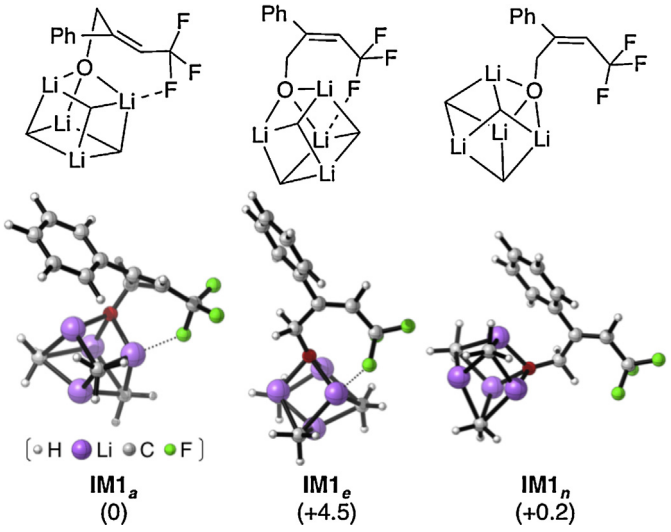


Fig. 1. Starting intermediates **IM1** generated from **1** with $(MeLi)_4$.

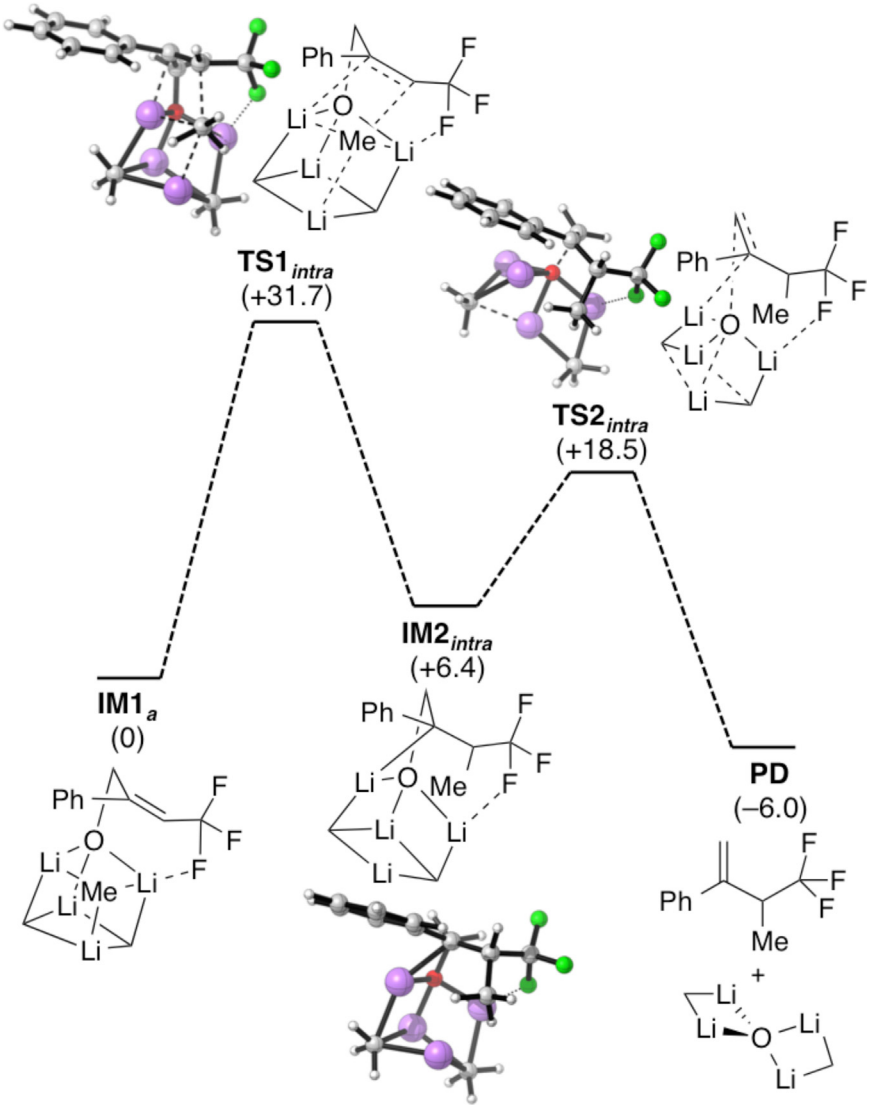


Fig. 2. Intramolecular pathway in the case of $\mathbf{IM1}_a$.

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yield. The chelation effect was considered to be important for controlling the stereochemistry in this reaction. The reaction in *n*-hexane led to a complex mixture, and **9** was recovered in only 12% yield after column chromatography. Fortunately, the crude mixture became relatively clean when Et_2O was used as a solvent, and **10** was obtained in 16% yield together with 58% of starting material **9**.

We then focused on the reactivity of other organometallic reagents, as chelation by the metal ion appeared to be essential for this reaction. Several alkyl metal reagents were screened under the standard conditions (Table 1). Considering the commercial availability of alkyl metal species, we selected methyl metal compounds for this screening. Since methyllithium reagent (MeLi) did not dissolve in *n*-hexane, diethyl ether (Et_2O) was used as a solvent in the screening experiments. Compound **11** bearing a naphthyl group was chosen as a substrate, due to the somewhat volatile nature of the product formed from the substrate bearing a phenyl group. The reaction of **11** with MeLi in Et_2O efficiently afforded the corresponding S_N2' product in 83% yield (entry 1). However, treatment of **11** with other methyl metal species was not effective (entries 2–4). In the case of MeMgBr, a complex mixture was obtained (entry 2), and Me_3Al and Me_2Zn lead to recovery of large amounts of starting material (entries 3 and 4). These results indicate that the nucleophilicity of the organometallic reagent, and

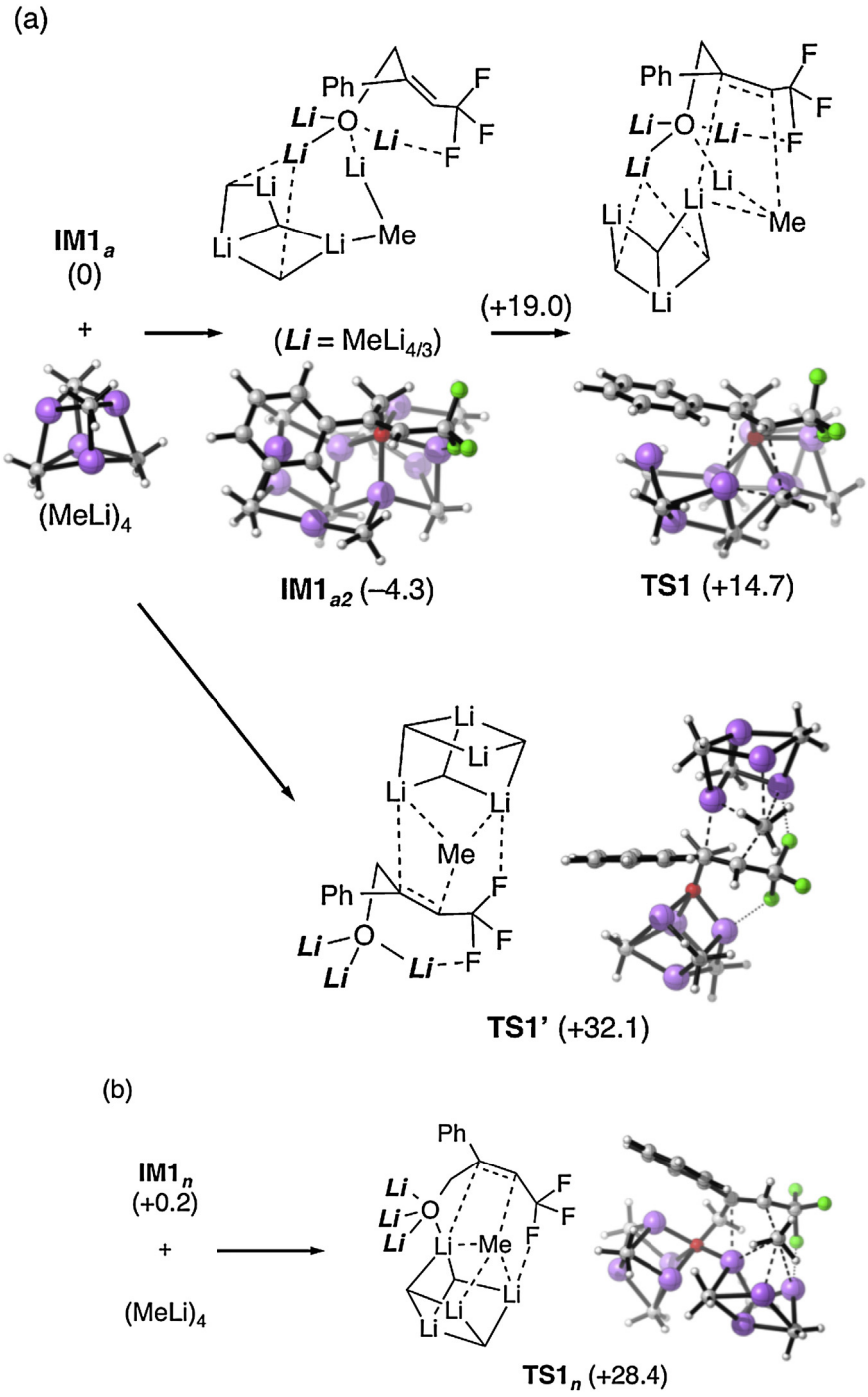

Fig. 3. Carbolithiation step of (a) $\mathbf{IM1}_a$ and (b) $\mathbf{IM1}_n$ with $(MeLi)_4$.

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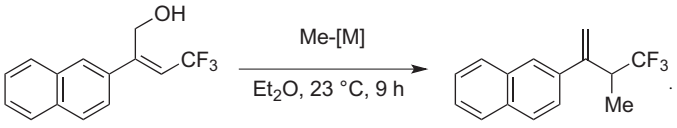
Table 1
Reaction with organometallic reagents[a].



11 12

Entry	Nucleophile	Yield of **12** [%][b]	Recovery of **11** [%][b]
1	MeLi	83	0
2	MeMgBr	Trace	43
3	Me_3Al	ND[c]	93
4	Me_2Zn	ND[c]	100

[a] The reactions were carried out with methyl metal species (5 equiv.) in Et_2O on a 0.2 mmol scale.
[b] Determined by ^1H NMR analysis.
[c] Not detected.

the unique chelation and aggregation modes of the lithium ion, are important.

In order to further examine the reaction mechanism, we conducted DFT calculations at the M06-2X/6-31+G(d,p) level of theory [15]. In this study, the starting material was modeled as **IM1** generated from allylic alcohol **1** and MeLi tetramer [16]. We first examined an influence of the Li–F interaction to the stability of the intermediate. The intermediate containing seven-membered ring bridged by Li–F interaction can adopt two types of conformer (**IM1$_a$**, and **IM1$_e$**). The free energies (kcal/mol) of the conformers and **IM1$_n$** without Li–F interaction were compared (Fig. 1). As anticipated from the experimental results, intermediate **IM1$_a$** was found to be the most stable conformer, and its C–O bond lies in a nearly perpendicular position with respect to the C=C double bond. The conformer with Li–F interaction (**IM1$_e$**), in which the hydroxyl group is directed inwards toward the double bond to generate allylic strain, was less stable than **IM1$_n$**. The slight energetic difference (0.2 kcal/mol) between **IM1$_a$** and **IM1$_n$** indicates that Li–F interaction does not significantly affect the thermal stability of these conformers. Bridging did not influence the length of the double bond (1.34 Å).

We then examined the intramolecular reaction pathway in the case of **IM1$_a$** (Fig. 2) [17]. Based on our experimental results and literature data [3–6], we assumed that the reaction proceeds via carbolithiation (**IM1$_a$** to **IM2$_{intra}$**) [18], followed by oxygen elimination (**IM2$_{intra}$** to **PD**). The calculation results showed that the highest activation energy was located between **IM1$_a$** and **TS1$_{intra}$**, which is the carbolithiation step. The activation energy of this step was +31.7 kcal/mol, which seems to be too large for the reaction proceeding at room temperature. Next, we focused on the intermolecular reaction of **IM1$_a$** with an extra MeLi tetramer $(MeLi)_4$ (Figs. 3 and 4). Carbolithiation of the double bond with $(MeLi)_4$ may occur from either the same (**TS1**) or the opposite (**TS1′**) side with respect to the lithium alkoxide substituent of **IM1$_a$**. **TS1** was obtained via formation of intermediate **IM1$_{a2}$**, in which

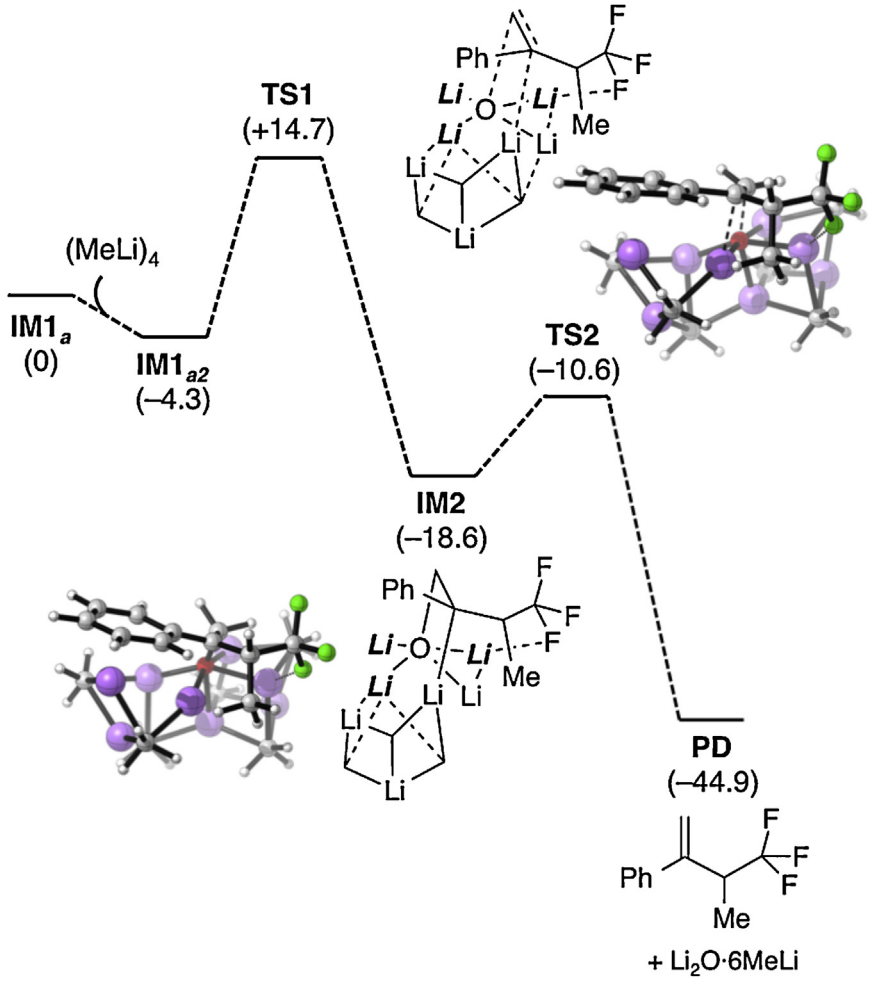


Fig. 4. Intermolecular pathway.

the lithium aggregates of **IM1$_a$** and $(MeLi)_4$ were combined, whilst **TS1′** was directly generated from **IM1$_a$**. Comparison of the energy levels of the transition states showed that the pathway through **TS1** (+14.7 kcal/mol from **IM1$_a$**, +19.0 kcal/mol from **IM1$_{a2}$**) is much more favorable than the pathway through **TS1′** (+32.1 kcal/mol) (Fig. 3a). In **TS1**, protruding MeLi of **IM1$_{a2}$** reacts with the double bond. Moreover, carbolithiation of **IM1$_n$** was also examined (Fig. 3b). The transition state of the carbolithiation of **IM1$_n$** with $(MeLi)_4$ (**TS1$_n$**) was obtained without formation of an intermediate and showed a higher energy barrier compared to **TS1**. We conclude that the lithium aggregate of **IM1$_a$** facilitates the desired reaction by serving as a directing group, which leads to the larger aggregate and generates reactive MeLi in close proximity to the double bond. The calculated activation energy of **TS1** from **IM1$_{a2}$** appears to be reasonable for the reaction to occur at room temperature.

We then calculated the entire reaction pathway for the intermolecular reaction of **IM1$_a$** with $(MeLi)_4$ (Fig. 4). In line with the intramolecular pathway in Fig. 2, the carbolithiation step requires the highest activation energy in the intermolecular reaction. Carbolithiated intermediate **IM2** and the transition state of the oxygen elimination step **TS2** were also energetically stabilized due to aggregate formation (−18.6, and −10.6 kcal/mol, respectively). The activation energy of the oxygen elimination step was +8.0 kcal/mol. In **TS2**, electrons of the π-orbital on the trigonal benzylic carbon move into the σ^*-orbital of C–O bond ($\angle$Ph–C–C–O: 87.2 deg.); this could induce C–O bond cleavage, where the $Li_2O{\cdot}6MeLi$ cluster acts as a good leaving group due to stabilization of the formal oxygen dianion by lithium aggregates.

3. Conclusion

We present the mechanistic insight into a S_N2'-type reaction of (*Z*)-trifluoromethylated allylic alcohol with alkyl lithium reagent in *n*-hexane in the absence of any additive. The stereochemistry of the substrate is important for the reaction, in order to accelerate the reaction and to control product formation through chelation of the alkoxide and a fluorine atom of the trifluoromethyl group to the lithium ion. The aryl group plays a role in controlling the regioselectivity and also accelerates the reaction. Computational studies were consistent with these pathways, and the lowest energy profile was obtained when two MeLi-tetramers were involved in the transition state. Overall, our results indicate that the hydroxyl group becomes a good leaving group for the S_N2'-type reaction through coordination to the lithium cluster. We believe that the basic understanding of the mechanism obtained in this work will be helpful to develop new molecular transformations with trifluoromethylated compounds in future.

4. Experimental

4.1. General

All reactions and manipulations were performed under an atmosphere of dry nitrogen.

^1H, ^{19}F NMR spectra were measured on a JEOL JNM-ECS-400 spectrometer at 400 and 376 MHz, respectively. ^{13}C NMR spectra were recorded on a JEOL JNM-ECS-400 spectrometer at 100 MHz. Chemical shifts are reported downfield from TMS (=0) or $CDCl_3$ for ^1H NMR. For ^{13}C NMR, chemical shifts are reported in the scale relative to $CDCl_3$. For ^{19}F NMR, chemical shifts are reported in the scale relative to a $CFCl_3$ external standard (0 ppm). Infrared spectra were measured on a Thermo Nicolet iS5, and only diagnostic absorptions are listed below. ESI-MS was taken on Bruker micrOTOF-QII-$_{RSL}$. EI-MS was taken on a JEOL JMS-700V. Column chromatography was performed with silica gel N-60 (40–100 μm) purchased from Kanto Chemical Co., Inc. In some cases, purification was carried out using a JIA recycling preparative HPLC system [LC-918R; column, JAIGEL-H; chloroform]. TLC analysis was performed on Silica gel 60 F_{254}-coated glass plates (Merck). Visualization was accomplished by means of ultraviolet (UV) irradiation at 254 nm or by spraying 12-molybdo(VI)phosphoric acid ethanol solution as the developing agent.

Dehydrated *n*-hexane, tetrahydrofuran (THF) and diethyl ether (Et_2O) were purchased from Kanto Chemical Co., Inc. Other reagents were purified by usual methods. Compounds **1** [11], **4** [19] and **7** [20] were prepared according to literature procedures. Compound **3** was obtained as a by-product in the oxy-trifuoromethylation of α-methylstyrene with copper-Togni reagent system [10i].

4.2. Preparation of (E)-4,4,4-trifluoro-2-phenyl-2-buten-1-ol (**6**)

Preparation of compound **6** was previously reported [11]. Colorless oil; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.86 (t, J = 6.2 Hz, 1H), 4.34–4.38 (m, 2H), 6.04 (qt, J = 8.3, 1.8 Hz, 1H), 7.19–7.22 (m, 2H), 7.36–7.40 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 66.6, 114.2 (q, J = 33.7 Hz), 123.6 (q, J = 270.7 Hz), 127.8, 128.6, 128.9, 135.6, 152.78 (q, J = 5.8 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ = −56.0 (d, J = 8.3 Hz); IR (neat): 3343, 3060, 2915, 1682, 1276, 1214 cm^{-1}; HRMS (ESI^+): Calcd. for $[C_{10}H_9F_3O+H]^+$: m/z = 203.0678, Found: 203.0677.

4.3. Synthesis of (Z)-4,4,4-trifluoro-2-phenethyl-2-buten-1-ol (**9**)

To a solution of 4,4,4-trifluoro-2-phenethyl-1-butene [11] (364 mg, 1.7 mmol) in CH_2Cl_2/phosphate buffer (pH = 7.0) (11 mL/11 mL) was added *m*-CPBA (2.2 g, 9.7 mmol) at 0 °C. After stirring for 4 h, the reaction was quenched with $Na_2S_2O_3$ and the mixture was extracted with CH_2Cl_2. The combined organic layer was dried over $MgSO_4$, and filtered. The filtrate was evaporated under reduced pressure. Flash column chromatography (SiO_2; *n*-hexane/ethyl acetate = 20/1) of the residue afforded 2-phenethyl-2-(2,2,2-trifluoroethyl)oxirane as a colorless oil (183 mg, 47%). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.91–2.25 (m, 3H), 2.59–2.75 (m, 5H), 7.17–7.22 (m, 3H), 7.27–7.31 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.6, 36.0, 39.8 (q, J = 28.9 Hz), 52.0, 54.3 (q, J = 2.9 Hz), 125.8 (q, J = 277.4 Hz), 126.3, 128.4, 128.7, 140.9; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −62.5 (t, J = 10.4 Hz); IR (neat): 3060, 3029, 2940, 1497, 1370, 1263 cm^{-1}; HRMS (ESI^+): Calcd. for $[C_{12}H_{13}F_3O+Na]^+$: m/z = 253.0811, Found: 253.0813.

To a solution of 2-phenethyl-2-(2,2,2-trifluoroethyl)oxirane (183 mg, 0.8 mmol) in THF (8 mL) was added a THF solution of NHMDS (1.9 mL, 1 M, 1.9 mmol) at −78 °C. After stirring for 2 h at the same temperature, the reaction was quenched with aqueous NH_4Cl. The mixture was extracted with ethyl acetate, dried over $MgSO_4$, and filtered. The filtrate was evaporated under reduced pressure. Flash column chromatography (SiO_2; *n*-hexane/ethyl actate = 5/1) of the residue afforded the title compound **9** as a colorless oil (61.4 mg, 33%). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.45 (t, J = 6.3 Hz, 1H), 2.60 (t, J = 7.9 Hz, 2H), 2.82 (t, J = 7.9 Hz, 2H), 4.36 (d, J = 6.3 Hz, 2H), 5.52 (q, J = 8.7 Hz, 1H), 7.18–7.24 (m, 3H), 7.29–7.32 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 34.1, 36.0, 60.4, 116.0 (q, J = 33.7 Hz), 123.2 (q, J = 271.6 Hz), 126.4, 128.5, 128.7, 140.8, 153.1 (q, J = 5.8 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ = −56.1 (t, J = 8.7 Hz); IR (neat): 3384, 3029, 2929, 1673, 1451, 1272 cm^{-1}; HRMS (ESI^+): Calcd. for $[C_{12}H_{13}F_3O+Na]^+$: m/z = 253.0811, Found: 253.0813.

4.4. Synthesis of (Z)-4,4,4-trifluoro-2-(2-naphthyl)-2-buten-1-ol (**11**)

To a solution of 4,4,4-trifluoro-2-(2-naphthyl)-1-butene [11] (2.3 g, 9.6 mmol) in CH_2Cl_2/phosphate buffer (pH = 7.0) (64 mL/64 mL) was added *m*-CPBA (11 g, 4.8 mmol) at 0 °C. After stirring

for 4 h, the reaction was quenched with $Na_2S_2O_3$ and the mixture was extracted with CH_2Cl_2. The combined organic layer was dried over $MgSO_4$, and filtered. The filtrate was evaporated under reduced pressure. Flash column chromatography (SiO_2; *n*-hexane/ethyl acetate = 20/1) of the residue afforded 2-(2-naphthyl)-2-(2,2,2-trifluoroethyl)oxirane as a colorless oil (1.1 g, 46%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.77–3.02 (m, 3H), 3.18 (d, J = 5.1 Hz, 1H), 7.48–7.51 (m, 3H), 7.83–7.88 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.0 (q, J = 28.9 Hz), 54.5, 55.8 (q, J = 2.9 Hz), 123.7, 125.5, 125.6 (q, J = 277.4 Hz), 126.6, 126.6, 127.8, 128.2, 128.5, 133.1, 135.5; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −61.6 (t, J = 10.4 Hz); IR (neat): 3059, 1768, 1575, 1425, 1366, 1131 cm^{-1}; HRMS (ESI$^+$): Calcd. for $[C_{14}H_{11}F_3O+H]^+$: m/z = 253.0835, Found: 253.0835.

To a solution of 2-(2-naphthyl)-2-(2,2,2-trifluoroethyl)oxirane (1.1 g, 4.4 mmol) in THF (44 mL) was added to a THF solution of NHMDS (5.3 mL, 1 M, 5.3 mmol) at −78 °C. After stirring for 2 h at the same temperature, the reaction was quenched with aqueous NH_4Cl. The mixture was extracted with ethyl acetate, dried over $MgSO_4$, and filtered. The filtrate was evaporated under reduced pressure. Flash column chromatography (SiO_2; *n*-hexane/diethyl ether = 5/1) of the residue afforded the title compound **11** as a colorless oil (818 mg, 74%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.64 (t, J = 6.8 Hz, 1H), 4.84 (d, J = 6.8 Hz, 2H), 6.08 (q, J = 8.7 Hz, 1H), 7.51–7.55 (m, 2H), 7.59 (dd, J = 8.5, 1.8 Hz, 1H), 7.84–7.90 (m, 3H), 8.01 (d, J = 1.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 59.8, 118.0 (q, J = 34.7 Hz), 123.3 (q, J = 270.7 Hz), 124.2, 126.8, 126.9, 127.1, 127.8, 128.6, 128.8 133.3, 133.7, 134.8, 151.4 (q, J = 5.8 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ = −55.6 (t, J = 8.7 Hz); IR (neat): 3370, 3061, 1647, 1436, 1326, 1195 cm^{-1}; HRMS (ESI$^+$): Calcd. for $[C_{14}H_{11}F_3O+H]^+$: m/z = 253.0835, Found: 253.0835.

4.5. Typical experimental procedure for S_N2'-type reaction of 1 in n-hexane

To a solution of **1** (21.0 mg, 0.1 mmol) in *n*-hexane (1 mL) was added an *n*-hexane solution of *n*-butyl lithium reagent (1.6 M, 0.33 mL, 0.5 mmol) at 0 °C. The reaction mixture was stirred for 3 h at 23 °C, and then the reaction was quenched with 1 N HCl on an ice bath. The mixture was extracted with ethyl acetate, and the combined organic layer was dried over $MgSO_4$, and filtered. The filtrate was evaporated under reduced pressure. Flash column chromatography (SiO_2; *n*-hexane) of the residue afforded compound **2** as a colorless oil (24.1 mg, 96%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.85–0.89 (m, 3H), 1.23–1.46 (m, 4H), 1.69–1.79 (m, 1H), 1.87–1.95 (m, 1H), 3.16–3.27 (m, 1H), 5.40 (s, 1H), 5.55 (s, 1H), 7.27–7.37 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8, 22.5, 28.9, 29.2, 48.2 (q, J = 26.0 Hz), 117.1 126.4, 127.0 (q, J = 279.4 Hz), 127.6, 128.4, 142.5, 143.8; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −69.2 (d, J = 8.7 Hz); IR (neat): 3060, 3026, 2958, 2933, 2874, 1631, 1600, 1262, 1163, 1131, 777, 699 cm^{-1}; HRMS (EI$^+$): Calcd. for $[C_{14}H_{17}F_3+H]^+$: m/z = 242.1282, Found: 242.1286.

4.5.1. 2-Phenyl-3-methyl-1-heptene (**5**)

Compound **5** was obtained using the same procedure as described for **2** in 3% yield. The spectra were consistent with reported data [21].

4.5.2. (E)-2-Butyl-4-fluoro-3-phenyl-3-octen-1-ol (**8**)

Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.80 (t, J = 7.4 Hz, 3H), 0.90 (t, J = 7.4 Hz, 3H), 1.15–1.47 (m, 11H), 1.98–2.07 (m, 2H), 3.06–3.14 (m, 1H), 3.36–3.43 (m, 1H), 3.51–3.56 (m, 1H), 7.11–7.14 (m, 2H), 7.28–7.35 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 14.2, 22.1, 22.9, 28.8 (d, J = 1.9 Hz), 29.0, 29.6 (d, J = 27.9 Hz), 29.8, 41.9 (d, J = 3.9 Hz), 64.6, 118.8 (d, J = 16.4 Hz), 127.2, 128.3, 130.2 (d, J = 2.9 Hz), 136.4 (d, J = 8.7 Hz), 159.8 (d, J = 254.3 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ = −110.2 (t, J = 23.0 Hz); IR (neat): 3368, 2958, 2930, 1684, 1467 cm^{-1}; HRMS (ESI$^+$): Calcd. for $[C_{18}H_{27}FO+Na]^+$: m/z = 301.1938, Found: 301.1934.

4.5.3. (2Z,3Z)-4-Fluoro-2-(2-phenylethylidene)-3-octen-1-ol (**10**)

Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94 (t, J = 7.4 Hz, 3H), 1.39 (sext, J = 7.4 Hz, 2H), 1.51–1.62 (m, 2H), 1.75–1.79 (m, 1H), 2.29 (dt, J = 17.9, 7.4 Hz, 2H), 3.44 (d, J = 7.4 Hz, 2H), 4.29 (d, J = 6.0 Hz, 2H), 5.38 (d, J = 43.2 Hz, 1H), 5.69 (t, J = 7.4 Hz, 1H), 7.18–7.22 (m, 3H), 7.27–7.31 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 22.2, 28.6, 32.8 (d, J = 27.9 Hz), 34.6, 66.9 (d, J = 5.78 Hz), 100.6 (d, J = 11.6 Hz), 126.3, 128.6, 128.6, 129.1, 133.6 (d, J = 2.9 Hz), 140.4, 161.2 (d, J = 264.9 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ = −99.2 (dt, J = 43.2, 17.9 Hz); IR (neat): 3421, 2958, 2930, 1683, 1454 cm^{-1}; HRMS (ESI$^+$): Calcd. for $[C_{16}H_{21}FO+Na]^+$: m/z = 271.1469, Found: 271.1471.

4.5.4. 4,4,4-Trifluoro-3-methyl-2-(2-naphthyl)-1-butene (**12**)

Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44 (d, J = 7.4 Hz, 3H), 3.49–3.61 (m, 1H), 5.51 (s, 1H), 5.63 (s, 1H), 7.45–7.51 (m, 3H), 7.78–7.85 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.0 (q, J = 2.89 Hz), 42.7 (q, J = 27.0 Hz), 117.4, 124.9, 125.4, 126.3, 126.5, 127.4 (q, J = 280.3 Hz), 127.7, 128.2, 128.3, 132.9, 133.4, 139.2, 145.0; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −70.4 (d, J = 8.7 Hz); IR (neat): 3059, 2991, 1626, 1641, 1382, 1167, 1137, 1091 cm^{-1}; HRMS (ESI$^+$): Calcd. for $[C_{15}H_{13}F_3O+H]^+$: m/z = 251.1042, Found: 251.1042.

4.6. DFT study

All calculations were carried out with the Gaussian 09 program package. Structural optimization and vibrational analyses were performed using M06-2X with the 6-31+G(d,p) basis set. Gibbs energies (kcal/mol) obtained by vibrational analyses are presented in the text. No imaginary frequency for intermediates and one imaginary frequency for each transition state were observed. Reaction pathways from the transition states were confirmed by IRC calculation and the vibration modes of their imaginary frequencies.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jfluchem.2015.07.024.

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