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Mechanistic Studies on α-Trifluoromethylation of Ketones via Silyl Enol Ethers and Its Application to Other Carbonyl Compounds

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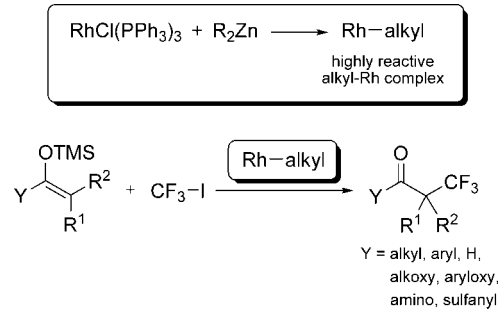

Synthesis of α-CF_3 carbonyl compounds has been recognized to be difficult up to now because the polarization of $CF_3^{\delta-}$-$I^{\delta+}$ is opposite to that of $CH_3^{\delta+}$-$I^{\delta-}$, and this makes it difficult to introduce CF_3^+ unit to enolates. We recently reported an effective α-trifluoromethylation of ketones by using Et_2Zn with Rh catalyst, but the mechanism has not fully been cleared. Now, we carried out the detailed mechanistic studies and found the involvement of a highly reactive alkylrhodium complex which derived from Et_2Zn and $RhCl(PPh_3)_3$ in this α-trifluoromethylation. Furthermore, this α-trifluoromethylation was applied to other types of carbonyl compounds in good yields.

Introduction

Organofluorine compounds have attracted much attention because of their important applications in medicines, pesticides, and/or liquid crystalline materials. Thus, many chemists have concentrated their efforts on their synthesis for many years.[1] Among those studies, trifluoromethylation of various aryl or alkyl halides is one of the most fascinating reactions as represented by Kobayashi−Kumadaki's trifluoromethylation,[2] which uses CF_3Cu derived from CF_3-X, and Burton's trifluoromethylation,[3] which uses CF_2X_2/Zn or Cd. These reactions gave the corresponding cross-coupling products. Taking advantage of their trifluoromethylation, many kinds of reactions for introducing a CF_3 group into various organic molecules have been developed, especially using nucleophilic trifluoromethylation.[4] For example, CF_3-TMS on treatment with a fluoride ion, by Prakash et al., or CF_3-I on treatment with tetrakis(dimethylamino)ethylene (TDAE), by Dolbier et al., reacted with

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(2) (a) Kobayashi, Y.; Kumadaki, I. *Tetrahedron Lett.* **1969**, *10*, 4095–4096. (b) Kobayashi, Y.; Yamamoto, K.; Kumadaki, I. *Tetrahedron Lett.* **1979**, *20*, 4071–4072.

(3) Burton, D. J.; Wiemers, D. M. *J. Am. Chem. Soc.* **1985**, *107*, 5014–5015.

(4) For a review for the nucleophilic trifluoromethylation reagents, see: Langlois, B. R.; Billard, T.; Roussel, S. *J. Fluorine Chem.* **2005**, *126*, 173–179, and references cited therein.

(5) For the nucleophilic trifluoromethylation by using CF_3-TMS, see: (a) Prakash, G. K. S.; Krishnamurti, R.; Olah, G. A. *J. Am. Chem. Soc.* **1989**, *111*, 393–395. (b) Krishnamurti, R.; Bellew, D. R.; Prakash, G. K. S. *J. Org. Chem.* **1991**, *56*, 984–989. (c) Ramaiah, P.; Krishnamurti, R.; Prakash, G. K. S. *Org. Synth.* **1995**, *72*, 232–240. (d) Singh, R. P.; Shreeve, J. M. *Tetrahedron* **2000**, *56*, 7613–7632. (e) Prakash, G. K. S.; Mandal, M. *J. Fluorine Chem.* **2001**, *112*, 123–131.

(6) For the nucleophilic trifluoromethylation by using CF_3-I with TDAE, see: (a) Aït-Mohand, S.; Takechi, N.; Medebielle, M.; Dolbier, W. R., Jr. *Org. Lett.* **2001**, *3*, 4271–4273. (b) Petrov, V. A. *Tetrahedron Lett.* **2001**, *42*, 3267–3269. (c) Xu, W.; Dolbier, W. R., Jr. *J. Org. Chem.* **2005**, *70*, 4741–4745. (d) Pooput, C.; Dolbier, W. R., Jr.; Medebielle, M. *J. Org. Chem.* **2006**, *71*, 3564–3568.

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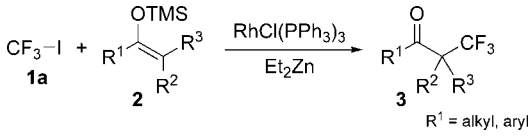
SCHEME 1. Zn-Mediated Rh-Catalyzed α-Trifluoromethylation of Ketones



carbonyl compounds to afford trifluoromethylated carbinols.[5,6] In additioin, a CF_3 radical derived from CF_3-I with SmI_2 or Et_3B was added to olefins.[7]

Although there are a number of methods for introducing a CF_3 unit to an organic molecule as mentioned above, it is difficult to introduce a CF_3 group at the α-position of carbonyl compounds. One of the most simple methods is the use of electrophilic trifluoromethylating reagents such as trifluoromethyl chalcogenium salts,[8] but their insolubility in most organic solvents inhibits their common use in organic synthesis. Another method is the use of radical trifluoromethylation protocols, but this method leads to low yields and requires special equipment or techniques in some cases.[9−11]

Recently, we have reported a Zn-mediated Rh-catalyzed α-trifluoromethylation of ketones via silyl enol ethers (**2**) (Scheme 1).[12] This reaction proceeded smoothly and made it possible to use the aromatic silyl enol ethers that could not be used in Mikami's procedure.[13] However, the mechanism of this effective α-trifluoromethylation of ketones was still unclear. This fact drove to investigate the reaction mechanism. We report herein the result of the mechanistic studies on the α-trifluoromethylation and the further application to other carbonyl compounds.

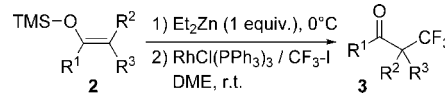
Results and Discussion

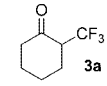
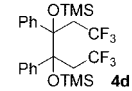
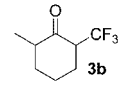
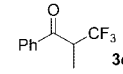
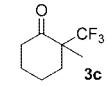
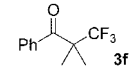
Mechanistic Studies on α-Trifluoromethylation. In a previous report, we disclosed an α-trifluoromethylation of ketones via silyl enol ethers (**2**) using Et_2Zn in the presence of $RhCl(PPh_3)_3$ (Table 1).[12] Various α-CF_3 ketones (**3**) for which synthesizing was difficult came to be easily obtained by using this method.

In this α-trifluoromethylation, we initially had assumed a participation of the SET mechanism, since a dimer product (**4d**) was obtained in an excellent yield on the α-trifluoromethylation of 1-phenyl-1-trimethylsiloxyethylene (**2d**) as shown in entry 4 of Table 1. In fact, Mikami's procedure was a radical α-trifluoromethylation of ketones by using Li, Ti, or Zn enolates assisted Et_3B/O_2.[13] Furthermore, Chen et al. also reported Pd(0)-induced addition of R_f-X to alkenes via a SET mechanism.[14] Thus, we tried to confirm the involvement of radical mechanism using the 1-(trimethylsiloxy)cyclohexene (**2a**) as a substrate (Table 2).

Although the yield was very low and a long reaction time was needed, this reaction gave **3a** even in the absence of the Rh catalyst (entry 2). Since a dialkylzinc such as Et_2Zn is generally not a good radical source, the need to add an additive such as O_2 has been recognized for the generation of alkyl radical,[15] and the yield of **3a** also improved slightly as expected (entry 3). However, although these results suggested the participation of the SET mechanism, the addition of a catalytic amount of radical scavengers such as galvinoxyl or TEMPO to

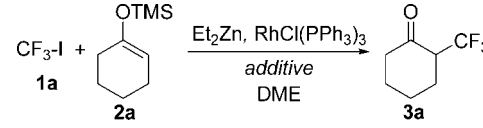
TABLE 1. α-Trifluoromethylation Using Silyl Enol Ethers of Various Ketones



entry	product	yield (%)[a]	ratio[b]	entry	product	yield (%)[a]	ratio[b]
1	 **3a**	74 (81)[c]		4	 **4d**	84[f]	[1:1]
2	 **3b**	- (62)[c,d,e]	[1:1]	5	 **3e**	53	
3	 **3c**	- (37)[c]		6	 **3f**	23	

[a] Isolated yield. [b] Diastereomeric ratio was calculated from ^{19}F NMR. [c] ^{19}F NMR yield calculated from benzotrifluoride (BTF). [d] Total yield of diastereomeric mixture. [e] **3c** was obtained in 15% as a by-product. [f] The dimer (**4d**) was isolated in the yield as the diastereomeric mixture.

TABLE 2. Examination about SET Mechanism



entry	$RhCl(PPh_3)_3$ (mol %)	additive	amount	time (h)	yield[a] (%)
1	2	none		0.5	81
2	none	none		24	16
3	none	O_2	25 mL	3	45
4	2	galvinoxyl	4 mol %	1.5	79
5	2	galvinoxyl	1 equiv	18	42
6	2	TEMPO	4 mol %	1.5	84
7	2	TEMPO	1 equiv	5	76

[a] ^{19}F NMR yield calculated from benzotrifluoride (BTF).

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(7) (a) Lu, X.; Ma, S.; Zhu, J. *Tetrahedron Lett.* **1988**, *29*, 5129–5130. (b) Takeyama, Y.; Ichinose, Y.; Oshima, K.; Utimoto, K. *Tetrahedron Lett.* **1989**, *30*, 3159–3162. (c) Yajima, T.; Nagano, H.; Saito, C. *Tetrahedron Lett.* **2003**, *44*, 7027–7029.

(8) (a) Umemoto, T.; Ishihara, S. *J. Am. Chem. Soc.* **1993**, *115*, 2156–2164. (b) Umemoto, T. *Chem. Rev.* **1996**, *96*, 1757–1777. (c) Ma, J.-A.; Cahard, D. *J. Org. Chem.* **2003**, *68*, 8726–8729.

(9) For the trifluoromethylation of silyl and germyl enolates of esters and ketones, see: (a) Miura, K.; Taniguchi, M.; Nozaki, K.; Oshima, K.; Utimto, K. *Tetrahedron Lett.* **1990**, *31*, 6391–6394. (b) Miura, K.; Takeyama, Y.; Oshima, K.; Utimoto, K. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 1542–1553.

(10) For the trifluoromethylation of lithium enolate of imides, see: (a) Iseki, K.; Nagai, T.; Kobayashi, Y. *Tetrahedron Lett.* **1993**, *34*, 2169–2170. (b) Iseki, K.; Nagai, T.; Kobayashi, Y. *Tetrahedron: Asymmetry* **1994**, *5*, 961–974.

(11) For the trifluoromethylation of enamines, see: (a) Cantacuzène, D.; Dorme, R. *Tetrahedron Lett.* **1975**, *25*, 2031–2034. (b) Cantacuzène, D.; Wakselman, C.; Dorme, R. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1365–1371. (c) Kitazume, T.; Ishikawa, N. *J. Am. Chem. Soc.* **1985**, *107*, 5186–5191. (d) Semisch, C.; Margaretha, P. *J. Fluorine Chem.* **1986**, *30*, 471–475.

(12) Sato, K.; Yuki, T.; Tarui, A.; Omote, M.; Kumadaki, I.; Ando, A. *Tetrahedron Lett.* **2008**, *49*, 3558–3561.

(13) (a) Itoh, Y.; Mikami, K. *Org. Lett.* **2005**, *7*, 649–651. (b) Itoh, Y.; Mikami, K. *Org. Lett.* **2005**, *7*, 4883–4885. (c) Itoh, Y.; Mikami, K. *Tetrahedron* **2006**, *62*, 7199–7203. (d) Mikami, K.; Tomita, Y.; Ichikawa, Y.; Amikura, K.; Itoh, Y. *Org. Lett.* **2006**, *8*, 4671–4673. (e) Itoh, Y.; Houk, K. N.; Mikami, K. *J. Org. Chem.* **2006**, *71*, 8918–8925.

(14) Chen, Q.-Y.; Yang, Z.-Y.; Zhao, C.-X.; Qiu, Z.-M. *J. Chem. Soc., Perkin Trans. 1* **1988**, 563–567.

(15) (a) Ryu, I.; Araki, F.; Minakata, S.; Komatsu, M. *Tetrahedron Lett.* **1998**, *39*, 6335–6336. (b) Bertrand, M. P.; Feray, L.; Nouguier, R.; Perfetti, P. *J. Org. Chem.* **1999**, *64*, 9189–9193. (c) Bertrand, M. P.; Coantic, S.; Feray, L.; Nouguier, R.; Perfetti, P. *Tetrahedron* **2000**, *56*, 3951–3961. (d) Yamada, K.; Fujihara, H.; Yamamoto, Y.; Miwa, Y.; Taga, T.; Tomioka, K. *Org. Lett.* **2002**, *4*, 3509–3511.

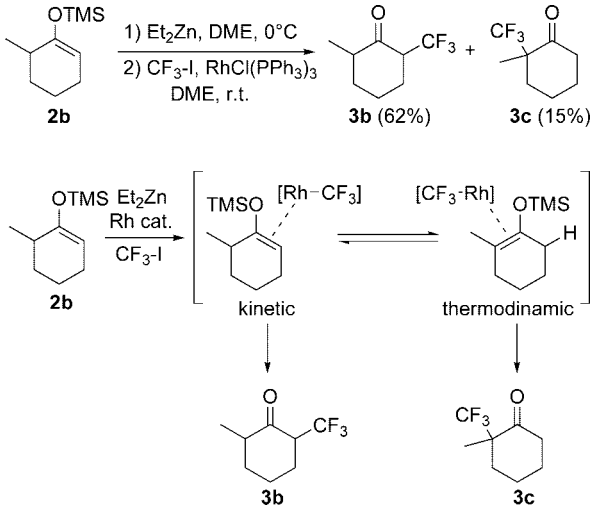
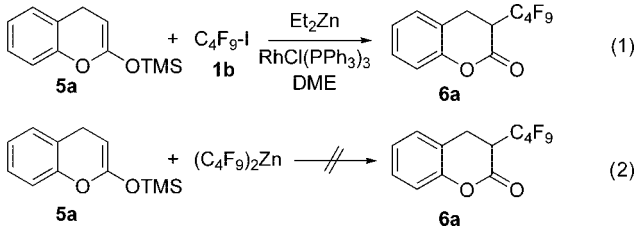


FIGURE 1. Zn-mediated Rh-catalyzed α-trifluoromethylation of **2b**.

SCHEME 2. Examination of α-Fluoroalkylation Using $(R_f)_2Zn$



the reaction mixture did not affect the yield of **3a** significantly (entries 4 and 6). Furthermore, the desired product (**3a**) was obtained even in the presence of a stoichiometric amount of the scavengers, although the yield was decreased slightly owing to formation of a complex mixture as shown in entries 5 and 7. These results mean that SET mechanism was not the main pathway in this Rh-catalyzed reaction.

In addition, the α-trifluoromethylation using 6-methyl-1-(trimethylsiloxy)cyclohexene (**2b**) gave the desired product (**3b**) along with a sizable amount of isomerized side product (**3c**) as shown in Table 1. Isomerization of olefins by Rh catalyst is well-known, and our result strongly suggests the coordination of a Rh complex onto the π-bond of silyl enol ether (Figure 1).

On the other hand, we had also assumed the formation of $(CF_3)_2Zn$ or CF_3ZnX from CF_3-I (**1a**) and Et_2Zn. We found that the reaction could apply to ketene silyl acetals (**5**) which derived from esters, as shown below. In addition, when C_4F_9-I (**1b**) was used in place of CF_3-I, the desired α-R_f carbonyl compound was obtained (eq 1 in Scheme 2). We tried the reaction by using $(C_4F_9)_2Zn$, which was synthesized according to Naumann's procedure,[16] but the desired product (**6a**) could not be obtained at all in the absence of Rh catalyst (eq 2 in Scheme 2). This means that the $(R_f)_2Zn$ is not involved as an active species and the formation of a Rh complex that derived from Et_2Zn is fundamental to give the α-CF_3 ketone (**3**).

We already reported that treatment of $RhCl(PPh_3)_3$ with Et_2Zn immediately gave Rh−Et complex (**7**) or Rh−H complex (**8**),[17]

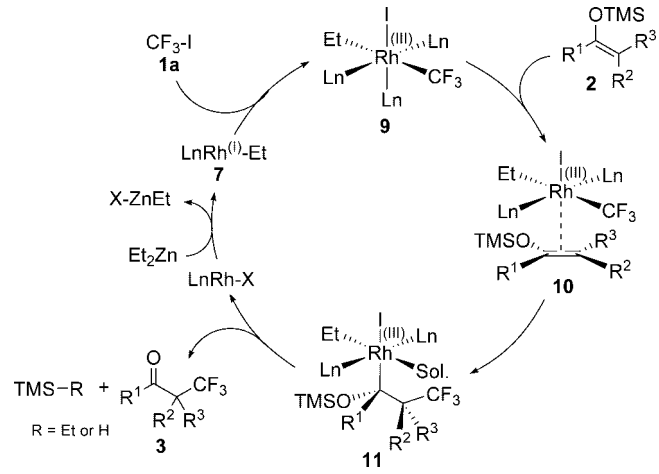


FIGURE 2. Reaction mechanism of Zn-mediated Rh-catalyzed α-trifluoromethylation of carbonyl compounds

and the formation of them is also strongly supported in this reaction. In particular, the key intermediate must be the Rh−Et complex (**7**) in this case, because the use of Me_2Zn instead of Et_2Zn also gave the α-trifluoromethylated product (**3a**) in a good yield (2 h, 66%). In addition, the catalytic effect of Et_2Zn was hardly detected in this reaction (0.5 equiv of Et_2Zn: 55%, 0.1 equiv of Et_2Zn: 18%).

Based on these results, we propose the formation of a highly reactive Rh−Et complex (**7**), which derived from Rh−X catalyst and Et_2Zn, in the mechanism of α-trifluoromethylation (Figure 2). Namely, the oxidative addition of CF_3-I onto **7** to form a Rh(III) complex (**9**) was followed by the coordination onto the π-bond of silyl enol ether. On subsequent addition of the CF_3 unit into the olefin, another Rh(III) complex (**11**) which suffered the reductive elimination was formed to give the desired α-CF_3 product (**3**) along with loss of ethyltrimethylsilane (TMS-Et) or trimethylsilane (TMS-H) with ethylene.

α-Trifluoromethylation of Esters via Ketene Silyl Acetals. We found out the reaction mechanism of the α-trifluoromethylation. Our proposed mechanism suggests that various silyl enol ethers will be able to be used in this reaction. In fact, the reaction could also apply to ketene silyl acetals (**5**) as already mentioned. Then, we attempted to synthesize of α-CF_3 esters (**12**) via ketene silyl acetals in place of silyl enol ethers (**2**). Generally, an ester group is stable, and can be easily transformed to other functional groups. Thus, synthesis of α-CF_3 esters is very important, but only a few methods are known for their synthesis.[18]

First, according to the previous procedure (method A),[12] we examined the reaction with 2-(trimethylsiloxy)-4*H*-chromene (**5a**) as the substrate (Table 3). As shown in entries 1−3, lowering the reaction temperature to 0 °C from room temperature increased the yield of α-CF_3 ester (**12a**), but further cooling to −30 °C decreased the yield. Next, we tried method B for the simplification of the procedure. Namely, the mixture of CF_3-I (**1a**) and **5a** in the presence of $RhCl(PPh_3)_3$ was treated with Et_2Zn. As expected, there were no significant differences in the yields (compare entry 4 with entry 2 of method A). We then examined the amount of the Rh catalyst (entries 4−7). Like as the previous results, the reaction gave the product only in a trace amount in the absence of $RhCl(PPh_3)_3$ as shown in entry

(16) Naumann, D.; Schorn, C.; Tyrra, W. *Z. Anorg. Allg. Chem.* **1999**, *625*, 827–830.

(17) (a) Sato, K.; Omote, M.; Ando, A.; Kumadaki, I. *Org. Lett.* **2004**, *6*, 4359–4361. (b) Sato, K.; Omote, M.; Ando, A.; Kumadaki, I. *Org. Synth.* **2006**, *83*, 177–183. (c) Sato, K.; Ishida, Y.; Murata, E.; Oida, Y.; Mori, Y.; Okawa, M.; Iwase, K.; Tarui, A.; Omote, M.; Kumadaki, I.; Ando, A. *Tetrahedron* **2007**, *63*, 12735–12739.

(18) (a) Molines, H.; Wakselman, C. *J. Fluorine Chem.* **1987**, *37*, 183–189. (b) Duan, J.-X.; Su, D.-B.; Chen, Q.-Y. *J. Fluorine Chem.* **1993**, *61*, 279–284. (c) Hagooly, A.; Rozen, S. *Chem. Commun.* **2004**, 594–595.

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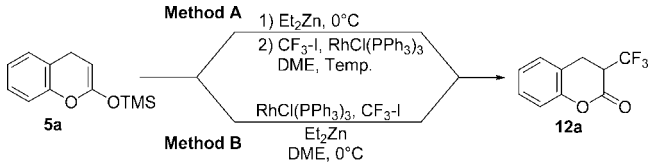
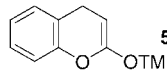
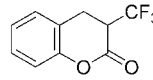
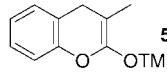
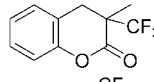
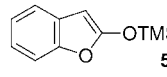
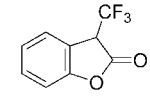
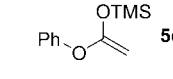
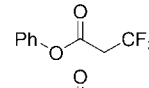
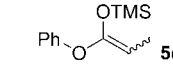
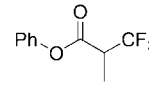
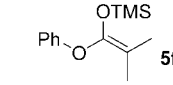
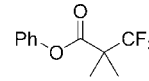
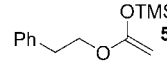
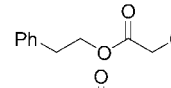
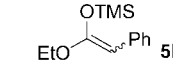
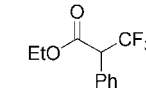
TABLE 3. Optimization of Reaction Conditions



entry	method	$RhCl(PPh_3)_3$ (mol %)	time (h)	T (°C)	yield[a] (%)
1	A	2	0.5	rt	69
2		2	1	0	76
3		2	24	−30	37
4	B	2	1	0	77
5		1	1.5	0	70
6		4	1	0	78
7		0	24	0	trace

[a] ^{19}F NMR yield calculated from benzotrifluoride (BTF).

TABLE 4. α-Trifluoromethylation Using Various Ketene Silyl Acetals

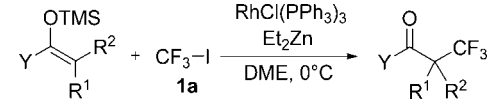
entry	substrate	time (h)	product	yield (%)[a]
1	 **5a**	1	 **12a**	63 (77)[b]
2	 **5b**	1.5	 **12b**	59
3	 **5c**	1	 **12c**	0
4	 **5d**	1	 **12d**	68
5	 **5e**	1	 **12e**	57
6	 **5f**	1	 **12f**	31
7	 **5g**	1	 **12g**	48
8	 **5h**	2	 **12h**	37

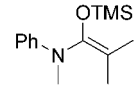
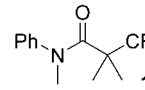
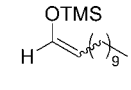
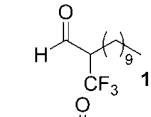
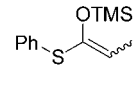
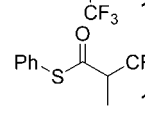
[a] Isolated yield. [b] ^{19}F NMR yield calculated from benzotrifluoride (BTF).

7. It is clear that the Rh catalyst was also playing an important role in this reaction.

In the next step, various substrates were examined on the basis of the condition in entry 4 of Table 3. The results are summarized in Table 4. All of the reactions smoothly proceeded. As shown in entries 1, 2, and 4−6, the ketene silyl acetals which have an aryloxy group gave the desired α-CF_3 esters in good yields. Also in this reaction, the more crowded the reaction centers were, the lower the yields were as shown in entries 4−6. However, it was interesting that the highly crowded product (**12b**) with a CF_3-attached quaternary carbon was obtained in a good yield as shown in entry 2. The substrate (**5b**) might have enough space for introduction of the CF_3 group due to its high planarity. In entries 7 and 8, the ketene silyl acetals which have alkoxy group also gave the products in moderate yields. On the other hand, the substrate (**5c**) did not give the product at all. The reason for this decreased reactivity might be attributed to the aromatization by the trimethylsilylation of coumaranone. For the same reason, trimethyl(phenoxy)silane did not give the product.

TABLE 5. α-Trifluoromethylation Using Other Silyl Enol Ethers



entry	substrate	time (h)	product	yield (%)[a]
1		1	 **13a**	55
2		2	 **14**	42
3		2	 **15**	41

[a] Isolated yield.

α-Trifluoromethylation of Other Carbonyl Compounds. Next, we investigated the α-trifluoromethylation of other carbonyl compounds. These results are summarized in Table 5. As shown in entry 1, the α-trifluoromethylation of an amide proceeded smoothly and gave the corresponding product (**13a**) in a moderate yield, even though it has two substituents on the α-position. An α-CF_3 aldehyde (**14**) was also obtained in a moderate yield as shown in entry 2. Furthermore, the reaction could be also applied to the synthesis of an α-CF_3 thioester (**15**) in a moderate yield (entry 3). It is well-known that amide group is found frequently in bioactive compounds such as peptides. However, there are a few methods for synthesizing α-CF_3 amides to the best of our knowledge.[19] Furthermore, the α-trifluoromethylation of aldehydes or thioesters has hardly ever reported, while most of them suffer cross-coupling reactions with sp^2-halides to give α-CF_3 enals.[20] This reaction is from the above results very useful because it could be applied to the directly synthesis of α-CF_3 carbonyl compounds.

In the last part, we tried to synthesize of α-CF_3 secondary amides. As already known, it is difficult to synthesize and to purify the *N,O*-silyl ketene acetals owing to the lone pair on the nitrogen that makes them less stable. In particular, the synthesis of them from the corresponding secondary amides is rarely reported owing to the influence of amide hydrogen. Thus, it is easily anticipated that the synthesis of α-CF_3 secondary amides would be difficult by using this reaction. However, we thought the difficulty would be overcome by transamidation with an α-CF_3 ester and a primary amine. Thus, the α-CF_3 ester

(19) (a) Chen, Q.; Wu, S. *J. Chem. Soc., Chem. Commun.* **1989**, 705–706. (b) Iseki, K.; Nagai, T.; Kobayashi, Y. *Tetrahedron Lett.* **1993**, *34*, 2169–70. (c) Xiao, J.-C.; Chen, Q.-Y. *J. Fluorine Chem.* **2003**, *123*, 189–195.

(20) (a) Paratian, J. M.; Labbe, E.; Sibille, S.; Perichon, J. *J. Organomet. Chem.* **1995**, *489*, 137–143. (b) Kamigata, N.; Udodaira, K.; Shimizu, T. *Phosphorus, Sulfur Silicon Relat. Elem.* **1997**, *129*, 155–168. (c) Nowak, I.; Robins, M. J. *J. Org. Chem.* **2007**, *72*, 2678–2681.

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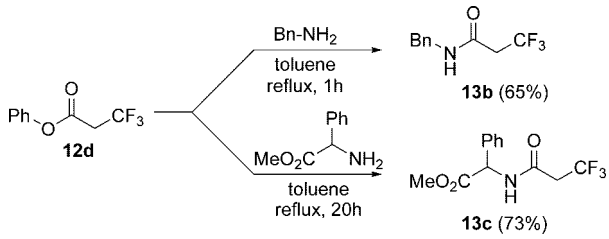
SCHEME 3. Synthesis of α-Trifluoromethylated Secondary Amides



(**12d**), synthesized by our reaction, was treated with primary amines to give the corresponding α-CF_3 secondary amides (**13b** and **13c**) in good yields (Scheme 3).

Conclusions

In conclusion, we clarified the reaction mechanism based on detailed mechanistic studies, where the highly reactive alkylrhodium complex that derived from Et_2Zn and $RhCl(PPh_3)_3$ played a very important role in this α-trifluoromethylation. Furthermore, we carried out the synthesis of various α-CF_3 carbonyl compounds. The α-trifluoromethylation reaction is one of the most important reactions not only in organofluorine chemistry but also in medicinal chemistry. Thus, we hope this reaction is used in various fields.

Experimental Section

General Procedure for the α-Trifluoromethylation of Ketones. The reaction procedure which was used for the mechanistic study was followed according to the previous report (method A).[12] Namely, to a solution of TMS enol ether (**2**, 1.0 mmol) in DME (3 mL) was added a solution of 1.0 M Et_2Zn in hexane (1.0 mmol) gradually at 0 °C and stirred for 1 h at this temperature. After the reaction mixture was cooled to −30 °C, CF_3−I (**1a**, ca. 1 mL at −78 °C) was introduced through a gas inlet tube, and then a solution of $RhCl(PPh_3)_3$ (2 mol%) and an additive in DME (2 mL) was immediately added. The reaction mixture was allowed to warm to room temperature and was stirred for 0.5 h. The resulting mixture was quenched with 10% HCl and extracted with Et_2O. The Et_2O layer was washed with satd NaCl and dried over $MgSO_4$. The solvent was removed in vacuo, and then benzotrifluoride (BTF) was added to the residue. The yield was calculated from the integration ratio of the **3** and BTF on ^{19}F NMR.

General Procedure for the Synthesis of α-CF_3 Esters (12) (Method B). To a solution of $RhCl(PPh_3)_3$ (2 mol %) and ketene silyl acetal (**5**, 1.0 mmol) in DME (5 mL) was added CF_3-I (**1a**, ca. 1 mL at −78 °C) at −40 °C. After the mixture was warmed to 0 °C, 1.0 M Et_2Zn in hexane (1 mL, 1.0 mmol) was slowly added, and the mixture was stirred for 1 h at the same temperature. The resulting mixture was quenched with 10% HCl and extracted with Et_2O. The Et_2O layer was washed with satd NaCl and dried over $MgSO_4$. The solvent was removed in vacuo, and then benzotrifluoride (BTF) was added in the residue. The yield was calculated from the integration ratio of the **12** and BTF on ^{19}F NMR. After the calculation, the residue was purified by column chromatography ($CHCl_3$/hexane = 1:1) to give **12**.

General Procedure for the Synthesis of α-CF_3 Secondary Amides (13b or 13c). A solution of phenyl 3,3,3-trifluoropropionate (**12d**, 0.5 mmol) and a primary amine (0.7 mmol) in toluene (2 mL) was refluxed until the disappearance of **12d** on the GLC analysis. The resulting mixture was quenched with 10% HCl and extracted with AcOEt. The AcOEt layer was washed with satd NaCl and dried over $MgSO_4$. The solvent was removed in vacuo, and the residue was purified by column chromatography to give the product.

Acknowledgment. We gratefully acknowledge TOSOH F-TECH, Inc., for the generous gift of CF_3I.

Supporting Information Available: Detailed experimental procedures and spectroscopic data for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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