

Iridium-Catalyzed Reactions of Trifluoromethylated Compounds with Alkenes: A C_{sp}³–H Bond Activation α to the Trifluoromethyl Group**

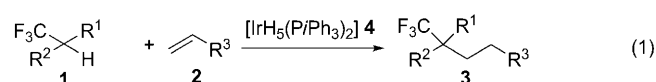
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Trifluoromethylated compounds play an important role in medicinal,^[1] agrochemical,^[2] and material science;^[3] therefore, exploitation of a general method for the synthesis of these compounds is highly desirable. Introduction of an α -trifluoromethyl group into the target molecule relies on either trifluoromethyl reagents or trifluoromethylated synthetic building blocks.^[4] It has been difficult to achieve carbon–carbon bond formation via α -trifluoromethyl carbanions because these carbanions and related organometallic species spontaneously release fluoride species to produce 1,1-difluoroolefins.^[4–5] This notorious decomposition of α -trifluoromethyl carbanions has hindered the development of this species for use in organic synthesis.^[6] Only few methods on the synthetic use of α -trifluoromethyl carbanions, under specific reaction conditions, have been reported.^[6–7]

Our research group has developed the transition-metal-catalyzed C_{sp}³–H functionalization reaction stemming from the α heteroatom effect.^[8] In light of the potent ability of the transition-metalated carbon nucleophiles to promote carbon–carbon bond forming reactions under neutral reaction conditions, we examined the activation of a C_{sp}³–H bond α to a trifluoromethyl group. Herein, we report the iridium- or ruthenium-catalyzed reactions of trifluoromethylated compounds with alkenes to afford alkylated products in an atom-economic and selective manner under neutral reaction conditions without the formation of any defluorinated by-product.

We found that [IrH₅(PiPr₃)₂] acts as an efficient catalyst for the reaction of trifluoromethyl compounds (**1**) with alkenes (**2**) at room temperature or at higher temperatures [Eq. (1)]. To our knowledge, no example of C–H bond activation α to a trifluoromethyl group with transition metal catalysts has been reported. Although recent progress on the transition-metal-catalyzed activation of carbon–fluorine bonds is striking.^[9]

Initially, we examined the reaction of methyl 1,1-trifluoroacetate (**1a**) with acrylonitrile (**2a**) at room temperature and found that the low valent hydride complexes of



iridium and ruthenium catalyzed the reaction highly efficiently (Table 1). [IrH₅(PiPr₃)₂] (**4**) proved to be the best catalyst among those examined. In the presence of 1 mol % of

Table 1: The reaction of methyl 1,1-bis(trifluoromethyl) acetate (**1a**) with acrylonitrile (**2a**) in the presence of Ru/Ir catalysts or conventional bases.^[a]

Entry ^[a]	Catalyst	Mol [%]	Solvent	t [h]	Conv. [%]	Yield [%] ^[b]
1	[IrH ₅ (PiPr ₃) ₂]	1	toluene	22	99	92 (89)
2	[IrH ₅ (PiPr ₃) ₂]	5	toluene	3	100	97 (94)
3	[Cp*RuH(PPh ₃) ₂]	1	toluene	24	94	94
4	[CpRuH(PPh ₃) ₂]	1	toluene	24	38	84
5	[RuH ₂ (PPh ₃) ₄]	1	toluene	24	18	78
6	[RuH ₂ (CO)(PPh ₃) ₃]	1	toluene	24	0	0
7	PiPr ₃	10	toluene	3	16	19
8	PPh ₃	100	THF	24	11	0
9	DBU	100	toluene	16	40	10
10	<i>t</i> BuOK	100	THF	16	50	0
11	MeONa	100	MeOH	16	50	0
12	Et ₃ N	100	MeCN	64	100	27
13	BnNMe ₃ ⁺ OH [–] ^[c]	100	MeOH	16	100	0

[a] Unless specified, the reaction was carried out with **1a** (0.2 mmol, 0.5 M in toluene) and acrylonitrile **2a** (0.6 mmol, 3 equiv) in the presence of a catalyst at room temperature. [b] Yield determined by ¹⁹F NMR spectroscopy using 1,3-bis(trifluoromethyl)benzene as an internal standard. Yield of the isolated product is shown in parenthesis. [c] 40% methanol solution. Bn = benzyl, Cp = cyclopentadienyl, Cp* = pentamethylcyclopentadienyl, DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene.

the catalyst **4** in toluene, the reaction gave methyl 4-cyano-2,2-bis(trifluoromethyl)butyrate (**3a**) in 92% yield and with 99% conversion of **1a** (Table 1, entry 1). [Cp*RuH(PPh₃)₂] was also useful as a catalyst (Table 1, entry 3). Notably, the desired product **3a** was not obtained by the reaction of **1a** in the presence of conventional bases such as DBU, *t*BuOK, MeONa, Et₃N, or BnNMe₃⁺OH[–] (Table 1, entries 9–13). Phosphines such as PiPr₃ and PPh₃ were not effective (Table 1, entries 7 and 8). Changing the solvent effect had a dramatic effect. The best yield was obtained in a nonpolar solvent such as toluene. The reactions of **1a** in DME (1,2-dimethoxyethane) and THF (tetrahydrofuran) gave **3a** in

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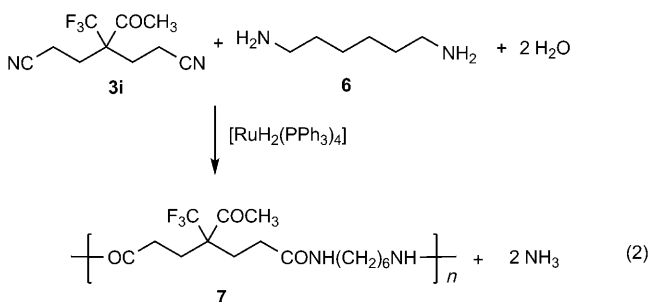
92% and 88% yield, respectively. Meanwhile, the same reaction in acetonitrile resulted in 5% yield.

The representative results of the iridium-catalyzed reaction of trifluoromethylated compounds with alkenes are shown in Table 2. The substrates bearing nitrile (**1b**) and ester (**1c**) functionalities were converted into the corresponding products in excellent yields (Table 2, entries 1–3). Notably, reactions that involved a substrate bearing an electron-donating substituent, such as a methoxy group, occurred readily. Thus, the iridium-catalyzed reaction of 1,1,1,3,3-pentafluoro-2-(trifluoromethyl)-3-methoxypropane (**1d**) gave the product **3d** in 56% yield (Table 2, entry 4).

The reaction of 2-(trifluoromethyl)cyclohexanone (**1e**) with acrylonitrile gave the product (**3e**) in 65% yield

(Table 2, entry 5). The reactions of trifluoromethylated compounds **1** with methyl vinyl ketone (**2b**) also proceeded but required a higher reaction temperature in comparison to the reaction with acrylonitrile (Table 2, entries 6 and 7). Thus, the reactions of **1a** and **1b** with **2b** at 110°C gave the corresponding compounds **3f** and **3g** in 82% and 61% yields, respectively. The reaction of trifluoromethyl compounds bearing two C–H bonds α to the trifluoromethyl group gave the double alkylation products exclusively. Thus, the reaction of 3,3,3-trifluoropropionitrile (**1f**) with **2a** gave 4-cyano-4-(trifluoromethyl)-heptane-1,7-dinitrile (**3h**) in 77% yield (Table 2, entry 8), and the reaction of 4,4,4-trifluoro-2-butanone (**1g**) with **2a** gave 4-acetyl-4-trifluoromethylheptane-1,7-dinitrile (**3i**) in good yield (Table 2, entry 9).

The products obtained are highly useful intermediates for the synthesis of industrially important trifluoromethylated compounds.^[9] Next, we demonstrated the catalytic production of polyamides bearing trifluoromethyl groups (which are useful for material science) by using our unique environmentally benign ruthenium-catalyzed method.^[10] The polycondensation of the dinitrile compound bearing a trifluoromethyl group **3i** with 1,6-hexanediamine (**6**) in the presence of [RuH₂(PPh₃)₄] catalyst (3 mol %) and two equivalents of water in DMF at 160°C gave the trifluoromethylated polyamide **7** in 96% yield along with ammonia as shown in Equation (2). The GPC analysis of **7** showed *M_n* = 2592 g mol^{−1} and *M_w* = 10878 g mol^{−1}, as well as PDI = 4.20.



The present iridium-catalyzed reaction can be rationalized by assuming that the C_{sp³}–H bond α to the trifluoromethyl group is activated with low valent iridium or ruthenium species,^[7] and subsequent insertion to alkenes and reductive elimination gives the product. It is noteworthy that the reaction occurs under heating conditions without the formation of defluorinated by-products. The lack of by-products may result from the stability of the fluoromethyl-iridium complex against decomposition that involves β -fluoro elimination, particularly under neutral reaction conditions.^[11]

In conclusion, we have found a novel and efficient iridium- or ruthenium-catalyzed reactions of trifluoromethylated compounds with alkenes without the formation of defluorinated by-products. The reaction is highly useful and will provide scope for finding other new types of catalytic reactions in fluorine chemistry.

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Table 2: Iridium-catalyzed reaction of α -trifluoromethylated compounds (**1**) with alkenes (**2**).^[a]

Entry	Substrate 1	Alkene 2	Product 3	<i>T</i> [°C]	<i>t</i> [h]	Yield [%] ^[b]
1				25	3	97 (94)
2				50	1	(91)
3				25	5	(93)
4				25	40	81 (56)
5 ^[c]				50	40	76 (65)
6				110	18	(82)
7				110	16	(61)
8				110	7	(77)
9				50	5	(70)

[a] The reaction was carried out with **1** (0.2 mmol) and **2** (0.3 mmol) in the presence of [IrH₅(PPr₃)₂] (5 mol %) in toluene (0.5 mL) under argon or in a sealed tube. [b] Yield determined by ¹⁹F NMR spectroscopy using 1,3-bis(trifluoromethyl)benzene as an internal standard. Yield of the isolated product is shown in parenthesis. [c] The ratio of **1e**/**2a** is 1.5:1 and the conversion was 86%.

Keywords: alkenes · C–H activation · fluorides · iridium · ruthenium

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