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The fluorine-containing π-allylmetal complex. The transition metal-catalyzed allylic substitution reaction of fluorinated allyl mesylates with various carbon nucleophiles

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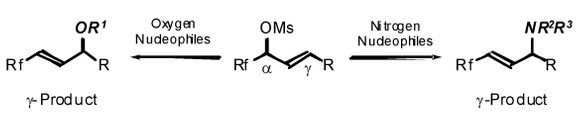
The allylic substitution reaction of α-fluoroalkylated allyl mesylates with various carbon nucleophiles in the presence of transition metal catalyst (Pd and Mo) proceeded with high regioselectivity to give the corresponding γ-fluoroalkylated products in excellent yields.

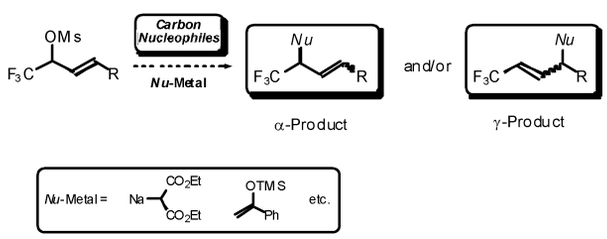
Introduction

Transition metal-catalyzed allylic substitution is one of the most efficient and the most versatile methods for carbon–carbon and carbon–heteroatom bond formation, and hence is the focus of intense synthetic attention.[1] To date, considerable effort has been devoted to the development of more efficient reactions catalyzed by various transition metals such as palladium,[2] molybdenum,[3] tungsten,[4] iridium,[5] rhodium,[6] ruthenium,[7] *etc.* As a result, a number of reactions are available today which very often afford high regio- and stereo-selectivity. In contrast to the remarkable progress made for the reaction of *non-fluorinated* allylic substrates, little attention has been paid to the transition metal-catalyzed allylic substitution reaction of *fluorine-containing* allylic esters so far. There have been quite limited studies on the allylic substitution reaction in fluorine chemistry.[8] Recently, we have reported that the reaction of α-fluoroalkylated allyl mesylates with various carboxylates and amines in the presence of palladium catalyst proceeds in a highly regio- and stereo-selective fashion to give the corresponding γ-products, allylic alcohol or amine derivatives in excellent yields, respectively[9] (Scheme 1).



Scheme 1

Herein we wish to report an extension of our studies to the allylic substitution reaction of fluorine-containing allylic mesylates with various carbon nucleophiles in detail (Scheme 2).

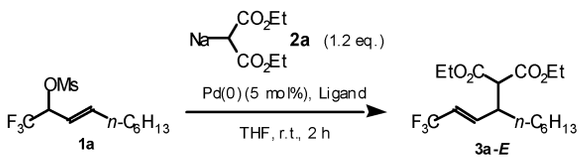


Scheme 2

Results and discussion

We initially examined the reaction of α-trifluoromethylated allyl mesylate **1a** with diethyl sodiomalonate **2a** using various palladium catalysts as listed in Table 1.[10] It was found that the ligand on palladium played an important role in the present allylic substitution reaction. Thus, the use of $Pd_2(dba)_3{\cdot}CHCl_3$ resulted in the complete recovery of the starting material. In contrast, the addition of various monodentate ligands such as triphenylphosphine, tri(2-furyl)phosphine, triphenyl phosphite, tributylphosphine, and *t*-octyl isocyanide was found to facilitate the reaction remarkably (entries 2–10). Additionally, the ratio of palladium and the ligand was crutial for effecting the high yield (entries 2–6). It was found that the palladium

Table 1 Investigation of the effect of the ligands



Entry	Catalyst	Yield of **3a-*E*** (%)[a]	Unreacted **1a** (%)[a]
1	$1/2[Pd_2(dba)_3{\cdot}CHCl_3]$	0	96
2	$1/2[Pd_2(dba)_3{\cdot}CHCl_3]$ + PPh_3	38[b]	44
3	$1/2[Pd_2(dba)_3{\cdot}CHCl_3]$ + $2PPh_3$	82[c]	0
4	$1/2[Pd_2(dba)_3{\cdot}CHCl_3]$ + $4PPh_3$	90	0
5	$Pd(OAc)_2$ + $5PPh_3$	93	0
6	$Pd(PPh_3)_4$	(99)	0
7	$1/2[Pd_2(dba)_3{\cdot}CHCl_3]$ + $4P(2\text{-furyl})_3$	87	0
8	$1/2[Pd_2(dba)_3{\cdot}CHCl_3]$ + $4P(OPh)_3$	61	32
9	$1/2[Pd_2(dba)_3{\cdot}CHCl_3]$ + $4P(n\text{-Bu})_3$	52	46
10	$1/2[Pd_2(dba)_3{\cdot}CHCl_3]$ + 4(*t*-Oct)NC	70	29
11	$1/2[Pd_2(dba)_3{\cdot}CHCl_3]$ + $4P(o\text{-Tol})_3$	0	quant.
12	$1/2[Pd_2(dba)_3{\cdot}CHCl_3]$ + 2dppe	20	75
13	$1/2[Pd_2(dba)_3{\cdot}CHCl_3]$ + dppf	0	94
14	$1/2[Pd_2(dba)_3{\cdot}CHCl_3]$ + 2bpy	19	77

[a] Determined by ^{19}F NMR. Value in parentheses is of isolated yield. [b] A diene was produced in 16% yield. [c] A diene was formed in 8% yield (see Scheme 3).

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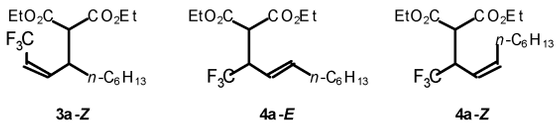


Fig. 1

complexes which were prepared from palladium(0) species and triphenylphosphine in a ratio of 4 : 1, gave the corresponding allylic substitution product **3a-*E*** in excellent yields (entry 4–6). On the other hand, bulky ligands such as $(o\text{-Tol})_3P$ did not provide the desired product at all (entry 8). Changing the ligand on palladium into a bidentate ligand such as dppe, dppf, and bpy caused a large decrease in the formation of **3a-*E*** (entries 9–11). In all cases, neither γ-*Z*-product **3a-*Z*** nor α-*E* or *Z*-products **4a-*E***, **4a-*Z*** were detected (Fig. 1).[11]

Having identified optimal catalyst, $Pd(PPh_3)_4$, a series of nucleophiles were applied to the reaction of **1a** and the results are summarized in Table 2.

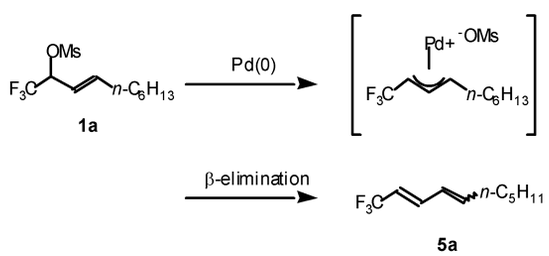
As shown in entries 1–5, the carbanions derived from diethyl malonate, ethyl acetoacetate, malononitrile, ethyl cyanoacetate, and Hornor–Wadsworth–Emmons reagent reacted smoothly with allyl mesylate **1a** in the presence of $Pd(PPh_3)_4$ to give the corresponding **3a-*E*** in almost quantitative yields. In all cases, the γ-products with *E* configuration at the newly created olefinic bond were formed exclusively. No trace of the α-products were detected at all. In entries 2, 4, and 5, the mixture of diastereomers was produced in a ratio of *ca.* 1 : 1.

We also examined the reaction of allyl mesylate **1a** with other carbon nucleophiles such as silyl enol ether, zinc acetylide, phenyl zinc reagent, and lithionitromethane, in the presence of the palladium catalyst at room temperature or 50 °C (entries 6–12). However, the desired products were not formed and the starting material was recovered in almost all cases. In the reaction with lithionitromethane, the decomposition of the π-allylpalladium complex occurred preferentially to lead to the diene **5a** in 80% yield (entry 12 and Scheme 3).

We next investigated the effect of the side chain R in the allylic mesylate **1** on the present reaction as compiled in Table 3. The substrate **1b** having a phenyl group as R was too unstable to isolate, so that the crude material after the mesylation of the corresponding allylic alcohol was employed for the reaction. In this case, a slight decrease in the stereoselectivity at the newly created olefinic bond was observed (entry 2). Changing the substituent from the phenyl to benzyloxymethyl group led to a further decrease in the stereoselectivity at the double bond (entry 3).

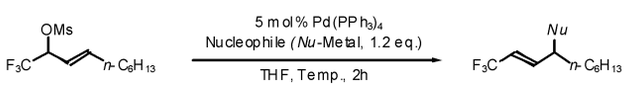
Interestingly, in the reaction of **1d** where R was H, the bisallylated products **6-*EE***, **6-*EZ***, and **6-*ZZ*** were obtained randomly, in addition to the monoallylated products **3h-*E*** and **3h-*Z*** (Table 4, entry 1). In order to obtain the allylic substitution products stereoselectively, we re-examined the effect of transition metal catalysts, as summarized in Table 4.

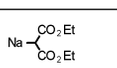
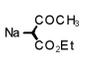
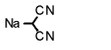
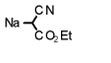
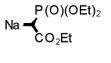
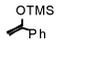
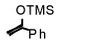
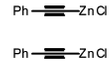
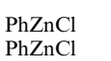
Palladium catalysts were employed bearing a variety of ligands such as $(o\text{-Tol})_3P$, dppe, 2,2′-bipyridyl **7**, and iminophosphine **8** (shown in Fig. 2). As shown in entries 2–6, the allylic substitution reaction of **1d** with **2a** proceeded smoothly to give the corresponding products **3** and **6** in good to excellent yields. In all cases, the γ-product was obtained exclusively and no trace of the α-product was detected. However, the monoallylated- and bisallylated products were obtained in almost 1 : 1 ratio and high *E* selectivity was obtained at the newly formed olefinic bond.



Scheme 3

Table 2 The palladium-catalyzed allylic substitution reaction of α-trifluoromethylated allylic mesylates with various carbon nucleophiles



Entry	Nucleophile (*Nu*-Metal)	Temp./°C	Product	Yield of **3** (%)[a]	Unreacted **1a** (%)[a]
1		rt	**3a-*E***	(99)	0
2		rt	**3b-*E***	(98)	0
3		rt	**3c-*E***	(86)	trace
4		rt	**3d-*E***	(99)	0
5		rt	**3e-*E***	(94)	0
6		rt	—	0	84
7		50	—	0[b]	13
8		rt	—	0	96
9		50	—	0	79
10	PhZnCl	rt	—	0	98
11	PhZnCl	50	—	0	80
12	$LiCH_2NO_2$	rt	—	0[c]	0

[a] Determined by ^{19}F NMR. Values in parentheses are of isolated yields. [b] An unidentified product was produced in 76% yield. [c] A diene was formed in 80% yield.

In search for more efficient catalysts affording high levels of regio- and stereo-selectivity, we tried using molybdenum catalysts for the allylic substitution reaction of **1d**. As shown in entry 7, molybdenum(cycroheptatriene)tricarbonyl did not give the desired product at all. Even when triphenylphosphine was employed as the ligand, in sharp contrast to the palladium catalyst, the product was not formed (entry 8). The use of dppe and iminophosphines (IP(Ph) **8** and IP(Cy) **9**) led to the preferential formation of **3**, but the stereoselectivity in **3** or the yield was greatly decreased (entries 9–11).

The use of bipyridyl ligand, on the other hand, gave exclusive *E*-stereoselection at the newly formed olefinic bond as shown in entry 12, although the yield was only 29%. Prolonged reaction time increased the yield from 29 to 42% (entry 13). The reaction in DME did not afford a dramatic change in the yield (entry 14). Of much interest is that the employment of 1,4-dioxane as the solvent improved the reaction markedly, giving a high yield (92%) as well as the high regio- and stereo-selectivity (**3** : **6** = 77 : 23, the exclusive *E* selectivity, entry 15). Phenanthroline **10** was also a good ligand, which afforded high regio- and stereo-selectivity, although the reaction was slightly slow (entries 17 and 18). It was also found that neither diimine **11** nor bispicolinylamide **12** gave the allylated product (entries 19 and 20). In all cases, only γ-products were obtained and no trace of the α-products was detected.

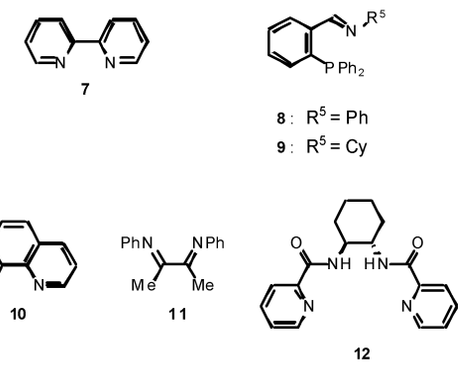
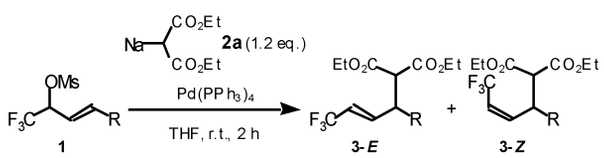


Fig. 2

Table 3 Examination of the effect of the side chain R



Entry	R	Product	Yield of **3** (%)[a]	*E* : *Z*[b]
1	n-C_6H_{13} (**a**)	**3a-*E***	99	100 : 0
2	Ph (**b**)	**3f-*E, Z***	81[c]	94 : 6
3	CH_2OBn (**c**)	**3g-*E, Z***	81	72 : 28

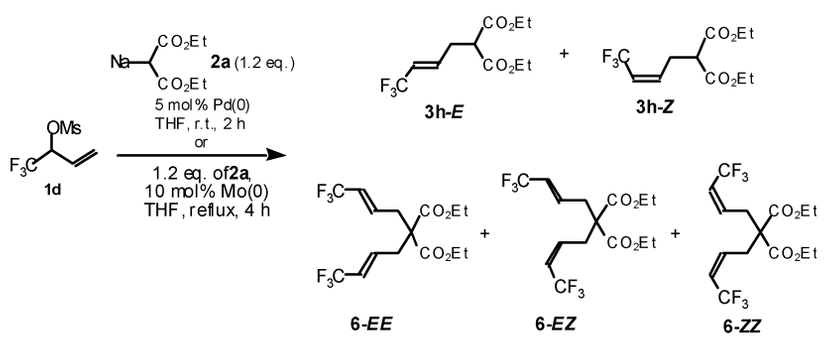
[a] Isolated yield. [b] Determined by ^{19}F NMR. [c] Based on the corresponding allylic alcohol.

Mechanism

The following mechanism might be proposed, as described in Schemes 4 and 5.

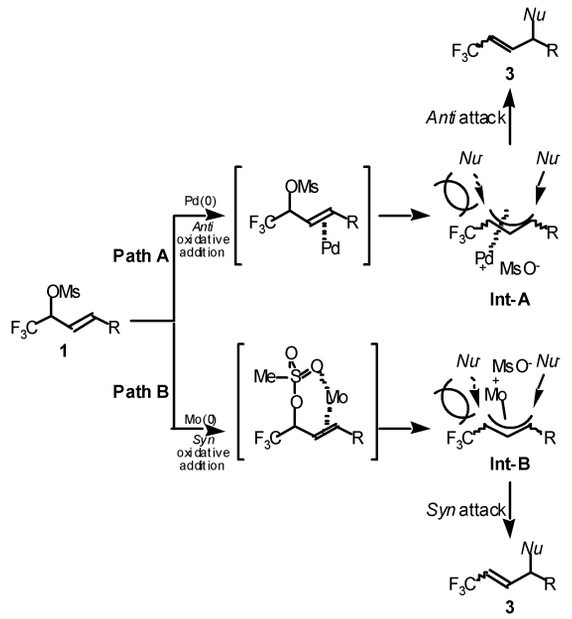
Generally, palladium-catalyzed allylic substitution reaction with stabilized carbon nucleophiles occurs *via anti* oxidative

Table 4 The reaction of α-trifluoromethylated allyl mesylate with sodiomalonate in the presence of palladium or molybdenum catalyst

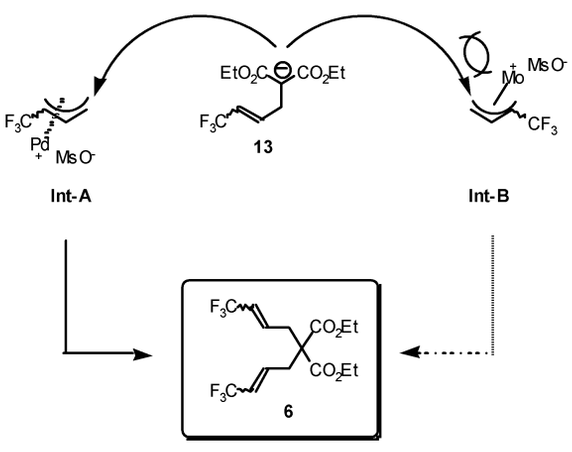


Entry	Catalyst	Yield of **3** and **6** (%)[a]	**3** (*E* : *Z*) : **6** (*EE* : *EZ* : *ZZ*)[a]	Unreacted **1d** (%)[a]
1	$Pd(PPh_3)_4$	95	56 (60 : 40) : 44 (43 : 45 : 12)	0
2	$1/2[Pd_2(dba)_3{\cdot}CHCl_3]$	64	39 (100 : 0) : 61 (95 : 5 : 0)	33
3	$1/2[Pd_2(dba)_3{\cdot}CHCl_3]$ + 4(*o*-Tol)$_3$P	68	57 (90 : 10) : 43 (90 : 10 : 0)	28
4	$1/2[Pd_2(dba)_3{\cdot}CHCl_3]$ + 2dppe	85	56 (100 : 0) : 44 (95 : 5 : 0)	13
5	$1/2[Pd_2(dba)_3{\cdot}CHCl_3]$ + 2bpy[b]	85	56 (100 : 0) : 44 (97 : 3 : 0)	5
6	$1/2[Pd_2(dba)_3{\cdot}CHCl_3]$ + 2IP(Ph)[c]	95	52 (100 : 0) : 48 (62 : 34 : 4)	0
7	$Mo(CO)_3(C_7H_8)$	0	—	88
8	$Mo(CO)_3(C_7H_8)$ + 2PPh_3	0	—	96
9	$Mo(CO)_3(C_7H_8)$ + dppe	71	86 (57 : 43) : 14 (50 : 40 : 10)	24
10	$Mo(CO)_3(C_7H_8)$ + IP(Ph)[c]	22	96 (77 : 23) : 4 (100 : 0 : 0)	67
11	$Mo(CO)_3(C_7H_8)$ + IP(Cy)[c]	18	100 (67 : 33) : 0	72
12	$Mo(CO)_3(C_7H_8)$ + bpy	29	93 (100 : 0) : 7 (100 : 0 : 0)	66
13[d]	$Mo(CO)_3(C_7H_8)$ + bpy	42	90 (100 : 0) : 10 (100 : 0 : 0)	58
14[e]	$Mo(CO)_3(C_7H_8)$ + bpy	41	91 (100 : 0) : 9 (100 : 0 : 0)	53
15[f]	$Mo(CO)_3(C_7H_8)$ + bpy	92	77 (100 : 0) : 23 (100 : 0 : 0)	4
16[d]	$Mo(CH_3CN)_3(C_7H_8)$ + bpy	57	84 (100 : 0) : 16 (100 : 0 : 0)	34
17	$Mo(CO)_3(C_7H_8)$ + phen[g]	51	88 (100 : 0) : 12 (100 : 0 : 0)	49
18	$Mo(CO)_3(C_7H_8)$ + phen[g]	54	87 (100 : 0) : 13 (100 : 0 : 0)	37
19	$Mo(CO)_3(C_7H_8)$ + DI[h]	0	—	80
20	$Mo(CO)_3(C_7H_8)$ + BPA[i]	0	—	quant.

[a] Determined by ^{19}F NMR and GC. [b] bpy: 2,2′-bipyridyl, **7**. [c] IP(Ph): iminophosphine, **8**. IP(Cy): iminophosphine, **9**. [d] Stirred for 24 h. [e] DME was used as a solvent. [f] 1,4-Dioxane was used as a solvent. [g] phen : 1,10-phenanthroline, **10**. [h] DI : diimine, **11**. [i] BPA : bis-picolinylamide, **12**.



Scheme 4



Scheme 5

addition-*anti* nucleophilic attack mode, providing the allylated products with overall retention of configuration (Scheme 4, Path A).[12] The molybdenum-catalyzed reaction has also been known to proceed with overall retention of configuration.[13] However it has been recently reported that the mode of action of molybdenum catalyst may differ from that of palladium (Path B). Thus, the molybdenum-catalyzed reaction is suggested to take place *via syn* oxidative addition-*syn* nucleophilic attack mode.[14] Based on this proposed mechanism, the molybdenum complex could coordinate with the allylic mesylate leaving group and an olefin, providing the oxidative product **Int-B** with the retention of configuration. The nucleophile attacks on the same face as that occupied by Mo, resulting in a net retention in this pathway.

In **Int-A** or **Int-B**, the transition metal might be closer to a CF_3 group than the R group due to the electron-withdrawing effect of the CF_3 group.[15] Therefore, the nucleophile reacts preferentially at the less hindered γ-carbon to give the γ-product **3**.

In the reaction of **1d** (R = H) with sodiomalonate, it is highly possible that sodiomalonate abstracts α-proton of γ-product **3**, forming the α-allylated sodiomalonate **13** (Scheme 5). The newly formed nucleophile **13** attacks the γ-carbon of **Int-A** or **Int-B**. In this case, **Int-A** may react more smoothly than **Int-B** does because of the large steric repulsion between molybdenum species and the bulky nucleophile **13**. As a result, higher selectivity of **3**/**6** was observed in the molybdenum-catalyzed reaction than in the palladium reaction.

For the molybdenum-catalyzed allylic substitution reaction, it has been also reported thus far that the reaction with stabilized carbon nucleophiles proceeds *via anti* oxidative addition-*anti* nucleophilic attack mode, like the palladium-catalyzed reaction.[16] Therefore, the detailed reaction mechanism for the present study remains unclear at present and an exact explanation for the mechanism awaits further investigation.

Conclusions

In summary, we have investigated the transition metal-catalyzed allylic substitution reaction of α-trifluoromethylated allyl mesylate with various carbon nucleophiles in detail. Only stabilized carbanions such as sodiomalonate, ethyl sodiocyanoacetate, *etc.* reacted with the mesylate smoothly to give the corresponding alkylation products in excellent yields. It was found that the side chain R in the mesylates affected the reaction significantly. Thus, the monoallylated product was obtained in high yields *via* palladium-catalyzed reaction in the case of R = n-C_6H_{13}, Ph *etc.*, however, the use of **1d** (R = H) led to the formation of bisallylated product along with the monoallylated one. The best yield and the best stereoselectivity were obtained when the molybdenum catalyst with a 2,2′-bipyridyl ligand was employed.

Experimental

General methods

Infrared spectra (IR) were taken on a Shimadzu FTIR-8200(PC) spectrometer as film on a NaCl plate. ^1H and ^{13}C NMR spectra were measured with a Bruker DRX-500 NMR spectrometer in a chloroform-d ($CDCl_3$) solution with tetramethylsilane (Me_4Si) as an internal reference. A JEOL JNM-EX90A (84.21 MHz) FT-NMR spectrometer was used for determining ^{19}F NMR spectra in a $CDCl_3$ solution with trichlorofluoromethane as internal standard. High-resolution mass spectra (HRMS) were taken on a Hitachi M-80B mass spectrometer by electron impact (EI), chemical ionization (CI), and fast atom bombardment (FAB) methods. Thin-layer chromatography (TLC) was done on aluminium sheets coated with silica gel (Merck 60 F_{254}), and column chromatography was carried out using silica gel (Wacogel C-200) as adsorbent.

Preparation of substrate 1d

To a THF solution of trifluoroacetaldehyde, prepared readily from trifluoroacetaldehyde monohydrate (40 mmol) and conc. H_2SO_4 (40 mmol), was added a THF solution of vinylmagnesium bromide (20 mmol) at −78 °C. The reaction mixture was stirred for several hours at that temperature, and the reaction was quenched with sat. NH_4Cl aq.. The mixture was extracted with ether three times, and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and filtered. The filtrate was gradually concentrated to remove solvents (THF and ether) to the yellow residue which was used without further purification.

To a CH_2Cl_2 solution of trifluoromethylated allylic alcohol (1 mmol) was added methanesulfonyl chloride (1.2 mmol) and Et_3N (1.2 mmol) at 0 °C. The whole was stirred for several hours at that temperature. After quenching the reaction with sat. NH_4Cl, the whole was extracted with CH_2Cl_2 three times, and the combined organic layers were dried over anhydrous Na_2SO_4, concentrated *in vacuo*. The residue was purified by silica gel column chromatography to give the corresponding allyl mesylate **1d** (~41% yield).

1-(Trifluoromethyl)-2-propenyl methanesulfonate (1d)

^1H NMR ($CDCl_3$) δ 3.11 (3H, s), 5.29 (1H, dq, J = 6.5 Hz, 6.5 Hz), 5.67 (1H, d, J = 10.5 Hz), 5.72 (1H, d, J = 17.2 Hz), 5.91

(1H, ddd, J = 6.5 Hz, 10.5 Hz, 17.2 Hz); ^{19}F NMR ($CDCl_3$) δ − 77.22 (3F, d, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$) δ 39.4, 77.1 (q, J = 34.4 Hz), 122.1 (q, J = 280.9 Hz), 125.3, 126.1; IR (neat) ν 725 (m), 764 (m), 843 (s), 870 (m), 949 (s), 1011 (s), 1109 (m), 1132 (s), 1182 (s), 1271 (s), 1337 (s), 1371 (s), 1418 (m), 2947 (w), 3038 (w); HRMS (CI) m/z 205.0146, found 205.0139 (M + H), calcd for $C_5H_8F_3O_3{}^{32}S$.

Typical procedure for the reaction of allyl mesylate 1a with sodiomalonate

To a solution of $Pd(PPh_3)_4$ (19 mg, 5 mol%, 0.02 mmol) in THF (3 mL) was added allyl mesylate **1a** (93 mg, 0.34 mmol) at 0 °C. After stirring of the reaction mixture for 10 min, sodiomalonate, **2a**, prepared from diethyl malonate (1.2 eq. 0.41 mmol) and NaH (1.2 eq. 0.41 mmol), was added to the reaction mixture, followed by warming of the solution to room temperature, then stirred for 2 h. The reaction was quenched with water, and the whole was extracted with ethyl acetate three times. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography to give the corresponding allylated product **3a-*E*** (119 mg, 99% yield).

Diethyl 1-(3,3,3-trifluoro-(1*E*)-propenyl)heptylmalonate (3a-*E*)

^{1}H NMR ($CDCl_3$) δ 0.87 (3H, t, J = 7.0 Hz), 1.23–1.43 (16H, m), 2.87 (1H, ddt, J = 3.5 Hz, 9.0 Hz, 9.0 Hz), 3.36 (1H, d, J = 9.0 Hz), 4.16 (2H, d, J = 7.5 Hz), 4.20 (2H, d, J = 7.5 Hz), 5.68 (1H, dq, J = 6.5 Hz, 15.5 Hz), 6.27 (1H, ddq, J = 2.0 Hz, 9.0 Hz, 15.5 Hz); ^{19}F NMR ($CDCl_3$) δ −64.74 (3F, d, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$) δ 13.9, 14.0, 22.5, 26.8, 28.9, 31.5, 31.9, 41.8, 56.0, 61.5, 61.6, 120.8 (q, J = 33.5 Hz), 122.6 (q, J = 269.2 Hz), 140.0 (q, J = 6.5 Hz), 167.6, 167.7; IR (neat) ν 671 (m), 795 (s), 856 (m), 979 (m), 1033 (m), 1126 (s), 1280 (s), 1369 (m), 1465 (m), 1681 (m), 1735 (s), 2858 (m), 2931 (s); HRMS (CI) m/z 353.1940, found 353.1938 (M + H), calcd for $C_{17}H_{28}F_3O_4$.

1-(3,3,3-Trifluoro-(1*E*)-propenyl)heptylmalononitrile (3c-*E*)

^{1}H NMR ($CDCl_3$) δ 0.89 (3H, t, J = 7.0 Hz), 1.26–1.35 (8H, m), 1.66–1.69 (1H, m), 1.76–1.78 (1H, m), 2.77 (1H, ddt, J = 5.5 Hz, 9.5 Hz, 9.5 Hz), 3.79 (1H, d, J = 5.5 Hz), 5.96 (1H, dq, J = 6.0 Hz, 16.0 Hz), 6.24 (1H, ddq J = 1.5 Hz, 9.5 Hz, 16.0 Hz); ^{19}F NMR ($CDCl_3$) δ −65.23 (3F, d, J = 6.0 Hz); ^{13}C NMR ($CDCl_3$) δ 13.9, 22.4, 26.5, 27.8, 28.7, 31.4, 43.0, 110.7, 110.9, 121.8 (q, J = 270.1 Hz), 124.7 (q, J = 34.8 Hz), 135.3 (q, J = 6.2 Hz); IR (neat) ν 864 (w), 976 (m), 1130 (s), 1211 (w), 1277 (m), 1315 (m), 1366 (w), 1466 (w), 1686 (w), 2862 (m), 2932 (s); HRMS (CI) m/z 259.1422, found 259.1421 (M + H), calcd for $C_{13}H_{18}F_3N_2$.

Ethyl 1-(3,3,3-trifluoro-(1*E*)-propenyl)heptylcyanoacetate (diastereomeric ratio = 60 : 40) (3d-*E*)

^{1}H NMR ($CDCl_3$) δ 0.87–0.90 (3H, m), 1.29–1.38 (13H, m), 2.83–2.89 (1H, m), 3.50 (1H, d, J = 6.3 Hz) (isomer), 3.64 (1H, d, J = 4.5 Hz) (another isomer), 4.23–4.27 (2H, m), 5.75–5.83 (1H, m), 6.22 (1H, ddq, J = 2.0 Hz, 9.6 Hz, 15.6 Hz) (isomer), 6.27 (1H, ddq, J = 2.0 Hz, 9.7 Hz, 15.6 Hz) (another isomer); ^{19}F NMR ($CDCl_3$) δ −64.65 (3F, d, J = 6.6 Hz) (isomer), −64.73 (3F, d, J = 6.6 Hz) (another isomer); ^{13}C NMR ($CDCl_3$) δ 13.9, 22.5, 26.6, 26.7, 28.7, 28.8, 28.8, 31.0, 31.5, 32.1, 42.3, 42.3, 43.3, 42.4, 63.1, 114.2, 120.3 (q, J = 38.3 Hz) (isomer), 120.5 (q, J = 269.3 Hz) (isomer), 122.7 (q, J = 269.9 Hz) (another isomer), 137.3 (q, J = 6.4 Hz) (isomer), 138.1 (q, J = 6.0 Hz) (another isomer), 164.6, 164.74; IR (neat) ν 856 (w), 980 (m), 1026 (m), 1126 (s), 1277 (m), 1369 (m), 1466 (m), 1682 (m), 1747 (s), 2341 (m), 2862 (m), 2932 (s); HRMS (CI) m/z 306.1681, found 306.1685 (M + H), calcd for $C_{15}H_{23}F_3NO_2$.

Ethyl 1-(3,3,3-trifluoro-(1*E*)-propenyl)heptyldiethylphosphonoacetate (diastereomeric ratio = 56 : 44) (3e-*E*)

^{1}H NMR ($CDCl_3$) δ 0.85–0.88 (3H, m), 1.20–1.47 (19H, m), 2.78–2.89 (1H, m), 2.96 (1H, dd, J = 9.8 Hz, 20.3 Hz) (isomer), 3.04 (1H, dd, J = 7.5 Hz, 21.5 Hz) (another isomer), 4.06–4.19 (4H, m), 4.23 (2H, q, J = 7.0 Hz) (isomer), 5.68 (1H, dq, J = 6.5 Hz, 15.5 Hz) (another isomer), 5.72 (1H, dq, J = 6.5 Hz, 15.5 Hz) (isomer), 6.17 (1H, ddq, J = 2.0 Hz, 10.0 Hz, 15.5 Hz) (isomer), 6.36 (1H, ddq, J = 2.0 Hz, 10.0 Hz, 15.5 Hz) (another isomer); ^{19}F NMR ($CDCl_3$) δ −64.66 (3F, d, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$) δ 13.9, 14.0, 14.1, 16.1–16.3 (m), 22.47, 22.48, 26.4, 26.7, 28.8, 31.5, 31.5, 32.31, 32.37, 41.0 (d, J = 3.4 Hz) (isomer), 41.1 (d, J = 4.1 Hz) (another isomer), 49.7 (d, J = 139.9 Hz) (isomer), 50.7 (d, J = 133.9 Hz) (another isomer), 61.4, 61.6, 62.5 (d J = 7.1 Hz) (isomer), 62.7 (d J = 7.4 Hz) (another isomer), 120.3 (q, J = 33.5 Hz) (isomer), 120.4 (q, J = 33.3 Hz) (another isomer), 122.7 (q, J = 269.2 Hz) (isomer), 140.2–140.5 (m), 167.8 (q, J = 3.9 Hz), 168.2 (q, J = 3.3 Hz); IR (neat) ν 675 (w), 795 (w), 860 (w), 972 (m), 1026 (s), 1123 (s), 1258 (s), 1369 (m), 1466 (m), 1682 (m), 1736 (s), 2858 (m), 2932 (w); HRMS (CI) m/z 417.2018, found 417.2022 (M + H), calcd for $C_{18}H_{33}F_{30}O_5P$.

Ethyl 1-(3,3,3-trifluoro-(1*E*)-propenyl)heptylacetoacetate (diastereomeric ratio = 58 : 42) (3b-*E*)

^{1}H NMR ($CDCl_3$) δ 0.86 (3H, t, J = 7.0 Hz), 1.22–1.45 (13H, m), 2.17 (3H, s) (isomer), 2.23 (3H, s) (another isomer), 2.90–2.92 (1H, m), 3.46 (1H, d, J = 9.0 Hz) (isomer), 3.50 (1H, d, J = 9.0 Hz) (another isomer), 4.14 (2H, q, J = 7.0 Hz) (isomer), 4.20 (2H, d, J = 7.0 Hz) (another isomer), 5.66 (1H, dq, J = 6.5 Hz, 16.0 Hz) (isomer), 5.67 (1H, dq, J = 6.5 Hz, 16.0 Hz) (another isomer), 6.14–6.21 (1H, m); ^{19}F NMR ($CDCl_3$) δ −64.72 (3F, d, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$) δ 13.95, 14.02, 22.5, 26.8, 26.9, 28.9, 29.6, 30.0, 31.5, 31.6, 32.0, 41.3, 61.6, 61.7, 63.6, 63.8, 120.9 (q, J = 33.6 Hz) (isomer), 121.0 (q, J = 33.6 Hz), 122.5 (q, J = 269.5 Hz) (isomer), 122.6 (q, J = 269.5 Hz) (another isomer), 139.9 (q, J = 6.8 Hz) (isomer), 140.1 (q, J = 6.6 Hz) (another isomer), 167.9, 168.0, 201.1, 201.2; IR (neat) ν 679 (w), 810 (w), 856 (w), 980 (m), 1026 (m), 1126 (s), 1277 (s), 1362 (s), 1466 (m), 1632 (w), 1682 (m), 1720 (s), 2858 (m), 2932 (s); HRMS (EI) m/z 323.1834, found 323.18434 (M + H), calcd for $C_{16}H_{26}F_3O_3$.

Diethyl 1-benzyloxymethyl-4,4,4-trifluoro-(2*E*)-butenyl malonate (3f-*E*)

^{1}H NMR ($CDCl_3$) δ 1.23 (6H, t, J = 7.0 Hz), 3.18–3.23 (1H, m), 3.53–3.64 (2H, m), 3.72 (1H, d, J = 8.0 Hz), 4.10–4.23 (4H, m), 4.45–4.83 (2H, m), 5.67–5.78 (1H, m), 6.47 (1H, ddq, J = 2.0 Hz, 9.5 Hz, 16.0 Hz), 7.28–7.30 (3H, m), 7.33–7.36 (2H, m); ^{19}F NMR ($CDCl_3$) δ −64.95 (3F, d, J = 6.6 Hz); ^{13}C NMR ($CDCl_3$) δ 13.96, 13.97, 41.7, 52.4, 61.6, 61.7, 69.8, 73.2, 121.3 (q, J = 269.2 Hz), 127.6, 127.8, 128.4, 137.5 (q J = 6.5 Hz), 137.7, 167.68, 167.72; IR (neat) ν 700 (m), 739 (m), 864 (w), 978 (m), 1030 (s), 1121 (s), 1369 (s), 1454 (m), 1680 (m), 1732 (s), 2870 (m), 2986 (m); HRMS (FAB) m/z 389.1576, found 389.1580 (M + H), calcd for $C_{19}H_{24}F_3O_5$.

Diethyl 1-benzyloxymethyl-4,4,4-trifluoro-(2*Z*)-butenyl malonate (3f-*Z*)

^{1}H NMR ($CDCl_3$) δ 1.23 (3H, t, J = 7.0 Hz), 3.18–3.23 (1H, m), 3.53–3.64 (2H, m), 3.76 (1H, d, J = 8.0 Hz), 4.10–4.23 (4H, m), 4.45–4.83 (2H, m), 5.67–5.78 (1H, m), 6.23 (1H, dd, J = 11.5 Hz, 11.5 Hz), 7.28–7.30 (3H, m), 7.33–7.36 (2H, m); ^{19}F NMR ($CDCl_3$) δ −58.69 (3F, d, J = 7.8 Hz); ^{13}C NMR ($CDCl_3$) δ 13.97, 14.03, 38.6, 52.2, 61.51, 61.53, 70.4, 73.1, 120.5 (q, J = 33.8 Hz), 122.6 (q, J = 269.2 Hz), 127.6, 127.7, 128.3, 137.8, 139.4 (q J = 6.5 Hz), 167.68, 167.72.

Diethyl 4,4,4-trifluoro-1-phenyl-(2*E*)-butenyl malonate (3g-*E*)

^{1}H NMR ($CDCl_3$) δ 1.00 (3H, t, J = 7.0 Hz), 1.27 (3H, t, J = 7.0 Hz), 3.84 (1H, d, J = 10.5 Hz), 3.97 (2H, dq, J = 2.5 Hz, 7.0 Hz), 4.18–4.24 (3H, m), 5.65 (1H, dq, J = 6.5 Hz, 15.6 Hz), 6.56 (1H, ddq, J = 2.0 Hz, 8.0 Hz, 15.6 Hz), 7.21–7.23 (1H, m), 7.25–7.28 (1H, m), 7.32–7.34 (2H, m); ^{19}F NMR ($CDCl_3$) δ −64.78 (3F, d, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$) δ 13.7, 14.0, 47.3, 56.8, 61.6, 61.9, 120.2 (q, J = 33.8 Hz), 122.6 (q, J = 269.8 Hz), 127.8, 128.1, 128.9, 137.8, 139.4 (q, J = 6.5 Hz), 166.8, 167.3; IR (neat) ν 559 (m), 608 (w), 673 (w), 700 (s), 766 (m), 862 (m), 978 (m), 1032 (s), 1138 (s), 1454 (m), 1497 (m), 1603 (w), 1678 (m), 1732 (m), 2909 (m), 2986 (s); HRMS (FAB) *m*/*z* 345.1314, found 345.1317 (M + H), calcd for $C_{17}H_{20}F_3O_4$.

Diethyl 4,4,4-trifluoro-(2*E*)-butenyl malonate (3h-*E*)

^{1}H NMR ($CDCl_3$) δ 1.27 (6H, t, J = 7.0 Hz), 2.73–2.75 (2H, m), 3.46 (1H, t, J = 7.2 Hz), 4.21 (4H, q, J = 7.0 Hz), 5.72 (1H, dq, J = 7.0 Hz, 16.0Hz), 6.35 (1H, dtq, J = 2.0 Hz, 7.0 Hz, 16.0 Hz); ^{19}F NMR ($CDCl_3$) δ −64.95 (3F, d, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 14.0, 30.4, 50.5, 61.7, 121.1 (q, J = 33.5 Hz), 122.5 (q, J = 269.3 Hz), 136.0 (q, J = 6.6 Hz), 168.2; IR (neat) ν 862 (w), 970 (m), 1034 (m), 1096 (m), 1128 (s), 1279 (s), 1371 (m), 1448 (m), 1682 (m), 1736 (s), 2988 (m); HRMS (CI) *m*/*z* 269.1001, found 269.1002 (M + H), calcd for $C_{11}H_{16}F_3O_4$.

Diethyl bis(4,4,4-trifluoro-(2*E*)-butenyl)malonate (6-*EE*)

^{1}H NMR ($CDCl_3$) δ 1.26 (6H, t, J = 7.3 Hz), 2.43 (4H, d, J = 7.5 Hz), 4.22 (4H, q, J = 7.3 Hz), 5.70 (2H, dq, J = 6.5 Hz, 15.8 Hz), 6.28 (2H, dtq, J = 2.0 Hz, 7.5 Hz, 15.5 Hz); ^{19}F NMR ($CDCl_3$) δ −65.07 (6F, d, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$) δ 13.9, 35.6, 56.4, 62.0, 122.3 (q, J = 269.5 Hz), 122.6 (q, J = 33.7 Hz), 134.3 (q, J = 6.5 Hz), 169.5; IR (neat) ν 681 (w), 856 (w), 974 (m), 1032 (m), 1124 (s), 1205 (s), 1275 (s), 1350 (m), 1447 (m), 1682 (m), 1732 (s), 2988 (s); HRMS (FAB) *m*/*z* 377.1188, found 377.1182 (M + H), calcd for $C_{15}H_{19}F_6O_4$.

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