Tetrahedron 67 (2011) 8238–8247

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Regioselective synthesis of trifluoromethyl group containing allylic amines by palladium-catalyzed allylic amination and sequential isomerization

Takuya Hirakawa, Kazunori Ikeda, Daiji Ikeda, Tomoko Tanaka, Hiroshi Ogasa, Motoi Kawatsura *, Toshiyuki Itoh *

Department of Chemistry and Biotechnology, Graduate School of Engineering, Tottori University, Koyama, Tottori 680-8552, Japan

ARTICLE INFO

Article history:
Received 4 August 2011
Received in revised form 30 August 2011
Accepted 31 August 2011
Available online 7 September 2011

ABSTRACT

The palladium-catalyzed regioselective allylic amination of the α-trifluoromethyl group-substituted allyl acetate has been accomplished using $Pd(OAc)_2$/DPPE and [Pd(π-allyl)(cod)]BF_4/DPPF as catalysts. The selective formation of the γ-product was attained in the presence of $Pd(OAc)_2$/DPPE, while the α-product was obtained using [Pd(π-allyl)(cod)]BF_4/DPPF. We also succeeded in the regioselective synthesis of the enantiomerically enriched aminated product from chiral allyl acetate using $Pd(OAc)_2$/DPPE and [Pd(π-allyl)(cod)]BF_4/(*S*)-BINAP. Furthermore, we found that kinetic resolution had occurred during the isomerization step from the γ-type product to the α-type product by the [Pd(π-allyl)(cod)]BF_4/(*S*)-BINAP catalyst.

1. Introduction

Recently, fluorine substituted organic compounds have attracted much interest in the field of medicinal chemistry and material science because of their unique properties due to the influence of fluorine. For example, the replacement of hydrogen atoms by fluorine atoms in organic molecules causes a relatively small steric change, but leads to major changes in the electron character of the molecules. Also, some fluorine-contained compounds sometimes exhibit an unusual stereoselectivity under standard organic reaction conditions. Therefore, the development of new transformation methods of fluorinated compounds should be one of the important subjects in organic chemistry. The transition metal-catalyzed allylic amination reaction of allylic esters is a versatile method to produce allylic amines, and several transition metal catalysts have realized these reactions.[1,2] However, most of them were the reactions involving non-fluorinated substrates, and there is only a limited example of the reaction of the α-trifluoromethylated allyl substrates.[3] In 2002, Konno and co-workers demonstrated the first example of the palladium-catalyzed regioselective (γ-selective) allylic amination of α-trifluoromethylated allyl mesylate, and found that the reaction produced the γ-product as a single regioisomer.[4] On the other hand, we recently reported on both the α-selective and γ-selective allylic aminations of α-trifluoromethylated allyl acetate using two types of palladium catalysts.[5] We further succeeded in obtaining the enantiomerically enriched α- and γ-allylic amines, although applicable combinations of the allylic esters and amines were limited. In this paper, we report the results of detailed study of our palladium-catalyzed regioselective allylic amination of α-trifluoromethylated allylic esters with several amines, including synthesis of the trifluoromethyl group containing optically active allylic amines.

2. Results and discussion

2.1. Regioselective allylic amination

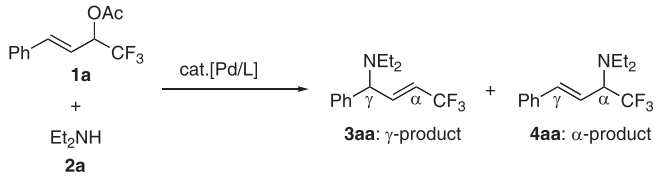
We examined the allylic amination of the α-trifluoromethylated allyl acetate **1a** with diethylamine (**2a**) using several palladium/phosphine catalysts (Table 1). We found that the $Pd(OAc)_2$ and [Pd(π-allyl)(cod)]BF_4 exhibited a catalytic activity for this intended reaction. On the contrary, palladium catalysts, which were generated from $Pd_2(dba)_3$ or [Pd(π-allyl)Cl]$_2$ with several phosphine ligands,[6] showed no catalytic activity toward the desired amination reaction or resulted in a low conversion of the substrate **1a** (<20%). The results obtained for the palladium-catalyzed allylic amination of **1a** with diethylamine (**2a**) are summarized in Table 1.

We first conducted the reaction using $Pd(OAc)_2$ with PPh_3 (4 equiv vs Pd). Although the desired product **3aa** was obtained, while poor reaction rate was recorded (Table 1, entry 1). Fortunately, we found that DPPE [1,2-bis(diphenylphosphino)ethane] (1 equiv to Pd) is an effective ligand for the allylic amination of **1a**, and the γ-trifluoromethyl group with substituted allyl amine **3aa** (γ-product) was obtained as a single regioisomer in 80% isolated yield (entry 2). We also examined the reaction with DPPF, but the

* Corresponding authors. E-mail addresses: kawatsur@chem.tottori-u.ac.jp (M. Kawatsura), titoh@chem.tottori-u.ac.jp (T. Itoh).

0040-4020/$ – see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2011.08.093

Table 1
Palladium-catalyzed allylic amination of **1a** with diethylamine **2a**[a]



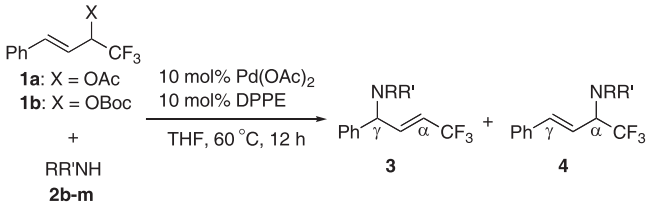
Entry	[Pd/L]	Solvent	Temp (°C)	Yield[b] (%) of **3aa**+**4aa**	**3aa**/**4aa**[c]
1	$Pd(OAc)_2/PPh_3$	THF	60	20	>98:2
2	$Pd(OAc)_2$/DPPE	THF	60	86 (80)[d]	>98:2
3	$Pd(OAc)_2$/DPPF	THF	60	64 (58)[d]	>98:2
4	$Pd(OAc)_2$/DPPE	Dioxane	100	68	>98:2
5	[Pd(π-allyl)(cod)]BF_4/PPh_3	THF	60	12	>98:2
6	[Pd(π-allyl)(cod)]BF_4/DPPE	THF	60	17	>98:2
7	[Pd(π-allyl)(cod)]BF_4/DPPF	THF	60	56	68:32
8	[Pd(π-allyl)(cod)]BF_4/DPPE	Dioxane	100	43	60:40
9	[Pd(π-allyl)(cod)]BF_4/DPPB	Dioxane	100	53	15:85
10[e]	[Pd(π-allyl)(cod)]BF_4/DPPF	Dioxane	100	95 (87)[d]	2:>98

[a] All reactions were carried out with **1a** (0.20 mmol), **2a** (0.31 mmol), palladium (0.020 mmol), and ligand (0.020 mmol for DPPE, DPPB, and DPPF, 0.084 mmol for PPh_3) in solvent (1.0 ml) for 12 h under nitrogen.
[b] The yields were determined by ^1H NMR.
[c] The ratio was determined by 400 MHz ^1H NMR spectral analysis of the crude materials.
[d] Isolated yield by silica gel column chromatography in parentheses.
[e] The reaction was carried out 9 h.

yield was not a satisfactory one (entry 3). A further investigation revealed that [Pd(π-allyl)(cod)]BF_4 also catalyzed the allylic amination of **1a** (entries 5–10). Again, the γ-selective amination was observed for the reaction using PPh_3 and DPPE ligated the palladium catalyst, but the yield was very low (entries 5 and 6). Interestingly, the palladium catalyst, which coordinated with DPPF, exhibited a higher reactivity and gave a mixture of two regioisomers, **3aa** and **4aa** (α-product) in the ratio of 68:32 (entry 7). This α-selectivity was improved by raising the reaction temperature to 100 °C in dioxane (entries 8–10), and **4aa** was obtained as a single regioisomer in 87% isolated yield (entry 10).

We demonstrated the regioselective allylic amination of **1** with several amines using these two types of palladium catalysts. The results of the $Pd(OAc)_2$/DPPE-catalyzed γ-selective allylic amination are summarized in Table 2. The reaction with aliphatic secondary amines, such as morpholine (**2b**), piperazine analogues (**2c** and **2d**), 4-phenylpiperidine (**2e**), and dibutyl- or dipropylamine (**2f** and **2g**), proceeded with a high regioselectivity and gave γ-products **3** in good yields (Table 2, entries 1–6). Unfortunately, it was found that the $Pd(OAc)_2$/DPPE-catalyzed allylic aminations were very sensitive to the steric factor of the amines; the reaction with *N*-ethylisopropylamine (**2h**) proceeded with a >98% γ-selectivity, but the yield was very low (12% NMR yield) (entry 7). In addition, the reaction with diisopropylamine (**2i**) resulted in no reaction (entry 8). We also demonstrated the reaction of **1a** with the aliphatic primary amines **2j**–**l**, and obtained the expected γ-products in moderate yields with >98% regioselectivities (entries 9, 11, and 13). In these reactions, ally alcohols were produced by the deacylation of **1a** with amines. Fortunately, however, we succeeded in preventing the formation of such an undesired reaction and increasing the yields of the desired products by changing the leaving group of allyl substrate from allyl acetate **1a** to allyl *tert*-butyl carbonate **1b** (entries 10, 12, and 14).

Table 2
Palladium-catalyzed allylic amination of **1a**,**b** with amines **2b**–**m**[a]



2b: morpholine
2c: 1-phenylpiperazine
2d: 1-methylpiperazine
2e: 4-phenylpiperidine
2f: dibutylamine
2g: dipropylamine
2h: *N*-ethylisopropylamine
2i: diisopropylamine
2j: n-butylamine
2k: isopropylamine
2l: benzylamine
2m: aniline

Entry	**1**	**2**	Yield[b,c] (%) of **3** and **4**	**3**/**4**[d]
1	**1a**	**2b**	92 (99)	97:3
2	**1a**	**2c**	88 (96)	>98:2
3	**1a**	**2d**	73 (76)	>98:2
4	**1a**	**2e**	91 (95)	>98:2
5	**1a**	**2f**	64 (72)	>98:2
6	**1a**	**2g**	68 (82)	>98:2
7	**1a**	**2h**	(12)	>98:2
8	**1a**	**2i**	0	—
9	**1a**	**2j**	54 (56)	>98:2
10	**1b**	**2j**	60 (80)	>98:2
11	**1a**	**2k**	60 (76)	>98:2
12	**1b**	**2k**	74 (85)	>98:2
13	**1a**	**2l**	66 (68)	>98:2
14	**1b**	**2l**	84 (84)	>98:2
15	**1a**	**2m**	(22)	>98:2

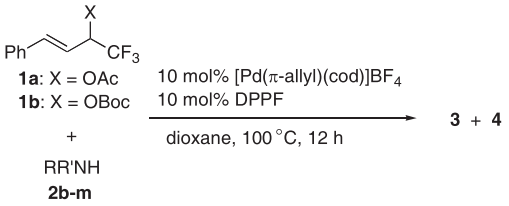
[a] All reactions were carried out with **1** (0.20 mmol), **2** (0.31 mmol), $Pd(OAc)_2$ (10 mol %), and DPPE (10 mol %) in THF (1.0 ml) at 60 °C for 12 h under nitrogen.
[b] Isolated yield by silica gel column chromatography.
[c] The NMR yield in parentheses.
[d] The ratio was determined by 400 MHz ^1H NMR spectral analysis of the crude materials.

The results of the [Pd(π-allyl)(cod)]BF_4/DPPF-catalyzed α-selective allylic amination are summarized in Table 3. As we expected, the α-products were obtained as the major regioisomers with high regioselectivity in the reaction using amines **2b**–**g** (Table 3, entries 1–6), while the [Pd(π-allyl)(cod)]BF_4/DPPF catalyst system was sensitive to the steric factor of the amines (entries 7 and 8) and no desired product was obtained when diisopropylamine (**2i**) was employed as substrate (entry 8). Changing the leaving group from acetate to *tert*-butyl carbonate effectively increased the yield of the desired α-product for the reaction of the aliphatic primary amines **2j**–**l** (entries 9–14). We further established that perfect α-selective reaction was accomplished when an aromatic primary amine **2m** was used in the presence of [Pd(π-allyl)(cod)]BF_4/DPPF as catalyst (entry 15).

We also examined the reaction of some 1,1,1-trifluoro-4-arylbut-3-en-2-yl acetates (**1a**–**e**)[7] with piperidine (**2n**) using the two types of palladium catalysts. As shown in Table 4, the reaction of **1a** with **2n** by $Pd(OAc)_2$/DPPE exhibited perfect γ-selectivity. On the other hand, as mentioned, the reaction by the [Pd(π-allyl)(cod)]BF_4/DPPF catalyst produced an α-product as a single regioisomer (Table 4, entries 1 and 2). The reactions of 1,1,1-trifluoro-4-arylbut-3-en-2-yl acetates **1c** and **1d**, which have an electron-donating or electron-withdrawing group at the *para*-position on the aromatic ring, did not show any significant difference in regioselectivity (entries 3–6). It should be noted that an increased yield was obtained for the γ-selective condition (entry 3), while a decreased yield was observed for the α-selective condition (entry 4).

We next studied the reaction pathway for the regioselective substitution, especially for the unusual selective formation of the α-

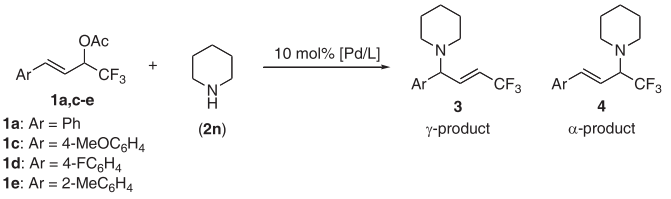
Table 3
Palladium-catalyzed allylic amination of **1a**,**b** with amines **2b**–**m**[a]



Entry	1	2	Yield[b,c] (%) of 3 and 4	3/4[d]
1	**1a**	**2b**	75 (79)	7:93
2	**1a**	**2c**	73 (73)	3:97
3	**1a**	**2d**	68 (69)	2:98
4	**1a**	**2e**	77 (78)	4:96
5	**1a**	**2f**	80	2:>98
6	**1a**	**2g**	70 (70)	2:98
7	**1a**	**2h**	(15)	75:25
8	**1a**	**2i**	0	—
9	**1a**	**2j**	61 (66)	2:>98
10	**1b**	**2j**	82 (82)	2:>98
11	**1a**	**2k**	57 (57)	2:>98
12	**1b**	**2k**	73 (73)	2:>98
13	**1a**	**2l**	79 (80)	2:>98
14	**1b**	**2l**	83 (83)	2:>98
15	**1a**	**2m**	58 (60)	2:>98

[a] All reactions were carried out with **1** (0.20 mmol), **2** (0.31 mmol), [Pd(π-allyl)(cod)]BF_4 (10 mol %), and DPPF (10 mol %) in dioxane (1.0 ml) at 100 °C for 12 h under nitrogen.
[b] Isolated yield by silica gel column chromatography.
[c] The NMR yield in parentheses.
[d] The ratio was determined by 400 MHz ^{1}H NMR spectral analysis of the crude materials.

Table 4
Palladium-catalyzed allylic amination of several allylic acetates **1a**–**e** with piperidine (**2n**)[a]

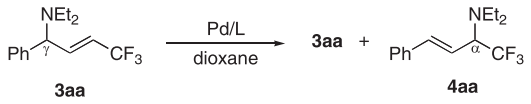


Entry	1	Condition[b]	Yield[c,d] (%) of 3 and 4 (%)	3/4[e]
1	**1a**	**A**	60 (74) (**3an**)	>98:2
2		**B**	64 (70) (**4an**)	2:>98
3	**1c**	**A**	78 (89) (**3cn**)	>98:2
4		**B**	52 (59) (**4cn**)	2:>98
5	**1d**	**A**	64 (84) (**3dn**)	>98:2
6		**B**	60 (62) (**4dn**)	2:>98
7	**1e**	**A**	63 (84) (**3en**)	>98:2
8		**B**	73 (75) (**4en**)	2:>98

[a] All reactions were carried out with **1** (0.20 mmol) and **2n** (0.31 mmol) in solvent (1.0 ml) for 12 h under nitrogen.
[b] Condition **A**: 10 mol % $Pd(OAc)_2$ and 10 mol % DPPE in THF at 60 °C for 12 h. Condition **B**: 10 mol % [Pd(π-allyl)(cod)]BF_4 and 10 mol % DPPF in dioxane at 100 °C for 12 h.
[c] Isolated yield by silica gel column chromatography.
[d] The NMR yield in parentheses.
[e] The ratio was determined by 400 MHz ^{1}H NMR spectral analysis of the crude materials.

product. Generally, the palladium catalyst forms the π-allylpalladium intermediate and nucleophiles attack the π-allyl terminus. According to a report on the allylic substitution of α-trifluoroalkylated allyl mesylates by Konno,[3d] the allyl substrate formed the π-allylpalladium complex, and nucleophiles selectively attacked the less sterically hindered π-allyl terminus to form the γ-product.[8] We believe the same mechanism might be involved in the reaction of **1a** with **2a** by $Pd(OAc)_2$/DPPE. In contrast, it is unclear whether or not a direct substitution occurred during the reaction of the [Pd(π-allyl)(cod)]BF_4/DPPF catalyst because, as we previously mentioned, the γ-product was obtained as the major product under several different conditions (Table 1, entries 7 and 8). Based on these results, we assumed that [Pd(π-allyl)(cod)]BF_4/DPPF had selectively formed the γ-product, thus causing isomerization to provide the α-product under the given reaction conditions.[9] To prove this hypothesis, the γ-product **3aa** was treated with the palladium catalyst, and the ^{1}H NMR spectrum was measured. When the reaction was carried out using 10 mol % [Pd(π-allyl)(cod)]BF_4 (without DPPF) in dioxane at 100 °C for 12 h, almost all **3aa** was consumed (>80% conversion), a complex mixture was produced and no desired product was produced (Table 5, entry 1). However, the reaction with 10 mol % of [Pd(π-allyl)(cod)]BF_4 and 10 mol % of DPPF showed formation of the α-product **4aa** (52% NMR yield) (entry 2), which suggested that **3aa** was isomerized to **4aa** by the [Pd(π-allyl)(cod)]BF_4/DPPF catalyst system.[10] Furthermore, the addition of excess Et_2NH (1.5 equiv to **3aa**) increased the formation of **4aa** up to a 73% NMR yield (entry 3). We also confirmed that the $Pd(OAc)_2$/DPPE did not catalyze the isomerization of **3aa** to **4aa** under the same conditions (entry 4). These results strongly support the idea that the γ-product was first selectively formed, and then was isomerized to the α-product by the [Pd(π-allyl)(cod)]BF_4/DPPF catalyst.

Table 5
The reaction of γ-product **3aa** using the palladium catalyst[a]



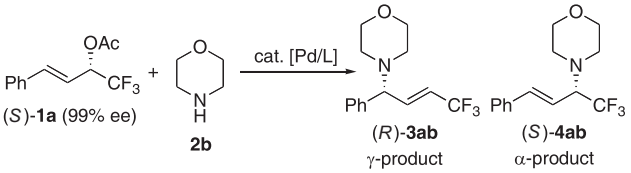
Entry	[Pd/L]	Et_2NH	Conversion[b] (%) of **3aa**	Yield[b] (%) of **4aa**
1	[Pd(π-allyl)(cod)]BF_4	—	>80	Trace
2	[Pd(π-allyl)(cod)]BF_4/DPPF	—	>99	52
3	[Pd(π-allyl)(cod)]BF_4/DPPF	1.5 equiv	>99	73
4	$Pd(OAc)_2$/DPPE	1.5 equiv	0	0

[a] All reactions were carried out with **3aa** (0.20 mmol), palladium (0.020 mmol), and ligand (0.020 mmol) in dioxane (1 ml) at 100 °C for 12 h under nitrogen.
[b] Determined by 400 MHz ^{1}H NMR spectral analysis of the crude materials.

2.2. Synthesis of enantiomerically enriched CF_3-group containing allylic amines

The *net retention* (*double inversion*) mechanism is a very popular stereochemical phenomenon for palladium-catalyzed allylic substitutions; the reaction of the optically active allyl substrates generally forms optically active substitution products without loss of any enantiomeric excess.[11] Based on this mechanism, we next examined the α- and γ-selective allylic aminations of enantiomerically enriched allyl acetate using two types of palladium catalysts to obtain optically active α- and γ-allylic amines. We expected that both the chiral α- and γ-allyl amines would be easily obtained by the net retention mechanism. However, we soon recognized that the enantiomeric excess of the allyl acetate was lost under the reaction conditions. For example, the reaction of the enantiomerically enriched allyl acetate (*S*)-**1a** (99% ee) with morpholine (**2b**) by the $Pd(OAc)_2$/DPPE catalyst at 60 °C gave the γ-product **3ab** in 99% yield with 81% ee (Table 6, entry 1). Furthermore, the α-selective reaction by [Pd(π-allyl)(cod)]BF_4/DPPF at 100 °C provided **4ab** in an 85% yield with a 0% ee (entry 3). We

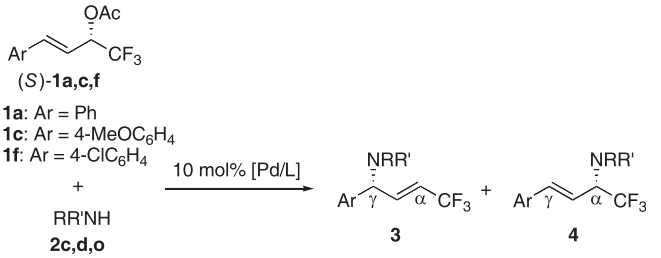
Table 6
Palladium-catalyzed allylic amination of chiral (*S*)-**1a** with morpholine (**2b**)[a]



Entry	[Pd/L]	Temp (°C)	Yield[b,c] (%) of **3ab** and **4ab**	**3ab**/**4ab**[d]	ee[e] (%) of (*R*)-**3ab**	ee[e] (%) of (*S*)-**4ab**
1	$Pd(OAc)_2$/DPPE	60	99	>98:2	81	n.d.
2	$Pd(OAc)_2$/DPPE	25	77 (66)	>98:2	98	n.d.
3	[Pd(π-allyl)(cod)]BF_4/DPPF	100	85	5:95	n.d.	0
4	[Pd(π-allyl)(cod)]BF_4/DPPF	60	94	18:82	n.d.	4
5	[Pd(π-allyl)(cod)]BF_4/(*S*)-BINAP	100	95	7:93	n.d.	33
6	[Pd(π-allyl)(cod)]BF_4/(*S*)-BINAP	40	95	7:93	n.d.	99
7[f]	[Pd(π-allyl)(cod)]BF_4/(*S*)-BINAP	40	98 (74)	3:97	n.d.	99
8	[Pd(π-allyl)(cod)]BF_4/(*R*)-BINAP	40	80	87:13	91	13[g]

[a] All reactions were carried out with (*S*)-**1a** (0.20 mmol), **2b** (0.31 mmol), palladium (0.020 mmol), and ligand (0.020 mmol) in solvent (1.0 ml) for 12 h under nitrogen.
[b] The yield were determined by ^{1}H NMR.
[c] Isolated yield by silica gel column chromatography in parentheses.
[d] The ratio was determined by 400 MHz ^{1}HMR spectral analysis of the crude materials.
[e] Values of ee were determined by chiral HPLC analysis.
[f] Reaction was conducted using 5 mol % [Pd] and ligand for 24 h.
[g] (*R*)-**4ab** was obtained as a major enantiomer.

Table 7
Palladium-catalyzed allylic amination of chiral allylic acetates (*S*)-**1a**–**f** with several amines **2c**–**o**[a]



Entry	**1**	**2**	Condition[b]	Time	Yield[c,d] (%) of **3** and **4**	**3**/**4**[e]	ee[f] (%) of major product
1	**1a**	**2c**	**A**	9 h	82 (91)	>98:2	97 (**3ac**)
2			**B** (40 °C)	12 h	81 (99)	6:94	97 (**4ac**)
3	**1a**	**2d**	**A**	12 h	80 (89)	>98:2	95 (**3ad**)
4			**B** (40 °C)	5 days	87 (93)	6:94	98 (**4ad**)
5	**1a**	**2o**	**A**	12 h	69 (83)	>98:2	96 (**3ao**)
6			**B** (25 °C)	25 h	61 (99)	13:87	96 (**4ao**)
7	**1c**	**2c**	**A**	12 h	84 (86)	>98:2	94 (**3cc**)
8			**B** (25 °C)	5 days	81 (97)	8:92	98 (**4cc**)
9	**1f**	**2c**	**A**	12 h	71 (71)	>98:2	83 (**3fc**)
10			**B** (25 °C)	5 days	65 (82)	8:92	95 (**4fc**)

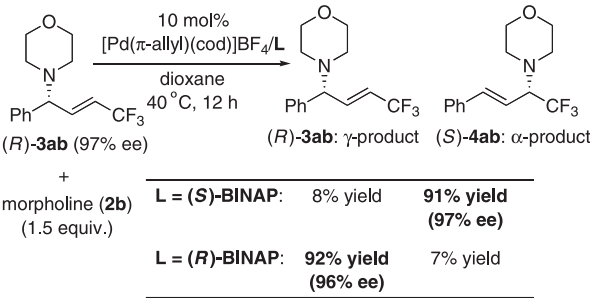
[a] All reactions were carried out with **1** (0.20 mmol) and **2** (0.31 mmol) in solvent (1.0 ml) for 12 h under nitrogen unless otherwise noted.
[b] Condition **A**: 10 mol % $Pd(OAc)_2$ and 10 mol % DPPE in THF at 25 °C. Condition **B**: 10 mol % [Pd(π-allyl)(cod)]BF_4 and 10 mol % (*S*)-BINAP in dioxane at 40 or 25 °C unless otherwise noted.
[c] Isolated yield by silica gel column chromatography.
[d] The NMR yield in parentheses.
[e] The ratio was determined by 400 MHz ^{1}H NMR spectral analysis of the crude materials.
[f] Values of ee were determined by chiral HPLC analysis.

then attempted to optimize the reaction conditions to retain the enantiomeric excess of the starting allyl substrate, which produces optically active trifluoromethyl group substituted aminated products. As mentioned, the allylic amination of (*S*)-**1a** by the $Pd(OAc)_2$/DPPE catalyst at 60 °C decreased the enantiopurity. Fortunately, reinvestigation of the reaction conditions revealed that the reaction proceeded at 25 °C with retention of the enantiomeric excess, and gave the optically active trifluoromethyl group substituted γ-type product (*R*)-**3ab** in 98% ee (entry 2). We next attempted formation of the chiral α-product **4ab** using the [Pd(π-allyl)(cod)]BF_4/ligand catalyst, but soon found that a reduced reaction temperature was not effective for retaining the enantiomeric excess. For example, the reaction at 60 °C gave primarily α-product **4ab** with low regioselectivity (entry 4). However, after the screening of several types of phosphine ligands, we succeeded in obtaining the enantiomerically enriched α-product (*S*)-**4ab** with complete chirality transfer using the chiral BINAP ligand. When (*S*)-BINAP was used as the ligand for the reaction of (*S*)-**1a** with morpholine (**2b**) at 100 °C, the α-product was produced as the major regioisomer with a 33% ee (entry 5). The racemization was prevented at 40 °C, then the enantiomerically pure α-product (*S*)-**4ab** was obtained in good yield even with 5 mol % [Pd(π-allyl)(cod)]BF_4/(*S*)-BINAP (entries 6 and 7).[12]

We demonstrated the $Pd(OAc)_2$/DPPE or [Pd(π-allyl)(cod)]BF_4/(*S*)-BINAP catalyzed reactions of other optically active allyl acetates and amines (Table 7). The reaction by $Pd(OAc)_2$/DPPE exhibited a perfect regioselectivity, and produced the enantiomerically enriched γ-products (entries 1, 3, 5, 7, 9). For the reaction of **1a** with **2c**, **2d** or **2o**, we succeeded in obtaining the enantiomerically enriched γ-product **3** with over a 95% ee (entries 1, 3, 5), although the enantiomeric excess of the γ-product from the reaction of **1c** and **1f** was slightly reduced during the reaction with **2c** (entries 7 and 9). On the other hand, as we expected, the [Pd(π-allyl)(cod)]BF_4/(*S*)-BINAP catalyst produced the enantiomerically enriched α-product with a high regioselectivity and enantiomeric excess. Although we observed a slow reaction rate and/or decreased regioselectivity,[13] a lower reaction temperature (25 °C)[14] and/or longer reaction time (5 days) gave the intended optically active α-product in a moderate to good yield with high regioselectivity (entries 2, 4, 6, 8, 10). Unfortunately, all reactions in Tables 6 and 7 were done by aliphatic secondary amines, because reactions by primary amines exhibited a decreased yield (<30%) owing to the deacylation of **1a**.

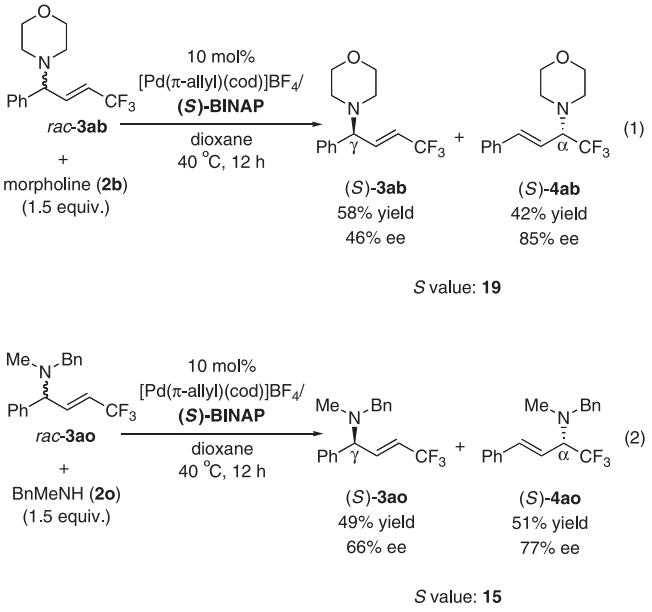
We further established that (*S*)-BINAP and (*R*)-BINAP exhibited different results of both the regiochemistry and enantiomeric excess for the allylic amination of (*S*)-**1a** with **2b**. As shown in Table 6, the reaction by (*S*)-BINAP gave the chiral α-product (*S*)-**4ab** with 99% ee (Table 6, entries 6 and 7). However, when the (*R*)-BINAP was used for the same reaction, the γ-product (*R*)-**3ab** was obtained as the major regioisomer with a high enantiomeric excess (91% ee) (entry 8). These results indicated that kinetic resolution might take place during the isomerization step from the γ-product to α-product. To clarify this, we next demonstrated the isomerization reaction of the chiral allyl amine (*R*)-**3ab** using chiral palladium/BINAP catalysts (Scheme 1). The isomerization reaction of (*R*)-**3ab** (97% ee) smoothly occurred when (*S*)-BINAP was used and the chiral α-product (*S*)-**4ab** was obtained in 91% yield without any loss of enantiomeric excess (97% ee). On the other hand, the isomerization of (*R*)-**3ab** proceeded very slowly when (*R*)-BINAP was used, and 92% of the γ-product was recovered. These two results strongly suggest that the (*S*)-BINAP ligand is a matching enantiomer for the stereospecific isomerization of the chiral allyl amine (*R*)-**3ab** to (*S*)-

4ab. To the best of our knowledge, this is the first example of the palladium-catalyzed isomerization of 1,3-disubstituted unsymmetrical allyl amines, though several examples have been reported of the kinetic resolution of the palladium-catalyzed allylic substitutions.[15,16]



Scheme 1.

We thus demonstrated the kinetic resolution of the racemic allyl amine *rac*-**3ab** by the [Pd(π-allyl)(cod)]BF_4/(*S*)-BINAP catalyzed isomerization (Eq. 1 in Scheme 2). As we intended, the selective kinetic resolution took place at 40 °C in 12 h and produced a 58% optically active γ-product **3ab** (46% ee (*S*)) and 42% chiral α-product **4ab** (85% ee (*S*)) (*S* value=19).[17,18] When the racemic allyl amine *rac*-**3ao** was treated with [Pd(π-allyl)(cod)]BF_4/(*S*)-BINAP, we observed that the resulting *S* value was 15 (Eq. 2 in Scheme 2).



Scheme 2.

In conclusion, we have demonstrated the regioselective formation of both the α- and γ-trifluoromethyl group-substituted allyl amines via the palladium-catalyzed allylic amination of α-trifluoromethylated allyl acetate. The conventional γ-product was obtained using the $Pd(OAc)_2$/DPPE catalyst, while the unusual α-product was obtained when the reaction was conducted in the presence of [Pd(π-allyl)(cod)]BF_4/DPPF as catalyst. We further revealed that the γ-product was easily isomerized to the α-product under the [Pd(π-allyl)(cod)]BF_4/DPPF catalyzed reaction conditions; the α-product was formed by isomerization of the γ-product. Furthermore, we demonstrated the regioselective synthesis of the chiral trifluoromethyl group substituted allylic amines from chiral allyl acetate using two types of palladium catalysts. We also found that kinetic resolution had occurred during the isomerization step using the chiral [Pd(π-allyl)(cod)]BF_4/BINAP catalyst.

3. Experimental section

3.1. General information

All manipulations were carried out under a nitrogen atmosphere. Nitrogen gas was dried by passage through P_2O_5. NMR spectra were recorded on a JEOL JNM-LA400 (400 MHz for ^{1}H), JEOL JNM-ECP500 (500 MHz for 1H, 125 MHz for ^{13}C, and 470 MHz for ^{19}F) or Bruker Biospin AVACNE II 600 (600 MHz for ^{1}H, 150 MHz for ^{13}C, and 564 MHz for ^{19}F). Chemical shifts are reported in δ parts per million referenced to an internal $SiMe_4$ standard for ^{1}H NMR and an internal C_6F_6 standard for ^{19}F NMR. Residual chloroform (δ 77.0 for ^{13}C) was used as internal reference for ^{13}C NMR. Data are reported as follows: chemical shift, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, quin=quintet, sep=septet, m=multiplet, br s=broad signal), coupling constant (Hz), and integration. $Pd(OAc)_2$, DPPE, DPPF, BINAP, and other reagents and solvents were purchased from common commercial sources and were used without further purification. [Pd(π-allyl)(cod)]BF_4,[19] racemic allyl acetates **1** and chiral allyl acetates (*S*)-**1**[20,21] were prepared according to the literatures.

3.2. General procedure for the allylic amination of 1,1,1-trifluoro-4-phenylbut-3-en-2-yl acetate (1a) with diethylamine (2a)

A typical procedure is given for the reaction of **1a** with **2a** (Table 1, entry 10). To a solution of [Pd(π-allyl)(cod)]BF_4 (7.0 mg, 0.020 mmol) and DPPF (11.4 mg, 0.020 mmol) in dioxane (1.0 ml) was added allyl acetate **1a** (50 mg, 0.20 mmol) and amine **2a** (23 mg, 0.31 mmol) at room temperature. The resultant mixture was stirred at 100 °C for 9 h. The reaction mixture was quenched with water, and extracted with ethyl acetate. The organic phase was washed with brine, dried over anhydrous $MgSO_4$, and evaporated. The NMR yield (95%, trioxane as an internal standard) and regioisomeric ratio were determined by 400 MHz ^{1}H NMR for crude material. The residue was purified by silica gel column chromatography (hexane/EtOAc/Et_3N=97/2/1) to give 46 mg (87%) of **4aa** (α-product) as a colorless oil.

*3.2.1. 1,1,1-Trifluoro-4-phenylbut-3-en-2-yl acetate (**1a**)*[5b,21]. Yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.18 (s, 3H), 5.80–5.85 (m, 1H), 6.11 (dd, *J*=7.8, 16.0 Hz, 1H), 6.86 (d, *J*=16.0 Hz, 1H), 7.30–7.42 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.6, 71.1 (q, J_{CF}=33.6 Hz), 117.3, 123.2 (q, J_{CF}=280.5 Hz), 127.0, 128.7, 129.0, 135.0, 138.8, 168.8. ^{19}F NMR (470 MHz, $CDCl_3$) δ 85.3 (d, *J*=6.8 Hz). IR (neat) 3034, 2971, 1760, 1657, 1370, 1277, 1223 cm^{-1}.

*3.2.2. tert-Butyl 1,1,1-trifluoro-4-phenylbut-3-en-2-yl carbonate (**1b**).* Colorless solid. Mp 53–55 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.51 (s, 9H), 5.59 (dquin, *J*=1.1, 6.6 Hz, 1H), 6.14 (dd, *J*=7.7, 16.0 Hz, 1H), 6.88 (d, *J*=16.0 Hz, 1H), 7.28–7.46 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.6, 73.9 (q, J_{CF}=34.0 Hz), 83.9, 117.1, 123.1 (q, J_{CF}=280.7 Hz), 127.0, 128.7, 129.0, 135.0, 138.7, 151.7. ^{19}F NMR (470 MHz, $CDCl_3$) δ 85.2 (d, *J*=6.5 Hz). IR (KBr) 2985, 1755, 1657, 1581, 1375, 1250, 1178, 1138 cm^{-1}. Anal. Calcd for $C_{15}H_{17}F_3O_3$: C, 59.60; H, 5.67. Found (%): C, 59.67; H, 5.67.

*3.2.3. 1,1,1-Trifluoro-4-(4-methoxyphenyl)but-3-en-2-yl acetate (**1c**).* White solid. Mp 51–52 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.17 (s, 3H), 3.82 (s, 3H), 5.76–5.82 (m, 1H), 5.97 (dd, *J*=8.0, 16.0 Hz, 1H), 6.80 (d, *J*=16.0 Hz, 1H), 6.87 (d, *J*=8.0 Hz, 2H), 7.36 (d, *J*=8.0 Hz, 2H). ^{13}C

NMR (125 MHz, $CDCl_3$) δ 20.6, 55.3, 71.3 (q, J_{CF}=33.2 Hz), 114.1, 114.8, 123.2 (q, J_{CF}=280.3 Hz), 127.7, 128.4, 138.4, 160.3, 168.9. ^{19}F NMR (470 MHz, $CDCl_3$) δ 85.2 (d, J=7.2 Hz). IR (KBr) 2963, 2936, 2842, 1760, 1608, 1514, 1379, 1353, 1192, 1031 cm^{-1}. HRMS (DART) m/z calcd for $[M+H]^+$: $C_{13}H_{14}F_3O_3$ 275.0895, found 275.0895.

*3.2.4. 1,1,1-Trifluoro-4-(4-fluorophenyl)but-3-en-2-yl acetate (**1d**).* Yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 2.18 (s, 3H), 5.77–5.83 (m, 1H), 6.03 (dd, J=7.7, 16.0 Hz, 1H), 6.82 (d, J=16.0 Hz, 1H), 7.02–7.06 (m, 2H), 7.38–7.42 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.3, 71.0 (q, J_{CF}=33.6 Hz), 115.6 (d, J_{CF}=21.6 Hz), 117.0, 123.2 (q, J_{CF}=280.3 Hz), 128.7 (d, J_{CF}=8.4 Hz), 131.2 (d, J_{CF}=2.4 Hz), 137.4, 163.1 (d, J_{CF}=249.5 Hz), 168.7. ^{19}F NMR (470 MHz, $CDCl_3$) δ 49.8 (tt, J=5.3, 8.5 Hz, 1F), 85.3 (d, J=6.7 Hz, 3F). IR (neat) 3052, 2927, 1764, 1661, 1514, 1375, 1218, 1035, 972 cm^{-1}. HRMS (ESI) m/z calcd for $[M+Na]^+$: $C_{12}H_{10}F_4NaO_2$ 285.0515, found 285.0514.

*3.2.5. 1,1,1-Trifluoro-4-o-tolylbut-3-en-2-yl acetate (**1e**).* Yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 2.19 (s, 3H), 2.36 (s, 3H), 5.80–5.86 (m, 1H), 5.99 (dd, J=8.0, 16.0 Hz, 1H), 7.10 (d, J=16.0 Hz, 1H), 7.16–7.24 (m, 3H), 7.43–7.45 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.6, 20.7, 71.3 (q, J_{CF}=33.2 Hz), 118.7, 123.2 (q, J_{CF}=279.5 Hz), 126.0, 126.2, 128.8, 130.5, 134.2, 136.1, 136.8, 168.8. ^{19}F NMR (470 MHz, $CDCl_3$) δ 85.2 (d, J=6.8 Hz). IR (neat) 3065, 3025, 2963, 1764, 1652, 1603, 1487, 1375, 1272, 1223, 1138, 1035 cm^{-1}. HRMS (ESI) m/z calcd for $[M+H]^+$: $C_{13}H_{14}F_3O_2$ 259.0946, found 259.0945.

*3.2.6. N,N-Diethyl-4,4,4-trifluoro-1-phenylbut-2-en-1-amine (**3aa**)[5a].* Colorless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 0.99 (t, J=6.9 Hz, 6H), 2.53 (q, J=6.9 Hz, 4H), 4.27 (d, J=8.2 Hz, 1H), 5.81 (dq, J=6.4, 16.0 Hz, 1H), 6.53 (ddq, J=1.8, 8.2, 16.0 Hz, 1H), 7.26–7.36 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.8, 43.1, 66.6, 119.3 (q, J_{CF}=33.6 Hz), 122.9 (q, J_{CF}=269.7 Hz), 127.6, 128.0, 128.6, 140.3, 141.4 (q, J_{CF}=6.1 Hz). ^{19}F NMR (470 MHz, $CDCl_3$) δ 98.0 (d, J=6.3 Hz). IR (neat) 2976, 2819, 1679, 1491, 1455, 1281, 1125 cm^{-1}. Anal. Calcd for $C_{14}H_{18}F_3N$: C, 65.35; H, 7.05; N, 5.44. Found: C, 65.26; H, 7.17; N, 5.31.

*3.2.7. 4-(4,4,4-Trifluoro-1-phenylbut-2-enyl)morpholine (**3ab**)[5b].* Colorless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 2.33–2.41 (m, 4H), 3.69 (t, J=4.8 Hz, 4H), 3.77 (d, J=8.2 Hz, 1H), 5.85 (dq, J=6.4, 15.6 Hz, 1H), 6.47 (ddq, J=2.1, 8.7, 15.6 Hz, 1H), 7.28–7.36 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 51.8, 67.0, 72.4, 119.7 (q, J_{CF}=33.9 Hz), 122.7 (q, J_{CF}=269.7 Hz), 128.1, 128.2, 128.9, 138.8, 141.2 (q, J_{CF}=6.1 Hz). ^{19}F NMR (564 MHz, $CDCl_3$) δ 97.8 (d, J=7.3 Hz). IR (neat) 2961, 2857, 2812, 1682, 1492, 1451, 1282, 1117 cm^{-1}. HRMS (EI) m/z calcd for [M]: $C_{14}H_{16}F_3NO$ 271.1184, found 271.1195.

*3.2.8. 1-(4,4,4-Trifluoro-1-phenylbut-2-enyl)-4-phenylpiperazine (**3ac**)[5b].* Colorless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 2.48–2.63 (m, 4H), 3.17 (t, J=5.2 Hz, 4H), 3.84 (d, J=8.6 Hz, 1H), 5.87 (dq, J=6.3, 15.5 Hz, 1H), 6.53 (ddq, J=2.0, 8.6, 15.5 Hz, 1H), 6.85 (t, J=7.4 Hz, 1H), 6.89 (d, J=8.0 Hz, 2H), 7.22–7.39 (m, 7H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 49.1, 51.1, 71.8, 115.9, 119.5 (q, J_{CF}=33.6 Hz), 119.6, 122.8 (q, J_{CF}=269.3 Hz), 127.9, 128.1, 128.8, 129.0, 139.1, 141.3 (q, J_{CF}=6.0 Hz), 151.1. ^{19}F NMR (470 MHz, $CDCl_3$) δ 97.9 (d, J=6.3 Hz). IR (neat) 3061, 3030, 2958, 2824, 1679, 1603, 1500, 1451, 1339, 1290, 1124 cm^{-1}. HRMS (EI) m/z calcd for [M]: $C_{20}H_{21}F_3N_2$ 346.1657, found 346.1663.

*3.2.9. 1-(4,4,4-Trifluoro-1-phenylbut-2-enyl)-4-methylpiperazine (**3ad**).* Colorless oil. ^1H NMR (600 MHz, $CDCl_3$) δ 2.27 (s, 3H), 2.10–2.80 (m, 8H), 3.80 (d, J=8.7 Hz, 1H), 5.84 (dq, J=6.4, 15.8 Hz, 1H), 6.49 (ddq, J=2.0, 8.7, 15.8 Hz, 1H), 7.27–7.35 (m, 5H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 45.9, 51.1, 55.2, 71.9, 119.5 (q, J_{CF}=33.8 Hz), 122.8 (q, J_{CF}=269.6 Hz), 127.9, 128.2, 128.8, 139.3, 141.5 (q, J_{CF}=6.4 Hz). ^{19}F NMR (564 MHz, $CDCl_3$) δ 97.8 (d, J=6.0 Hz). IR (neat) 2945, 2802, 1679, 1455, 1344, 1277, 1125, 1008 cm^{-1}. HRMS (ESI) m/z calcd for $[M+H]^+$: $C_{15}H_{20}F_3N_2$ 285.1579, found 285.1569.

*3.2.10. 1-(4,4,4-Trifluoro-1-phenylbut-2-enyl)-4-phenylpiperidine (**3ae**).* Yellow solid. Mp 59–65 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 1.70–1.84 (m, 4H), 1.91 (dt, J=3.4, 11.0 Hz, 1H), 2.12 (dt, J=3.4, 11.0 Hz, 1H), 2.43–2.48 (m, 1H), 2.82 (d, J=11.3 Hz, 1H), 3.11 (d, J=11.3 Hz, 1H), 3.88 (d, J=7.9 Hz, 1H), 5.85 (dq, J=6.4, 15.4 Hz, 1H), 6.55 (ddq, J=2.3, 7.9, 15.4 Hz, 1H), 7.17–7.21 (m, 3H), 7.27–7.36 (m, 7H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 33.6, 33.7, 42.7, 51.7, 52.6, 72.1, 119.4 (q, J_{CF}=33.6 Hz), 123.0 (q, J_{CF}=269.7 Hz), 126.2, 126.9, 127.9, 128.3, 128.5, 128.8, 139.5, 141.8 (q, J_{CF}=6.3 Hz), 146.3. ^{19}F NMR (564 MHz, $CDCl_3$) δ 97.9 (d, J=6.1 Hz). IR (KBr) 3034, 2935, 2802, 2752, 1679, 1599, 1493, 1453, 1286, 1123 cm^{-1}. HRMS (ESI) m/z calcd for $[M+H]^+$: $C_{21}H_{23}F_3N$ 346.1783, found 346.1781.

*3.2.11. N,N-Dibutyl-4,4,4-trifluoro-1-phenylbut-2-en-1-amine (**3af**).* Colorless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 0.86 (t, J=7.3 Hz, 6H), 1.21–1.29 (m, 4H), 1.37–1.43 (m, 4H), 2.41 (t, J=7.6 Hz, 4H), 4.30 (d, J=8.2 Hz, 1H), 5.79 (dq, J=6.4, 16.0 Hz, 1H), 6.54 (ddq, J=1.8, 8.2, 16.0 Hz, 1H), 7.25–7.35 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.0, 20.4, 29.5, 49.8, 66.3, 119.9 (q, J_{CF}=33.6 Hz), 122.9 (q, J_{CF}=269.7 Hz), 127.5, 128.1, 128.4, 140.2, 140.8 (q, J=5.8 Hz). ^{19}F NMR (564 MHz, $CDCl_3$) δ 98.0 (d, J=6.3 Hz). IR (neat) 2958, 2869, 2819, 1679, 1455, 1281, 1125, 981 cm^{-1}. HRMS (ESI) m/z calcd for $[M+H]^+$: $C_{18}H_{27}F_3N$ 314.2096, found 314.2092.

*3.2.12. 4,4,4-Trifluoro-1-phenyl-N,N-dipropylbut-2-en-1-amine (**3ag**).* Colorless oil. ^1H NMR (600 MHz, $CDCl_3$) δ 0.83 (t, J=7.5 Hz, 6H), 1.41–1.47 (m, 4H), 2.34–2.42 (m, 4H), 4.30 (d, J=8.3 Hz, 1H), 5.79 (dq, J=6.4, 15.8 Hz, 1H), 6.54 (ddq, J=2.3, 8.3, 15.8 Hz, 1H), 7.25–7.28 (m, 1H), 7.31–7.35 (m, 4H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 11.7, 20.5, 52.2, 66.3, 120.0 (q, J_{CF}=33.8 Hz), 123.0 (q, J_{CF}=269.6 Hz), 127.5, 128.2, 128.4, 140.2, 140.8 (q, J_{CF}=5.9 Hz). ^{19}F NMR (564 MHz, $CDCl_3$) δ 98.1 (d, J=5.6 Hz). IR (neat) 2963, 2873, 2819, 1675, 1496, 1455, 1281, 1125, 981 cm^{-1}. HRMS (ESI) m/z calcd for $[M+H]^+$: $C_{16}H_{23}F_3N$ 286.1783, found 286.1774.

*3.2.13. N-Ethyl-4,4,4-trifluoro-N-isopropyl-1-phenylbut-2-en-1-amine (**3ah**).* Colorless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 0.92–1.00 (m, 9H), 2.53 (ddd, J=1.8, 6.9, 14.2 Hz, 2H), 2.95–3.03 (m, 1H), 4.38 (d, J=8.2 Hz, 1H), 5.78 (dq, J=6.4, 15.6 Hz, 1H), 6.57 (ddq, J=2.1, 8.2, 15.6 Hz, 1H), 7.24–7.36 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.3, 19.3, 19.9, 39.3, 48.6, 65.8, 118.8 (q, J_{CF}=33.6 Hz), 123.0 (q, J_{CF}=269.7 Hz), 127.4, 128.0, 128.5, 141.4, 142.2 (q, J_{CF}=6.1 Hz). ^{19}F NMR (564 MHz, $CDCl_3$) δ 98.0 (d, J=6.2 Hz). IR (neat) 2971, 2931, 2873, 1675, 1286, 1125, 981 cm^{-1}. HRMS (EI) m/z calcd for [M]: $C_{15}H_{20}F_3N$ 271.1548, found 271.1542.

*3.2.14. N-Butyl-4,4,4-trifluoro-1-phenylbut-2-en-1-amine (**3aj**).* Colorless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 0.89 (t, J=7.3 Hz, 3H), 1.30–1.51 (m, 5H), 2.48–2.59 (m, 2H), 4.27–4.28 (m, 1H), 5.87 (ddq, J=1.4, 6.4, 15.6 Hz, 1H), 6.43–6.49 (m, 1H), 7.27–7.37 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.9, 20.4, 32.3, 47.4, 63.6, 118.1 (q, J_{CF}=34.2 Hz), 123.2 (q, J_{CF}=270.6 Hz), 127.3, 127.9, 128.8, 140.9, 142.4 (q, J_{CF}=6.4 Hz). ^{19}F NMR (564 MHz, $CDCl_3$) δ 97.9 (d, J=6.4 Hz). IR (neat) 3329, 2961, 2932, 2874, 1678, 1603, 1493, 1455, 1287, 1120 cm^{-1}. HRMS (EI) m/z calcd for [M]: $C_{14}H_{18}F_3N$ 257.1391, found 257.1393.

*3.2.15. 4,4,4-Trifluoro-N-isopropyl-1-phenylbut-2-en-1-amine (**3ak**).* Colorless oil. ^1H NMR (600 MHz, $CDCl_3$) δ 1.04 (d, J=6.0 Hz, 3H), 1.07 (d, J=6.4 Hz, 3H), 1.27 (br s, 1H), 2.70–2.77 (m, 1H), 4.41–4.42 (m, 1H), 5.84 (ddq, J=1.5, 6.4, 15.8 Hz, 1H), 6.45–6.50 (m, 1H), 7.27–7.37 (m, 5H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 22.8, 23.4, 45.8, 60.5, 118.1 (q, J_{CF}=33.4 Hz), 123.3 (q, J_{CF}=269.6 Hz), 127.3, 127.8,

128.9, 141.1, 142.8 (q, J_{CF}=5.9 Hz). ^{19}F NMR (564 MHz, $CDCl_3$) δ 98.0 (d, J=6.7 Hz). IR (neat) 3325, 3030, 2967, 1679, 1491, 1455, 1290, 1125, 977 cm^{-1}. HRMS (ESI) m/z calcd for $[M+H]^+$: $C_{13}H_{17}F_3N$ 244.1313, found 244.1304.

*3.2.16. N-Benzyl-4,4,4-trifluoro-1-phenylbut-2-en-1-amine (**3al**).* Colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.72 (s, 2H), 4.32–4.34 (m, 1H), 5.90 (ddq, J=1.4, 6.4, 15.6 Hz, 1H), 6.46–6.51 (m, 1H), 7.24–7.39 (m, 10H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 51.3, 62.3, 118.4 (q, J_{CF}=33.9 Hz), 123.2 (q, J_{CF}=269.7 Hz), 127.2, 127.4, 128.0, 128.1, 128.5, 128.9, 139.7, 140.4, 142.1 (q, J_{CF}=6.1 Hz). ^{19}F NMR (564 MHz, $CDCl_3$) δ 97.9 (d, J=6.0 Hz). IR (neat) 3325, 3061, 3030, 2842, 1679, 1603, 1491, 1455, 1290, 1120, 1026, 977 cm^{-1}. HRMS (EI) m/z calcd for [M]: $C_{17}H_{16}F_3N$ 291.1235, found 291.1233.

*3.2.17. N-(4,4,4-Trifluoro-1-phenylbut-2-enyl)benzenamine (**3am**).* Colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.97 (d, J=4.1 Hz, 1H), 5.01–5.04 (m, 1H), 5.94 (ddq, J=1.8, 6.4, 15.6 Hz, 1H), 6.57–6.62 (m, 3H), 6.76 (tt, J=1.1, 7.6 Hz, 1H), 7.16–7.20 (m, 2H), 7.32–7.41 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 59.1, 113.5, 118.4, 119.5 (q, J_{CF}=33.9 Hz), 123.2 (q, J_{CF}=270.6 Hz), 127.4, 128.4, 129.2, 129.3, 139.6, 140.2 (q, J_{CF}=5.8 Hz), 146.5. ^{19}F NMR (564 MHz, $CDCl_3$) δ 98.1 (d, J=5.8 Hz). IR (neat) 3410, 3056, 3030, 1684, 1603, 1500, 1455, 1429, 1290, 1120, 972 cm^{-1}. HRMS (EI) m/z calcd for [M]: $C_{16}H_{14}F_3N$ 277.1078, found 277.1078.

*3.2.18. N,N-Diethyl-1,1,1-trifluoro-4-phenylbut-3-en-2-amine (**4aa**)[5a].* Colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.09 (t, J=7.1 Hz, 6H), 2.59–2.66 (m, 2H), 2.75–2.82 (m, 2H), 3.78–3.85 (m, 1H), 6.22 (dd, J=7.8, 16.0 Hz, 1H), 6.68 (d, J=16.0 Hz, 1H), 7.25–7.41 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.0, 44.8, 63.8 (q, J_{CF}=27.5 Hz), 120.1, 126.2 (q, J_{CF}=285.0 Hz), 126.6, 128.2, 128.6, 136.2, 136.4. ^{19}F NMR (564 MHz, $CDCl_3$) δ 90.9 (d, J=8.1 Hz). IR (neat) 2976, 2833, 1451, 1388, 1268, 1107, 968 cm^{-1}. Anal. Calcd for $C_{14}H_{18}F_3N$: C, 65.35; H, 7.05; N, 5.44. Found: C, 65.24; H, 7.14; N, 5.40.

*3.2.19. 4-(1,1,1-Trifluoro-4-phenylbut-3-en-2-yl)morpholine (**4ab**)[5b].* Colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.72–2.80 (m, 4H), 3.57–3.64 (m, 1H), 3.73 (t, J=4.6 Hz, 4H), 6.18 (dd, J=8.2, 16.0 Hz, 1H), 6.72 (d, J=16.0 Hz, 1H), 7.25–7.42 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 50.4, 67.2, 68.6 (q, J_{CF}=27.5 Hz), 118.5, 125.7 (q, J_{CF}=285.0 Hz), 126.7, 128.5, 128.7, 135.7, 137.5. ^{19}F NMR (470 MHz, $CDCl_3$) δ 92.0 (d, J=8.2 Hz). IR (neat) 2963, 2857, 1453, 1362, 1264, 1108, 1012 cm^{-1}. HRMS (EI) m/z calcd for [M]: $C_{14}H_{16}F_3NO$ 271.1184, found 271.1195.

*3.2.20. 1-(1,1,1-Trifluoro-4-phenylbut-3-en-2-yl)-4-phenylpiperazine (**4ac**)[5b].* White solid. Mp 135–137 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.87–2.97 (m, 4H), 3.21 (t, J=4.9 Hz, 4H), 3.71 (quin, J=8.0 Hz, 1H), 6.22 (dd, J=8.0, 16.0 Hz, 1H), 6.74 (d, J=16.0 Hz, 1H), 6.86 (t, J=7.4 Hz, 1H), 6.91 (d, J=7.4 Hz, 2H), 7.21–7.47 (m, 7H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 49.7, 49.9, 68.1 (q, J_{CF}=27.6 Hz), 116.2, 118.7, 119.9, 125.8 (q, J_{CF}=285.5 Hz), 126.7, 128.4, 128.6, 129.0, 135.8, 137.4, 151.3. ^{19}F NMR (470 MHz, $CDCl_3$) δ 92.1 (d, J=8.5 Hz). IR (KBr) 2806, 1652, 1603, 1581, 1500, 1388, 1303, 1268, 1236, 1187 cm^{-1}. HRMS (EI) m/z calcd for [M]: $C_{20}H_{21}F_3N_2$ 346.1657, found 346.1661.

*3.2.21. 1-(1,1,1-Trifluoro-4-phenylbut-3-en-2-yl)-4-methylpiperazine (**4ad**).* Yellow oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.28 (s, 3H), 2.20–2.60 (m, 4H), 2.76–2.84 (m, 4H), 3.62–3.68 (m, 1H), 6.18 (dd, J=8.0, 16.0 Hz, 1H), 6.70 (d, J=16.0 Hz, 1H), 7.27–7.29 (m, 1H), 7.33 (t, J=7.4 Hz, 2H), 7.39–7.41 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 46.0, 49.8, 55.4, 68.1 (q, J_{CF}=13.8 Hz), 118.9, 125.8 (q, J_{CF}=285.4 Hz), 126.7, 128.4, 128.7, 135.9, 137.3. ^{19}F NMR (564 MHz, $CDCl_3$) δ 92.0 (d, J=8.2 Hz). IR (neat) 2939, 2844, 2799, 1679, 1457, 1376, 1268, 1163, 1109, 1012 cm^{-1}. HRMS (DART) m/z calcd for $[M+H]^+$: $C_{15}H_{20}F_3N_2$ 285.1579, found 285.1576.

*3.2.22. 1-(1,1,1-Trifluoro-4-phenylbut-3-en-2-yl)-4-phenylpiperidine (**4ae**).* Yellow solid. Mp 85–90 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.77–1.85 (m, 4H), 2.46–2.51 (m, 1H), 2.61 (dt, J=3.0, 11.1 Hz, 1H), 2.69 (dt, J=2.9, 11.1 Hz, 1H), 3.03–3.05 (m, 1H), 3.14–3.17 (m, 1H), 3.69–3.74 (m, 1H), 6.25 (dd, J=7.9, 15.8 Hz, 1H), 6.74 (d, J=15.8 Hz, 1H), 7.18–7.23 (m, 3H), 7.28–7.31 (m, 3H), 7.34–7.37 (m, 2H), 7.43–7.45 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 33.9, 34.0, 42.5, 50.7, 51.3, 68.5 (q, J_{CF}=27.4 Hz), 119.4, 126.1 (q, J_{CF}=286.5 Hz), 126.2, 126.7, 126.9, 128.3, 128.5, 128.7, 136.0, 136.8, 146.2. ^{19}F NMR (564 MHz, $CDCl_3$) δ 92.3 (d, J=8.3 Hz). IR (KBr) 3025, 2940, 2810, 1652, 1599, 1496, 1451, 1397, 1272, 1098 cm^{-1}. HRMS (DART) m/z calcd for $[M+H]^+$: $C_{21}H_{23}F_3N$ 346.1783, found 346.1780.

*3.2.23. N,N-Dibutyl-1,1,1-trifluoro-4-phenylbut-3-en-2-amine (**4af**).* Colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.92 (t, J=7.3 Hz, 6H), 1.25–1.51 (m, 8H), 2.50–2.55 (m, 2H), 2.64–2.70 (m, 2H), 3.72–3.79 (m, 1H), 6.21 (dd, J=7.8, 16.0 Hz, 1H), 6.66 (d, J=16.0 Hz, 1H), 7.25–7.41 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.0, 20.2, 31.0, 51.0, 64.1 (q, J_{CF}=27.5 Hz), 120.0, 126.3 (q, J_{CF}=285.7 Hz), 126.6, 128.1, 128.6, 136.2, 136.4. ^{19}F NMR (564 MHz, $CDCl_3$) δ 91.1 (d, J=8.9 Hz). IR (neat) 2960, 2933, 2874, 1686, 1497, 1468, 1379, 1268, 1173, 1111 cm^{-1}. Anal. Calcd for $C_{18}H_{26}F_3N$: C, 68.93; H, 8.36; N, 4.47. Found: C, 68.98; H, 8.55; N, 4.33.

*3.2.24. 1,1,1-Trifluoro-4-phenyl-N,N-dipropylbut-3-en-2-amine (**4ag**).* Colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.90 (t, J=7.3 Hz, 6H), 1.45–1.51 (m, 4H), 2.50–2.54 (m, 2H), 2.60–2.64 (m, 2H), 3.72–3.78 (m, 1H), 6.22 (dd, J=7.9, 15.8 Hz, 1H), 6.67 (d, J=15.8 Hz, 1H), 7.27–7.29 (m, 1H), 7.33–7.36 (m, 2H), 7.41–7.42 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 11.5, 21.9, 53.2, 64.2 (q, J_{CF}=27.5 Hz), 120.0, 126.3 (q, J_{CF}=285.3 Hz), 126.6, 128.2, 128.7, 136.2, 136.4. ^{19}F NMR (564 MHz, $CDCl_3$) δ 91.0 (d, J=8.4 Hz). IR (neat) 2964, 2935, 2875, 1469, 1380, 1267, 1177, 1155, 1110, 968 cm^{-1}. HRMS (ESI) m/z calcd for $[M+H]^+$: $C_{16}H_{23}F_3N$ 286.1783, found 286.1780.

*3.2.25. N-Ethyl-1,1,1-trifluoro-N-isopropyl-4-phenylbut-3-en-2-amine (**4ah**).* Colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.01 (d, J=6.4 Hz, 3H), 1.07 (t, J=6.9 Hz, 3H), 1.10 (d, J=6.4 Hz, 3H), 2.61–2.68 (m, 1H), 2.78–2.85 (m, 1H), 3.17–3.25 (m, 1H), 3.81–3.88 (m, 1H), 6.26 (dd, J=7.8, 16.0 Hz, 1H), 6.66 (d, J=16.0 Hz, 1H), 7.25–7.41 (m, 5H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 15.4, 19.5, 21.7, 40.3, 49.5, 61.3 (q, J_{CF}=28.6 Hz), 121.8, 126.2 (q, J_{CF}=284.0 Hz), 126.5, 128.1, 128.7, 135.9, 136.4. ^{19}F NMR (564 MHz, $CDCl_3$) δ 89.2 (d, J=8.9 Hz). IR (neat) 2971, 2936, 2873, 1455, 1384, 1268, 1111, 972 cm^{-1}. HRMS (EI) m/z calcd for [M]: $C_{15}H_{20}F_3N$ 271.1548, found 271.1544.

*3.2.26. N-Butyl-1,1,1-trifluoro-4-phenylbut-3-en-2-amine (**4aj**).* Colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.91 (t, J=7.3 Hz, 3H), 1.30–1.55 (m, 4H), 2.62–2.76 (m, 2H), 3.68–3.74 (m, 1H), 6.04 (dd, J=8.2, 15.6 Hz, 1H), 6.70 (d, J=15.6 Hz, 1H), 7.27–7.42 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.9, 20.2, 32.1, 47.1, 62.8 (q, J_{CF}=28.8 Hz), 122.1, 125.5 (q, J=286.0 Hz), 126.7, 128.3, 128.7, 135.8, 136.0. ^{19}F NMR (470 MHz, $CDCl_3$) δ 87.0 (d, J=7.2 Hz). IR (neat) 3347, 2961, 2932, 2874, 1468, 1336, 1258, 1155, 1114, 968 cm^{-1}. HRMS (DART) m/z calcd for $[M+H]^+$: $C_{14}H_{19}F_3N$ 258.1470, found 258.1466.

*3.2.27. 1,1,1-Trifluoro-N-isopropyl-4-phenylbut-3-en-2-amine (**4ak**).* Colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.07 (d, J=6.3 Hz, 3H), 1.10 (d, J=6.3 Hz, 3H), 1.16 (br s, 1H), 2.96 (sep, J=6.3 Hz, 1H), 3.78 (quin, J=7.4 Hz, 1H), 6.02 (dd, J=8.2, 16.0 Hz, 1H), 6.67 (d, J=16.0 Hz, 1H), 7.24–7.43 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.2, 23.6, 45.8, 60.2 (q, J_{CF}=29.2 Hz), 122.4, 125.6 (q, J_{CF}=280.7 Hz), 126.7, 128.3, 128.6, 135.6, 135.8. ^{19}F NMR (470 MHz, $CDCl_3$) δ 86.7 (d,

J=7.4 Hz). IR (neat) 3329, 3030, 2967, 2873, 1719, 1447, 1379, 1263, 1183, 1156, 1116, 963 cm^{-1}. HRMS (DART) m/z calcd for $[M+H]^+$: $C_{13}H_{17}F_3N$ 244.1313, found 244.1314.

*3.2.28. N-Benzyl-1,1,1-trifluoro-4-phenylbut-3-en-2-amine (**4al**).* Colorless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 3.70–3.76 (m, 1H), 3.84 (d, J=13.3 Hz, 1H), 3.96 (d, J=13.3 Hz, 1H), 6.06 (dd, J=8.2, 16.0 Hz, 1H), 6.66 (d, J=16.0 Hz, 1H), 7.26–7.42 (m, 10H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 50.7, 61.4 (q, J_{CF}=28.8 Hz), 121.6, 125.6 (q, J_{CF}=283.1 Hz), 126.7, 127.3, 128.1, 128.4, 128.6, 128.7, 135.7, 136.4, 139.1. ^{19}F NMR (470 MHz, $CDCl_3$) δ 87.1 (d, J=7.2 Hz). IR (neat) 3347, 3030, 2927, 2855, 1657, 1603, 1500, 1455, 1259, 1174, 1125, 1031 cm^{-1}. HRMS (EI) m/z calcd for [M]: $C_{17}H_{16}F_3N$ 291.1235, found 291.1225.

*3.2.29. N-(1,1,1-Trifluoro-4-phenylbut-3-en-2-yl)benzenamine (**4am**).* Colorless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 3.91 (d, J=8.7 Hz, 1H), 4.58–4.66 (m, 1H), 6.20 (dd, J=6.2, 15.8 Hz, 1H), 6.73 (d, J=8.2 Hz, 2H), 6.79–6.83 (m, 2H), 7.20–7.39 (m, 7H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 58.2 (q, J_{CF}=30.1 Hz), 113.8, 119.3, 120.8, 125.2 (q, J_{CF}=283.1 Hz), 126.8, 128.5, 128.7, 129.5, 135.5, 135.6, 145.7. ^{19}F NMR (564 MHz, $CDCl_3$) δ 86.5 (t, J=5.6 Hz). IR (neat) 3410, 3056, 3030, 1603, 1509, 1250, 1125, 968 cm^{-1}. HRMS (EI) m/z calcd for [M]: $C_{16}H_{14}F_3N$ 277.1078, found 277.1086.

*3.2.30. 1-(4,4,4-Trifluoro-1-phenylbut-2-en-1-yl)piperidine (**3an**).* Colorless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 1.36–1.47 (m, 2H), 1.55 (quin, J=5.7 Hz, 4H), 2.21–2.43 (m, 4H), 3.81 (d, J=8.3 Hz, 1H), 5.81 (dq, J=6.3, 15.6 Hz, 1H), 6.51 (ddq, J=1.9, 8.3, 15.6 Hz, 1H), 7.25–7.37 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.4, 26.1, 52.3, 72.3, 119.1 (q, J_{CF}=33.6 Hz), 122.9 (q, J_{CF}=269.3 Hz), 127.7, 128.2, 128.6, 139.6, 141.9 (q, J_{CF}=5.8 Hz). ^{19}F NMR (470 MHz, $CDCl_3$) δ 98.0 (d, J=6.6 Hz). IR (neat) 3034, 2936, 2797, 1679, 1455, 1281, 1125 cm^{-1}. Anal. Calcd for $C_{15}H_{18}F_3N$: C, 66.90; H, 6.74; N, 5.20. Found: C, 66.56; H, 6.75; N, 5.11.

*3.2.31. 1-(1,1,1-Trifluoro-4-phenylbut-3-en-2-yl)piperidine (**4an**).* Colorless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 1.43 (quin, J=5.7 Hz, 2H), 1.59 (quin, J=5.7 Hz, 4H), 2.65–2.74 (m, 4H), 3.62 (quin, J=8.3 Hz, 1H), 6.21 (dd, J=7.7, 15.8 Hz, 1H), 6.70 (d, J=15.8 Hz, 1H), 7.25–7.44 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.3, 26.5, 51.2, 68.8 (q, J_{CF}=27.2 Hz), 119.6, 126.1 (q, J_{CF}=286.6 Hz), 126.7, 128.2, 128.6, 136.1, 136.5. ^{19}F NMR (470 MHz, $CDCl_3$) δ 92.4 (d, J=8.5 Hz). IR (neat) 3025, 2936, 2851, 2815, 1455, 1263, 1156, 1107 cm^{-1}. Anal. Calcd for $C_{15}H_{18}F_3N$: C, 66.90; H, 6.74; N, 5.20. Found: C, 67.02; H, 7.02; N, 5.15.

*3.2.32. 1-(4,4,4-Trifluoro-1-(4-methoxyphenyl)but-2-en-1-yl)piperidine (**3cn**).* Colorless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 1.41 (quin, J=5.5 Hz, 2H), 1.55 (quin, J=5.5 Hz, 4H), 2.25–2.31 (m, 4H), 3.76 (d, J=7.8 Hz, 1H), 3.80 (s, 3H), 5.78 (dq, J=6.4, 15.6 Hz, 1H), 6.49 (ddq, J=2.1, 7.8, 15.6 Hz, 1H), 6.87 (d, J=8.8 Hz, 2H), 7.19 (d, J=8.8 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.5, 26.1, 52.3, 55.2, 71.6, 114.0, 118.8 (q, J_{CF}=33.6 Hz), 123.0 (q, J_{CF}=269.7 Hz), 129.3, 131.6, 142.1 (q, J_{CF}=6.1 Hz), 159.1. ^{19}F NMR (470 MHz, $CDCl_3$) δ 98.0 (d, J=6.3 Hz). IR (neat) 2940, 2851, 2797, 1679, 1612, 1514, 1250, 1120, 1040, 977 cm^{-1}. Anal. Calcd for $C_{16}H_{20}F_3NO$: C, 64.20; H, 6.73; N, 4.68. Found: C, 64.05; H, 6.72; N, 4.66.

*3.2.33. 1-(1,1,1-Trifluoro-4-(4-methoxyphenyl)but-3-en-2-yl)piperidine (**4cn**).* Colorless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 1.42 (quin, J=5.7 Hz, 2H), 1.59 (quin, J=5.7 Hz, 4H), 2.63–2.73 (m, 4H), 3.58 (quin, J=8.4 Hz, 1H), 3.81 (s, 3H), 6.06 (dd, J=8.0, 16.0 Hz, 1H), 6.62 (d, J=16.0 Hz, 1H), 6.87 (d, J=8.8 Hz, 2H), 7.35 (d, J=8.8 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.3, 26.5, 51.2, 55.3, 68.9 (q, J_{CF}=27.2 Hz), 114.0, 117.1, 126.2 (q, J_{CF}=279.9 Hz), 127.9, 128.9, 136.0, 159.7. ^{19}F NMR (470 MHz, $CDCl_3$) δ 92.3 (d, J=8.8 Hz). IR (neat) 2940, 2837, 1608, 1514, 1460, 1254, 1160, 1107, 1035 cm^{-1}. Anal. Calcd for $C_{16}H_{20}F_3NO$: C, 64.20; H, 6.73; N, 4.68. Found: C, 64.32; H, 7.00; N, 4.47.

*3.2.34. 1-(4,4,4-Trifluoro-1-(4-fluorophenyl)but-2-en-1-yl)piperidine (**3dn**).* Colorless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 1.41 (quin, J=5.7 Hz, 2H), 1.55 (quin, J=5.7 Hz, 4H), 2.24–2.39 (m, 4H), 3.80 (d, J=8.2 Hz, 1H), 5.80 (dq, J=6.4, 15.6 Hz, 1H), 6.46 (ddq, J=2.0, 8.2, 15.6 Hz, 1H), 7.00–7.06 (m, 2H), 7.22–7.28 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.4, 26.1, 52.2, 71.5, 115.5 (d, J_{CF}=21.1 Hz), 119.3 (q, J_{CF}=33.9 Hz), 122.8 (q, J_{CF}=269.3 Hz), 129.6 (d, J_{CF}=8.6 Hz), 135.4, 141.6 (q, J_{CF}=6.1 Hz), 162.2 (d, J_{CF}=245.7 Hz). ^{19}F NMR (470 MHz, $CDCl_3$) δ 47.0–47.1 (m, 1F), 97.9 (d, J=6.3 Hz, 3F). IR (neat) 2940, 2855, 2802, 2757, 1679, 1608, 1509, 1227, 1125, 977 cm^{-1}. Anal. Calcd for $C_{15}H_{17}F_4N$: C, 62.71; H, 5.96; N, 4.88. Found: C, 62.80; H, 6.19; N, 4.84.

*3.2.35. 1-(1,1,1-Trifluoro-4-(4-fluorophenyl)but-3-en-2-yl)piperidine (**4dn**).* Colorless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 1.44 (quin, J=5.6 Hz, 2H), 1.59 (quin, J=5.6 Hz, 4H), 2.70 (t, J=5.2 Hz, 4H), 3.61 (quin, J=8.3 Hz, 1H), 6.12 (dd, J=7.7, 15.8 Hz, 1H), 6.66 (d, J=15.8 Hz, 1H), 7.03 (t, J=8.6 Hz, 2H), 7.38 (dd, J=5.4, 8.6 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.2, 26.5, 51.2, 68.7 (q, J_{CF}=27.2 Hz), 115.6 (d, J_{CF}=21.1 Hz), 119.4, 126.1 (q, J_{CF}=286.9 Hz), 128.3 (d, J_{CF}=7.7 Hz), 132.3 (d, J_{CF}=3.8 Hz), 135.2, 162.65 (d, J_{CF}=247.6 Hz). ^{19}F NMR (470 MHz, $CDCl_3$) δ 48.2–48.3 (m, 1F), 92.4 (d, J=8.5 Hz, 3F). IR (neat) 2940, 2855, 2819, 1603, 1509, 1227, 1160, 1111, 972 cm^{-1}. Anal. Calcd for $C_{15}H_{17}F_4N$: C, 62.71; H, 5.96; N, 4.88. Found: C, 62.79; H, 4.94; N, 6.19.

*3.2.36. 1-(4,4,4-Trifluoro-1-(o-tolyl)but-2-en-1-yl)piperidine (**3en**).* Colorless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 1.43 (quin, J=5.6 Hz, 2H), 1.48–1.61 (m, 4H), 2.26–2.33 (m, 4H), 2.35 (s, 3H), 3.96 (d, J=8.9 Hz, 1H), 5.77 (dq, J=6.4, 15.8 Hz, 1H), 6.44 (ddq, J=2.0, 8.9, 15.8 Hz, 1H), 7.11–7.23 (m, 3H), 7.43 (d, J=7.4 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.6, 24.6, 26.1, 52.6, 68.5, 118.4 (q, J_{CF}=33.9 Hz), 122.8 (q, J_{CF}=269.7 Hz), 126.4, 127.2, 127.9, 130.7, 136.3, 138.1, 141.6 (q, J_{CF}=5.8 Hz). ^{19}F NMR (470 MHz, $CDCl_3$) δ 98.0 (d, J=6.3 Hz). IR (neat) 2936, 2855, 2797, 2757, 1675, 1451, 1290, 1125, 977 cm^{-1}. Anal. Calcd for $C_{16}H_{20}F_3N$: C, 67.83; H, 7.11; N, 4.94. Found: C, 67.80; H, 7.10; N, 5.00.

*3.2.37. 1-(1,1,1-Trifluoro-4-(o-tolyl)but-3-en-2-yl)piperidine (**4en**).* Colorless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 1.44 (quin, J=5.6 Hz, 2H), 1.60 (quin, J=5.6 Hz, 4H), 2.36 (s, 3H), 2.71 (t, J=5.0 Hz, 4H), 3.65 (quin, J=8.4 Hz, 1H), 6.06 (dd, J=7.7, 15.8 Hz, 1H), 6.93 (d, J=15.6 Hz, 1H), 7.13–7.22 (m, 3H), 7.42–7.48 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.8, 24.3, 26.6, 51.3, 68.9 (q, J_{CF}=27.2 Hz), 121.0, 125.0, 125.9, 126.1 (q, J_{CF}=286.6 Hz), 128.0, 130.3, 134.4, 135.5, 135.6. ^{19}F NMR (470 MHz, $CDCl_3$) δ 92.3 (d, J=8.8 Hz). IR (neat) 2940, 2851, 2819, 1460, 1254, 1165, 1107, 968 cm^{-1}. Anal. Calcd for $C_{16}H_{20}F_3N$: C, 67.83; H, 7.11; N, 4.94. Found: C, 67.80; H, 7.18; N, 4.98.

3.3. General procedure for the allylic amination of (*S*)-1,1,1-trifluoro-4-phenylbut-3-en-2-yl acetate ((*S*)-1a) with morpholine (2b)

A typical procedure is given for the reaction of (*S*)-1,1,1-trifluoro-4-phenylbut-3-en-2-yl acetate ((*S*)-**1a**) with morpholine (**2b**) (Table 6, Entry 2). To a solution of $Pd(OAc)_2$ (4.5 mg, 0.020 mmol), DPPE (8.0 mg, 0.020 mmol), (*S*)-1,1,1-trifluoro-4-phenylbut-3-en-2-yl acetate ((*S*)-**1a**) (50 mg, 0.20 mmol) in THF (1.0 ml) was added morpholine (**2b**) and stirred at 25 °C for 12 h. The reaction mixture was quenched with brine and H_2O (1 ml), then extracted with ethyl

acetate. The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The NMR yield (77%, trioxane as an internal standard) and ratio of **3ab** and **4ab** was determined by ^1H NMR of the crude materials. The residue was purified by silica gel preparative thin-layer chromatography (hexane/EtOAc/Et_3N=10/1/0.1) to give 37 mg (66%) of (*R*)-**3ab** (98% ee) as a colorless oil.

*3.3.1. (S)-1,1,1-Trifluoro-4-phenylbut-3-en-2-yl acetate ((S)-**1a**)*[5b,20]. Yellow oil. $[\alpha]_D^{26}$ +143.14 (*c* 0.89, $CHCl_3$) (99% ee). Enantiomeric purity was determined by HPLC using a Daicel CHIRALPAK AD-H (hexane/2-propanol=99/1, flow: 1.0 ml/min, 254 nm, 35 °C, t_R 4.4 min (major); t_R 5.6 min (minor)).

*3.3.2. (S)-1,1,1-Trifluoro-4-(4-methoxyphenyl)but-3-en-2-yl acetate ((S)-**1c**).* White solid. Mp 71–75 °C. $[\alpha]_D^{26}$ +170.5 (*c* 1.09, $CHCl_3$) (99% ee). Enantiomeric purity was determined by HPLC using a Daicel CHIRALPAK AD-H (hexane/2-propanol=99/1, flow: 1.0 ml/min, 254 nm, 35 °C, t_R 7.5 min (major); t_R 9.2 min (minor)).

*3.3.3. (S)-4-(4-Chlorophenyl)-1,1,1-trifluorobut-3-en-2-yl acetate ((S)-**1f**)*[5b]. Yellow solid. Mp 77–79 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 2.19 (s, 3H), 5.78–5.84 (m, 1H), 6.09 (dd, *J*=7.4, 16.0 Hz, 1H), 6.81 (d, *J*=16.0 Hz, 1H), 7.31–7.36 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.6, 70.9 (q, J_{CF}=33.6 Hz), 118.0, 123.1 (q, J_{CF}=280.3 Hz), 128.2, 128.9, 133.5, 134.9, 137.4, 168.8. ^{19}F NMR (470 MHz, $CDCl_3$) δ 85.3 (d, *J*=6.8 Hz). IR (KBr) 2958, 2931, 1760, 1491, 1375, 1272, 1223, 1187, 1031 cm^{-1} $[\alpha]_D^{26}$ +118.3 (*c* 0.81, $CHCl_3$) (99% ee). Enantiomeric purity was determined by HPLC using a Daicel CHIRALCEL OD-H (hexane/2-propanol=99/1, flow: 0.5 ml/min, 254 nm, 35 °C, t_R 11.3 min (major); t_R 12.3 min (minor)).

*3.3.4. 4-((R)-4,4,4-Trifluoro-1-phenylbut-2-enyl)morpholine ((R)-**3ab**)*[5b]. Colorless oil. $[\alpha]_D^{26}$ −40.3 (*c* 0.73, $CHCl_3$) (96% ee). Enantiomeric purity was determined by HPLC using a Daicel CHIRALCEL OD-H (hexane/2-propanol=99/1, flow: 1.0 ml/min, 254 nm, 35 °C, t_R 5.9 min (major); t_R 6.9 min (minor)).

*3.3.5. 4-((S)-1,1,1-Trifluoro-4-phenylbut-3-en-2-yl)morpholine ((S)-**4ab**)*[5b]. Colorless oil. $[\alpha]_D^{26}$ +69.2 (*c* 1.37, $CHCl_3$) (99% ee). Enantiomeric purity was determined by HPLC using a Daicel CHIRALPAK AD-H (hexane/2-propanol=99/1, flow: 1.0 ml/min, 254 nm, 35 °C, t_R 11.2 min (major); t_R 13.0 min (minor)).

*3.3.6. 1-((R)-4,4,4-Trifluoro-1-phenylbut-2-enyl)-4-phenylpiperazine ((R)-**3ac**)*[5b]. Colorless oil. $[\alpha]_D^{26}$ −22.2 (*c* 0.18, $CHCl_3$) (97% ee). Enantiomeric purity was determined by HPLC using a Daicel CHIRALCEL OD-H (hexane/2-propanol=99/1, flow: 1.0 ml/min, 254 nm, 35 °C, t_R 11.1 min (minor); t_R 12.6 min (major)).

*3.3.7. 1-((S)-1,1,1-Trifluoro-4-phenylbut-3-en-2-yl)-4-phenylpiperazine ((S)-**4ac**)*[5b]. White solid. Mp 135–137 °C. $[\alpha]_D^{26}$ +61.1 (*c* 0.36, $CHCl_3$) (99% ee). Enantiomeric purity was determined by HPLC using a Daicel CHIRALPAK AD-H (hexane/2-propanol=9/1, flow: 1.0 ml/min, 254 nm, 35 °C, t_R 6.2 min (major); t_R 9.2 min (minor)).

*3.3.8. 1-((R)-4,4,4-Trifluoro-1-phenylbut-2-enyl)-4-methylpiperazine ((R)-**3ad**).* Colorless oil. $[\alpha]_D^{24}$ −45.7 (*c* 1.88, $CHCl_3$) (95% ee). Enantiomeric purity was determined by HPLC using a Daicel CHIRALPAK AD-H (hexane/2-propanol/diethylamine=99/1/0.1, flow: 1.0 ml/min, 254 nm, 35 °C, t_R 5.9 min (major); t_R 6.5 min (minor)).

*3.3.9. 1-((S)-1,1,1-Trifluoro-4-phenylbut-3-en-2-yl)-4-methylpiperazine ((S)-**4ad**).* Colorless oil. $[\alpha]_D^{25}$ +63.4 (*c* 2.03, $CHCl_3$) (98% ee). Enantiomeric purity was determined by HPLC using a Daicel CHIRALCEL OJ-H (hexane/2-propanol/diethylamine=99/1/0.1, flow: 1.0 ml/min, 254 nm, 35 °C, t_R 5.8 min (minor); t_R 10.1 min (major)).

*3.3.10. (R)-N-Benzyl-4,4,4-trifluoro-N-methyl-1-phenylbut-2-en-1-amine ((R)-**3ao**)*[5b]. Colorless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 2.11 (s, 3H), 3.42 (d, *J*=13.5 Hz, 1H), 3.53 (d, *J*=13.5 Hz, 1H), 4.07 (d, *J*=7.8 Hz, 1H), 5.87 (dq, *J*=6.4, 15.6 Hz, 1H), 6.59 (ddq, *J*=2.0, 7.8, 15.6 Hz, 1H), 7.20–7.40 (m, 10H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 39.1, 58.9, 69.9, 119.9 (q, J_{CF}=33.6 Hz), 122.9 (q, J_{CF}=269.3 Hz), 127.0, 127.8, 128.2, 128.3, 128.6, 128.7, 139.1, 139.5, 141.0 (q, J_{CF}=6.4 Hz). ^{19}F NMR (470 MHz, $CDCl_3$) δ 97.9–98.1 (m). IR (neat) 3065, 2846, 2797, 1684, 1496, 1455, 1286, 1125, 981 cm^{-1}. HRMS (MALDI-TOF) *m*/*z* calcd for $[M+H]^+$: $C_{18}H_{19}F_3N$ 306.1470, found 306.1470 (matrix: SA). $[\alpha]_D^{26}$ −26.8 (*c* 1.38, $CHCl_3$) (96% ee). Enantiomeric purity was determined by HPLC using a Daicel CHIRALPAK AD-H (hexane/2-propanol=199/1, flow: 1.0 ml/min, 254 nm, 35 °C, t_R 3.8 min (major); t_R 4.6 min (minor)).

*3.3.11. (S)-N-Benzyl-1,1,1-trifluoro-N-methyl-4-phenylbut-3-en-2-amine ((S)-**4ao**)*[5b]. Colorless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 2.40 (s, 3H), 3.67 (d, *J*=13.2 Hz, 1H), 3.75 (quin, *J*=8.0 Hz, 1H), 3.81 (d, *J*=13.2 Hz, 1H), 6.24 (dd, *J*=8.0, 16.0 Hz, 1H), 6.67 (d, *J*=16.0 Hz, 1H), 7.18–7.45 (m, 10H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 38.2, 59.1, 65.5 (q, J_{CF}=28.0 Hz), 118.8, 126.3 (q, J_{CF}=286.3 Hz), 126.7, 127.3, 128.3, 128.4, 128.6, 128.7, 136.0, 137.2, 138.7. ^{19}F NMR (470 MHz, $CDCl_3$) δ 92.1 (d, *J*=8.2 Hz). IR (neat) 2956, 2808, 1496, 1453, 1370, 1269, 1168, 1107, 1025 cm^{-1}. HRMS (MALDI-TOF) *m*/*z* calcd for $[M+H]^+$: $C_{18}H_{19}F_3N$ 306.1470, found 306.1458 (matrix: SA). $[\alpha]_D^{27}$ +150.3 (*c* 0.74, $CHCl_3$) (96% ee). Enantiomeric purity was determined by HPLC using a Daicel CHIRALCEL OJ-H (hexane/2-propanol=99/1, flow: 1.0 ml/min, 254 nm, 35 °C, t_R 8.4 min (major); t_R 9.4 min (minor)).

*3.3.12. 1-((R)-4,4,4-Trifluoro-1-(4-methoxyphenyl)but-2-enyl)-4-phenylpiperazine ((R)-**3cc**).* Yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 2.50–2.60 (m, 4H), 3.17 (t, *J*=5.2 Hz, 4H), 3.79–3.81 (m, 1H), 3.81 (s, 3H), 5.85 (dq, *J*=6.3, 16.0 Hz, 1H), 6.51 (ddq, *J*=2.3, 8.6, 16.0 Hz, 1H), 6.84 (t, *J*=7.4 Hz, 1H), 6.89 (d, *J*=8.6 Hz, 4H), 7.23–7.26 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 49.1, 51.1, 55.2, 71.2, 114.2, 115.9, 119.2 (q, J_{CF}=33.6 Hz), 119.7, 122.8 (q, J_{CF}=268.7 Hz), 129.1, 129.2, 131.0, 141.6 (q, J_{CF}=6.0 Hz), 151.2, 159.3. ^{19}F NMR (564 MHz, $CDCl_3$) δ 97.9 (d, *J*=6.2 Hz). IR (neat) 2958, 2819, 1679, 1603, 1509, 1455, 1384, 1344, 1250, 1116 cm^{-1}. HRMS (ESI) *m*/*z* calcd for $[M+H]^+$: $C_{21}H_{24}F_3N_2O$ 377.1841, found 377.1833. $[\alpha]_D^{25}$ −22.1 (*c* 2.82, $CHCl_3$) (94% ee). Enantiomeric purity was determined by HPLC using a Daicel CHIRALCEL OD-H (hexane/2-propanol=99/1, flow: 1.0 ml/min, 254 nm, 35 °C, t_R 14.7 min (minor); t_R 16.9 min (major)).

*3.3.13. 1-((S)-1,1,1-Trifluoro-4-(4-methoxyphenyl)but-3-en-2-yl)-4-phenylpiperazine ((S)-**4cc**).* White solid. Mp 176–184 °C. ^1H NMR (600 MHz, $CDCl_3$) δ 2.87–2.95 (m, 4H), 3.18–3.23 (m, 4H), 3.65–3.71 (m, 1H), 3.81 (s, 3H), 6.07 (dd, *J*=8.3, 15.8 Hz, 1H), 6.67 (d, *J*=15.8 Hz, 1H), 6.84–6.88 (m, 3H), 6.90–6.92 (m, 2H), 7.23–7.27 (m, 2H), 7.34–7.36 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 49.8, 50.0, 55.4, 68.4 (q, J_{CF}=27.6 Hz), 114.1, 116.2, 116.3, 120.0, 126.0 (q, J_{CF}=285.1 Hz), 128.1, 128.6, 129.2, 137.0, 151.4, 159.9. ^{19}F NMR (564 MHz, $CDCl_3$) δ 91.9 (d, *J*=8.2 Hz). IR (KBr) 3003, 2909, 2842, 1652, 1608, 1581, 1514, 1308, 1250, 1183, 1142, 1102 cm^{-1}. HRMS (DART) *m*/*z* calcd for $[M+H]^+$: $C_{21}H_{24}F_3N_2O$ 377.1841, found 377.1838. $[\alpha]_D^{25}$ +86.7 (*c* 1.17, $CHCl_3$) (98% ee). Enantiomeric purity was determined by HPLC using a Daicel CHIRALPAK AD-H (hexane/2-propanol=9/1, flow: 1.0 ml/min, 254 nm, 35 °C, t_R 9.4 min (major); t_R 12.5 min (minor)).

*3.3.14. 1-((R)-1-(4-Chlorophenyl)-4,4,4-trifluorobut-2-enyl)-4-phenylpiperazine ((R)-**3fc**)*[5b]. Yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 2.49–2.60 (m, 4H), 3.17 (t, *J*=5.0 Hz, 4H), 3.83 (d, *J*=8.6 Hz, 1H),

5.87 (dq, J=6.3, 15.8 Hz, 1H), 6.47 (ddq, J=2.0, 8.6, 15.8 Hz, 1H), 6.86 (t, J=7.2 Hz, 1H), 6.90 (d, J=8.6 Hz, 2H), 7.24–7.35 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 49.2, 51.1, 71.2, 116.0, 119.9, 120.0 (q, J_{CF}=34.0 Hz), 122.6 (q, J_{CF}=269.9 Hz), 129.2, 129.2, 129.4, 133.8, 137.8, 140.8 (q, J_{CF}=6.4 Hz), 151.1. ^{19}F NMR (470 MHz, $CDCl_3$) δ 97.7 (d, J=6.1 Hz). IR (neat) 2958, 2825, 1681, 1600, 1490, 1453, 1344, 1286, 1123, 1006 cm^{-1}. HRMS (MALDI-TOF) m/z calcd for $[M+H]^+$: $C_{20}H_{21}ClF_3N_2$ 381.1345, found 381.1348 (matrix: SA). $[\alpha]_D^{25}$ −22.3 (c 2.39, $CHCl_3$) (83% ee). Enantiomeric purity was determined by HPLC using a Daicel CHIRALCEL OJ-H (hexane/2-propanol=9/1, flow: 1.0 ml/min, 254 nm, 35 °C, t_R 14.8 min (major); t_R 19.8 min (minor)). Recrystallization of isolated product from hexane gave an enantiomerically pure (*R*)-**3fc** (>99% ee).

*3.3.15. 1-((S)-4-(4-Chlorophenyl)-1,1,1-trifluorobut-3-en-2-yl)-4-phenylpiperazine ((S)-**4fc**)*[5b]. White solid. Mp 151–153 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.89–2.96 (m, 4H), 3.21 (t, J=4.9 Hz, 4H), 3.72 (quin, J=8.0 Hz, 1H), 6.19 (dd, J=8.0, 16.0 Hz, 1H), 6.71 (d, J=16.0 Hz, 1H), 6.87 (t, J=7.4 Hz, 1H), 6.92 (d, J=8.0 Hz, 2H), 7.24–7.36 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 49.8, 49.9, 68.1 (q, J_{CF}=28.0 Hz), 116.3, 119.5, 120.0, 125.7 (q, J_{CF}=285.5 Hz), 127.9, 128.9, 129.1, 134.1, 134.3, 136.0, 151.3. ^{19}F NMR (470 MHz, $CDCl_3$) δ 92.1 (d, J=8.9 Hz). IR (KBr) 2884, 2823, 1602, 1492, 1455, 1388, 1268, 1245, 1150, 1105, 1013, 976 cm^{-1}. HRMS (MALDI-TOF) m/z calcd for $[M+H]^+$: $C_{20}H_{21}ClF_3N_2$ 381.1345, found 381.1340 (matrix: SA). $[\alpha]_D^{25}$ +71.4 (c 0.95, $CHCl_3$) (95% ee). Enantiomeric purity was determined by HPLC using a Daicel CHIRALPAK AD-H (hexane/2-propanol=9/1, flow: 1.0 ml/min, 254 nm, 35 °C, t_R 7.1 min (major); t_R 10.2 min (minor)). Recrystallization of isolated product from hexane gave an enantiomerically pure (*S*)-**4fc** (>99% ee).

Acknowledgements

This study was financially supported in part by Grant-in-Aid for Scientific Research (C) (No. 23550123) from the Japan Society for the Promotion of Science.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2011.08.093.

References and notes

1. (a) Jørgensen, K. A. In *Modern Amination Methods*; Ricci, A., Ed.; Wiley-VCH: Weinheim, 2000; Chapter 1, p 1; (b) Johannsen, M.; Jørgensen, K. A. *Chem. Rev.* **1998**, *98*, 1689.
2. Selected examples of transition metal-catalyzed allylic aminations of allylic esters: (a) For [Pd] Dubovyk, I.; Watson, I. D. G.; Yudin, A. K. *J. Am. Chem. Soc.* **2007**, *129*, 14172; (b) Johns, A. M.; Liu, Z.; Hartwig, J. F. *Angew. Chem., Int. Ed.* **2007**, *46*, 7259; (c) Faller, J. W.; Wilt, J. C. *Org. Lett.* **2005**, *7*, 633 and references therein; (d) For [Ir] Takeuchi, R.; Ue, N.; Tanabe, K.; Yamashita, K.; Shiga, N. *J. Am. Chem. Soc.* **2001**, *123*, 9525; (e) Ohmura, T.; Hartwig, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 15164; (f) Leitner, A.; Shekhar, S.; Pouy, M. J.; Hartwig, J. F. *J. Am. Chem. Soc.* **2005**, *127*, 15506; (g) Polet, D.; Alexakis, A.; Tissot-Croset, K.; Corminboeuf, C.; Ditrich, K. *Chem.—Eur. J.* **2006**, *12*, 3596; (h) Weihofen, R.; Tverskoy, O.; Helmchen, G. *Angew. Chem., Int. Ed.* **2006**, *45*, 5546 and references therein; (i) For [Rh] Evans, P. A.; Robinson, J. E.; Nelson, J. D. *J. Am. Chem. Soc.* **1999**, *121*, 6761; (j) Evans, P. A.; Robinson, J. E.; Nelson, J. D. *J. Am. Chem. Soc.* **1999**, *121*, 12214; (k) For [Ru] Morisaki, Y.; Kondo, T.; Mitsudo, T. *Organometallics* **1999**, *18*, 4742; (l) Matsushima, Y.; Onitsuka, K.; Kondo, T.; Mitsudo, T.; Takahashi, S. *J. Am. Chem. Soc.* **2001**, *123*, 10405; (m) Matsushima, Y.; Onitsuka, K.; Takahashi, S. *Organometallics* **2004**, *23*, 3763; (n) Kawatsura, M.; Ata, F.; Hirakawa, T.; Hayase, S.; Itoh, T. *Tetrahedron Lett.* **2008**, *49*, 4873 and references therein.
3. Examples of allylic substitutions of fluorinated allyl substrates: (a) Hanzawa, Y.; Ishizawa, S.; Kobayashi, Y. *Chem. Pharm. Bull.* **1988**, *36*, 4209; (b) Hanzawa, Y.; Ishizawa, S.; Ito, H.; Kobayashi, Y.; Taguchi, T. *J. Chem. Soc., Chem. Commun.* **1990**, 394; (c) Fish, P. V.; Reddy, S. P.; Lee, C. H.; Johnson, W. S. *Tetrahedron Lett.* **1992**, *33*, 8001; (d) Konno, T.; Ishihara, T.; Yamanaka, H. *Tetrahedron Lett.* **2000**, *41*, 8467; (e) Okano, T.; Matsubara, H.; Kusukawa, T.; Fujita, M. *J. Organomet. Chem.* **2003**, *676*, 43; (f) Konno, T.; Takehana, T.; Ishihara, T.; Yamanaka, H. *Org. Biomol. Chem.* **2004**, *2*, 93; (g) Konno, T.; Takehana, T.; Mishima, M.; Ishihara, T. *J. Org. Chem.* **2006**, *71*, 3545; (h) Kawatsura, M.; Wada, S.; Hayase, S.; Itoh, T. *Synlett* **2006**, 2483.
4. Konno, T.; Nagata, K.; Ishihara, T.; Yamanaka, H. *J. Org. Chem.* **2002**, *67*, 1768.
5. (a) Kawatsura, M.; Hirakawa, T.; Tanaka, T.; Ikeda, D.; Hayase, S.; Itoh, T. *Tetrahedron Lett.* **2008**, *49*, 2450; (b) Hirakawa, T.; Ikeda, K.; Ogasa, H.; Kawatsura, M.; Itoh, T. *Synlett* **2010**, 2887.
6. We examined PPh_3, DPPE, and DPPF as a phosphine ligand.
7. The reaction of alkyl group substituted acetates, such as 1,1,1-trifluorohept-3-en-2-yl acetate, didn't provide any aminated products.
8. The electronic effect of trifluoromethyl group is also important for this regioselectivity.
9. (a) Åkermark, B.; Åkermark, G.; Hegedus, L. S.; Zetterberg, K. *J. Am. Chem. Soc.* **1981**, *103*, 3037; (b) Amatore, C.; Génin, E.; Jutand, A.; Mensah, L. *Organometallics* **2007**, *26*, 1875; (c) Watson, I. D. G.; Yudin, A. K. *J. Am. Chem. Soc.* **2005**, *127*, 17516; (d) Watson, I. D. G.; Styler, S. A.; Yudin, A. K. *J. Am. Chem. Soc.* **2004**, *126*, 5086.
10. The examples of Pd-catalyzed allylic substitution of allyl amines, see: (a) Murahashi, S.-I.; Imada, Y.; Nishimura, K. *J. Chem. Soc., Chem. Commun.* **1988**, 1578; (b) Miyazawa, M.; Wang, S.-Z.; Takeda, H.; Yamamoto, K. *Synlett* **1992**, 323; (c) Miyazawa, M.; Yamamoto, K. *Chem. Lett.* **1994**, 491; (d) Doi, T.; Yanagisawa, A.; Miyazawa, M.; Yamamoto, K. *Tetrahedron: Asymmetry* **1995**, *6*, 389.
11. Examples of net retention mechanism in the palladium-catalyzed allylic substitutions: (a) Hayashi, T.; Hagihara, T.; Konishi, M.; Kumada, M. *J. Am. Chem. Soc.* **1983**, *105*, 7767; (b) Hayashi, T.; Yamamoto, A.; Hagihara, T. *J. Org. Chem.* **1986**, *51*, 723; (c) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **1999**, *121*, 4545.
12. The absolute configuration of (*R*)-**3ab** and (*S*)-**4ab** were determined by the comparison of the X-ray crystallographic analysis of (*R*)-**3fc** and (*S*)-**4fc**. Crystallographic data for compounds (*R*)-**3fc** and (*S*)-**4fc** have been deposited with Cambridge Crystallographic Data Center as supplementary publication number CCDC 792223 (for (*R*)-**3fc**) and CCDC 792751 (for (*S*)-**4fc**). Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(1223)336033 or e-mail: data_request@ccdc.cam.ac.uk].
13. We confirmed that the α-selectivity in the [Pd(π-allyl)(cod)]BF_4/(*S*)-BINAP catalyst system is inferior to the [Pd(π-allyl)(cod)]BF_4/DPPF catalyst system.
14. The reaction of **1a** (99% ee) with **2o** at 40 °C under the condition B gave **4ao** (94% ee) with 93% regioselectivity.
15. Selected examples of kinetic resolution in the palladium-catalyzed allylic substitutions of disubstituted symmetrical or monosubstituted allylic esters: (a) Cook, G. R. *Curr. Org. Chem.* **2000**, *4*, 869; (b) Robinson, D. E. J. E.; Bull, S. D. *Tetrahedron: Asymmetry* **2003**, *14*, 1407; (c) Longmire, J. M.; Wang, B.; Zhang, X. *Tetrahedron Lett.* **2000**, *41*, 5435; (d) Reetz, M. T.; Sostmann, S. *J. Organomet. Chem.* **2000**, *603*, 105; (e) Gilbertson, S. R.; Lan, P. *Org. Lett.* **2001**, *3*, 2237; (f) Cook, G. R.; Sankaranarayanan, S. *Org. Lett.* **2001**, *3*, 3531; (g) Lüssem, B. J.; Gais, H.-J. *J. Org. Chem.* **2004**, *69*, 4041; (h) Castillo, A. B.; Favier, I.; Teuma, E.; Castillón, S.; Godard, C.; Aghmiz, A.; Claver, C.; Gómez, M. *Chem. Commun.* **2008**, 6197; (i) Hou, X. L.; Zheng, B. H. *Org. Lett.* **2009**, *11*, 1789 and references therein.
16. Examples of kinetic resolution in the palladium-catalyzed allylic substitutions of 1,3-disubstituted unsymmetrical allylic esters: (a) Hayashi, T.; Yamamoto, A.; Ito, Y. *J. Chem. Soc., Chem. Commun.* **1986**, 1090; (b) Faller, J. W.; Wilt, J. C. *Tetrahedron Lett.* **2004**, *45*, 7613.
17. Calculated by ee_P and ee_S. $S=\ln[(1-c)(1+ee_P)]/\ln[(1-c)(1-ee_P)]$. $c=ee_S/(ee_S+ee_P)$.
18. Kagan, H. B.; Fiaud, J. C. *Top. Stereochem.* **1988**, *18*, 249.
19. White, D. A.; Doyle, J. R.; Lewis, H. *Inorg. Synth.* **1972**, *13*, 55.
20. Prakash, G. K. S.; Mandal, M.; Schweizer, S.; Petasis, N. A.; Olah, G. A. *Org. Lett.* **2000**, *2*, 3173.
21. Kitazume, T.; Lin, J. T.; Yamazaki, T.; Takeda, M. *J. Fluorine Chem.* **1989**, *43*, 177.