Preprint Title Efficient and Convenient Access to Optically Active Tetrafluoroethylenated Amines Based on [1,3]-Proton Shift Reaction

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Publication Date 23 Juli 2024

Article Type Full Research Paper

Supporting Information File 1 SI.pdf; 8.0 MB

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Efficient and Convenient Access to Optically Active Tetrafluoroethylenated Amines Based on [1,3]-Proton Shift Reaction

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Abstract

Treatment of various (*R*)-*N*-(2,2,3,3-tetrafluoropent-4-en-1-ylidene)-1-phenylethylamine derivatives with 2.4 equiv. of DBU in toluene at room temperature to 50 °C for 24 h led to a smooth [1,3]-proton shift reaction with a high chirality transfer, affording the corresponding rearranged products in acceptable yields. Without purification, these products were subjected to acid hydrolysis and the subsequent *N*-Cbz protection, providing the optically active tetrafluoroethylenated amides in moderate three-step yields.

Keywords

Tetrafluoroethylene fragment; optically active; amine; [1,3]-proton shift reaction

Introduction

A fluorine atom has quite peculiar chemical and physical properties compared to others, and hence changes in molecular properties resulting from the introduction of fluorine atom(s) into organic molecules are also significantly unique, and often extremely noticeable even when the number of the atom introduced is small [1]. By skillfully utilizing such characteristics, fluorine-containing organic molecules have established themselves as indispensable compounds in various frontlines, such as medicinal, agrochemical, and material fields [2].

In particular, tetrafluoroethylenated compounds possessing two fluorine atoms on each of two adjacent carbons, has been attracting an enormous attention these days. This stems from the fact that substances with a tetrafluoroethylene fragment exhibit significantly different molecular properties compared to monofluorinated, difluorinated, or trifluoromethylated molecules [3]. Therefore, more and more tetrafluoroethylenated molecules having a variety of applications, such as bioactive substances (Figure 1a, **1**, **2**) [4], liquid crystals (Figure 1b, **3**, **4**) [5], fluorescent molecule (Figure 1c, **5**) [6], and so on, have been developed in recent years.

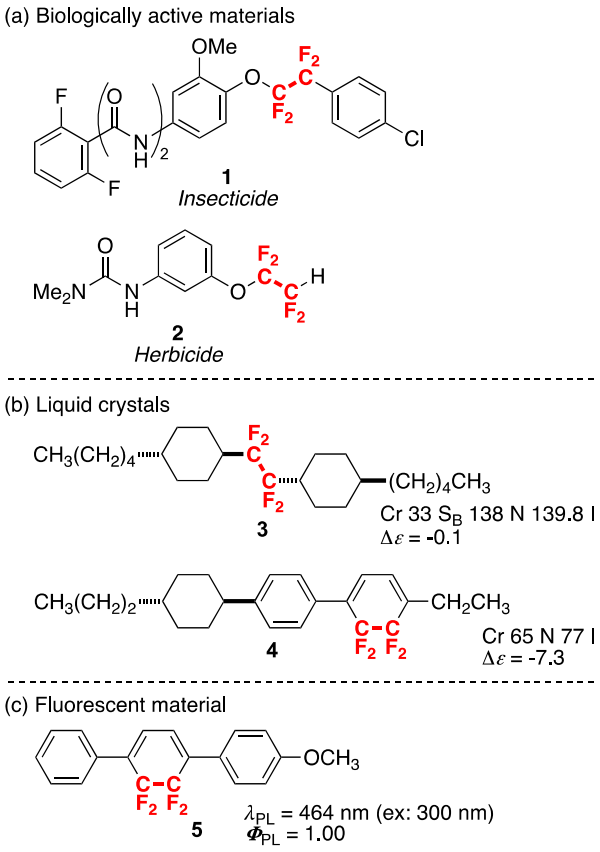


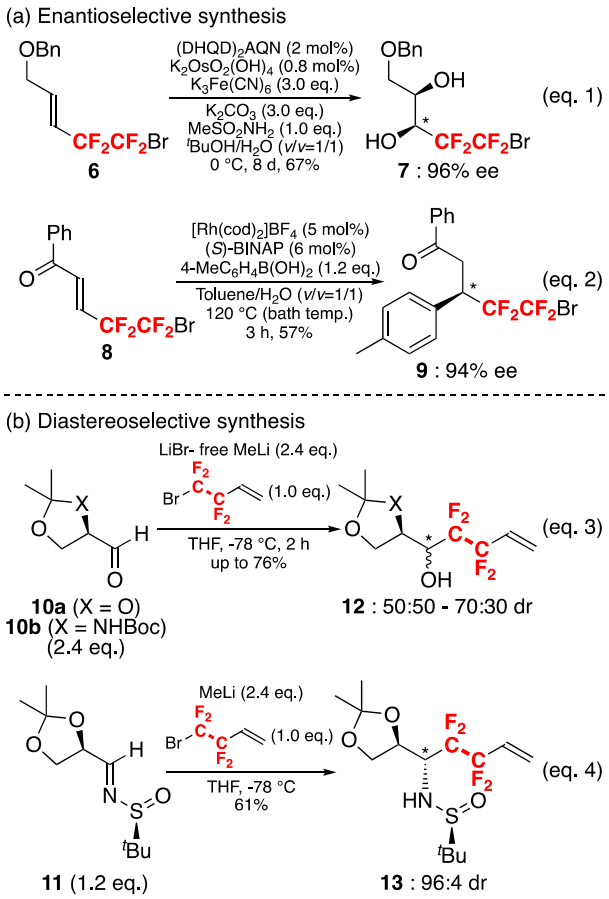
Figure 1: Various applications of tetrafluoroethylenated molecules.

In sharp contrast to the major development of such *non-chiral* tetrafluoroethylenated compounds, there have been quite a few reports on the preparation of *chiral* molecules possessing a tetrafluoroethylene unit on an asymmetric carbon center in a high optical purity, and to the best of our knowledge, only the following have been published so far (Scheme 1).

As a highly enantioselective synthesis, there has been a pioneering work by Linclau et al. They have reported that asymmetric Sharpless dihydroxylation of readily available (*E*)-5-bromo-4,4,5,5-tetrafluoro-2-penten-1-ol derivative **6** led to the corresponding chiral diols **7** with an excellent enantiomeric excess, 96% ee (eq. 1) [7]. It has also been published that the asymmetric conjugate addition of 4-methylphenylboronic acid towards (*E*)-5-bromo-4,4,5,5-tetrafluoro-1-phenyl-2-penten-1-one (**8**) in the presence

of the rhodium catalyst coordinated with (*S*)-BINAP gave the corresponding Michael adduct **9** in 94% enantiomeric excess (eq. 2) [8].

As a diastereoselective synthesis have been reported reductive coupling reactions of commercially available 4-bromo-3,3,4,4-tetrafluoro-1-butene and glyceraldehyde **10a** or its imine derivative **11**, or Garner's aldehyde **10b** [9, 10]. Although the diastereoselectivities are somehow low in some cases, the diastereomers **12**, **13** are often easily separable, and each diastereomer of optically active alcohols or amines can be obtained with an excellent optical purity (eq. 3, 4).

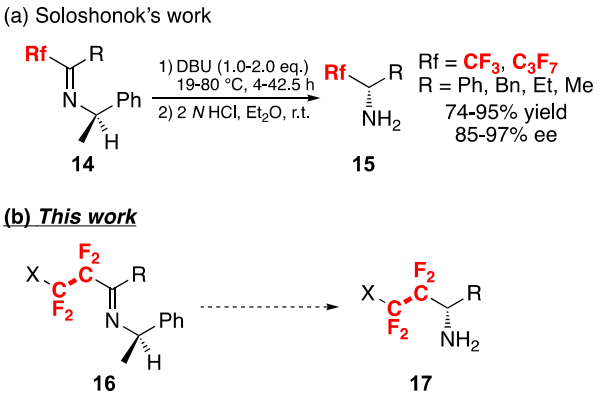


Scheme 1: Precedented synthetic approaches to optically active compounds possessing a tetrafluoroethylene group on an asymmetric carbon center.

These are the only four precedented works for the preparation of optically active substances having a tetrafluoroethylene group on an asymmetric carbon center. In order to overcome the current lack of synthetic methods for preparing such molecules, we came up with the idea of utilizing the [1,3]-proton shift reaction reported by Soloshonok et al.

In 1997, Soloshonok et al. reported that fluoroalkylated amines **15** with high optical purity could be easily prepared through [1,3]-proton shift reactions of optically active imines **14** which were readily prepared by dehydration condensation of various perfluoroalkyl ketones with optically active (*R*)-phenethylamine (Scheme 2a) [11]. Therefore, we envisioned that optically active tetrafluoroethylenated amines **17** could be synthesized by applying the [1,3]-proton shift to optically active imines **16** derived from readily-prepared tetrafluoroethylenated ketones (Scheme 2b).

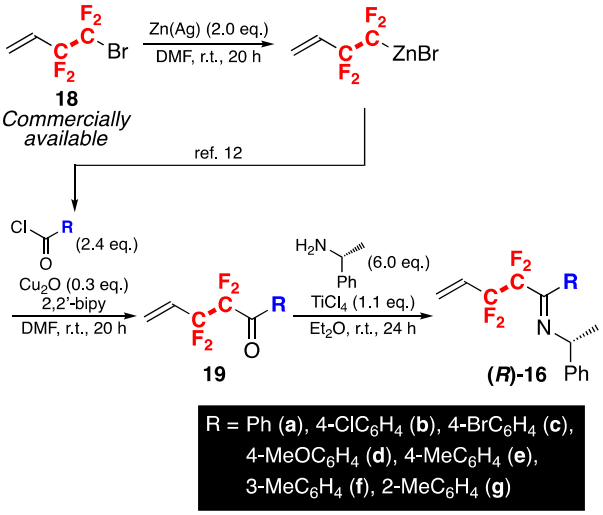
In this paper, we describe the details of the [1,3]-proton shift reaction of various tetrafluoroethylenated imines.



Scheme 2: Synthetic strategy for preparing fluorine-containing amines *via* [1,3]-proton shift reaction.

Results and Discussion

As for the preparation of substrates used in this study, tetrafluoroethylenated ketones **19**, which could be prepared in one step from commercially available 3,3,4,4-tetrafluoro-1-butene (**18**) [12], were employed to synthesize various optically active imines **(*R*)-16** in high yields by dehydration condensation with (*R*)-1-phenylethylamine under the influence of $TiCl_4$ [13] (Scheme 3).



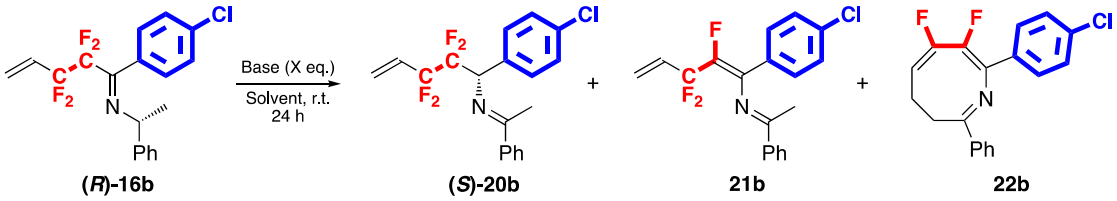
Scheme 3: Preparation of the substrates used in this study.

Among the imines thus obtained, **(*R*)-16b** was used to investigate the optimum reaction conditions (Table 1). Treatment of **(*R*)-16b** with 1.2 equiv. of DBU (1,8-diazabicyclo[5.4.0]-7-undecene) in THF at room temperature for 24 h gave the corresponding [1,3]-proton shift adduct **(*S*)-20b** in 31% yield. In this case, HF-elimination product **21b** was also given in 16% [14], and the starting material was recovered in 53%. As shown in Entry 2-7, the reactions in various solvents were next examined. When CH_3CN or CH_2Cl_2 was used, 17% or 36% of the target **(*S*)-20b** was obtained and almost no HF elimination product, **21b** was provided, while about 40% of azocine derivative **22b** was afforded as a byproduct [15], along with the recovery of

(*R*)-16b. In the case of diethyl ether, toluene, hexane, and cyclohexane, **(*S*)-20b** was given in 30% to 40% yield and significant amount of unreacted substrate was still observed, although formation of the byproduct **22b** could be generally suppressed.

We also examined the reaction using other bases instead of DBU. As shown in Entry 9 and 10, the reaction did not proceed at all with triethylamine or DABCO, and **(*R*)-16b** was quantitatively recovered. The influence of the amount of DBU upon the reaction was also investigated (Entry 11-13). The results showed that when 2.4 equiv. of DBU were used, the target compound (*S*)-**20b** was obtained in 50% yield, along with a formation of 43% yield of the byproduct **22b** (Entry 11), while increasing the number of equivalents of DBU decreased the yield of the target (*S*)-**20b** and increased the yield of the byproduct **22b** (Entry 12 and 13). Therefore, the reaction at 0 °C was also carried out to have unsatisfactory result that a large amount of **(*R*)-16b** was recovered (Entry 14).

Table 2: Investigation of the reaction conditions.



(*R*)-16b (*S*)-20b 21b 22b

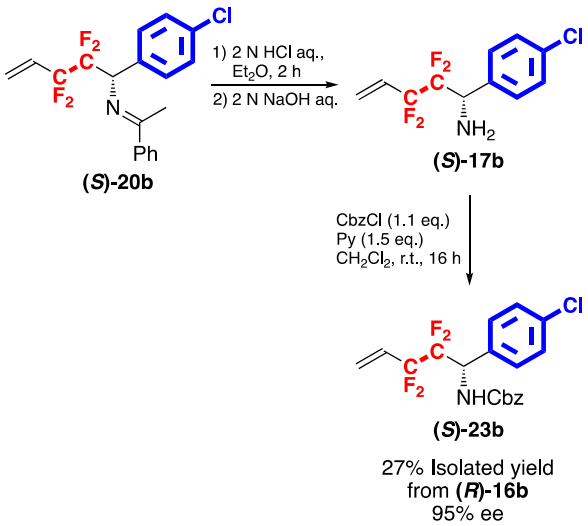
Entry	Base/X eq.	Solvent	Yield[a]/% of **(*S*)-20b**	Yield[a]/% of **21b**	Yield[a]/% of **22b**	Recovery[a]/% of **(*R*)-16b**
1	DBU/1.2	THF	31	16	0	53
2	DBU/1.2	CH_3CN	17	0	39	44
3	DBU/1.2	Et_2O	38	14	17	31
4	DBU/1.2	Toluene	37	13	0	50
5	DBU/1.2	Hexane	26	12	0	62
6	DBU/1.2	CH_2Cl_2	36	3	38	23
7	DBU/1.2	Cyclohexane	32	17	0	51
8	DBU/1.2	Toluene	33	18	0	49
9	Et_3N/1.2	Toluene	0	0	0	100
10	DABCO/1.2	Toluene	0	0	0	100
11	DBU/2.4	Toluene	50	2	43	5

12	DBU/4.8	Toluene	29	0	71	0
13	DBU/6.8	Toluene	31	0	69	0
14[b]	DBU/2.4	Toluene	8	13	0	79

[a]Determined by ^{19}F NMR; [b]The reaction was carried out at 0 °C.

Based on these results, the reaction conditions in Entry 11 was determined as an optimum one, which gave the highest yield, although the byproduction of azocine derivative **22b** could not be completely suppressed.

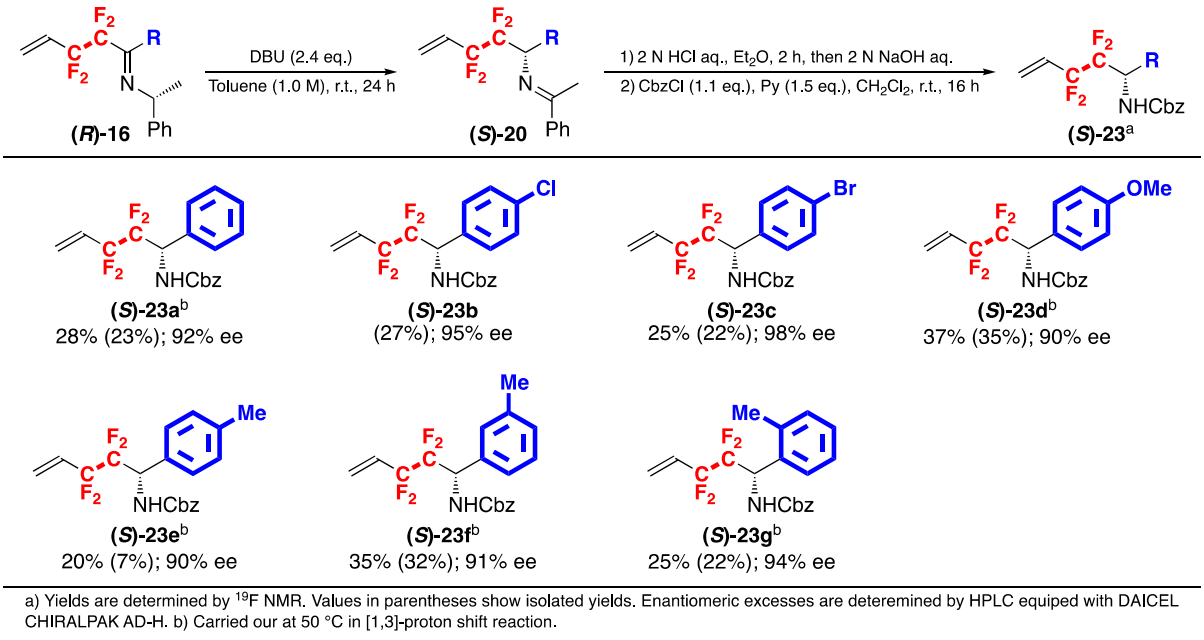
Thus obtained [1,3]-proton shift product **(*S*)-20b** was subjected to 2 N HCl aq. in Et_2O for 2 h, and subsequently 2 N NaOH aq., affording the corresponding free amine **(*S*)-17b**. Then, treatment of the amine with CbzCl and pyridine in CH_2Cl_2 gave the corresponding amide **(*S*)-23b** in 27% three-step isolated yield. The measurement of HPLC equipped with a chiral column, CHIRALPAK AD-H for **(*S*)-23b** showed that the amide had an optical purity of 95% ee (Scheme 4).



Scheme 4: Derivatization of **(*S*)-20b** to **(*S*)-23b** for determining the optical purity of **(*S*)-20b**.

On the next stage, the substrate scope for the present reaction was explored by using various imines **(*R*)-16** (Scheme 5). When the substituent R is an aromatic ring

substituted by a halogen such as chlorine and bromine atoms, the amides **(*S*)-23** were obtained in approximately 30-40% yield and with very high optical purity (**(*S*)-23b**, **(*S*)-23c**), although the satisfactory result (92% ee) was given in the case of the reaction at 50 °C for **(*S*)-23a**. The substrates with an aromatic ring substituted by not only an electron-withdrawing halogen atom but also an electron-donating group such as methoxy and methyl group also underwent a smooth [1,3]-proton shift reaction, affording the desired products with high enantiomeric excess (90% ee for **(*S*)-23d** and **(*S*)-23e**). Furthermore, it was found that the substituent position on the aromatic ring did not significantly influence upon the reaction efficiency as well as optical purity, the reaction proceeding in a highly enantioselective manner (91% ee for **(*S*)-23f** and 94% ee for **(*S*)-23g**) [16].



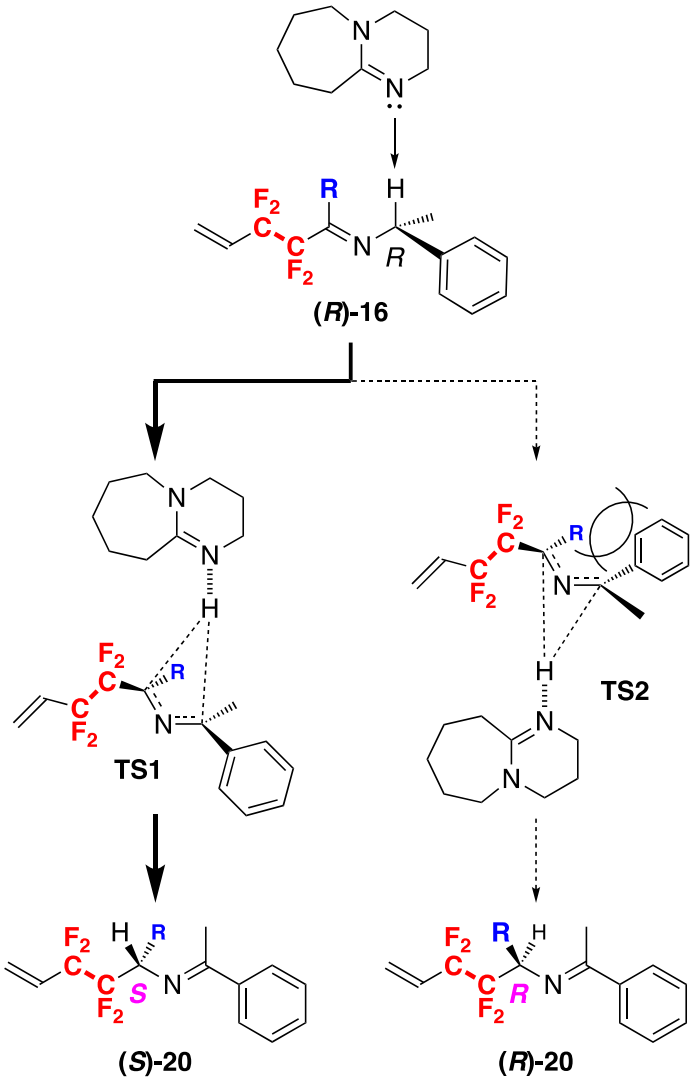
a) Yields are determined by ^{19}F NMR. Values in parentheses show isolated yields. Enantiomeric excesses are deteremined by HPLC equiped with DAICEL CHIRALPAK AD-H. b) Carried our at 50 °C in [1,3]-proton shift reaction.

Scheme 5: Substrate scope for the present [1,3]-proton shift reaction.

Although the absolute configuration of the products has not been determined yet, the [1,3]-proton shift reaction in this study is expected to proceed via the reaction

mechanism reported by Soloshonok [11], as shown in Scheme 6, so we believe that all products have *S* configuration at the chiral carbon center.

First, DBU interacts with the benzylic hydrogen of the imine **(*R*)-16**, and this hydrogen is about to be abstracted as a proton. This hydrogen which is being abstracted simultaneously interacts with the carbon possessing a tetrafluoroethylene fragment as well. At this time, transition states **TS1** or **TS2** are possible, but the reaction proceeds exclusively through the transition state **TS1** to avoid significant steric repulsion between R substituent and phenyl group. Therefore, the product **(*S*)-20** with *S* configuration might be obtained preferentially.



Scheme 6: Proposed reaction mechanism.

Conclusion

In summary, we have succeeded in synthesizing optically active amines having a tetrafluoroethylene group on the asymmetric carbon center by applying the [1,3]-proton shift reaction using various optically active imines, which can be easily prepared starting from commercially available 4-bromo-3,3,4,4-tetrafluoro-1-butene. In this reaction, although the byproduction of azocine derivatives could not be completely suppressed, the [1,3]-proton shift reaction proceeded in relatively good yield and high asymmetric transfer was achieved. As a result, it was found that various optically active amine derivatives could be obtained with high optical purity.

Experimental

General Information

All air and/or moisture sensitive reactions were carried out in anhydrous solvents under an Ar atmosphere in flame-dried glassware. All commercially available starting materials and reagents were used as received without further purification. Reactions were monitored by thin-layer chromatography (TLC) using Merck silica gel 60 F_{254} plate, and column chromatography was carried out by using Wakogel® 60N (38–100 μm) as an adsorbent.

Specific optical rotations $[\alpha]_D$ were given in 10^{-1} deg cm^2 g^{-1} and were measured using HORIBA SEPA-200 high sensitive polarimeter. Infrared spectra (IR) were determined in a liquid film on a NaCl plate or KBr method with a JASCO FT/IR-4100 type spectrometer, and reported in wavenumber (cm^{-1}). High-resolution mass spectra

(HRMS) were taken on a JEOL JMS-700MS spectrometer by fast atom bombardment (FAB) methods.

^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) were measured on a Bruker AVANCE Ⅲ 400 NMR spectrometer, and chemical shifts were reported in parts per million (ppm, δ) using the residual solvents peaks. Coupling constants (J) were reported in herts (Hz). ^{19}F NMR (376 MHz) was also measured on the Bruker AVANCE Ⅲ 400 NMR spectrometer, and chemical shifts were reported ppm using hexafluorobenzene (C_6F_6) as an internal standard. ^{19}F NMR spectra of the crude materials were used for determining the yield of the products with hexafluorobenzene (C_6F_6). HPLC was carried out on a Shimadzu LC-10AT *vp* Liquid Chromatograph equipped with a SPD-10A *vp* UV-vis detector using a chiral column (CHIRALPAK AD-H, DAICEL CEMICAL IND. Ltd., 0.46 cm ϕ × 25 cm).

Typical procedure for the preparation of imine (*R*)-16

To a solution of the ketone **19a** (0.25 g, 1.09 mmol) and (*R*)-1-phenyethlamine (0.84 mL, 6.0 equiv., 6.54 mmol) in 5.0 mL of dry diethyl ether was added 0.13 mL of titanium (IV) chloride (1.1 equiv., 1.20 mmol) at 0 °C. After stirring the reaction mixture overnight, a mixture of 10 mL of an aqueous 0.5 M NaOH solution and 2.4 mL of diethyl ether was added into the reaction mixture. After separation of the organic phase, the aqueous phase was extracted with diethyl ether three times. The combined organic phases were dried over anhydrous sodium sulfate and the solvent was evaporated. The residue was purified by silica gel column chromatography to give the corresponding imine **(*R*)-16a** (0.30 g, 0.89 mmol, 82%).

(*R*)-*N*-(2,2,3,3-Tetrafluoro-1-phenylpent-4-en-1-ylidene)-1-phenylethylamine ((*R*)-16a)

Isolated yield: 82% (0.30 g, 0.89 mmol); Colorless oil; $[\alpha]^{28}_{D}$= +100.2 (*c* 1.44, $CHCl_3$); the solvent of the column chromatography, Hexane/AcOEt = 20/1, R_f = 0.24; ^{1}H NMR ($CDCl_3$): *δ* 7.15-7.50 (m, 10H), 6.24 (dq, *J* = 17.21, 11.60 Hz, 1H, CH_2=C*H*CF_2), 5.90 (dt, *J* = 17.21, 2.00 Hz, 1H, C*H*$_2$=$CHCF_2$), 5.67 (d, *J* = 11.60 Hz, 1H, C*H*$_2$=$CHCF_2$), 4.55 (q, *J* = 6.40 Hz, 1H, C=NC*H*(CH_3)Ph), 1.47 (d, *J* = 6.40 Hz, 3H, C=NCH(C*H*$_3$)Ph); ^{13}C NMR ($CDCl_3$): *δ* 159.9 (t, *J* = 27.5 Hz, *C*=NCH(CH_3)Ph), 144.3 (Ar), 131.8 (Ar), 129.7 (Ar), 128.63 (Ar), 128.55 (Ar), 127.9 (t, *J* = 23.9 Hz, CH_2=*C*HCF_2), 127.8 (Ar), 127.2 (Ar), 126.5 (Ar), 123.3 (t, *J* = 9.7 Hz, *C*H_2=$CHCF_2$), 115.7 (tt, *J* = 250.2, 32.8 Hz, *C*F_2), 113.1 (tt, *J* = 255.4, 33.4 Hz, *C*F_2), 61.8 (C=N*C*H(CH_3)Ph), 24.7 (C=NCH(*C*H_3)Ph); ^{19}F NMR ($CDCl_3$): *δ* -112.51 (dd, *J* = 261.64, 11.60 Hz, 1F, CH_2=CHC*F*$_2$$CF_2$), -113.20 (d, *J* = 275.57 Hz, 1F, CH_2=$CHCF_2$C*F*$_2$), -113.30 (dd, *J* = 261.64, 11.60 Hz, 1F, CH_2=CHC*F*$_2$$CF_2$), -114.06 (d, *J* = 275.57 Hz, 1F, CH_2=$CHCF_2$C*F*$_2$),; IR (neat): *ν* 3029, 2976, 2927, 1660, 1419, 1242, 1168, 1101, 1037, 1010, 866, 701 cm^{-1}; HRMS (FAB) Calcd for $C_{19}H_{18}F_4N$ $[M+H]^+$: 336.1375, Found 336.1366.

(*R*)-*N*-(1-(4-Chlorophenyl)-2,2,3,3-tetrafluoropent-4-en-1-ylidene)-1-phenyethylamine ((*R*)-16b)

Isolated yield: 86% (0.64 g, 1.74 mmol); Colorless oil; $[\alpha]^{31}_{D}$= +164.5 (*c* 1.25, $CHCl_3$); the solvent of the column chromatography, Hexane/AcOEt = 20/1, R_f = 0.26; ^{1}H NMR ($CDCl_3$): *δ* 7.50 (d, *J* = 8.80 Hz, 2H, Ar–*H*), 7.30-7.46 (m, 5H, Ar–*H*), 7.21 (d, *J* = 8.80 Hz, 2H, Ar-*H*), 6.32 (dq, *J* = 17.61, 11.60 Hz, 1H, CH_2=C*H*CF_2), 5.96 (dt, *J* = 17.61, 2.40 Hz, 1H, C*H*$_2$=$CHCF_2$), 5.74 (d, *J* = 11.60 Hz, 1H, C*H*$_2$=$CHCF_2$), 4.61 (q, *J* = 6.40 Hz, 1H, C=NC*H*(CH_3)Ph), 1.56 (d, *J* = 6.40 Hz, 3H, C=NCH(C*H*$_3$)Ph); ^{13}C NMR ($CDCl_3$): *δ* 158.6 (t, *J* = 27.7 Hz, *C*=NCH(CH_3)Ph), 143.9 (Ar), 135.8 (Ar), 130.0 (Ar), 129.2 (Ar), 128.8 (Ar), 128.6 (Ar), 127.5 (t, *J* = 23.9 Hz, CH_2=*C*HCF_2), 127.1 (Ar), 126.3

(Ar), 123.3 (t, *J* = 9.3 Hz, *C*CH_2=$CHCF_2$), 115.4 (tt, *J* = 250.2, 32.9 Hz, *C*F_2), 112.8 (tt, *J* = 255.5, 33.7 Hz, *C*F_2), 61.9 (C=N*C*H(CH_3)Ph), 24.6 (C=NCH(*C*H_3)Ph); ^{19}F NMR ($CDCl_3$): *δ* -112.43 (dm, *J* = 262.77 Hz, 1F, CH_2=CHC*F*$_2$$CF_2$), -113.19 (dm, *J* = 262.77 Hz, 1F, CH_2=CHC*F*$_2$$CF_2$), -113.20 (d, *J* = 275.19 Hz, 1F, CH_2=$CHCF_2$C*F*$_2$), -114.05 (d, *J* = 275.19, 1F, CH_2=$CHCF_2$C*F*$_2$); IR (neat): *ν* 3060, 3032, 2973, 1662, 1595, 1491, 1243, 1093, 1011, 877, 821, 700 cm^{-1}; HRMS (FAB) Calcd for $C_{19}H_{17}{}^{35}ClF_4N$ $[M+H]^+$: 370.0986, Found 370.0994.

(*R*)-*N*-(1-(4-Bromophenyl)-2,2,3,3-tetrafluoropent-4-en-1-ylidene)-1-phenyethylamine ((*R*)-16c)

Isolated yield: 88% (0.62 g, 1.99 mmol); Colorless oil; $[\alpha]^{31}{}_D$= +88.0 (*c* 1.30, $CHCl_3$); the solvent of the column chromatography, Hexane/AcOEt = 10/1, R_f = 0.46; ^{1}H NMR ($CDCl_3$): *δ* 7.57 (d, *J* = 8.80 Hz, 2H, Ar–*H*), 7.22-7.35 (m, 5H, Ar–*H*), 7.02 (d, *J* = 8.80 Hz, 2H, Ar-*H*), 6.17 (dq, *J* = 17.21, 12.00 Hz, 1H, CH_2=C*H*CF_2), 5.85 (dt, *J* = 17.21, 2.40 Hz, 1H, C*H*$_2$=$CHCF_2$), 5.65 (d, *J* = 12.00 Hz, 1H, C*H*$_2$=$CHCF_2$), 4.46 (q, *J* = 6.40 Hz, 1H, C=NC*H*(CH_3)Ph), 1.42 (d, *J* = 6.40 Hz, 3H, C=NCH(C*H*$_3$)Ph); ^{13}C NMR ($CDCl_3$): *δ* 158.6 (t, *J* = 27.6 Hz, *C*=NCH(C*H*$_3$)Ph), 143.8 (Ar), 131.7 (Ar), 130.5 (Ar), 129.4 (Ar), 128.6 (Ar), 127.5 (t, *J* = 23.8 Hz, CH_2=*C*HCF_2), 127.1 (Ar), 126.3 (Ar), 124.1 (Ar), 123.4 (t, *J* = 9.5 Hz, *C*CH_2=$CHCF_2$), 115.4 (tt, *J* = 250.1, 33.0 Hz, CF_2), 112.7 (tt, *J* = 255.6, 33.9 Hz, CF_2), 61.9 (C=N*C*H(CH_3)Ph), 24.6 (C=NCH(*C*H_3)Ph); ^{19}F NMR ($CDCl_3$): *δ* -113.27 (dm, *J* = 262.77 Hz, 1F, CH_2=CHC*F*$_2$$CF_2$), -114.04 (dm, *J* = 262.77 Hz), -114.05 (d, *J* = 275.57 Hz, 1F, CH_2=$CHCF_2$C*F*$_2$), -114.90 (d, *J* = 275.57 Hz, 1F, CH_2=$CHCF_2$C*F*$_2$); IR (neat): *ν* 2974, 1726, 1653, 1589, 1486, 1451, 1419, 1393, 1243, 1167, 1104, 1072, 1010, 911, 877, 816, 736 cm^{-1}; HRMS (FAB) Calcd for $C_{19}H_{17}{}^{79}BrF_4N$ $[M^+]$: 413.0402, Found 413.0394.

(*R*)-*N*-(2,2,3,3-Tetrafluoro-1-(4-methoxyphenyl)pent-4-en-1-ylidene)-1-phenylethylamine ((*R*)-16d)

Isolated yield d: 72% (1.06 g, 2.90 mmol); Colorless oil; $[\alpha]^{28}_{D}$= +165.1 (*c* 1.10, $CHCl_3$); the solvent of the column chromatography, Hexane/AcOEt = 20/1, R_f = 0.28; ^{1}H NMR ($CDCl_3$): *δ* 7.35-7.55 (m, 5H, Ar-*H*), 7.28 (d, *J* = 8.80 Hz, 2H, Ar-*H*), 7.09 (d, *J* = 8.80 Hz, 2H, Ar-*H*), 6.39 (dq, *J* = 17.61, 11.60 Hz, 1H, CH_2=C*H*CF_2), 5.99 (dt, *J* = 17.61, 2.00 Hz, 1H, C*H*$_2$=$CHCF_2$), 5.75 (d, *J* = 11.60 Hz, 1H, C*H*$_2$=$CHCF_2$), 4.78 (q, *J* = 6.40 Hz, 1H, C=NC*H*(CH_3)Ph), 3.91 (s, 3H, OC*H*$_3$), 1.61 (d, *J* = 6.40 Hz, 3H, C=NCH(C*H*$_3$)Ph); ^{13}C NMR ($CDCl_3$): *δ* 160.4 (Ar), 159.5 (t, *J* = 27.4 Hz, *C*=NCH(CH_3)Ph), 144.3 (Ar), 129.2 (Ar), 128.4 (Ar), 127.9 (t, *J* = 23.6 Hz, CH_2=*C*HCF_2), 126.9 (Ar), 126.3 (Ar), 123.6 (Ar), 122.9 (t, *J* = 9.6 Hz, *C*H_2=$CHCF_2$), 115.5 (tt, *J* = 250.2, 32.6 Hz, *C*F_2), 113.8 (Ar), 113.0 (tt, *J* = 255.4, 33.2 Hz, *C*F_2), 61.5 (C=N*C*H(CH_3)Ph), 54.9 (O*C*H_3), 24.6 (C=NCH(*C*H_3)Ph); ^{19}F NMR ($CDCl_3$): *δ* -112.54 (dm, *J* = 276.70 Hz, 1F, CH_2=CHC*F*$_2$$CF_2$), -113.28 (d, *J* = 274.44 Hz, 1F, CH_2=$CHCF_2$C*F*$_2$), -113.36 (dm, *J* = 276.70 Hz, 1F, CH_2=CHC*F*$_2$$CF_2$), -114.15 (d, *J* = 274.44 Hz, 1F, CH_2=$CHCF_2$C*F*$_2$); IR (neat): *ν* 2971, 2930, 1608, 1511, 1296, 1254, 1168, 1103, 1035, 1008, 700 cm^{-1}; HRMS (FAB) Calcd for $C_{20}H_{20}F_4NO$ $[M+H]^+$: 366.1481, Found 366.1479.

(*R*)-*N*-(2,2,3,3-Tetrafluoro-1-(4-methylphenyl)pent-4-en-1-ylidene)-1-phenylethylamine ((*R*)-16e)

Isolated yield: 63%; Colorless oil ; $[\alpha]^{28}_{D}$ = +148.9 (*c* 1.33, $CHCl_3$); the solvent of the column chromatography, Hexane/AcOEt = 20/1, R_f = 0.24; ^{1}H NMR ($CDCl_3$): *δ* 7.32–7.45 (m, 7H, Ar-*H*), 7.18 (d, *J* = 8.00 Hz, 2H, Ar-*H*), 6.33 (dq, *J* = 17.61, 11.60 Hz, 1H, CH_2=C*H*CF_2), 5.95 (dt, *J* = 17.61, 2.40 Hz, 1H, C*H*$_2$=$CHCF_2$), 5.72 (d, *J* = 11.60 Hz, 1H, C*H*$_2$=$CHCF_2$), 4.68 (q, *J* = 6.40 Hz, 1H, C=NC*H*(CH_3)Ph), 2.49 (s, 3H,

Ar-C*H*$_3$), 1.55 (d, *J* = 6.40 Hz, 3H, C=NCH(C*H*$_3$)Ph); ^{13}C NMR ($CDCl_3$): *δ* 159.8 (t, *J* = 27.3 Hz, *C*=NCH(CH_3)Ph), 144.2 (Ar), 139.6 (Ar), 129.1 (Ar), 128.7 (Ar), 128.5 (Ar), 127.8 (t, *J* = 25.1 Hz, CH_2=*C*HCF_2), 127.6 (Ar), 127.0 (Ar), 126.4 (Ar), 123.0 (t, *J* = 9.5 Hz, *C*H_2=CHCF_2), 115.5 (tt, *J* = 250.2, 32.8 Hz, *C*F_2), 112.9 (tt, *J* = 255.5, 33.4 Hz, *C*F_2), 61.6 (C=N*C*H(CH_3)Ph), 24.6 (Ar-*C*H_3), 21.2 (C=NCH(*C*H_3)Ph); ^{19}F NMR ($CDCl_3$): *δ* -113.36 (dm, *J* = 261.64 Hz, 1F, CH_2=CHC*F*$_2$CF_2), -114.11 (d, *J* = 274.44 Hz, 1F, CH_2=CHCF_2C*F*$_2$), -114.17 (dm, *J* = 261.64 Hz, 1F, CH_2=CHC*F*$_2$CF_2), -114.98 (d, *J* = 274.44 Hz, 1F, CH_2=CHCF_2C*F*$_2$); IR (neat): *ν* 3032, 2975, 2925, 1658, 1451, 1418, 1243, 1165, 1100, 1029, 1009, 876, 700 cm^{-1}; HRMS (FAB) Calcd for $C_{20}H_{20}F_4N$ $[M+H]^+$: 350.1532, Found 350.1532.

***N*-(2,2,3,3-Tetrafluoro-1-(3-methylphenyl)pent-4-en-1-ylidene)-1-phenylethylamine ((*R*)-16f)**

Isolated yield: 96%; Colorless oil; $[\alpha]^{31}_D$ = +154.4 (*c* 1.36, $CHCl_3$); the solvent of the column chromatography, Hexane/AcOEt = 10/1, R_f = 0.47; ^{1}H NMR ($CDCl_3$): *δ* 7.22–7.37 (m, 7H Ar-*H*), 6.94-6.99 (m, 2H, Ar-*H*), 6.22 (dq, *J* = 17.21, 12.00 Hz, 1H, CH_2=C*H*CF_2), 5.86 (dt, *J* = 17.21, 2.00 Hz, 1H, C*H*$_2$=CHCF_2), 5.65 (d, *J* = 12.00 Hz, 1H, C*H*$_2$=CHCF_2), 4.51 (q, *J* = 6.40 Hz, 1H, C=NC*H*(CH_3)Ph), 2.38 (s, 3H, Ar-C*H*$_3$), 1.44 (d, *J* = 6.40 Hz, 3H, C=NCH(C*H*$_3$)Ph); ^{13}C NMR ($CDCl_3$): *δ* 159.9 (t, *J* = 27.5 Hz, *C*=NCH(CH_3)Ph), 144.3 (Ar), 138.2 (Ar), 131.7 (Ar), 130.2 (Ar), 128.4 (Ar), 128.3 (Ar), 128.1 (Ar), 127.9 (t, *J* = 23.7 Hz, CH_2=*C*HCF_2), 127.0 (Ar), 126.4 (Ar), 124.7 (Ar), 123.0 (t, *J* = 9.4 Hz, *C*H_2=CHCF_2), 115.5 (tt, *J* = 250.0, 32.6 Hz, CF_2), 112.9 (tt, *J* = 255.3, 33.5 Hz, CF_2), 61.6 (C=N*C*H(CH_3)Ph), 24.6 (Ar-*C*H_3), 21.3 (C=NCH(*C*H_3)Ph); ^{19}F NMR ($CDCl_3$): *δ* -113.31 (dm, *J* = 262.02 Hz, 1F, CH_2=CHC*F*$_2$CF_2), -113.94 (dm, *J* = 262.02 Hz, 1F, CH_2=CHC*F*$_2$CF_2), -113.94 (dm, *J* = 276.57 Hz, 1F, CH_2=CHCF_2C*F*$_2$), -114.82 (dm, *J* = 276.57 Hz, 1F, CH_2=CHCF_2C*F*$_2$); IR (neat): *ν* 3028, 2974, 2929, 1662, 1652,

1604, 1585, 1493, 1451, 1419, 1370, 1249, 1209, 1099, 1029, 1008, 959, 926, 841, 772, 717 cm^{-1}; MS (FAB): *m/z* 350 (M^+, 44), 272 (M^+-PhH, 14), 246 ($[M+H]^+$-PhC_2H_4, 31), 105 ($PhC_2H_4^+$, 100), 77 (Ph^+, 15).

(*R*)-*N*-(2,2,3,3-Tetrafluoro-1-(2-methylphenyl)pent-4-en-1-ylidene)-1-phenylethylamine ((*R*)-16g)

Isolated yield: 45%, This is a mixture of atropisomers.; Colorless oil; $[\alpha]^{28}_D$ = +96.7 (*c* 0.97, $CHCl_3$); the solvent of the column chromatography, Hexane/AcOEt = 10/1, R_f = 0.54; ^{1}H NMR ($CDCl_3$): *δ* 7.13-7.40 (m, 9H, Ar-H), **Major isomer**: 6.32 (dq, *J* = 17.21, 11.60 Hz, 1H, CH_2=C*H*CF_2), 5.91 (dt, *J* = 17.21, 2.40 Hz, 1H, C*H*$_2$=CHCF_2), 5.68 (d, *J* = 11.60 Hz, 1H, C*H*$_2$=CHCF_2), 4.31 (q, *J* = 6.40 Hz, 1H, C=NC*H*(CH_3)Ph), 1.93 (s, 3H, Ar-C*H*$_3$), 1.36 (d, *J* = 6.40 Hz, 3H, C=NCH(C*H*$_3$)Ph); **Minor isomer**: 6.22 (dq, *J* = 17.21, 11.60 Hz, 1H, CH_2=C*H*CF_2), 5.84 (dt, *J* = 17.21, 2.40 Hz, 1H, C*H*$_2$=CHCF_2), 5.64 (d, *J* = 11.60 Hz, 1H, C*H*$_2$=CHCF_2), 4.34 (q, *J* = 6.40 Hz, 1H, C=NC*H*(CH_3)Ph), 2.33 (s, 3H, Ar-C*H*$_3$), 1.48 (d, *J* = 6.40 Hz, 3H, C=NCH(C*H*$_3$)Ph); ^{13}C NMR ($CDCl_3$): Only two signals were detected for a CF_2CF_2 unit. 115.6 (tt, *J* = 249.8, 32.5 Hz, CF_2), 113.1 (tt, *J* = 256.0, 32.6 Hz, CF_2); **Major isomer**: *δ* 160.3 (dd, *J* = 32.4, 27.8 Hz, *C*=NCH(CH_3)Ph), 143.9 (Ar), 136.3 (Ar), 132.7 (Ar), 131.6 (Ar), 130.2 (Ar), 129.5 (Ar), 128.4 (Ar), 128.2 (t, *J* = 23.6 Hz, CH_2=*C*HCF_2), 127.5 (Ar), 126.5 (Ar), 125.7 (Ar), 122.8 (t, *J* = 9.5 Hz, *C*H_2=CHCF_2), 62.0 (C=N*C*H(CH_3)Ph), 24.7 (Ar-*C*H_3), 19.3 (C=NCH(*C*H_3)Ph); **Minor isomer**: *δ* 160.8 (dd, *J* = 32.1, 25.6 Hz, *C*=NCH(CH_3)Ph), 143.9 (Ar), 139.8 (Ar), 135.8 (Ar), 131.9 (Ar), 130.2 (Ar), 129.4 (Ar), 128.0 (t, *J* = 23.8 Hz, CH_2=*C*HCF_2), 127.7 (Ar), 127.0 (Ar), 126.4 (Ar), 125.6 (Ar), 123.0 (t, *J* = 9.7 Hz, *C*H_2=CHCF_2), 62.1 (C=N*C*H(CH_3)Ph), 24.0 (Ar-*C*H_3), 19.7 (C=NCH(*C*H_3)Ph); ^{19}F NMR ($CDCl_3$): *δ* **Major isomer**: -114.50 to -113.50 (m, 2F, CH_2=CHC*F*$_2$$CF_2$), -113.77 (dt, *J* = 281.59, 4.14 Hz, 1F, CH_2=$CHCF_2$C*F*$_2$), -115.60 (dt, *J* = 281.59, 4.52 Hz, 1F, CH_2=$CHCF_2$C*F*$_2$); **Minor isomer**: -112.67 (dm, *J* = 276.70 Hz, 1F, CH_2=$CHCF_2$C*F*$_2$), -

113.38 (dm, *J* = 259.38 Hz, 1F, CH_2=CHC*F*$_2$$CF_2$), -114.21 (dm, *J* = 259.38 Hz, 1F, CH_2=CHC*F*$_2$$CF_2$), -116.58 (dt, *J* = 276.70, 4.14 Hz, 1F, CH_2=CHCF_2C*F*$_2$); IR (neat): ν 3064, 3029, 2975, 2929, 2868, 1710, 1653, 1602, 1494, 1451, 1419, 1385, 1370, 1354, 1305, 1242, 1204, 1166, 1104, 1049, 1007, 980, 959, 911, 879, 861, 764 cm^{-1}; MS (FAB): *m/z* 350 (M^+, 39), 272 (M^+-PhH, 8), 246 ($[M+H]^+$-PhC_2H_4, 24), 105 ($PhC_2H_4^+$, 100), 77 (Ph^+, 14).

Typical procedure for the synthesis of carbamate (*S*)-23b via [1,3]-proton shift reaction

To a solution of imine **(*R*)-16b** (0.37 g, 1.00 mmol) in Toluene (1.0 mL) was added 0.36 mL of DBU (2.4 equiv., 2.40 mmol) at room temperature, and the mixture was stirred at that temperature for 24 h. Then, the whole was diluted with MeOH (5.0 mL) and to this mixture was added 2 N HCl aqueous solution (5.0 mL) at room temperature. After 2 h, a large amount of 2 N NaOH aqueous solution was added, and then the whole was extracted with diethyl ether three times. The combined organic layers were dried over anhydrous sodium sulfate and the solvent was evaporated. The residue was purified by silica gel column chromatography (elution: Hexane : EtOAc = 5 : 1) to give the corresponding amine (0.10 g, 0.39 mmol).

The above amine (0.10 g, 0.39 mmol) was dissolved in CH_2Cl_2, and benzyl chloroformate (0.061 mL, 1.1 equiv. 0.43 mmol) and pyridine (0.048 mL, 1.5 equiv., 0.59 mmol) was gradually added into the above solution at 0 °C. After stirring for 16 h at room temperature, the mixture was poured into crushed ice and diluted with CH_2Cl_2. The organic phase was separated, washed with water three times, dried over anhydrous sodium sulfate, and then evaporated *in vacuo*. The residue was purified by silica gel column chromatography to give the corresponding carbamate **(*S*)-23b** as a crystal (0.11 g, 0.27 mmol, 27% for three-step yield).

(*S*)-Benzyl *N*-(2,2,3,3-tetrafluoro-1-phenylpent-4-en-1-yl)carbamate ((*S*)-23a)

Isolated yield: 23% (three-step yield): White solid; M.P.: 80.7-82.2 °C; $[\alpha]^{28}_{D}$ = +16.9 (*c* 0.33, $CHCl_3$); Enantiomeric excess was established by HPLC analysis, ee = 92% [CHIRALPAK AD-H; Hexane/*i*-PrOH = 80/20, 254 nm, 0.7 mL/m ($t_{S\ isomer}$ = 11.3 min, $t_{R\ isomer}$ = 17.8 min)]; the solvent of the column chromatography, Hexane/AcOEt = 3/1, R_f = 0.57; ^{1}H NMR ($CDCl_3$): δ 7.30-7.43 (m, 10H), 5.94 (dq, *J* = 17.61, 11.60 Hz, 1H, CH_2=C*H*CF_2), 5.81 (d, *J* = 17.61 Hz, 1H, C*H*$_2$=$CHCF_2$), 5.62 (d, *J* = 11.60 Hz, 1H, C*H*$_2$=$CHCF_2$), 5.56-5.65 (m, 1H, CHN*H*Cbz), 5.37-5.53 (m, 1H, C*H*NHCbz), 5.15 (d, *J* = 12.00 Hz, 1H, NHCOOC*H*$_2$Ph), 5.07 (d, *J* = 12.00 Hz, 1H, NHCOOC*H*$_2$Ph); ^{13}C NMR ($CDCl_3$): δ 155.2 (NH*C*OOCH_2Ph), 135.8 (Ar), 134.0 (Ar), 128.8 (Ar), 128.6 (Ar), 128.5 (Ar), 128.3 (Ar), 128.2 (Ar), 128.1 (Ar), 126.3 (t, *J* = 24.9 Hz, CH_2=*C*HCF_2), 124.0 (t, *J* = 9.1 Hz, *C*H_2=$CHCF_2$), 115.9 (tt, *J* = 256.8, 33.2 Hz, CF_2), 115.3 (tt, *J* = 250.9, 33.1 Hz, CF_2), 67.4 (NHCOO*C*H_2Ph), 55.0 (dd, *J* = 28.2, 22.3 Hz, *C*HNHCbz); ^{19}F NMR ($CDCl_3$): δ -112.58 (dd, *J* = 263.52, 9.79 Hz, 1F, CH=CHC*F*$_2$$CF_2$), -114.49 (dd, *J* = 263.52, 9.79 Hz, 1F, CH=CHC*F*$_2$$CF_2$), -117.03 (d, *J* = 273.69 Hz, 1F, CH=$CHCF_2$C*F*$_2$), -122.80 (dd, *J* = 273.69, 19.58 Hz, 1F, CH=$CHCF_2$C*F*$_2$); IR (KBr): ν 3355, 2960, 2923, 1694, 1540, 1326, 1251, 1184, 1112, 1043, 1029, 979, 711 cm^{-1}; HRMS (FAB) Calcd for $C_{19}H_{18}F_4NO_2$ $[M+H]^+$: 368.1274, Found 368.1270.

(*S*)-Benzyl *N*-(2,2,3,3-tetrafluoro-1-(4-chlorophenylpent-4-en-1-yl)carbamate ((*S*)-23b)

Isolated yield: 27% (three-step yield): White solid; M.P: 113.6-115.4 °C; $[\alpha]^{31}_{D}$ = +30.6 (*c* 1.08, $CHCl_3$); Enantiomeric excess was established by HPLC analysis, ee = 95% [CHIRALPAK AD-H; Hexane/*i*-PrOH = 80/20, 254 nm, 0.7 mL/m ($t_{S\ isomer}$ = 9.86 min, $t_{R\ isomer}$ = 15.1 min)]; the solvent of the column chromatography, Hexane/AcOEt = 5/1, R_f = 0.34; ^{1}H NMR ($CDCl_3$): δ 7.25-7.39 (m, 9H), 5.93 (dq, *J* = 17.61, 11.20 Hz, 1H,

C*H*$_2$=C*H*CF$_2$), 5.81 (d, *J* = 17.61 Hz, 1H, C*H*$_2$=CHCF$_2$), 5.64 (d, *J* = 11.20 Hz, 1H, C*H*$_2$=CHCF$_2$), 5.56 (br d, *J* = 9.20 Hz, 1H, N*H*Cbz), 5.35-5.50 (m, 1H, C*H*NHCbz), 5.14 (d, *J* = 12.40 Hz, 1H, NHCOOC*H*$_2$Ph), 5.08 (d, *J* = 12.40 Hz, 1H, NHCOOC*H*$_2$Ph); ^{13}C NMR ($CDCl_3$): *δ* 155.3 (NH*C*OOCH$_2$Ph), 135.9 (Ar), 135.1 (Ar), 132.8 (Ar), 129.8 (Ar), 129.1 (Ar), 128.7 (Ar), 128.5 (Ar), 128.4 (Ar), 126.3 (t, *J* = 24.2 Hz, CH$_2$=*C*HCF$_2$), 124.5 (t, *J* = 9.6 Hz, *C*H$_2$=CHCF$_2$), 115.9 (tt, *J* = 256.0, 34.6 Hz, CF$_2$), 115.4 (tt, *J* = 250.3, 33.3 Hz, CF$_2$), 67.8 (NHCOO*C*H$_2$Ph), 54.7 (t, *J* = 24.8 Hz, *C*HNHCbz); ^{19}F NMR ($CDCl_3$): *δ* -113.26 (dm, *J* = 270.67 Hz, 1F), -115.08 (dm, *J* = 270.67 Hz, 1F), -117.48 (d, *J* = 275.57 Hz 1F), -123.66 (dd, *J* = 275.57, 18.07 Hz, 1F); IR (KBr): *ν* 3744, 3347, 3038, 2980, 2778, 1699, 1652, 1597, 1532, 1493, 1457, 1419, 1377, 1335, 1264, 1180, 1117, 1040, 1014, 992, 941, 916, 857, 829, 787 cm^{-1}; HRMS (FAB) Calcd for $C_{19}H_{17}{}^{35}ClF_4NO_2$ $[M+H]^+$: 402.0884, Found 402.0879.

(*S*)-Benzyl *N*-(2,2,3,3-tetrafluoro-1-(4-bromophenylpent-4-en-1-yl)carbamate ((*S*)-23c)

Isolated yield: 22% (three-step yield): White solid; M.P.: 110.4-111.6 °C; $[\alpha]^{28}_D$ = +20.8 (*c* 0.92, $CHCl_3$); 98% ee [CHIRALPAK AD-H; Hexane/*i*-PrOH = 80/20, 254 nm, 0.7 mL/m ($t_{S\ isomer}$ = 14.6 min, $t_{R\ isomer}$ = 25.4 min)]; the solvent of the column chromatography, Hexane/AcOEt = 10/1, R_f = 0.40; ^{1}H NMR ($CDCl_3$): *δ* 7.51 (d, *J* = 8.20 Hz, 2H, Ar-H), 7.30-7.39 (m, 5H, Ar-H), 7.22 (d, *J* = 8.20 Hz, 2H, Ar-H), 5.95 (dq, *J* = 17.21, 11.20 Hz, 1H, CH$_2$=C*H*CF$_2$), 5.81 (d, *J* = 17.21 Hz, 1H, C*H*$_2$=CHCF$_2$), 5.65 (d, *J* = 11.20 Hz, 1H, C*H*$_2$=CHCF$_2$), 5.50 (d, *J* = 8.80 Hz, 1H, N*H*Cbz), 5.32-5.46 (m, 1H, C*H*NHCbz), 5.14 (d, *J* = 12.00 Hz, 1H, NHCOOC*H*$_2$Ph), 5.07 (d, *J* = 12.00 Hz, NHCOOC*H*$_2$Ph); ^{13}C NMR ($CDCl_3$): *δ* 155.3 (NH*C*OOCH$_2$Ph), 135.9 (Ar), 133.3 (Ar), 132.0 (Ar), 130.1 (Ar), 128.7 (Ar), 128.5 (Ar), 128.3 (Ar), 126.3 (t, *J* = 18.6 Hz, CH$_2$=*C*HCF$_2$), 124.5 (t, *J* = 9.5 Hz, *C*H$_2$=CHCF$_2$), 123.3 (Ar), 115.8 (tt, *J* = 259.5, 32.4 Hz, CF$_2$), 115.4 (tt, *J* = 250.6, 33.6 Hz, CF$_2$), 67.7 (NHCOO*C*H$_2$Ph), 54.8 (t, *J* = 24.0

Hz, *C*HNHCbz); ^{19}F NMR ($CDCl_3$): δ -113.16 (dm, *J* = 265.78 Hz, 1F), -114.96 (dm, *J* = 265.78 Hz, 1F), -117.33 (d, *J* = 276.70 Hz 1F), -123.59 (dd, *J* = 276.70, 15.43 Hz, 1F); IR (KBr): ν 3350, 3090, 3066, 3035, 2976, 2778, 1692, 1531, 1491, 1456, 1419, 1409, 1377, 1331, 1269, 1181, 1103, 1040, 1010, 991, 964, 917, 828, 781 cm^{-1}; HRMS (FAB) Calcd for $C_{19}H_{17}{}^{79}BRF_4NO_2$ $[M+H]^+$: 446.0379, Found 446.0380.

(*S*)-Benzyl *N*-(2,2,3,3-tetrafluoro-1-(4-methoxyphenylpent-4-en-1-yl)carbamate ((*S*)-23d)

Isolated yield: 35% (three-step yield): White solid; M.P.: 65.6-67.2 °C; $[\alpha]^{28}_D$ = +26.1 (*c* 0.51, $CHCl_3$); 90% ee [CHIRALPAK AD-H; Hexane/*i*-PrOH = 80/20, 254 nm, 0.7 mL/m ($t_{S\ isomer}$ = 19.7 min, $t_{R\ isomer}$ = 49.4 min)]; the solvent of the column chromatography, Hexane/AcOEt =3/1, R_f = 0.39; ^{1}H NMR ($CDCl_3$): δ 7.30-7.38 (m, 5H, Ar-H), 7.26 (d, *J* = 8.20 Hz, 2H, Ar-H), 6.89 (d, *J* = 8.20 Hz, 2H, Ar-H), 5.91 (dq, *J* = 17.21, 11.20 Hz, 1H, CH_2=C*H*CF_2), 5.79 (d, *J* = 17.21 Hz, 1H, C*H*$_2$=$CHCF_2$), 5.61 (d, *J* = 11.20 Hz, 1H, C*H*$_2$=$CHCF_2$), 5.51 (br d, *J* = 10.00 Hz, 1H, N*H*Cbz), 5.32-5.47 (m, 1H, C*H*NHCbz), 5.14 (d, *J* = 12.100 Hz, 1H, NHCOOC*H*$_2$Ph), 5.07 (d, *J* = 12.00 Hz, 1H, NHCOOC*H*$_2$Ph), 3.81 (s, 3H, ArOC*H*$_3$); ^{13}C NMR ($CDCl_3$): δ 159.9 (NH*C*OOCH$_2$Ph), 155.2 (Ar), 135.9 (Ar), 129.5 (Ar), 128.5 (Ar), 128.3 (Ar), 128.2 (Ar), 126.4 (t, *J* = 24.2 Hz, CH_2=*C*HCF_2), 126.1 (Ar), 123.9 (t, *J* = 9.5 Hz), 116.0 (tt, *J* = 255.4, 36.1 Hz, CF_2), 115.3 (tt, *J* = 250.5, 32.4 Hz, CF_2), 114.1 (Ar), 67.4 (NHCOO*C*H$_2$Ph), 55.2 (ArO*C*H$_3$), 54.5 (dd, *J* = 28.4, 22.0 Hz, *C*HNHCbz); ^{19}F NMR ($CDCl_3$): δ -112.57 (dd, *J* = 264.65, 10.16 Hz, 1F), -114.49 (dd, *J* = 264.65, 10.16 Hz, 1F), -117.48 (dd, *J* = 272.18, 7.91 Hz ,1F), -122.70 (dd, *J* = 272.18, 17.32 Hz, 1F); IR (KBr): ν 3371, 2963, 1699, 1533, 1516, 1243, 1122, 1093, 1038, 993, 798 cm^{-1}; HRMS (FAB) Calcd for $C_{19}H_{18}F_4NO_2$ $[M+H]^+$: 398.1379, Found 398.1366.

(*S*)-Benzyl *N*-(2,2,3,3-tetrafluoro-1-(4-methylphenylpent-4-en-1-yl)carbamate ((*S*)-23e)

Isolated yield: 7% (three-step yield): White solid; M.P.: 92.8-94.1 °C; $[\alpha]^{28}_{D}$ = +26.3 (*c* 0.07, $CHCl_3$); 90% ee [CHIRALPAK AD-H; Hexane/*i*-PrOH = 80/20, 254 nm, 0.7 mL/m ($t_{S\ isomer}$ = 10.5 min, $t_{R\ isomer}$ = 20.7 min)]; the solvent of the column chromatography, Hexane/AcOEt =3/1, R_f = 0.62; ^{1}H NMR ($CDCl_3$): δ 7.30-7.40 (m, 5H, Ar-H), 7.25 (d, *J* = 8.00 Hz, 2H, Ar-H), 7.19 (d, *J* = 8.00 Hz, 2H, Ar-H), 5.94 (dq, *J* = 17.21, 11.20 Hz, 1H, C*H*$_2$=C*H*CF_2), 5.81 (d, *J* = 17.21 Hz, 1H, C*H*$_2$=$CHCF_2$), 5.62 (d, *J* = 11.20 Hz, 1H, C*H*$_2$=$CHCF_2$), 5.58 (br d, *J* = 10.00 Hz, 1H, N*H*Cbz), 5.35-5.49 (m, 1H, C*H*NHCbz), 5.15 (d, *J* = 12.00 Hz, 1H, NHCOOC*H*$_2$Ph), 5.07 (d, *J* = 12.00 Hz, 1H, NHCOOC*H*$_2$Ph), 2.37 (s, 3H, ArC*H*$_3$); ^{13}C NMR ($CDCl_3$): δ 155.2 (NH*C*OOCH_2Ph), 138.8 (Ar), 135.9 (Ar), 131.1 (Ar), 129.4 (Ar), 128.5 (Ar), 128.3 (Ar), 128.2 (Ar), 128.1 (Ar), 126.4 (t, *J* = 24.1 Hz, CH_2=*C*HCF_2), 124.0 (t, *J* = 9.6 Hz, *C*H_2=$CHCF_2$), 116.0 (tt, *J* = 257.4, 32.6 Hz, CF_2), 115.3 (tt, *J* = 250.5, 33.6 Hz, CF_2), 67.4 (NHCOO*C*H_2Ph), 54.8 (dd, *J* = 27.7, 21.9 Hz, *C*HNHCbz), 21.1 (Ar*C*H_3); ^{19}F NMR ($CDCl_3$): δ -112.52 (dd, *J* = 263.52, 9.79 Hz, 1F), -114.55 (dd, *J* = 263.52, 11.67 Hz, 1F), -117.23 (dm, *J* = 272.18 Hz ,1F), -122.82 (dd, *J* = 272.18, 18.07 Hz, 1F),; IR (KBr): ν 3366, 3037, 2962, 1704, 1324, 1244, 1208, 1098, 1034, 991, 791, 696 cm^{-1}; HRMS (FAB) Calcd for $C_{19}H_{18}F_4NO_2$ $[M+H]^+$: 382.1430, Found 382.1434.

(*S*)-Benzyl N-(2,2,3,3-tetrafluoro-1-(3-methylphenyl)pent-4-en-1-yl)carbamate ((*S*)-23f)

Isolated yield: 32% (three-step yield): White solid; M.P.: 73.5-75.3 °C; $[\alpha]^{28}_{D}$ = +43.1 (*c* 0.44, $CHCl_3$); 91% ee [CHIRALPAK AD-H; Hexane/*i*-PrOH = 80/20, 254 nm, 0.7 mL/m ($t_{S\ isomer}$ = 10.4 min, $t_{R\ isomer}$ = 15.1 min)]; the solvent of the column chromatography, Hexane/AcOEt =5/1, R_f = 0.41; ^{1}H NMR ($CDCl_3$): δ 7.15-7.44 (m, 9H, Ar-H), 5.97 (dq,

J = 17.21, 11.60 Hz, 1H, CH_2=C*H*CF_2), 5.84 (d, *J* = 17.21 Hz, 1H, C*H*$_2$=$CHCF_2$), 5.70 (d, *J* = 9.60 Hz, 1H, CHN*H*Cbz), 5.63 (d, *J* = 11.60 Hz, 1H, C*H*$_2$=$CHCF_2$), 5.40-5.53 (m, 1H, C*H*NHCbz), 5.17 (d, *J* = 12.00 Hz, 1H, $NHCO_2CH_2$Ph), 5.09 (d, *J* = 12.00 Hz, 1H, $NHCO_2CH_2$Ph), 2.38 (s, 3H, Ar-C*H*$_3$); ^{13}C NMR ($CDCl_3$): *δ* 155.2 (NH*C*OOCH$_2$Ph), 138.3 (Ar), 135.9 (Ar), 134.0 (Ar), 129.6 (Ar), 129.0 (Ar), 128.50 (Ar), 128.47 (Ar), 128.2 (Ar), 128.1 (Ar), 126.4 (t, *J* = 24.2 Hz, CH_2=*C*HCF_2), 125.2 (Ar), 123.9 (t, *J* = 9.6 Hz, *C*H_2=$CHCF_2$), 116.0 (tt, *J* = 256.6, 31.7 Hz, CF_2), 115.3 (tt, *J* = 250.6, 33.6 Hz, CF_2), 67.4 (NHCOO*C*H$_2$Ph), 55.0 (dd, *J* = 28.1, 21.5, Hz, *C*HNHCbz), 21.2 (Ar-*C*H$_3$); ^{19}F NMR ($CDCl_3$): *δ* -113.03 (dd, *J* = 264.27, 10.16 Hz, 1F), -115.10 (dd, *J* = 264.27, 9.41 Hz, 1F), -117.33 (d, *J* = 272.56 Hz ,1F), -123.48 (dd, *J* = 272.56, 18.45 Hz, 1F); IR (KBr): *ν* 3354, 3034, 2961, 2898, 1683, 1530, 1465, 1455, 1415, 1335, 1247, 1171, 1118, 1045, 1009, 962, 913, 898, 855, 828, 779 cm^{-1}; HRMS (FAB) Calcd for $C_{19}H_{18}F_4NO_2$ $[M+H]^+$: 382.1430, Found 382.1426.

(*S*)-Benzyl N-(2,2,3,3-tetrafluoro-1-(2-methylphenylpent-4-en-1-yl)carbamate ((*S*)-23g)

Isolated yield: 22% (three-step yield): White solid; M.P.: 51.9-52.5 °C; $[\alpha]^{28}_D$ = +23.0 (*c* 0.43, $CHCl_3$); 94% ee [CHIRALPAK AD-H; Hexane/*i*-PrOH = 80/20, 254 nm, 0.7 mL/m ($t_{S\ isomer}$ = 9.3 min, $t_{R\ isomer}$ = 16.1 min)]; the solvent of the column chromatography, Hexane/AcOEt = 5/1 R_f = 0.47; ^{1}H NMR ($CDCl_3$): *δ* 7.20-7.38 (m, 9H), 5.95 (dq, *J* = 17.21, 10.80, Hz, 1H, CH_2=C*H*CF_2), 5.83 (d, *J* = 17.21 Hz, 1H, C*H*$_2$=$CHCF_2$), 5.75-5.85 (m, 1H, C*H*NHCbz), 5.62 (d, *J* = 10.80 Hz, 1H, C*H*$_2$=$CHCF_2$), 5.51 (d, *J* = 9.60 Hz, 1H, CHN*H*Cbz), 5.14 (d, *J* = 12.40 Hz, 1H, NHCOOC*H*$_2$Ph), 5.04 (d, *J* = 12.40 Hz, 1H, NHCOOC*H*$_2$Ph), 2.44 (s, 3H, Ar-C*H*$_3$); ^{13}C NMR ($CDCl_3$): *δ* 155.2 (C=O), 137.1 (Ar), 135.9 (Ar), 133.1 (Ar), 130.7 (Ar), 128.7 (Ar), 128.6 (Ar), 128.3 (Ar), 128.2 (Ar), 127.1 (Ar), 126.37 (Ar), 126.35 (t, *J* = 24.3 Hz, CH_2=*C*HCF_2), 124.0 (t, *J* = 9.5 Hz, *C*H_2=$CHCF_2$), 116.2 (tt, *J* = 253.8, 33.3 Hz, CF_2), 115.3 (tt, *J* = 252.0, 33.6 Hz, CF_2),

67.5 (CO_2CH_2Ph), 50.1 (dd, *J* = 29.4, 21.5 Hz, *C*HNHCbz), 19.5 (Ar-CH_3); ^{19}F NMR ($CDCl_3$): δ -114.10 (dm, *J* = 270.67 Hz, 1F), -115.87 (dm, *J* = 270.67 Hz, 1F), -117.67 (d, *J* = 275.57 Hz ,1F), -124.70 (dm, *J* = 275.57 Hz, 1F); IR (KBr): ν 3382, 3037, 2963, 2925, 1707, 1532, 1451, 1421, 1377, 1343, 1321, 1248, 1189, 1126, 1095, 1035, 1011, 987, 957, 917, 824, 748 cm^{-1}; HRMS (FAB) Calcd for $C_{20}H_{19}F_4NNaO_2$ $[M+Na]^+$: 404.1250, Found 404.1241.

Supporting Information

Supporting Information File 1:

^1H, ^{13}C, ^{19}F NMR spectra of **16a**-**g**, **23a**-**g** and HPLC charts of racemic as well as chiral **23a**-**g**

Acknowledgements

We thank TOSOH FINECHEM for the general gift of 4-bromo-3,3,4,4-tetrafluoro-1-butene (**1**).

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14. The HF elimination product, **21b**, was too unstable in silica gel column chromatography to be isolated in a pure form, and hence its identification by ^{1}H NMR analysis could not be carried out. A similar compound, however, *N*-benzylidene-(1-phenyl)-2,3,3-trifluoro-1,4-pentdienylamine, could be easily isolated, and the structure could be completely identified (see SI). Accordingly, it was determined unambiguously that **21b** also has an azatriene structure, on the basis of the comparison of the ^{19}F

NMR chemical shifts for **21b** and *N*-benzylidene-(1-phenyl)-2,3,3-trifluoro-1,4-pentdienylamine.

15. Electrocyclization of 5,6-difluoro-3-azaocta-1,3,5,7-tetraene derivative which resulted from two HF eliminations of the imine **(*R*)-16b** under the influence of DBU might take place, giving the corresponding azocine derivative **22b**. The details are currently under investigation. See SI.

16. When R is an alkyl group, the desired rearranged product was rarely obtained, leading to unidentified products, together with a large amount of starting material.