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Metal-mediated *gem*-Difluoroallylation of *N*-Acylhydrazones: Highly Efficient Synthesis of *α*,*α*-Difluorohomoallylic Amines†

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Indium-mediated *gem*-difluoroallylation of aldehyde-derived *N*-acylhydrazones **1a**—**1q** and **4a**—**4g** with 3-bromo-3,3-difluoropropene **2** afforded *α*,*α*-difluorohomoallylic hydrazides **3a**—**3q** and **5a**—**5g** in high yields, respectively. Functional groups such as nitro, phenolic hydroxyl, benzyloxy and even C=C bonds of *α*,*β*-unsaturated aldehydes were compatible under this mild and operationally simple *gem*-difluoroallylic reaction condition. By means of substitution of Zn powder for indium, *gem*-difluoroallylation of ketone-derived *N*-acylhydrazones **6a**—**6d** also provided the corresponding *α*,*α*-difluorohomoallylic hydrazides **7a**—**7d** in medium yields. The N—N bond cleavage of the hydrazide **3a** proceeded smoothly to give the corresponding primary *gem*-difluorohomoallylic amine **8**, which could be converted to *gem*-difluoro-*δ*-substituted *α*,*β*-unsaturated lactam **11** via acryloylation followed by ring closing metathesis (RCM) reaction.

Keywords metal-mediated, hydrazone, *gem*-difluorohomoallylic amine

Introduction

The addition of allylic metal derivatives to imines[1] is generally recognized as one of the most efficient methods for the access to homoallylic amine derivatives, which are compounds of interest themselves because they can be versatile intermediates in the synthesis of other bioactive molecules.[2] Recently, continuous endeavors of organic chemists have documentated a lot of reports about highly asymmetric and catalytic allylation of imine compounds with nonfluorinated allylic precursors,[3-5] however, we found that scant attentions were given to *gem*-difluoroallylation reaction, due to the hard introduction of fluorine moiety and the weak reactivity of *gem*-difluoro-containing building block in contrast to nonfluorinated counterpart.[6] *gem*-Difluoromethylene moiety is a key structural unit in many fluorinated compounds of biological and pharmaceutical significance and some building blocks have been developed to introduce CF_2 into organic compounds.[7] Among them, 3-bromo-3,3-difluoropropene (BDFP) and its derivatives are some of the most important building blocks. The coupling of the *gem*-difluoroallylic metal species, with carbonyl compounds is one of the most important procedures to prepare *gem*-difluorohomoallylic alcohols.[6] For example, 4-deoxy-4,4-difluoro-glycosides have been synthesized via a direct sequence involving ring-closing metathesis and indium-mediated difluoroallylation of aldehydes with BDFP.[8] As the counterparts of *gem*-difluorohomoallylic alcohols, most of *gem*-difluorohomoallylic amines were obtained via conversion of *gem*-difluorohomoallylic alcohols (three steps)[9] or diethylaminosulfur trifluoride (DAST)-mediated difluorination of *α*,*β*-unsaturated ketone amines (low yield).[10] Thus, a novel method should be developed to efficiently synthesize *gem*-difluorohomoallylic amines.

Theoretically, *gem*-difluoroallylation of imines or imine oxides would be the alternative method to address the synthesis of *gem*-difluorohomoallylic amines. However, to the best of our knowledge, none of this kind of *gem*-difluoroallylation was reported so far, which may be ascribed to the following facts: (1) the addition of organometallic reagents to the C=N double bonds of imines or imine oxides is severely restricted either by the poor electrophilicity of the azomethine carbon or by the tendency of enolisable imines and imine derivatives to undergo deprotonation rather than addition;[11] (2) imines may be readily hydrolyzed to the corresponding carbonyl compounds before allylation occurs, thus giving the corresponding *gem*-difluorohomoallylic alcohols;[12] (3) the less reactivity of *gem*-difluoroallylation reagent (such as BDFP) comparing to the nonfluorinated counterparts. On the other hand, it is well-known that the advantages of hydrazones over imines or imine oxides as nucleophilic

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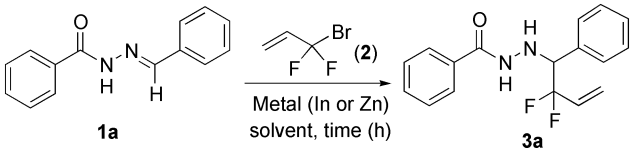
receptors featured a favorable equilibrium in the formation, ease of purification and handling and resistance to tautomerization. Thus, herein we wish to report highly efficient metal-mediated *gem*-difluoroallylation of *N*-acylhydrazones with BDFP and *gem*-difluorohomoallylic amine was accessed in a straightforward fashion. Furthermore, the resultant *α*,*α*-difluorohomoallylic amine could be readily transformed to *gem*-difluoro-*δ*-substituted *α*,*β*-unsaturated lactam.

Results and discussion

Our initial experiments were performed with benzaldehyde-derived acylhydrazone **1a**[13] as a model substrate (Table 1). Firstly, acid-washed zinc powder was used to mediate the *gem*-difluoroallylation between **1a** and BDFP **2**. With toluene as solvent, no reaction occurred due to the poor solubility of **1a** (Entry 1). Slightly gratifyingly, *gem*-difluoroallylation proceeded smoothly via substitution of DMF for toluene and desired *α*,*α*-difluorohomoallylic hydrazide **3a** was provided in 78% yield (Entry 2). Further, the yield could be improved to 87% when zinc was replaced with indium powder (Entry 3). Finally, we are glad to find that **3a** could be obtained in almost quantitative yield when the reaction time was prolonged from 17 to 46 h (Entry 4).

Table 1 Exploring the reaction condition of *gem*-difluoroallylation of model substrate **1a** with BDFP **2**



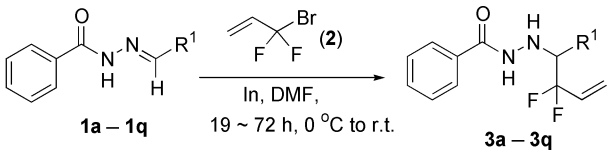
1a **3a**

Entry	Metal (equiv.)	Solvent	Time/h	Yield[a]/%
1	Zn (1.7)	Toluene	24	NR
2	Zn (1.7)	DMF	24	78
3	In (1.7)	DMF	17	87
4	In (1.7)	DMF	46	97

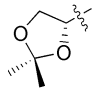
[a] Isolated yield after chromatography (silica gel) based on the starting material **1a**.

On the basis of above results, we investigated the substrate generality using optimized reaction condition (Table 2). Overall, the reactions progressed well on a variety of aldehyde-derived *N*-acylhydrazones **1a**—**1q**. Firstly, *gem*-difluoroallylation displayed good results for a lot of aromatic aldehyde-derived hydrazones **1b**—**1j**, regardless of aromatic aldehydes bearing electron-donating substituents (**1b**—**1d**, Entries 2—4), electron-withdrawing substituents (**1e**—**1i**, Entries 5—9) and even phenolic hydroxyl group (**1j**, Entry 10). In the case of *ortho*-substituted substrates, 2.6 equiv. of BDFP **2** and 2.5 equiv. of indium powder were used for the complete transformation of hydrazones (**1e**, **1h**, Entries 5, 8). We were also pleased to find that *α*,*β*-unsaturated aromatic aldehyde-derived hydrazones **1k**, **1l** only underwent regioselective 1,2-addition (no any 1,4-addition product was detected) and corresponding *α*,*α*-difluorohomoallylic hydrazides **3k**, **3l** were afforded in 84% and 76% yields, respectively (Entries 11—12). In addition, aliphatic aldehyde-derived substrates **1m**—**1p** also delivered the desired products **3m**—**3p** in medium to good yields (Entries 13—16) no matter whether the aliphatic chains were straight chain (**1m**, **1o**), branched chain (**1n**) or cyclic chain (**1p**). (*R*)-Glyceraldehyde acetonide-derived hydrazone **1q** gave two separable diastereomers in a 1.3/1 ratio determined by ^{19}F NMR and *syn* isomer was the major product.

Table 2 Substrate generality of indium-mediated *gem*-difluoroallylation on aldehyde-derived hydrazones **1a**—**1q**



1a – 1q **3a – 3q**

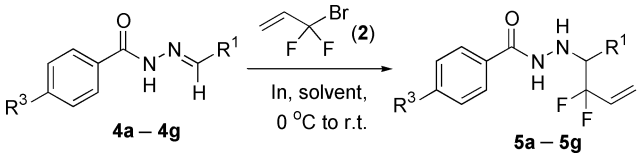
Entry	Hydrazone	R^1	Time/h	Yield[a]/%
1	**1a**	Ph	46	97
2	**1b**	*p*-MeO-C_6H_4	26	90
3	**1c**	*p*-Me-C_6H_4	24	91
4	**1d**	*o*-MeO-C_6H_4	29	65
5	**1e**	*o*-Cl-C_6H_4	72	72[b]
6	**1f**	*p*-Cl-C_6H_4	60	69
7	**1g**	*m*-Cl-C_6H_4	40	89
8	**1h**	2,4-di-Cl-C_6H_3	36	80[c]
9	**1i**	*m*-NO_2-C_6H_4	24	52
10	**1j**	2,4-di-OH-C_6H_3	24	69
11	**1k**	PhCH=CH	24	84[d]
12	**1l**	MeCH=CH	23	76
13	**1m**	*n*-Heptyl	19	85
14	**1n**	*i*-Pr	21	87
15	**1o**	$BnOCH_2$	24	76
16	**1p**	*c*-Hexyl	32	89
17	**1q**		25	90[e] *syn/anti* 1.3/1

[a] Isolated yield after column chromatography. [b] 6 equiv. indium and 6 equiv. **2** were used. [c] 2.5 equiv. indium and 2.6 equiv. **2** were used. [d] 2.5 equiv. **2** was used. [e] The diastereoisomeric ratio was determined by ^{19}F NMR analysis.

Then, we turned our attention to study the substitution effect of auxiliary benzoyl moiety and the result is summarized in Table 3. Clearly, hydrazones **4a**—**4f** derived from *p*-methoxybenzohydrazides underwent the *gem*-difluoroallylation smoothly in slightly lower yields comparing to the benzohydrazide-derived counterparts

(Entries 1—6 in Table 3 vs. Entries 1, 12—14 and 16 in Table 2). Once *p*-methoxyl group was replaced with *p*-nitro group, compound **4g** did not furnish any product in DMF due to its poor solubility in this solvent (Entry 7). Although *gem*-difluoroallylation of **4g** could occur with DMSO as solvent, the yield was very low (19%) (Entry 8), which, in our opinion, was ascribed to the incompatibility between strong electron-withdrawing nitro group and indium powder in strong polar solvent.

Table 3 Substitution effect of auxiliary benzoyl moiety on indium-mediated *gem*-difluoroallylation



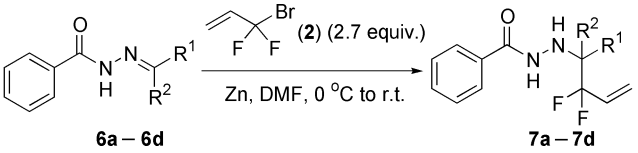
4a – 4g **5a – 5g**

Entry	Hydrazone	R^3	R^1	Solvent	Time/h	Yield[a]/%
1	**4a**	MeO	Ph	DMF	40	87
2	**4b**	MeO	*p*-Me_2N-C_6H_4	DMF	70	71
3	**4c**	MeO	CH_3CH_2=CH	DMF	24	79
4	**4d**	MeO	*n*-Heptyl	DMF	26	79
5	**4e**	MeO	*i*-Pr	DMF	24	82
6	**4f**	MeO	*c*-Hexyl	DMF	26	87
7	**4g**	NO_2	Ph	DMF	20	0
8	**4g**	NO_2	Ph	DMSO	19	19

[a] Isolated yield after column chromatography.

Next, we examined the *gem*-difluoroallylation of ketone-derived *N*-acylhydrazones **6a**—**6d** with BDFP **2** (Table 4). Interestingly, no reaction occurred when the reaction was performed with indium powder in DMF. Fortunately, the *gem*-difluoroallylation proceeded smoothly if zinc powder was used instead of indium powder and the desired tertiary amine derivatives **7a**—**7d** were afforded in medium yields, even for the sterically hindered cyclopentanone-derived *N*-benzoylhydrazone **6d**. According to the above results, one conclusion could be made that the reactivity of the *gem*-difluoroallylation of ketone-derived *N*-acylhydrazones mediated by zinc powder was higher than that mediated by indium powder, which is in line with Burton[6g] and Kirihara's[6j] results.

Table 4 Zinc-mediated *gem*-difluoroallylation of ketone-derived *N*-acylhydrazones



6a – 6d **7a – 7d**

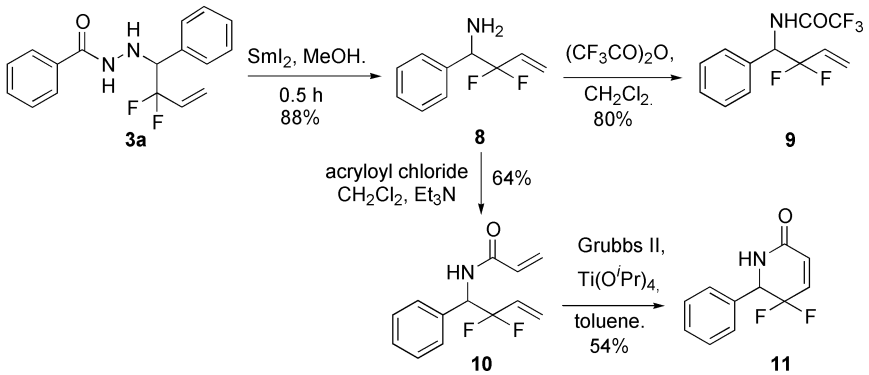
Entry	Hydrazone	R^1	R^2	Time/h	Yield[a]/%
1	**6a**	Ph	Me	24	45
2	**6b**	Me	Me	14	47
3	**6c**	Et	Me	24	40
4	**6d**	-$(CH_2)_4$-		24	45

[a] Isolated yield after column chromatography.

The synthesized *α*,*α*-difluorohomoallylic hydrazide derivatives were easily subjected to cleavage of the N—N bond to afford the corresponding *gem*-difluorohomoallylic amines, which could be further converted to other versatile building blocks and *gem*-difluorinated intermediates. As a representative example, treatment of benzohydrazide **3a** in methanol with SmI_2 utilizing the N—N bond cleavage method developed by Friestad group[14] smoothly provided the desired primary *gem*-difluorohomoallylic amine **8** in 88% yield (Scheme 1). Since the boiling point of amine **8** was low and slightly difficult to handle, trifluoroacetylation of **8** would give the trifluoroacetamide **9** in 80% yield, which, in our opinion, could be recognized as a novel *gem*-difluorinated building block for synthesis of other *gem*-difluoromethylene-containing compounds. In addition, *gem*-difluorohomoallylic amine **8** was also readily transformed to a versatile intermediate, *gem*-difluoro-*δ*-substituted *α*,*β*-unsaturated lactam **11** via acryloylation followed by RCM catalyzed by Grubbs II catalyst (8 mol%).

In conclusion, we reported the practical *gem*-difluoroallylation of aldehyde-derived acylhydrazones mediated by indium powder with 3-bromo-3,3-difluoropropene.

Scheme 1



This general and easily repeatable procedure afforded various *gem*-difluorohomoallylic hydrazine derivatives in high yields. A lot of functional groups were tolerable for this mild and operationally simple reaction condition. Via substitution of zinc powder for indium powder, *gem*-difluoroallylation of ketone-derived *N*-acylhydrazones also provided the corresponding *α*,*α*-difluorohomoallylic hydrazides in medium yields. The N—N bond cleavage of the hydrazide proceeded smoothly to give the corresponding *gem*-difluorohomoallylic amine, which could be converted to *gem*-difluoro-*δ*-substituted *α*,*β*-unsaturated lactam via acryloylation followed by RCM. Further developing asymmetric *gem*-difluoroallylation of the hydrazones using chiral catalysts or chiral auxiliaries is in active progress.

Experimental section

Reagents and apparatus

All reagents were used as received from commercial sources, unless specified otherwise, or prepared as described in the literature. Dichloromethane and DMF were distilled from CaH_2. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker AM300 spectrometer. ^{19}F NMR was recorded on a Bruker AM300 spectrometer ($CFCl_3$ as outside standard and low field is positive). Chemical shifts (δ) are reported in ppm, and coupling constants (J) are in Hz. Melting points are uncorrected. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad.

Representative general procedure for the preparation of hydrazones

The benzoic hydrazide **1a** (25 mmol) was added to a hexane solution (120 mL) containing benzaldehyde (37 mmol). The resulting mixture was stirred at reflux for 4 h. The crystallized solid was filtered and washed with hexane. The pure hydrazone was obtained by recrystallization from absolute EtOH (5.43 g, 97% yield).

(*E*)-*N′*-Octylidenebenzohydrazide (1m): White solid, m.p. 77—78 ℃; ^1H NMR ($CDCl_3$, 300 MHz) δ: 9.98 (s, 1H), 7.82 (d, J=6.9 Hz, 2H), 7.67 (t, J=5.4 Hz, 1H), 7.47 (t, J=7.5 Hz, 1H), 7.36 (t, J=7.5 Hz, 2H), 2.35—2.28 (m, 2H), 1.47—1.45 (m, 2H), 1.26 (br, 8H), 0.87 (t, J=5.4 Hz, 3H); IR (KBr) v: 3261, 3063, 1651, 1627, 1539, 1286 cm^{-1}; ESI-MS *m/z*: 247 $(M+H)^+$. Anal. calcd for $C_{15}H_{22}N_2O$: C 73.13, H 9.00, N 11.37; found C 73.10, H 9.02, N 11.35.

(*E*)-*N′*-(2-(Benzyloxy)ethylidene)benzohydrazide (1o): White solid, m.p. 110—112 ℃; ^1H NMR (CD_3OD, 300 MHz) δ: 8.34 (d, J=7.2 Hz, 2H), 8.20 (t, J=4.8 Hz, 1H), 8.05 (t, J=7.5 Hz, 1H), 7.96 (t, J=7.5 Hz, 2H), 7.82—7.74 (m, 5H), 5.35 (s, 2H), 4.71 (d, J=4.8 Hz, 2H); IR (KBr) v: 3196, 3034, 1645, 1571, 1359 cm^{-1}; ESI-MS *m/z*: 269 $(M+H)^+$, 286 $(M+NH_4)^+$, 291 $(M+Na)^+$. Anal. calcd for $C_{16}H_{16}N_2O_2$: C 71.62, H 6.01, N 10.44; found C 71.51, H 6.00, N 10.36.

(*S*,*E*)-*N′*-[(2,2-Dimethyl-1,3-dioxolan-4-yl)methylene]benzohydrazide (1q): White solid, m.p. 163—165 ℃; $[\alpha]_D^{25}$ 44.5 (*c* 0.83, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ: 10.03 (br, 1H), 7.83 (d, J=7.8 Hz, 2H), 7.64 (d, J=3.6 Hz, 1H), 7.51 (t, J=7.2 Hz, 1H), 7.41 (t, J=7.5 Hz, 2H), 4.74 (d, J=5.4 Hz, 1H), 4.17 (t, J=8.7 Hz, 1H), 3.90—3.86 (m, 1H), 1.42 (s, 3H), 1.38 (s, 3H); IR (KBr) v: 3315, 3074, 1648, 1557, 1368, 1058 cm^{-1}; ESI-MS *m/z*: 249 $(M+H)^+$, 271 $(M+Na)^+$, 519 $(2M+Na)^+$; HRMS calcd for $C_{13}H_{16}N_2O_3Na$ 271.1053, found 271.1064. Anal. calcd for $C_{13}H_{16}N_2O_3$: C 62.89, H 6.50, N 11.28; found C 63.01, H 6.47, N 11.29.

(*E*)-*N′*-(4-(Dimethylamino)benzylidene)-4-methoxybenzohydrazide (4b): Pale yellow solid, m.p. 232—234 ℃; ^1H NMR (CD_3OD, 300 MHz) δ: 8.17 (s, 1H), 7.88 (d, J=7.8 Hz, 2H), 7.65 (d, J=8.1 Hz, 2H), 7.02 (d, J=8.4 Hz, 2H), 6.75 (d, J=8.1 Hz, 2H), 3.85 (s, 3H), 3.01 (s, 6H); IR (KBr) v: 3244, 3056, 1645, 1606, 1180 cm^{-1}; ESI-MS *m/z*: 298 $(M+H)^+$, 320 $(M+Na)^+$. Anal. calcd for $C_{17}H_{19}N_3O_2$: C 68.67, H 6.44, N 14.13; found C 68.32, H 6.54, N 13.91.

(*E*)-*N′*-((*E*)-But-2-enylidene)-4-methoxybenzohydrazide (4c): Pale yellow solid, m.p. 184—186 ℃; ^1H NMR (CD_3OD, 300 MHz) δ: 7.91 (d, J=8.1 Hz, 1H), 7.84 (d, J=8.1 Hz, 2H), 6.99 (d, J=7.8 Hz, 2H), 6.36—6.19 (m, 2H), 3.83 (s, 3H), 1.88 (d, J=4.8 Hz, 3H); IR (KBr) v: 3268, 3054, 3002, 1639, 1606, 1509 cm^{-1}; ESI-MS *m/z*: 219 $(M+H)^+$, 241 $(M+Na)^+$. Anal. calcd for $C_{12}H_{14}N_2O_2$: C 66.04, H 6.47, N 12.84; found C 65.66, H 6.28, N 12.73.

(*E*)-4-Methoxy-*N′*-octylidenebenzohydrazide (4d): White solid, m.p. 89—90 ℃; ^1H NMR (CD_3OD, 300 MHz) δ: 9.67 (s, 1H), 7.81 (d, J=7.8 Hz, 2H), 7.62 (br, 1H), 6.88 (d, J=8.4 Hz, 2H), 3.83 (s, 3H), 2.34—2.29 (m, 2H), 1.49—1.46 (m, 2H), 1.27 (br, 8H), 0.87 (t, J=5.7 Hz, 3H); IR (KBr) v: 3234, 1648, 1624, 1510, 1256 cm^{-1}; ESI-MS *m/z*: 277 $(M+H)^+$. Anal. calcd for $C_{16}H_{24}N_2O_2$: C 69.53, H 8.75, N 10.14; found C 69.34, H 8.67, N 10.02.

(*E*)-4-Methoxy-*N′*-(2-methylpropylidene)benzohydrazide (4e): White solid, m.p. 183—185 ℃; ^1H NMR ($CDCl_3$, 300 MHz) δ: 9.47 (br, 1H), 7.81 (br, 2H), 7.48 (s, 1H), 6.89 (d, J=8.4 Hz, 2H), 3.83 (s, 3H), 2.64 (br, 1H), 1.11 (s, 3H), 1.09 (s, 3H); ESI-MS *m/z*: 221 $(M+H)^+$. Anal. calcd for $C_{12}H_{16}N_2O_2$: C 65.43, H 7.32, N 12.72; found C 65.41, H 7.36, N 12.76.

(*E*)-*N′*-(Cyclohexylmethylene)-4-methoxybenzohydrazide (4f): White solid, m.p. 169—170 ℃; ^1H NMR (CD_3OD, 300 MHz) δ: 7.83 (d, J=8.4 Hz, 2H), 7.52 (d, J=6.0 Hz, 1H), 6.99 (d, J=8.4 Hz, 2H), 3.84 (s, 3H), 2.31 (br, 1H), 1.83—1.67 (m, 5H), 1.38—1.25 (m, 5H); IR (KBr) v: 3229, 1647, 1606, 1509, 1179 cm^{-1}; ESI-MS *m/z*: 261 $(M+H)^+$. Anal. calcd for $C_{15}H_{20}N_2O_2$: C 69.20, H 7.74, N 10.76; found C 69.14, H 7.71, N 10.65.

Representative procedure for the *gem*-difluoroallylation of hydrazones (Reaction mediated by indium powder or zinc powder using the same typical procedure as follows)

To a heterogeneous solution of benzaldehyde-derived acylhydrazone **1a** (45 mg, 0.20 mmol) and indium powder (39 mg, 0.34 mmol) in anhydrous DMF was added 3-bromo-3,3-difluoropropene **2** (54 mg, 0.34 mmol) at 0 ℃. Then, the reaction mixture was warmed up to room temperature and stirred until the starting material **1a** was completely consumed. After that, the reaction was quenched with 1 mol/L HCl (3 mL) and EtOAc (10 mL) was added. After the system was neutralized with saturated $NaHCO_3$, the mixture was extracted with EtOAc (20 mL×3). The combined organic layers were dried over anhydrous sodium sulfate, and the solvent was removed *in vacuo*. The residue was purified using chromatography on silica gel to give *N′*-(2,2-difluoro-1-phenylbut-3-enyl)benzohydrazide (**3a**) as a white solid (59 mg, 97% yield). m.p. 93—94 ℃; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.71 (br, 1H), 7.62—7.59 (m, 2H), 7.51—7.31 (m, 8H), 5.98—5.80 (m, 1H), 5.63—5.58 (m, 1H), 5.45 (d, J=11.1 Hz, 1H), 4.51 (dd, J=12.3, 9.3 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 167.38, 134.23, 132.53, 132.02, 130.42 (t, J=24.8 Hz), 129.37, 128.90, 128.69, 128.51, 126.92, 121.32 (t, J=8.8 Hz), 119.97 (t, J=244.8 Hz), 77.08 (t, J=32.3 Hz), 68.63 (t, J=25.4 Hz); ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −105.26 (dt, J=246.8, 11.3 Hz), −106.50 (dt, J=245.1, 13.8 Hz); IR (KBr) v: 3303, 3226, 3062, 1642, 1531 cm^{-1}; ESI-MS *m/z*: 303 $(M+H)^+$; HRMS calcd for $C_{17}H_{17}F_2N_2O$ 303.1304, found 303.1310.

***N′*-(2,2-Difluoro-1-(4-methoxyphenyl)but-3-enyl)benzohydrazide (3b)**: Liquid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.89 (s, 1H), 7.62 (d, J=7.5 Hz, 2H), 7.47 (t, J=7.5 Hz, 1H), 7.39—7.32 (m, 4H), 6.85 (d, J=8.4 Hz, 2H), 5.96—5.79 (m, 1H), 5.59 (d, J=17.4 Hz, 1H), 5.43 (d, J=11.1 Hz, 1H), 4.67 (br, 1H), 4.49—4.41 (m, 1H), 3.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 167.37, 159.93, 132.56, 131.96, 130.56 (t, J=26.7 Hz), 130.50, 128.65, 126.96, 126.21, 121.15 (t, J=10.8 Hz), 120.09 (t, J=245.5 Hz), 113.90, 67.97 (t, J=24.5 Hz), 55.24; ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −105.43 (dt, J=245.6, 13.0 Hz), −106.52 (dt, J=247.0, 9.9 Hz); IR (thin film) v: 3296, 3209, 3068, 1633, 1253 cm^{-1}; ESI-MS *m/z*: 333 $(M+H)^+$; HRMS calcd for $C_{18}H_{19}F_2N_2O_2$ 333.1409, found 333.1422.

***N′*-(2,2-Difluoro-1-*p*-tolylbut-3-enyl)benzohydrazide (3c)**: White solid, m.p. 82—83 ℃; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.71 (d, J=8.1 Hz, 1H), 7.63—7.60 (m, 2H), 7.51—7.46 (m, 1H), 7.40—7.30 (m, 4H), 7.15 (d, J=8.1 Hz, 2H), 5.98—5.80 (m, 1H), 5.61 (d, J=17.1 Hz, 1H), 5.45 (d, J=10.8 Hz, 1H), 4.46 (dd, J=12.6, 9.3 Hz, 1H), 4.20 (br, 1H), 2.34 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 167.26, 138.71, 132.57, 131.95, 131.15, 131.11, 130.51 (t, J=24.0 Hz), 129.22, 128.70, 126.90, 121.20 (t, J=9.7 Hz), 120.04 (t, J=244.2 Hz), 68.44 (t, J=24.8 Hz), 21.22; ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −105.26 (dt, J=247.6, 11.0 Hz), −106.44 (dt, J=247.3, 9.9 Hz); IR (KBr) v: 3254, 1643, 1531, 1516, 1472 cm^{-1}; ESI-MS *m/z*: 317 $(M+H)^+$; HRMS calcd for $C_{18}H_{19}F_2N_2O$ 317.1460, found 317.1473.

***N′*-(2,2-Difluoro-1-(2-methoxyphenyl)but-3-enyl)benzohydrazide (3d)**: Pale yellow solid, m.p. 103—104 ℃; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.71 (s, 1H), 7.65—7.62 (m, 2H), 7.57 (d, J=8.1 Hz, 1H), 7.51—7.46 (m, 1H), 7.41—7.37 (m, 2H), 7.33—7.26 (m, 1H), 7.00—6.95 (m, 1H), 6.87 (d, J=8.4 Hz, 1H), 6.02—5.85 (m, 1H), 5.58 (dt, J=17.1, 2.1 Hz, 1H), 5.40 (d, J=11.1 Hz, 1H), 5.09 (dd, J=15.6, 8.4 Hz, 1H), 3.76 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 166.88, 157.99, 132.76, 131.83, 130.87 (t, J=26.9 Hz), 129.76, 129.18, 128.66, 126.90, 122.78, 120.65 (t, J=5.5 Hz), 120.45 (t, J=245.8 Hz), 111.08, 60.35 (t, J=26.9 Hz), 55.73; ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −104.77 (dt, J=243.6, 9.9 Hz), −107.95 (dt, J=243.6, 11.6 Hz); IR (KBr) v: 3255, 1641, 1531, 1495, 1253 cm^{-1}; ESI-MS *m/z*: 333 $(M+H)^+$; HRMS calcd for $C_{18}H_{18}F_2N_2NaO_2$ 355.1229, found 355.1243.

***N′*-(1-(2-Chlorophenyl)-2,2-difluorobut-3-enyl)benzohydrazide (3e)**: White solid, m.p. 108—110 ℃; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.73 (d, J=6.3 Hz, 1H), 7.64—7.61 (m, 3H), 7.49 (t, J=7.8 Hz, 1H), 7.41—7.36 (m, 3H), 7.33—7.27 (m, 2H), 6.03—5.85 (m, 1H), 5.62 (d, J=17.4 Hz, 1H), 5.46 (d, J=11.4 Hz, 1H), 5.18 (dd, J=12.9, 9.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 167.43, 135.58, 132.48, 132.28, 132.25, 132.00, 130.38 (t, J=25.4 Hz), 130.09, 129.87, 129.76, 128.70, 126.96, 121.51 (d, J=9.2 Hz), 119.84 (t, J=246.6 Hz), 63.72 (t, J=25.4 Hz); ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −105.96 (dt, J=245.3, 12.1 Hz), −107.39 (dt, J=245.1, 12.4 Hz); IR (KBr) v: 3294, 3238, 3061, 1641, 1534, 1475 cm^{-1}; ESI-MS *m/z*: 337 $(M+H)^+$, 359 $(M+Na)^+$, 375 $(M+K)^+$, 695 $(2M+Na)^+$; HRMS calcd for $C_{17}H_{16}ClF_2N_2O$ 337.0914, found 337.0924.

***N′*-(1-(4-Chlorophenyl)-2,2-difluorobut-3-enyl)benzohydrazide (3f)**: Pale yellow solid, m.p. 73—74 ℃; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.63—7.60 (m, 3H), 7.54—7.48 (m, 1H), 7.43—7.26 (m, 6H), 5.98—5.80 (m, 1H), 5.62 (d, J=17.1 Hz, 1H), 5.53 (d, J=12.0 Hz, 1H), 4.51 (dd, J=12.3, 9.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 167.49, 134.88, 132.76, 132.21, 132.16, 130.73, 130.13 (t, J=26.0 Hz), 128.77, 126.88, 121.72 (t, J=8.6 Hz), 119.62 (t, J=244.7 Hz), 67.96 (t, J=24.8 Hz); ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −105.03 (dt, J=247.3, 10.4 Hz), −107.14 (dt, J=248.2, 9.0 Hz); IR (KBr) v: 3290, 1647, 1491, 1467, 1092 cm^{-1}; ESI-MS *m/z*: 337 $(M+H)^+$; HRMS calcd for $C_{17}H_{16}ClF_2N_2O$ 337.0914, found 337.0929.

***N′*-(1-(3-Chlorophenyl)-2,2-difluorobut-3-enyl)benzohydrazide (3g)**: Liquid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.75 (d, J=9.9 Hz, 1H), 7.64—7.61 (m, 2H), 7.53—7.47 (m, 2H), 7.41—7.31 (m, 2H), 7.30—7.25 (m, 3H), 5.98—5.81 (m, 1H), 5.63 (d, J=17.4 Hz, 1H), 5.50 (d, J=11.4 Hz, 1H), 4.50 (dd, J=12.3, 9.6 Hz, 1H); ^{13}C

NMR ($CDCl_3$, 75.5 MHz) δ: 167.65, 136.34 (t, J=2.0 Hz), 134.40, 132.29, 132.13, 130.08 (t, J=25.5 Hz), 129.37, 129.12, 128.72, 127.79, 126.97, 126.84, 121.76 (t, J=10.0 Hz), 119.55 (t, J=244.8 Hz), 68.07 (t, J=26.5 Hz); ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −104.69 (dt, J=246.8, 13.5 Hz), −107.12 (dt, J=246.5, 12.1 Hz); IR (KBr) v: 3306, 3256, 3064, 1633, 1532, 694 cm^{-1}; ESI-MS *m/z*: 337 $(M+H)^+$; HRMS calcd for $C_{17}H_{16}ClF_2N_2O$ 337.0914, found 337.0928.

***N′*-(1-(2,4-Dichlorophenyl)-2,2-difluorobut-3-enyl)-benzohydrazide (3h)**: Liquid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.71—7.61 (m, 4H), 7.53—7.47 (m, 1H), 7.41—7.36 (m, 3H), 7.29—7.26 (m, 1H), 6.02—5.85 (m, 1H), 5.67—5.59 (m, 1H), 5.49 (d, J=11.4 Hz, 1H), 5.40 (br, 1H), 5.13 (t, J=11.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 167.62, 136.29, 135.17, 132.26, 132.15, 131.05 (t, J=2.6 Hz), 130.15 (t, J=26.3 Hz), 129.52, 128.73, 127.36, 126.96, 121.84 (t, J=9.8 Hz), 119.53 (t, J=246.6 Hz), 63.28 (t, J=24.2 Hz); ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −106.80 (d, J=7.1 Hz); IR (thin film) v: 3308, 3059, 1641, 1473, 1313 cm^{-1}; ESI-MS *m/z*: 371 $(M+H)^+$, 391 $(M+Na)^+$; HRMS calcd for $C_{17}H_{15}Cl_2F_2N_2O$ 371.0524, found 371.0537.

***N′*-(2,2-Difluoro-1-(3-nitrophenyl)but-3-enyl)benzohydrazide (3i)**: Liquid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 8.37 (s, 1H), 8.20 (dd, J=8.4, 1.2 Hz, 1H), 7.91 (s, 1H), 7.78 (d, J=7.5 Hz, 1H), 7.63—7.60 (m, 2H), 7.56—7.47 (m, 2H), 7.38 (t, J=7.8 Hz, 2H), 6.05—5.88 (m, 1H), 5.64 (d, J=17.1 Hz, 1H), 5.55 (d, J=11.1 Hz, 1H), 4.69 (t, J=9.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 167.90, 148.25, 136.59 (t, J=2.6 Hz), 135.87, 132.33, 131.96, 129.70 (t, J=25.4 Hz), 129.45, 128.79, 126.92, 124.27, 123.93, 122.38 (t, J=4.9 Hz), 119.12 (t, J=243.9 Hz), 67.76 (t, J=26.3 Hz); ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −103.23 (dt, J=250.1, 9.9 Hz), −108.36 (dt, J=249.3, 15.5 Hz); IR (thin film) v: 3294, 1645, 1581, 1532, 1353 cm^{-1}; ESI-MS *m/z*: 348 $(M+H)^+$; HRMS calcd for $C_{17}H_{16}F_2N_3O_3$ 348.1154, found 348.1168.

***N′*-(1-(2,4-Dihydroxyphenyl)-2,2-difluorobut-3-enyl)benzohydrazide (3j)**: White solid, m.p. 78—80 ℃; ^{1}H NMR (CD_3SOCD_3, 300 MHz) δ: 9.45 (s, 1H), 8.96 (s, 1H), 8.37 (s, 1H), 7.82—7.79 (m, 2H), 7.54—7.48 (m, 1H), 7.44—7.39 (m, 2H), 7.16 (d, J=8.1 Hz, 1H), 6.38—6.32 (m, 2H), 6.18—6.01 (m, 1H), 5.64—5.57 (m, 2H), 5.48 (d, J=11.4 Hz, 1H), 4.82 (t, J=11.4 Hz, 1H); ^{13}C NMR (CD_3SOCD_3, 75.5 MHz) δ: 205.63, 166.86, 158.66, 157.92, 133.03, 131.57 (t, J=12.5 Hz), 131.07, 128.35, 127.25, 120.57, 120.04 (t, J=9.7 Hz), 118.50, 106.99 (dd, J=330.7, 324.0 Hz), 63.08 (t, J=25.6 Hz); ^{19}F NMR (CD_3SOCD_3, 282 MHz) δ: −104.73 (dt, J=245.6, 9.6 Hz), −107.23 (dt, J=243.9, 13.5 Hz); IR (KBr) v: 3280, 1623, 1518, 1313, 997 cm^{-1}; ESI-MS *m/z*: 335 $(M+H)^+$, 357 $(M+Na)^+$, 691 $(2M+Na)^+$; HRMS calcd for $C_{17}H_{16}F_2N_2NaO_3$ 357.1021, found 357.1038.

(*E*)-*N′*-(4,4-Difluoro-1-phenylhexa-1,5-dien-3-yl)-benzohydrazide (3k): Liquid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 8.00 (s, 1H), 7.71 (d, J=7.5 Hz, 2H), 7.49 (t, J=7.2 Hz, 1H), 7.41—7.25 (m, 7H), 6.74 (d, J=15.9 Hz, 1H), 6.13—5.96 (m, 1H), 5.74 (d, J=17.7 Hz, 1H), 5.54 (d, J=11.1 Hz, 1H), 4.25 (br, 1H), 4.10—4.07 (m, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 167.50, 137.73, 135.98, 132.51, 132.07, 130.57 (t, J=25.9 Hz), 128.79, 128.68, 128.41, 126.96, 126.79, 121.38 (t, J=8.6 Hz), 119.96 (t, J=245.7 Hz), 67.21 (t, J=26.2 Hz); ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −105.13 (dt, J=262.8, 9.6 Hz), −107.21 (dt, J=263.1, 12.9 Hz); IR (KBr) v: 3279, 1641, 1579, 1319, 969 cm^{-1}; ESI-MS *m/z*: 329 $(M+H)^+$, 351 $(M+Na)^+$; HRMS calcd for $C_{19}H_{18}F_2N_2NaO$ 351.1279, found 351.1296.

(*E*)-*N′*-(3,3-Difluorohepta-1,5-dien-4-yl)benzohydrazide (3l): Liquid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 8.05 (s, 1H), 7.75—7.72 (m, 2H), 7.54—7.49 (m, 1H), 7.42 (t, J=7.5 Hz, 2H), 6.05—5.83 (m, 2H), 5.70 (d, J=17.4 Hz, 1H), 5.54—5.49 (m, 1H), 5.42—5.34 (m, 1H), 4.67 (br, 1H), 3.90—3.81 (m, 1H), 1.71 (dd, J=6.3, 1.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 167.30, 134.70, 132.62, 131.98, 130.65 (t, J=27.4 Hz), 128.71, 126.95, 123.34 (t, J=2.0 Hz), 120.94 (t, J=9.2 Hz), 120.10 (t, J=245.3 Hz), 67.03 (t, J=25.1 Hz), 18.16; ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −105.43 (dt, J=213.9, 12.7 Hz), −107.47 (ddd, J=247.6, 12.1, 7.9 Hz); IR (thin film) v: 3286, 3064, 1642, 1537, 1317 cm^{-1}; ESI-MS *m/z*: 267 $(M+H)^+$; HRMS calcd for $C_{14}H_{17}F_2N_2O$ 267.1304, found 267.1299.

***N′*-(3,3-Difluoroundec-1-en-4-yl)benzohydrazide (3m)**: Liquid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.89 (s, 1H), 7.74 (d, J=7.2 Hz, 2H), 7.52 (t, J=6.9 Hz, 1H), 7.43 (t, J=8.1 Hz, 2H), 6.16—5.98 (m, 1H), 5.73 (d, J=9.0 Hz, 1H), 5.54 (d, J=11.1 Hz, 1H), 4.65 (br, 1H), 3.22—3.12 (m, 1H), 1.74—1.67 (m, 1H), 1.63—1.60 (m, 2H), 1.57—1.26 (m, 9H), 0.88 (t, J=6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 166.79, 132.64, 131.92, 130.35 (t, J=26.2 Hz), 128.71, 126.92, 121.90 (t, J=243.4 Hz), 120.74 (t, J=9.1 Hz), 65.33 (dd, J=26.9, 21.5 Hz), 31.80, 29.65, 29.01, 27.73 (d, J=2.7 Hz), 26.15, 22.65, 4.73; ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −102.96 (dt, J=249.6 Hz, 10.7 Hz), −107.26 (ddd, J=249.3, 14.1, 8.2 Hz); IR (thin film) v: 3304, 1639, 1536, 1468, 989 cm^{-1}; ESI-MS *m/z*: 325 $(M+H)^+$, 671 $(2M+Na)^+$; HRMS calcd for $C_{18}H_{27}F_2N_2O$ 325.2086, found 325.2100.

***N′*-(4,4-Difluoro-2-methylhex-5-en-3-yl)benzohydrazide (3n)**: Liquid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.96 (s, 1H), 7.72—7.69 (m, 2H), 7.50—7.45 (m, 1H), 7.42—7.36 (m, 2H), 6.17—5.99 (m, 1H), 5.77—5.70 (m, 1H), 5.50 (d, J=11.1 Hz, 1H), 4.67 (br, 1H), 3.05—2.96 (m, 1H), 2.01—1.92 (m, 1H), 1.15 (dd, J=6.9, 1.2 Hz, 3H), 1.08 (d, J=7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 166.57, 132.70, 131.88, 131.13 (t, J=25.3 Hz), 128.70, 126.90, 122.06 (t, J=246.2 Hz), 120.34 (t, J=8.8 Hz), 69.79 (dd, J=25.1, 22.1 Hz), 27.13, 21.00, 17.94; ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −100.05 (dt, J=251.8, 10.4 Hz), −103.22 (dt, J=251.3, 12.4 Hz); IR (KBr) v: 3300, 3066, 1713, 1639, 1506, 1224 cm^{-1}; ESI-MS *m/z*: 269 $(M+H)^+$, 291

$(M + Na)^+$, 559 $(2M + Na)^+$; HRMS calcd for $C_{14}H_{19}F_2N_2O$ 269.1460, found 269.1467.

***N′*-(1-(Benzyloxy)-3,3-difluoropent-4-en-2-yl)benzohydrazide (3o)**: Liquid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 8.09 (s, 1H), 7.72 (d, J=7.2 Hz, 2H), 7.52 (t, J=7.8 Hz, 1H), 7.43—7.28 (m, 7H), 6.18—6.01 (m, 1H), 5.75 (d, J=17.7 Hz, 1H), 5.53 (d, J=10.8 Hz, 1H), 5.05 (br, 1H), 4.69 (d, J=11.4 Hz, 1H), 4.55 (d, J=11.4 Hz, 1H), 3.80—3.75 (m, 1H), 3.72—3.63 (m, 2H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 166.64, 137.55, 132.67, 131.89, 130.39 (t, J=25.6 Hz), 128.69, 128.55, 127.96, 127.92, 126.93, 120.89 (t, J=9.7 Hz), 120.14 (t, J=242.4 Hz), 73.39, 67.06 (q, J=2.9 Hz), 63.72 (t, J=25.1 Hz); ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −102.56 (dt, J=254.6, 8.7 Hz), −106.32 (dt, J=255.5, 12.4 Hz); IR (thin film) ν: 3300, 3065, 1651, 1535, 1455 cm^{-1}; ESI-MS *m/z*: 347 $(M+H)^+$, 369 $(M+Na)^+$, 384 $(M+K)^+$; HRMS calcd for $C_{19}H_{21}F_2N_2O_2$ 347.1566, found 347.1582.

***N′*-(1-Cyclohexyl-2,2-difluorobut-3-enyl)benzohydrazide (3p)**: White solid, m.p. 42—44 ℃; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.92 (s, 1H), 7.74—7.72 (m, 2H), 7.53—7.48 (m, 1H), 7.42 (t, J=7.5 Hz, 2H), 6.19—6.02 (m, 1H), 5.75 (d, J=17.4 Hz, 1H), 5.53 (d, J=11.1 Hz, 1H), 5.12 (br, 1H), 3.04—2.95 (m, 1H), 2.00 (d, J=9.0 Hz, 1H), 1.77—1.50 (m, 6H), 1.31—1.15 (m, 4H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 166.44, 132.68, 131.89, 131.19 (t, J=25.2 Hz), 128.71, 126.88, 122.14 (t, J=244.6 Hz), 120.34 (t, J=9.7 Hz), 69.96 (dd, J=26.8, 22.1 Hz), 37.32, 31.18, 28.17, 26.62, 26.45, 26.11; ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −99.17 (dt, J=249.6, 12.7 Hz), −102.97 (dt, J=251.0, 12.1 Hz); IR (KBr) ν: 3297, 3066, 1635, 1451, 990 cm^{-1}; ESI-MS *m/z*: 309 $(M+H)^+$; HRMS calcd for $C_{17}H_{23}F_2N_2O$ 309.1773, found 309.1773.

***N′*-((*R*)-1-((*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl)-2,2-difluorobut-3-enyl)benzohydrazide (*anti*-3q)**: Liquid, $[\alpha]_D^{28}$ −41.2 (*c* 1.90, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.84 (s, 1H), 7.72—7.69 (m, 2H), 7.53—7.48 (m, 1H), 7.39 (t, J=7.5 Hz, 2H), 6.26—6.08 (m, 1H), 5.77 (d, J=17.4 Hz, 1H), 5.58 (d, J=10.8 Hz, 1H), 4.75 (br, 1H), 4.26—4.19 (m, 1H), 4.14—4.05 (m, 2H), 3.34 (dd, J=16.2, 9.0 Hz, 1H), 1.51 (s, 3H), 1.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 166.53, 132.77, 131.93, 130.22 (t, J=23.9 Hz), 128.73, 126.84, 121.11 (t, J=9.7 Hz), 117.17 (t, J=243.0 Hz), 109.75, 73.16 (d, J=6.1 Hz), 67.62 (t, J=4.8 Hz), 66.39 (dd, J=28.3, 24.8 Hz), 26.39, 25.51; ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −98.64 (dt, J=255.8, 10.4 Hz), −107.01 (ddd, J=259.9, 13.3, 9.9 Hz); IR (thin film) ν: 3304, 1652, 1422, 1063, 991 cm^{-1}; ESI-MS *m/z*: 327 $(M+H)^+$, 349 $(M+Na)^+$, 675 $(2M+Na)^+$; HRMS calcd for $C_{16}H_{21}F_2N_2O_3$ 327.1515, found 317.1521.

***N′*-((*S*)-1-((*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl)-2,2-difluorobut-3-enyl)benzohydrazide (*syn*-3q)**: White solid, m.p. 86—88 ℃; $[\alpha]_D^{28}$ +12.2 (*c* 2.10, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.88 (s, 1H), 7.71 (d, J=7.2 Hz, 2H), 7.49 (t, J=6.9 Hz, 1H), 7.40 (t, J=7.5 Hz, 2H), 6.15—5.98 (m, 1H), 5.74 (d, J=17.4 Hz, 1H), 5.55 (d, J=11.1 Hz, 1H), 4.34—4.33 (m, 1H), 4.18 (t, J=8.4 Hz, 1H), 4.00 (t, J=7.5 Hz, 1H), 3.62—3.53 (m, 1H), 1.52 (s, 3H), 1.34 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 166.36, 132.58, 131.96, 130.84 (t, J=24.2 Hz), 128.75, 126.86, 121.23 (t, J=9.6 Hz), 116.85 (t, J=245.1 Hz), 108.98, 73.32 (t, J=2.6 Hz), 65.41, 64.95 (d, J=2.9 Hz), 26.32, 24.78; ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −103.85 (dt, J=253.0, 9.9 Hz), −105.69 (dt, J=251.8, 11.8 Hz); IR (KBr) ν: 3315, 1644, 1534, 1473, 1056 cm^{-1}; ESI-MS *m/z*: 327 $(M+H)^+$, 349 $(M+Na)^+$, 675 $(2M+Na)^+$; HRMS calcd for $C_{16}H_{21}F_2N_2O_3$ 327.1515, found 317.1523.

***N′*-(2,2-Difluoro-1-phenylbut-3-enyl)-4-methoxybenzohydrazide (5a)**: White solid, m.p. 106—108 ℃; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.67 (s, 1H), 7.58 (d, J=8.4 Hz, 2H), 7.41—7.34 (m, 2H), 7.26 (br, 3H), 6.86 (d, J=8.4 Hz, 2H), 5.98—5.80 (m, 1H), 5.60 (d, J=17.4 Hz, 1H), 5.45 (d, J=11.1 Hz, 1H), 4.53—4.45 (m, 1H), 3.81 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 166.95, 162.59, 134.34, 130.48 (t, J=24.7 Hz), 129.39, 128.84, 128.74, 124.73, 121.25 (t, J=9.7 Hz), 119.97 (t, J=245.6 Hz), 113.94, 68.69 (t, J=25.6 Hz), 55.41; ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −105.13 (dt, J=245.6, 12.4 Hz), −106.63 (dt, J=247.9, 13.0 Hz); IR (KBr) ν: 3296, 3227, 1627, 1607, 1523 cm^{-1}; ESI-MS *m/z*: 333 $(M+H)^+$; HRMS calcd for $C_{18}H_{19}F_2N_2O_2$ 333.1409, found 333.1412.

***N′*-(1-(4-(Dimethylamino)phenyl)-2,2-difluorobut-3-enyl)-4-methoxybenzohydrazide (5b)**: Pale yellow solid, m.p. 142—144 ℃; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.60 (d, J=8.7 Hz, 3H), 7.28 (d, J=8.4 Hz, 2H), 6.87 (d, J=8.7 Hz, 2H), 6.68 (d, J=8.4 Hz, 2H), 5.98—5.81 (m, 1H), 5.61 (d, J=17.7 Hz, 1H), 5.43 (d, J=11.1 Hz, 1H), 5.30 (br, 1H), 4.37 (t, J=11.1 Hz, 1H), 3.18 (s, 3H), 2.95 (s, 6H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 166.75, 162.48, 150.61, 130.90 (t, J=26.3 Hz), 130.11, 128.75, 124.96, 121.71, 120.81 (t, J=9.5 Hz), 120.31 (t, J=245.1 Hz), 113.88, 112.25, 68.20 (t, J=24.8 Hz), 55.40, 40.47; ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −105.86 (s, 2F); IR (KBr) ν: 3288, 3240, 3072, 1637, 1612, 1525 cm^{-1}; ESI-MS *m/z*: 376 $(M+H)^+$; HRMS calcd for $C_{20}H_{23}F_2N_3NaO_2$ 398.1651, found 398.1659.

(*E*)-*N′*-(3,3-Difluorohepta-1,5-dien-4-yl)-4-methoxybenzohydrazide (5c): Liquid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.85 (s, 1H), 7.73—7.69 (m, 2H), 6.94—6.90 (m, 2H), 6.05—5.84 (m, 2H), 5.71 (d, J=17.1 Hz, 1H), 5.52 (d, J=10.8 Hz, 1H), 5.43—5.34 (m, 1H), 4.02 (br, 1H), 3.84 (s, 3H), 3.81—3.79 (m, 1H), 1.72 (dd, J=6.3, 1.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 166.84, 162.57, 134.61, 130.75 (t, J=24.8 Hz), 128.73, 124.86, 123.41 (t, J=4.5 Hz), 120.85 (t, J=10.0 Hz), 120.13 (t, J=244.2 Hz), 113.94, 67.08 (t, J=26.0 Hz), 55.42, 18.14; ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −115.39 (dt, J=247.9, 11.8 Hz), −117.53 (dt, J=246.5, 11.6 Hz); IR (thin film) ν: 3289, 1637, 1608, 1463, 1259 cm^{-1}; ESI-MS *m/z*: 297 $(M+H)^+$, 319 $(M+Na)^+$, 351 $(M+MeOH+Na)^+$; HRMS calcd for $C_{15}H_{19}F_2N_2O_2$ 297.1409, found 297.1423.

***N′*-(3,3-Difluoroundec-1-en-4-yl)-4-methoxybenzohydrazide (5d)**: Liquid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.79 (s, 1H), 7.73—7.69 (m, 2H), 6.95—6.91 (m, 2H), 6.15—5.98 (m, 1H), 5.73 (d, J=17.4 Hz, 1H), 5.54 (d, J=11.1 Hz, 1H), 4.08 (br, 1H), 3.84 (s, 3H), 3.21—3.11 (m, 1H), 1.73—1.66 (m, 1H), 1.62—1.59 (m, 2H), 1.56—1.27 (m, 9H), 0.87 (t, J=6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 166.45, 162.53, 130.44 (t, J=24.0 Hz), 128.71, 124.88, 121.90 (t, J=243.6 Hz), 120.67 (t, J=8.0 Hz), 113.94, 65.36 (dd, J=27.3, 23.0 Hz), 55.40, 31.80, 29.67, 28.99, 27.73 (d, J=4.7 Hz), 26.14, 22.63, 14.06; ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −103.01 (dt, J=249.3, 10.4 Hz), −107.32 (ddd, J=249.9, 14.1, 8.2 Hz); IR (thin film) v: 3298, 1637, 1608, 1467, 1258 cm^{-1}; ESI-MS m/z: 355 $(M+H)^+$; HRMS calcd for $C_{19}H_{29}F_2N_2O_2$ 355.2192, found 355.2203.

***N′*-(4,4-Difluoro-2-methylhex-5-en-3-yl)-4-methoxybenzohydrazide (5e)**: Liquid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.79 (br, 1H), 7.72—7.67 (m, 2H), 6.94—6.89 (m, 2H), 6.19—6.02 (m, 1H), 5.79—5.72 (m, 1H), 5.53 (d, J=11.1 Hz, 1H), 4.17 (br, 1H), 3.84 (s, 3H), 3.05—2.97 (m, 1H), 2.05—1.94 (m, 1H), 1.17 (dd, J=6.9, 1.2 Hz, 3H), 1.11 (d, J=6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 166.23, 162.49, 131.22 (t, J=25.5 Hz), 128.68, 124.94, 122.08 (t, J=244.9 Hz), 120.26 (t, J=9.7 Hz), 113.94, 69.80 (dd, J=26.2, 21.6 Hz), 55.40, 27.16, 21.03, 17.96; ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −100.07 (dt, J=267.6, 9.9 Hz), −103.31 (dt, J=267.6, 12.3 Hz); IR (thin film) v: 3299, 1631, 1609, 1512, 1258 cm^{-1}; ESI-MS m/z: 299 $(M+H)^+$, 321 $(M+Na)^+$; HRMS calcd for $C_{15}H_{21}F_2N_2O_2$ 299.1566, found 299.1576.

***N′*-(1-Cyclohexyl-2,2-difluorobut-3-enyl)-4-methoxybenzohydrazide (5f)**: Liquid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.75 (s, 1H), 7.70 (d, J=9.0 Hz, 2H), 6.92 (d, J=8.1 Hz, 2H), 6.20—6.02 (m, 1H), 5.76 (d, J=17.4 Hz, 1H), 5.53 (d, J=11.1 Hz, 1H), 4.21 (br, 1H), 3.82 (s, 3H), 3.03—2.94 (m, 1H), 2.04—1.99 (m, 1H), 1.77—1.54 (m, 6H), 1.31—1.21 (m, 4H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 166.12, 162.50, 131.26 (t, J=25.4 Hz), 128.67, 124.92, 122.14 (t, J=243.2 Hz), 120.23 (t, J=10.0 Hz), 113.93, 69.96 (dd, J=25.0, 22.1 Hz), 55.40, 37.31, 31.18 (d, J=3.0 Hz), 28.17, 26.64, 26.46, 26.13; ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −99.24 (dt, J=252.7, 8.2 Hz), −103.10 (dt, J=251.5, 13.0 Hz); IR (thin film) v: 3298, 1634, 1608, 1257, 1180 cm^{-1}; ESI-MS m/z: 339 $(M+H)^+$, 361 $(M+Na)^+$; HRMS calcd for $C_{18}H_{25}F_2N_2O_2$ 339.1879, found 339.1892.

***N′*-(2,2-Difluoro-1-phenylbut-3-enyl)-4-nitrobenzohydrazide (5g)**: Pale yellow solid, m.p. 122—124 ℃; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 8.26 (d, J=8.7 Hz, 2H), 7.78 (d, J=9.0 Hz, 2H), 7.66 (d, J=3.3 Hz, 1H), 7.44—7.37 (m, 5H), 5.97—5.80 (m, 1H), 5.62 (d, J=17.1 Hz, 1H), 5.48 (d, J=11.4 Hz, 1H), 5.39 (br, 1H), 4.52 (t, J=11.1 Hz, 1H); ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −105.81 (d, J=12.4 Hz), −105.89 (d, J=12.1 Hz); IR (KBr) v: 3313, 3004, 1641, 1600, 1523 cm^{-1}; ESI-MS m/z: 348 $(M+H)^+$; HRMS calcd for $C_{17}H_{15}F_2N_3NaO_3$ 370.0974, found 370.0973. Anal. calcd for $C_{17}H_{15}F_2N_3O_3$: C 58.79, H 4.35, N 12.10; found C 56.95, H 4.55, N 10.01.

***N′*-(3,3-Difluoro-2-phenylpent-4-en-2-yl)benzohydrazide (7a)**: White solid, m.p. 64—66 ℃; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.63 (t, J=6.3 Hz, 4H), 7.47 (t, J=7.5 Hz, 1H), 7.41—7.34 (m, 5H), 5.99—5.81 (m, 1H), 5.51 (d, J=17.7 Hz, 1H), 5.41 (d, J=10.8 Hz, 1H), 1.73 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 166.89, 138.27, 132.49, 131.93, 130.02 (t, J=24.5 Hz), 128.72, 128.36, 128.26, 128.11, 126.85, 121.18 (t, J=9.5 Hz), 117.88 (t, J=210.5 Hz), 67.38 (t, J=25.7 Hz), 17.62 (t, J=2.1 Hz); ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −107.37 (dd, J=245.1, 11.8 Hz), −109.52 (dd, J=244.2, 14.1 Hz); IR (KBr) v: 3284, 3063, 1711, 1648, 1456 cm^{-1}; ESI-MS m/z: 317 $(M+H)^+$, 339 $(M+Na)^+$, 655 $(2M+Na)^+$; HRMS calcd for $C_{18}H_{19}F_2N_2O$ 317.1460, found 317.1466.

***N′*-(3,3-Difluoro-2-methylpent-4-en-2-yl)benzohydrazide (7b)**: White solid, m.p. 130—132 ℃; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.75 (d, J=7.2 Hz, 2H), 7.56—7.51 (m, 2H), 7.45 (t, J=7.5 Hz, 2H), 6.25—6.07 (m, 1H), 5.73 (d, J=17.4 Hz, 1H), 5.55 (d, J=11.1 Hz, 1H), 4.51 (br, 1H), 1.23 (s, 6H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 167.17, 132.57, 131.98, 130.13 (t, J=25.4 Hz), 128.79, 126.33, 122.63 (t, J=279.4 Hz), 120.89 (t, J=9.7 Hz), 61.51 (t, J=22.6 Hz), 19.89, 19.86; ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −110.59 (d, J=9.3 Hz, 2F); IR (KBr) v: 3279, 3197, 1637, 1462, 1056 cm^{-1}; ESI-MS m/z: 255 $(M+H)^+$, 277 $(M+Na)^+$, 313 $(M+K)^+$; HRMS calcd for $C_{13}H_{16}F_2N_2NaO$ 277.1123, found 277.1129.

***N′*-(4,4-Difluoro-3-methylhex-5-en-3-yl)benzohydrazide (7c)**: Liquid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.72 (d, J=7.8 Hz, 2H), 7.55—7.47 (m, 2H), 7.42 (t, J=7.5 Hz, 2H), 6.25—6.08 (m, 1H), 5.70 (d, J=17.4 Hz, 1H), 5.51 (d, J=11.4 Hz, 1H), 4.71 (br, 1H), 1.69—1.55 (m, 2H), 1.18 (s, 3H), 1.00 (t, J=7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 166.67, 132.69, 131.85, 130.38 (t, J=27.1 Hz), 128.75, 126.85, 123.38 (t, J=247.6 Hz), 120.61 (t, J=10.1 Hz), 63.51 (t, J=24.7 Hz), 25.38 (t, J=1.7 Hz), 15.35 (t, J=2.3 Hz), 7.42; ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −107.34 (dd, J=245.9, 9.0 Hz), −108.46 (dd, J=250.4, 14.1 Hz); IR (thin film) v: 3294, 3066, 1641, 1467, 1174, 1082 cm^{-1}; ESI-MS m/z: 269 $(M+H)^+$, 291 $(M+Na)^+$; HRMS calcd for $C_{14}H_{19}F_2N_2O$ 269.1460, found 269.1474.

***N′*-(1-(1,1-Difluoroallyl)cyclopentyl)benzohydrazide (7d)**: White solid, m.p. 84—86 ℃; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.74—7.72 (m, 2H), 7.57—7.46 (m, 2H), 7.43—7.41 (m, 2H), 6.31—6.13 (m, 1H), 5.79—5.72 (m, 1H), 5.54 (d, J=11.1 Hz, 1H), 4.66 (br, 1H), 1.87 (br, 4H), 1.67 (br, 4H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 166.73, 132.57, 131.91, 130.86 (t, J=25.0 Hz), 128.75, 126.83, 122.79 (t, J=245.4 Hz), 120.52 (t, J=9.7 Hz), 72.66 (t, J=24.8 Hz), 31.24 (t, J=2.4 Hz), 25.25; ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −107.10 (d, J=11.6 Hz); IR (KBr) v: 3294, 3213, 1622, 1557, 1465

cm^{-1}; ESI-MS *m/z*: 281 $(M+H)^+$, 303 $(M+Na)^+$, 583 $(2M+Na)^+$; HRMS calcd for $C_{15}H_{19}F_2N_2O$ 281.1460, found 281.1473.

2,2-Difluoro-1-phenylbut-3-en-1-amine (8): To a solution of **3a** (45 mg, 0.15 mmol) in MeOH (0.5 mL) under N_2 was added SmI_2 (5 mL, 0.1 mol/L in THF) dropwise. After 30 min, the dark blue solution was opened to air, and the color changed to yellow. Removal of all the solvent in vacuo and flash chromatography [*V*(hexane) ∶ *V*(EtOAc) ∶ *V*(Et_3N) = 4 ∶ 1 ∶ 0.005] of the residue gave the compound **8** (24 mg, 88% yield) as a clear oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.36—7.26 (m, 5H), 5.90—5.73 (m, 1H), 5.57 (d, J=17.7 Hz, 1H), 5.42 (d, J=10.5 Hz, 1H), 4.23 (t, J=11.7 Hz, 1H), 2.21 (br, 2H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 137.63, 130.41 (t, J=19.6 Hz), 128.30, 128.23, 128.15, 120.88 (t, J=7.0 Hz), 120.61 (t, J=183.2 Hz), 60.86 (t, J=21.3 Hz); ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −106.80 (dt, J=241.1, 10.7 Hz), −109.00 (dt, J=241.4, 11.8 Hz); IR (thin film) *v*: 3105, 3035, 1455, 1404, 990 cm^{-1}; ESI-MS *m/z*: 184 $(M+H)^+$; HRMS calcd for $C_{10}H_{11}F_2N$ 184.0932, found 184.0937.

***N*-(2,2-Difluoro-1-phenylbut-3-enyl)-2,2,2-trifluoroacetamide (9)**: Trifluoroacetic anhydride (207 mg, 0.98 mmol) was added dropwise to a solution of **8** in 3 mL of anhydrous CH_2Cl_2 at room temperature. After 12 h the reaction was concentrated *in vacuo* and flash chromatography gave compound **9** (110 mg, 80% yield). White solid, m.p. 78—79 ℃; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.40—7.26 (m, 5H), 6.97 (d, J=7.2 Hz, 1H), 5.84—5.66 (m, 2H), 5.53—5.49 (m, 1H), 5.42—5.30 (m, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 156.54 (q, J=28.7 Hz), 132.76, 129.49 (t, J=19.1 Hz), 129.19, 128.86, 128.09, 122.20 (t, J=6.7 Hz), 118.65 (t, J=184.9 Hz), 114.05 (t, J=216.4 Hz), 57.69 (t, J=20.2 Hz); ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −76.16 (s, 3F), −106.67 (ddd, J=244.8, 11.3, 4.2 Hz, 1F), −108.22 (ddd, J=245.5, 14.7, 6.2 Hz, 1F); IR (KBr) *v*: 3316, 1712, 1560, 1212, 1184 cm^{-1}; ESI-MS *m/z*: 297 $(M+NH_4)^+$, 302 $(M+Na)^+$; HRMS calcd for $C_{12}H_{10}F_5NO$ 279.0683, found 279.0674. Anal. calcd for $C_{12}H_{10}F_5NO$: C 51.62, H 3.61, N 5.02; found C 51.60, H 3.64, N 5.03.

***N*-(2,2-Difluoro-1-phenylbut-3-enyl)acrylamide (10)**: White solid, m.p. 99—100 ℃; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.38—7.24 (m, 6H), 6.34—6.20 (m, 2H), 5.86—5.73 (m, 1H), 5.66—5.50 (m, 3H), 5.40 (d, J=10.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ: 165.65, 135.23, 135.21, 130.88 (t, J=19.3 Hz), 128.87, 128.80, 128.77, 127.89, 121.57 (t, J=7.2 Hz), 119.68 (t, J=184.1 Hz), 57.52 (t, J=20.4 Hz); ^{19}F NMR ($CDCl_3$, 282 MHz) δ: −104.91 (dt, J=242.8, 13.8 Hz, 1F), −105.99 (dt, J=245.3, 12.7 Hz, 1F); IR (KBr) *v*: 3337, 1660, 1629, 1540, 1232, 995 cm^{-1}; ESI-MS *m/z*: 238 $(M+H)^+$; HRMS calcd for $C_{13}H_{14}F_2NO$ 238.1038, found 238.1042. Anal. calcd for $C_{13}H_{13}F_2NO$: C 65.81, H 5.52, N 5.90; found C 65.58, H 5.69, N 5.73.

5,5-Difluoro-6-phenyl-5,6-dihydropyridin-2(1*H*)-one (11): White solid, m.p. 171—173 ℃; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.43 (s, 5H), 6.65—6.58 (m, 1H), 6.29—6.25 (m, 2H), 4.97 (dd, J=19.8, 9.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100.7 MHz) δ: 164.0, 134.7 (dd, J=32.3, 27.2 Hz), 132.0, 130.2 (t, J=10.3 Hz), 129.9, 129.0, 128.9, 114.2 (dd, J=247.1, 236.7 Hz), 61.6 (dd, J=33.0, 26.5 Hz); ^{19}F NMR ($CDCl_3$, 282 MHz,) δ: −100.34 (dd, J=278.9, 18.3 Hz, 1F), −103.54 (d, J=274.4 Hz, 1F); IR (KBr) *v*: 3189, 3072, 1702, 1631, 1411, 1062 cm^{-1}; ESI-MS *m/z*: 210 $(M+H)^+$; HRMS calcd for $C_{11}H_{10}F_2NO$ 210.0725, found 210.0726.

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