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Heck-type 5-*endo-trig* cyclizations promoted by vinylic fluorines: Ring-fluorinated indene and 3*H*-pyrrole syntheses from 1,1-difluoro-1-alkenes

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Abstract

Arylpalladium or aminopalladium species bearing a 2,2-difluorovinyl group undergo an unusual 5-*endo* alkene insertion followed by β-fluorine elimination. These processes provide a facile access to ring-fluorinated five-membered carbocyclic and heterocyclic compounds starting from an *o*-(3,3-difluoroallyl)phenyl trifluoromethanesulfonate and 3,3-difluoroallyl ketone *O*-pentafluorobenzoyloximes. In both systems, the two vinylic fluorine atoms are essential for Heck-type 5-*endo-trig* cyclizations.

Keywords: 5-*endo-trig* Cyclization; Heck-type reaction; Pyrrole; Indene; 5-*endo* Alkene insertion; β-Fluorine elimination; Palladium

1. Introduction

In contemporary organic synthesis, the Heck reaction is one of the most valuable bond-forming processes promoted by transition metals [1]. The Heck reaction proceeds via alkene insertion and β-hydrogen elimination, which are a palladium-catalyzed coupling of alkenes. The intramolecular version of the Heck reaction has been widely used to construct a variety of ring systems. Normally, *exo*-mode cyclization is the favored path, as *endo*-mode cyclization is less likely to form smaller rings (Scheme 1) [2].

In particular, 5-*endo-trig* cyclizations in the Heck reaction are limited [3,4], and all reports on such 5-*endo* Heck cyclizations have been confined to the palladium-catalyzed reaction of *N*-vinyl-2-haloarylamines [5] or *N*-vinyl-2-haloalkenylamines (Scheme 2, Path A) [6]. To the best of our knowledge, one exception is the efficient cyclopentenone formation via an alka-2,4-dienoylpalladium species [7]. However, the reactions of these vinylamine (enamine-type) substrates can be interpreted in terms of a mechanism other than a 5-*endo-trig* cyclization (Path B), which involves: (i) the oxidative addition of halides **1** to Pd(0); (ii) the formation of six-membered palladacycles **2** through nucleophilic substitution with the enamine on the palladium; (iii) a subsequent reductive elimination, which leads to the 5-*endo-trig* type products [6a,8].

In general, according to Baldwin's rules [9], the 5-*endo-trig* cyclization has long been considered a disfavored process for the construction of five-membered rings, because of the severe distortions required in the reaction geometry. In recent publications, we have reported on nucleophilic 5-*endo-trig* cyclizations of 1,1-difluoro-1-alkenes **3** with an *N*-, *O*-, or a *C*-nucleophile, providing five-membered ring-fluorinated hetero- and carbocycles, such as indoles, 2-pyrrolines, benzo[*b*]furans, 2,3-dihydrofurans, indenes, and cyclopentenes (Scheme 3) [10]. The remarkable reactivity of these alkenes towards nucleophilic 5-*endo-trig* cyclizations is probably due to: (i) the polarization of the carbon–carbon double bond caused by the two fluorine atoms [11], which exerts an electrostatic attraction for the intramolecular nucleophile, overcoming the difficulty of the initial ring formation; (ii) the leaving group ability of fluoride ions, which suppresses the reverse ring opening.

In the above 5-*endo-trig* cyclizations, typical metal species, such as lithium, sodium, and potassium compounds, were employed as intramolecular nucleophiles (Scheme 3). Thus, we turned our attention to organotransition metal chemistry to

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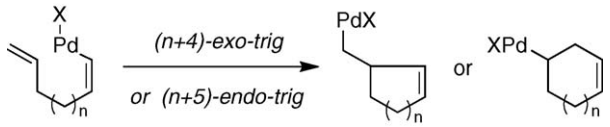
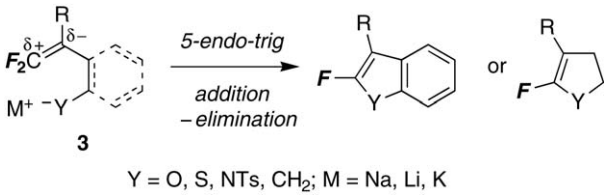
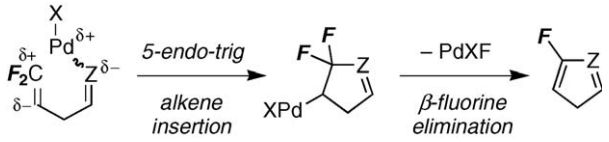


Scheme 1. *exo* or *endo* Alkene insertion in intramolecular Heck reactions.



Scheme 3. Nucleophilic 5-*endo-trig* cyclizations of 1,1-difluoro-1-alkenes.



Scheme 4. Heck-type 5-*endo-trig* cyclizations of 1,1-difluoro-1-alkenes.

broaden the scope of the 5-*endo-trig* cyclization of 1,1-difluoro-1-alkenes, as well as to open up a new 5-*endo-trig* pathway in Heck-type cyclizations. There is only one example describing a Heck-type reaction of a 1,1-difluoro-1-alkene [12]. Heitz reported that arylpalladium iodide complexes replaced the fluorine atom of 1,1-difluoroethene to afford α-fluorostyrenes via alkene insertion and subsequent β-fluorine elimination [13]. Based on these considerations, we expected that a Heck-type 5-*endo-trig* cyclization of difluoroalkenes could be promoted by the electrostatic attraction between the palladium species and the polarized difluoroalkene double bonds, even though this pathway is sterically hindered (Scheme 4). Herein, we report on the results of our studies on Heck-type 5-*endo-trig* cyclizations of 1,1-difluoro-1-alkenes, which provide an approach to ring-fluorinated five-membered carbocyclic and heterocyclic compounds.

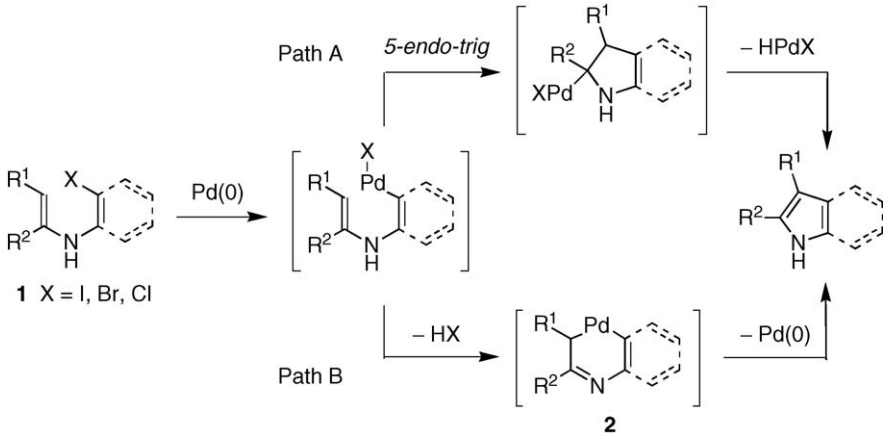
2. Results and discussion

2.1. Heck-type 5-endo-trig cyclizations with arylpalladium species

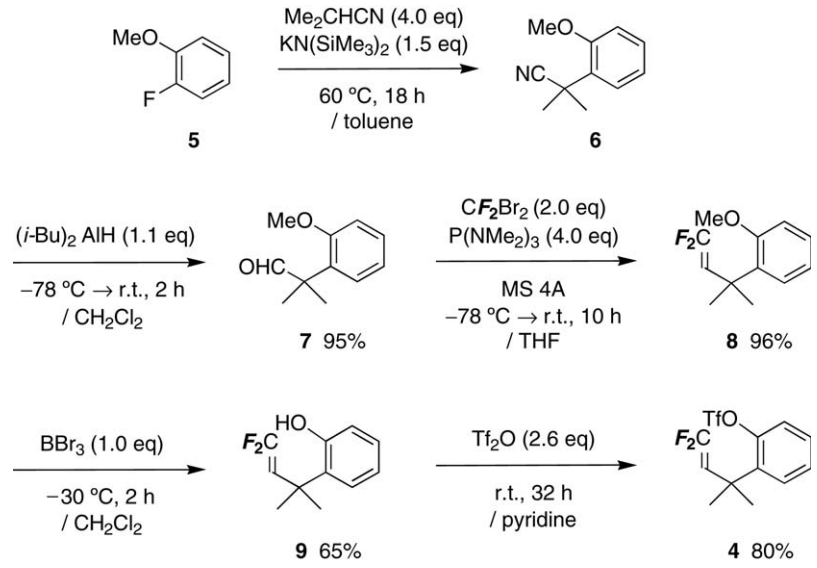
In the reported Heck-type reaction of 1,1-difluoroethene described above, arylpalladium species were employed as the intermolecular coupling partners. We first attempted an intramolecular version of this reaction using an aryl triflate substrate. Aryl triflate **4** bearing a 3,3-difluoroallyl group at the *ortho* position was designed and prepared as follows. Using the literature method, 2-methylpropanenitrile was treated with potassium hexamethyldisilazide to generate the corresponding carbanion, which reacted with 2-fluoroanisole (**5**) to replace the fluorine, leading to formation of nitrile **6** [14]. The cyano group of **6** was transformed by reduction with diisobutylaluminum hydride (DIBAL-H) followed by difluoromethylenation to give difluoroalkene **8** via aldehyde **7**. Demethylation of the methoxy group in **8** and successive trifluoromethanesulfonylation afforded the desired substrate **4** for the cyclization (Scheme 5).

When **4** was heated with a stoichiometric amount of $Pd(PPh_3)_4$ and PPh_3 in *N*,*N*-dimethylacetamide (DMA), the Heck-type 5-*endo-trig* cyclization proceeded to give indanone **12** (57% yield), instead of the expected 3-fluoroindene **11**. As the formation of **12** seemed to be caused by the hydrolysis of **11**, presumably due to the complexation with a Pd(II) generated during the reaction, the reaction mixture was treated with PhSH before quenching. Thus, the formation of fluoroindene **11** was confirmed, and we showed that the 5-*endo-trig* cyclization was achieved by arylpalladium(II) species **10**, generated via the oxidative addition of aryl triflate **4** to Pd(0) (Scheme 6). An attempt to promote this cyclization with a catalytic amount (10 mol%) of $Pd(PPh_3)_4$ and PPh_3 (1.0 equiv. vide infra) gave only a 15% yield of **12**.

To confirm the effect of fluorine, we examined the reaction of a fluorine-free substrate **13**, which gave only a trace amount of the cyclized product **14** (Scheme 7). These results clearly show that fluorine functions as an activator of the substrates in the Heck-type 5-*endo-trig* cyclization.



Scheme 2. Plausible mechanisms for the palladium-catalyzed cyclization of vinylamines.

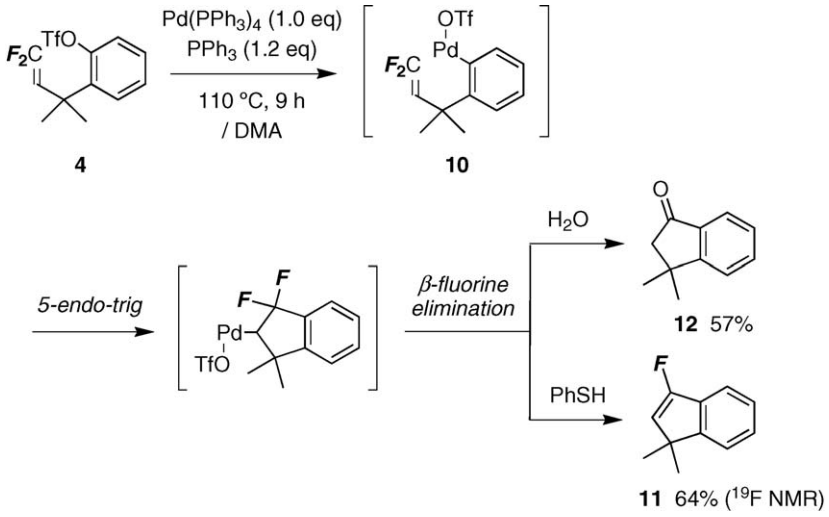


Scheme 5. Preparation of *o*-(3,3-difluoroallyl)phenyl triflate **4**.

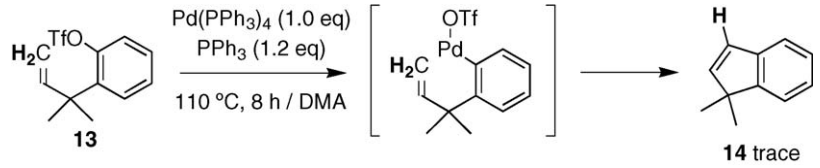
2.2. Heck-type 5-endo-trig cyclizations with aminopalladium species

Having accomplished a Heck-type 5-*endo-trig* cyclization with *C*-palladium species, as described above, we aimed to form ring-fluorinated heterocycles via the Heck-type cyclization with aminopalladium species. Recently, Narasaka reported that homoallyl ketone *O*-pentafluorobenzoyloximes underwent oxidative addition to Pd(0) to generate alkylideneaminopalladium species, which afforded nitrogen heterocycles via the insertion of an alkene moiety in a 5-*exo* fashion [15]. This prompted us to investigate the 5-*endo* insertion of an intramolecular difluoroalkene moiety in 3,3-difluoroallyl ketone *O*-pentafluorobenzoyloximes **15**, which provides a synthetic method for ring-fluorinated 3*H*-pyrrole derivatives **16** (Scheme 8).

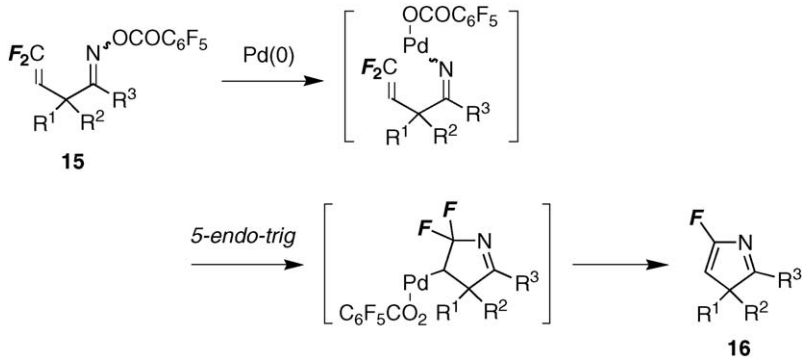
To synthesize the substrates (3,3-difluoroallyl ketone *O*-pentafluorobenzoyloximes **15**), we acylated enamines **17**,



Scheme 6. Heck-type 5-*endo-trig* cyclizations of difluoroalkene **4** via C–Pd species.



Scheme 7. Effect of the vinylic substituent on 5-*endo* Heck-type cyclizations with C–Pd species.



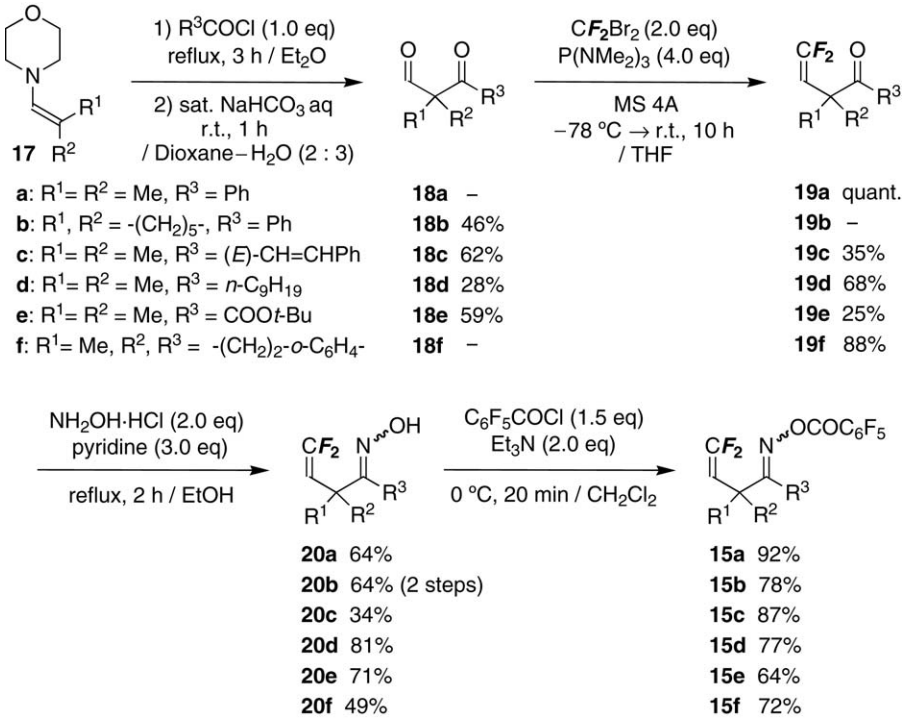
Scheme 8. Heck-type 5-*endo-trig* cyclizations of difluoroalkenes **15** via N–Pd species.

derived from aldehydes, with acid chlorides to prepare β-ketoaldehyde intermediates **18**. The selective Wittig-type difluoromethylenation of **18** gave difluoroallyl ketones **19** [16], which were further transformed into *O*-pentafluorobenzoyloximes **15** via oximation followed by pentafluorobenzoylation (Scheme 9).

Then, we investigated the Heck-type cyclization of **15a** ($R^1 = R^2 = Me$ and $R^3 = Ph$, *Z*-form [17]) in *N*,*N*-dimethylformamide (DMF) at 80 °C (Scheme 8 and Table 1). The catalytic reaction gave the desired compound, 5-fluoro-3*H*-pyrrole **16a**, albeit in only 19% yield (Entry 2). We examined the reagents required for the reduction of the in situ generated palladium(II) species to Pd(0). On treatment with $Pd(PPh_3)_4$ (10 mol%) and NEt_3 (5.0 equiv.) [12], **16a** was obtained in low yield (Entry 3). After the screening of suitable reductants, we found that a stoichiometric amount of PPh_3 was effective in reducing $C_6F_5CO_2Pd(II)F$ to Pd(0), which allowed the cyclization to proceed under palladium catalysis with the generation of $Ph_3P{=}O$ and Ph_3PF_2 [18,19]. When the reaction was conducted in DMA at higher temperatures (110 °C), the yield of **16a** improved to 71% (Entry 5) [20].

We tried to synthesize other fluoropyrroles **16** under the above optimized conditions (Table 2). The cyclization of substrate **15b** with a cyclohexane ring successfully afforded the spiro-type product **16b** (Entry 2). Substrate **15c** bearing a conjugated alkene moiety on the oxime carbon readily underwent cyclization to give the corresponding pyrrole **16c** (Entry 3). The reactions of substrates **15d** and **15e** bearing a primary alkyl or an acyl group as R^3 resulted in poor yield (Entries 4 and 5). Furthermore, the construction of a fused tricyclic system of 4,5-dihydro-3a*H*-benzo[*g*]indole **16f**, where the transition state is more strained, was achieved using this method (Scheme 10). Thus, the catalytic process provides a facile access to 5-fluoro-3*H*-pyrroles [21,22].

To elucidate the role of the vinylic fluorines, we examined the reaction of substrates that had atoms other than fluorine at



Scheme 9. Preparation of 3,3-difluoroallyl ketone oximes **15**.

Table 1
Effect of reductant and conditions on the Heck-type cyclization of **15a** ($R^1 = R^2 = Me$ and $R^3 = Ph$)

Entry	$Pd(PPh_3)_4$ (equiv.)	Reductant (equiv.)	Solvent	Conditions	Yield (%)
1	0.3	None	DMF	80 °C, 1 h	71
2	0.1	None	DMF	80 °C, 2 h, then 110 °C, 2 h	19
3	0.1	NEt_3 (5.0)	DMF	80 °C, 2 h, then 110 °C, 9 h	<30
4	0.1	PPh_3 (1.0)	DMF	100 °C, 4 h	57
5	0.1	PPh_3 (1.0)	DMA	110 °C, 8 h	71

the vinylic positions, such as the corresponding monofluoroalkene **21a**, fluorine-free alkene **21b**, dichloroalkene **21c**, and dibromoalkene **21d**. These oximes **21a–d** were prepared via the corresponding allyl ketones **23a–d** (Scheme 11). Monofluoroketone **23a** was derived from difluoroallyl ketone **19a** via hydride reduction of its dimethyl acetal **22** [23]. Dichloroketone **23c** [24,25] and dibromoketone **23d** [26] were prepared via dihalomethylenation of ketoaldehyde **18a**. Ketones **23a**, **23c**, and **23d** thus obtained and **23b** [27] were transformed into the desired substrates **21** via oximation followed by pentafluorobenzoylation [28].

When **21a–d** were subjected to the same reaction conditions as above, no cyclized products were observed (Scheme 12). Instead, the corresponding ketones were obtained via hydrolysis of the oxime moiety of **21a–c**, and **21d** gave a complex mixture, presumably due to its vinylic bromides reactive toward Pd(0). These results clearly show that the two vinylic fluorines play an important role in this Heck-type 5-*endo-trig* cyclization. The major distinction of the 1,1-difluoro-1-alkenes appears to be the remarkable polarization of the double bond, which is caused by the repulsive interaction between the lone pairs of fluorine and the π-electrons. Such repulsion is much stronger for fluorine than for other halogens, due to the 2p-orbital occupancy of both the lone pairs and the π-electrons.

2.3. Conclusion

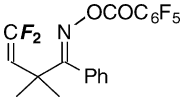
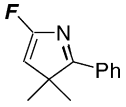
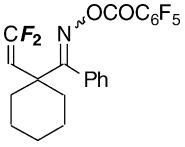
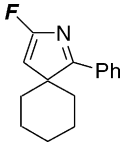
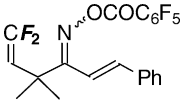
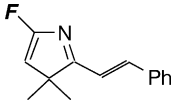
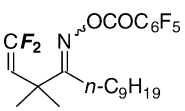
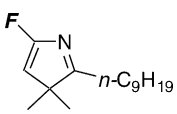
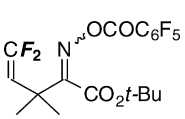
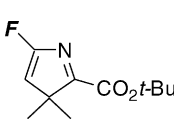
We have accomplished a 5-*endo-trig* alkene insertion in the Heck-type cyclization of an *o*-(3,3-difluoroallyl)phenyl triflate and 3,3-difluoroallyl ketone oximes by taking advantage of the polarized double bond of 1,1-difluoro-1-alkenes. The two vinylic fluorine atoms were confirmed to be essential for the 5-*endo* Heck-type cyclizations. The alkene insertion followed by β-fluorine elimination provides a facile method for ring-fluorinated indene and 3*H*-pyrrole syntheses.

3. Experimental

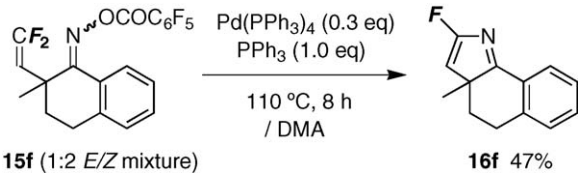
3.1. General experimental procedure

IR spectra were recorded on a Horiba FT-300S spectrometer by ATR (attenuated total reflectance) method. ^1H NMR, ^{13}C

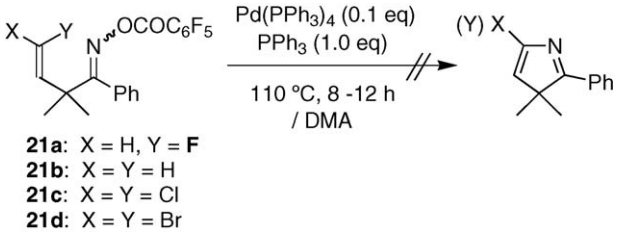
Table 2
Synthesis of 5-fluoro-3*H*-pyrroles **16** from difluoroalkenes **15**[a]

Entry	Substrate **15**[b]	Product **16**	Time (h)	Yield (%)
1	 **15a**		8	71
2	 **15b**		8	78
3	 **15c**		1	76
4	 **15d**		8	29
5	 **15e**		12	14

[a] All the reactions were performed with $Pd(PPh_3)_4$ (0.1 equiv.) and PPh_3 (1.0 equiv.) in DMA at 110 °C.
[b] Each of substrates **15** was a single isomer, while the stereochemistry of **15b–e** was not determined.



Scheme 10. Construction of a fused tricyclic system via a Heck-type 5-*endo-trig* cyclization.



Scheme 12. Effect of the vinylic substituent on 5-*endo* Heck-type cyclizations with N–Pd species.

NMR, and ^{19}F NMR spectra were recorded on a Bruker Avance 500 spectrometer, a Bruker DRX 500, or a JEOL JNM-AL-400 spectrometer. ^{1}H NMR chemical shifts (δ) are given in ppm downfield from internal Me_4Si. ^{13}C NMR chemical shifts (δ) are given in ppm downfield from Me_4Si, relative to chloroform-*d* (δ = 77.00). ^{19}F NMR chemical shifts (δ_F) are given in ppm downfield from internal C_6F_6. Mass spectra were taken with a JEOL MS-700M spectrometer. Elemental analyses were performed with a YANAKO MT-6 CHN Corder apparatus. All reactions were carried out under argon. Dichloromethane (CH_2Cl_2) was distilled from P_2O_5 and then from CaH_2, and stored over molecular sieves (4 Å). THF and Et_2O were purchased as an anhydrous solvent from Kanto Chemical Co., Inc. and stored over 4 Å molecular sieves. Methanol was distilled from $Mg(OMe)_2$ and stored over molecular sieves (3 Å). Ethanol was distilled from NaOEt and stored over molecular sieves (3 Å). *N*,*N*-dimethylacetamide (DMA) was distilled under reduced pressure from BaO and stored over molecular sieves (4 Å). DMF was dried over P_2O_5, then distilled under reduced pressure from CaH_2, and stored over molecular sieves (4 Å). Toluene was dried over $CaCl_2$, then distilled, and stored over molecular sieves (4 Å). Pyridine was distilled from CaH_2 and stored over molecular sieves (4 Å). Column chromatography and preparative thin-layer chromatography (PTLC) were performed on silica gel (Kanto Chemical Co. Inc., Silica Gel 60 and Wako Pure Chemical Industries, Ltd., B5-F), respectively.

3.2. Heck-type 5-endo-trig cyclizations with arylpalladium species

3.2.1. 2-(2-Methoxyphenyl)-2-methylpropanal (7)

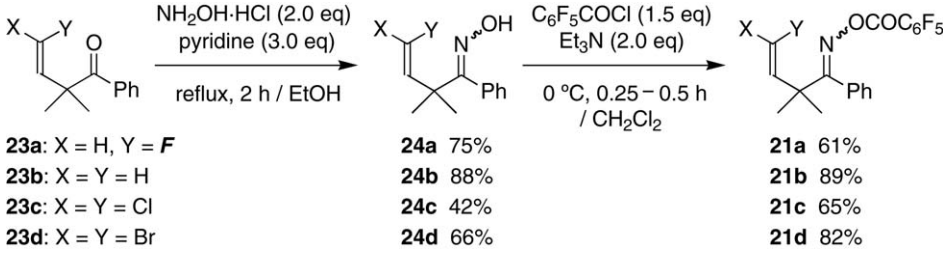
To a solution of 2-(2-methoxyphenyl)-2-methylpropionitrile (6.87 g, 39.2 mmol) in CH_2Cl_2 (80 mL) was added diisobutylaluminum hydride (DIBAL-H, 39.2 mL, 1.0 M in toluene, 39.2 mmol) dropwise at −78 °C. After the reaction mixture was stirred for 1.5 h at room temperature, an additional DIBAL-H (4.0 mL, 1.0 M in toluene, 4.0 mmol) was added dropwise at −78 °C. The mixture was stirred for 0.5 h, and then hexane, methanol, saturated aqueous NH_4Cl, and 10% sulfuric acid were added to quench the reaction. Organic materials were extracted with CH_2Cl_2 three times. The combined extracts were washed with brine and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (AcOEt–hexane 1:4) to give **7** (6.66 g, 95%) as a colorless liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.38 (6H, s), 3.76 (3H, s), 6.89 (1H, dm, *J* = 8.0 Hz), 7.00 (1H, ddd, *J* = 8.0, 8.0, 1.2 Hz), 7.25–7.32 (2H, m), 9.51 (1H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.1, 48.2, 55.1, 110.9, 120.9, 126.7, 128.5, 131.8, 156.4, 203.5. IR (neat) 2970, 2704, 1724, 1489, 1458, 1437, 1240, 1092, 1026, 752 cm^{-1}. HRMS (FAB): calcd for $C_{11}H_{15}O_2$ ($[M + H]^+$) 179.1072, found 179.1045.

3.2.2. 2-(4,4-Difluoro-2-methylbut-3-en-2-yl)anisole (8)

To a mixture of dibromodifluoromethane (CF_2Br_2, 5.92 mL, 64.8 mmol) and microwave-dried molecular sieves (4 Å) powder (6.6 g) in THF (50 mL) was added tris(dimethylamino)phosphine ($P(NMe_2)_3$, 23.5 mL, 130 mmol) at −78 °C. The mixture was stirred for 30 min at that temperature, and then warmed to room temperature. Aldehyde **7** (5.78 g, 32.4 mmol) was added and the mixture was stirred for 10 h. The reaction was quenched with phosphate buffer (pH 7) and organic materials were extracted with Et_2O three times. The combined extracts were washed with brine and dried over $MgSO_4$. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (AcOEt–hexane 1:4) to give **8** (6.18 g, 96%) as a colorless liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.53 (6H, s), 3.82 (3H, s), 4.54 (1H, dd, J_{HF} = 28.4, 5.8 Hz), 6.85–6.93 (2H, m), 7.19–7.24



Scheme 11. Preparation of allyl ketone oximes **21**.

(1H, m), 7.27–7.30 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.3 (dd, J_{CF} = 4, 2 Hz), 35.1 (dd, J_{CF} = 5, 3 Hz), 55.1, 88.3 (dd, J_{CF} = 22, 14 Hz), 111.5, 120.2, 125.9, 127.6, 135.9, 154.7 (dd, J_{CF} = 290, 280 Hz), 157.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ_F 72.1 (1F, dd, J_{FF} = 54 Hz, J_{FH} = 6 Hz), 74.2 (1F, dd, J_{FF} = 54 Hz, J_{FH} = 28 Hz). IR (neat) 2968, 1734, 1458, 1437, 1329, 1290, 1242, 1215, 1030, 999, 746 cm^{-1}. HRMS (FAB): calcd for $C_{12}H_{15}F_2O$ ($[M + H]^+$) 213.1091, found 213.1135.

3.2.3. 2-(4,4-Difluoro-2-methylbut-3-en-2-yl)phenol (**9**)

To a solution of **8** (1.11 g, 5.21 mmol) in CH_2Cl_2 (25 mL) was added a solution of tribromoborane (BBr_3, 5.2 mL, 1.0 M in CH_2Cl_2, 5.2 mmol) dropwise at −30 °C. After the reaction mixture was stirred for 2 h at −30 °C, phosphate buffer (pH 7) was added to quench the reaction. Organic materials were extracted with CH_2Cl_2 three times. The combined extracts were washed with brine and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (AcOEt–hexane 1:19) to give **9** (0.67 g, 65%) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.54 (6H, s), 4.59 (1H, dm, J_{HF} = 26.7 Hz), 5.10–5.15 (1H, m), 6.72 (1H, d, J = 7.7 Hz), 6.89 (1H, dd, J = 7.7, 7.7 Hz), 7.11 (1H, ddd, J = 7.7, 7.7, 1.6 Hz), 7.26 (1H, dd, J = 7.7, 1.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.3 (dd, J_{CF} = 3, 2 Hz), 34.8 (dd, J_{CF} = 5, 3 Hz), 87.4 (dd, J_{CF} = 21, 13 Hz), 116.7, 120.6, 126.1, 127.8, 133.5, 153.6, 155.1 (dd, J_{CF} = 294, 285 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ_F 75.5 (1F, dd, J_{FF} = 45 Hz, J_{FH} = 5 Hz), 77.2 (1F, dd, J_{FF} = 45 Hz, J_{FH} = 27 Hz).

3.2.4. 2-(4,4-Difluoro-2-methylbut-3-en-2-yl)phenyl trifluoromethanesulfonate (**4**)

To a solution of **9** (94 mg, 0.47 mmol) in pyridine (2 mL) was added trifluoromethanesulfonic anhydride (0.105 mL, 0.62 mmol). After the reaction mixture was stirred for 24 h at room temperature, an additional trifluoromethanesulfonic anhydride (0.105 mL, 0.62 mmol) was added, and the reaction mixture was stirred for 8 h at room temperature. Aqueous 1 M HCl was added to quench the reaction, and organic materials were extracted with Et_2O three times. The combined extracts were washed with aqueous 1 M HCl and brine, and then dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by thin-layer chromatography on silica gel (AcOEt–hexane 1:19) to give **4** (126 mg, 80%) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.55 (6H, s), 4.61 (1H, dd, J_{HF} = 27.2, 4.0 Hz), 7.29–7.35 (3H, m), 7.46–7.51 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.1 (dd, J_{CF} = 3, 2 Hz), 34.8 (dd, J_{CF} = 6, 2 Hz), 88.1 (dd, J_{CF} = 22, 14 Hz), 118.3 (q, J_{CF} = 319 Hz), 121.2 (dd, J_{CF} = 4, 3 Hz), 127.7, 127.8, 128.4, 139.7, 148.6, 155.2 (dd, J_{CF} = 292, 286 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ_F 75.0 (1F, dd, J_{FF} = 44 Hz, J_{FH} = 4 Hz), 77.4 (1F, dd, J_{FF} = 44 Hz, J_{FH} = 27 Hz), 87.5 (3F, s). IR (neat) 2979, 1736, 1419, 1325, 1211, 1140, 1066, 895, 879, 766, 598 cm^{-1}. Anal. Calcd for $C_{12}H_{11}F_5O_3S$: C, 43.64; H, 3.36%. Found: C, 43.49; H, 3.54%.

3.2.5. 3-Fluoro-1,1-dimethyl-1H-indene (**11**)

To a solution of triphenylphosphine (PPh_3, 124 mg, 0.47 mmol) and tetrakis(triphenylphosphine)palladium ($Pd(PPh_3)_4$, 455 mg, 0.394 mmol) in DMA (20 mL) was added **4** (130 mg, 0.39 mmol). After the reaction mixture was stirred at 110 °C for 9 h, thiophenol (0.16 mL, 1.58 mmol) was added. Phosphate buffer (pH 7) was added and organic materials were extracted with Et_2O three times. The combined extracts were washed with water three times and brine, and dried over $MgSO_4$. After removal of the solvent under reduced pressure, the residue was purified by preparative thin-layer chromatography (pentane) to give **11** (64%, determined before extraction by ^{19}F NMR relative to internal $C_6H_5CF_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (6H, s), 5.62 (1H, s), 7.24–7.34 (4H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.9 (d, J_{CF} = 3 Hz), 44.7 (d, J_{CF} = 5 Hz), 117.9 (d, J_{CF} = 13 Hz), 117.9 (d, J_{CF} = 5 Hz), 121.2 (d, J_{CF} = 3 Hz), 126.5, 126.5, 134.6 (d, J_{CF} = 27 Hz), 151.7 (d, J_{CF} = 7 Hz), 157.4 (d, J_{CF} = 280 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ_F 23.6 (s). IR (neat) 2956, 2924, 2854, 2360, 2332, 1458, 1375, 1219, 771 cm^{-1}. HRMS (FAB): calcd for $C_{11}H_{12}F$ ($[M + H]^+$) 163.0923, found 163.0924.

3.2.6. 3,3-Dimethylindan-1-one (**12**) [29]

To a solution of PPh_3 (50.8 mg, 0.194 mmol) and $Pd(PPh_3)_4$ (180 mg, 0.156 mmol) in DMA (10 mL) was added **4** (51.5 mg, 0.156 mmol). After the reaction mixture was stirred at 110 °C for 9 h, phosphate buffer (pH 7) was added to quench the reaction. Organic materials were extracted with Et_2O three times. The combined extracts were washed with water three times and brine, and dried over $MgSO_4$. After removal of the solvent under reduced pressure, the residue was purified by preparative thin-layer chromatography on silica gel (AcOEt–hexane 1:4) to give **12** (14.2 mg, 57%) as a colorless liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.43 (6H, s), 2.60 (2H, s), 7.36–7.71 (4H, m). IR (neat) 2958, 1709, 1604, 1471, 1323, 1290, 1246, 766 cm^{-1}.

3.3. Heck-type 5-endo-trig cyclizations with aminopalladium species

3.3.1. 1-Benzoylcyclohexane-1-carbaldehyde (**18b**)

To a solution of benzoyl chloride (11.6 g, 83 mmol) in Et_2O (14 mL) was added 4-(cyclohexylidenemethyl)morpholine (**17b**, 12.5 g, 69 mmol) [30] with vigorous stirring over 1 h at 0 °C, and the solution was heated to reflux for 3 h. Saturated aqueous sodium bicarbonate ($NaHCO_3$) was added (23 mL) at 0 °C, and the mixture was stirred for 1 h at that temperature. Organic materials were extracted with Et_2O three times. The combined extracts were washed with brine and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (AcOEt–hexane 1:20) to give **18b** (6.9 g, 46%) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.41–1.47 (2H, m), 1.49–1.57 (4H, m), 2.04 (2H, ddd, J = 13.1, 7.5, 4.4 Hz), 2.16 (2H, ddd, J = 13.1, 7.8, 4.6 Hz), 7.41 (2H, t, J = 7.6 Hz), 7.51 (1H, tt, J = 7.6, 1.2 Hz), 7.69 (2H, d, J = 7.6 Hz), 9.70 (1H, s). ^{13}C

NMR (126 MHz, $CDCl_3$) δ 22.1, 25.1, 29.6, 64.9, 128.4, 128.5, 132.3, 137.1, 199.6, 201.0. IR (neat) 2935, 1720, 1670, 1446, 1228, 949, 783, 694 cm^{-1}. HRMS (FAB): calcd for $C_{14}H_{17}O_2$ ($[M + H]^+$) 217.1229, found 217.1213.

3.3.2. (E)-2,2-Dimethyl-3-oxo-5-phenylpent-4-enal (18c)

Compound **18c** was prepared by the method described for **18b** using (*E*)-cinnamoyl chloride (5.00 g, 30.0 mmol), Et_2O (6 mL), 4-(2-methylpropenyl)morpholine (**17a**, 4.23 g, 30.0 mmol), and saturated aqueous $NaHCO_3$ (10 mL). Purification by column chromatography on silica gel (AcOEt–hexane 1:20) gave **18c** (3.74 g, 62%) as a white solid.

^1H NMR (500 MHz, $CDCl_3$) δ 1.30 (6H, s), 6.82 (1H, d, J = 15.6 Hz), 7.17–7.35 (3H, m), 7.38–7.49 (2H, m,), 7.61 (1H, d, J = 15.6 Hz), 9.59 (1H, s). ^{13}C NMR (126 MHz, $CDCl_3$) δ 18.9, 59.3, 120.5, 128.3, 128.8, 131.1, 134.0, 144.6, 197.2, 201.0. IR (neat) 1732, 1722, 1684, 1674, 1599, 1576, 1448, 1329, 1065, 980, 899, 762, 710, 685, 567, 519 cm^{-1}. HRMS (FAB): calcd for $C_{13}H_{15}O_2$ ($[M + H]^+$) 203.1072, found 203.1092.

3.3.3. 2,2-Dimethyl-3-oxododecanal (18d)

Compound **18d** was prepared by the method described for **18b** using decanoyl chloride (5.47 g, 28.7 mmol), Et_2O (7 mL), and **17a** (4.05 g, 28.7 mmol). The reaction mixture was heated to reflux for 5 h, and saturated aqueous $NaHCO_3$ (10 mL) was added. Purification by column chromatography on silica gel (Et_2O–hexane 1:10) gave **18d** (1.82 g, 28%) as a colorless liquid.

^1H NMR (500 MHz, $CDCl_3$) δ 0.88 (3H, t, J = 7.0 Hz), 1.21–1.32 (12H, m), 1.33 (6H, s), 1.45 (2H, tt, J = 7.3, 7.3 Hz), 2.44 (2H, t, J = 7.3 Hz), 9.62 (1H, s). ^{13}C NMR (126 MHz, $CDCl_3$) δ 14.0, 19.1, 22.6, 23.3, 29.0, 29.2, 29.3, 29.3, 31.8, 39.0, 60.3, 201.1, 209.3. IR (neat) 2924, 2854, 1734, 1700, 1466, 1366, 1072, 1035, 914, 838, 722 cm^{-1}. HRMS (FAB): calcd for $C_{14}H_{27}O_2$ ($[M + H]^+$) 227.2011, found 227.2006.

3.3.4. tert-Butyl 3,3-dimethyl-2,4-dioxobutyrate (18e)

Compound **18e** was prepared by the method described for **18b** using *tert*-butyl 2-chloro-2-oxoacetate (3.34 g, 20.3 mmol) [31], Et_2O (4 mL), **17a** (2.87 g, 20.3 mmol), and saturated aqueous $NaHCO_3$ (7 mL). Purification by column chromatography on silica gel (Et_2O–hexane 1:10) gave **18e** (3.40 g, 59%) as a colorless oil.

^1H NMR (500 MHz, $CDCl_3$) δ 1.38 (6H, s), 1.54 (9H, s), 9.68 (1H, s). ^{13}C NMR (126 MHz, $CDCl_3$) δ 18.8, 27.8, 57.8, 85.5, 160.6, 193.9, 197.8. IR (neat) 2981, 1712, 1460, 1371, 1317, 1259, 1155, 1049, 978, 843, 742 cm^{-1}. HRMS (FAB): calcd for $C_{10}H_{17}O_4$ ($[M + H]^+$) 201.1127, found 201.1132.

3.3.5. 4,4-Difluoro-2,2-dimethyl-1-phenylbut-3-en-1-one (19a)

To a mixture of CF_2Br_2 (1.68 g, 7.99 mmol) and microwave-dried molecular sieves (4 Å) powder (1.4 g) in THF (10.5 mL) was added $P(NMe_2)_3$ (4.11 g, 25.2 mmol) at −78 °C. The reaction mixture was stirred for 15 min at that temperature, and then warmed to room temperature. To the mixture was added 2,2-dimethyl-3-oxo-3-phenylpropanal **18a** (1.23 g, 6.98 mmol) [32]. After the mixture was stirred 10 h, the reaction was quenched with phosphate buffer (pH 7) at 0 °C. After suction filtration, organic materials were extracted with AcOEt three times. The combined extracts were washed with brine and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (AcOEt–hexane 1:20) to give **19a** (1.46 g, quant.) as a white solid.

^1H NMR (500 MHz, $CDCl_3$) δ 1.46 (6H, s), 4.65 (1H, dd, J_{HF} = 27.8, 3.0 Hz), 7.39 (2H, t, J = 7.4 Hz), 7.47 (1H, t, J = 7.4 Hz), 7.94 (2H, d, J = 7.4 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 26.8, 43.6 (dd, J_{CF} = 3, 3 Hz), 85.7 (dd, J_{CF} = 22, 16 Hz), 128.0, 129.0, 132.0, 135.1, 155.2 (dd, J_{CF} = 293, 288 Hz), 202.0 (dd, J_{CF} = 2, 2 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 77.2 (1F, dd, J_{FF} = 42 Hz, J_{FH} = 3 Hz), 77.8 (1F, dd, J_{FF} = 42 Hz, J_{FH} = 28 Hz). IR (neat) 1734, 1682, 1323, 1215, 997, 795, 715, 700, 690 cm^{-1}. HRMS (FAB): calcd for $C_{12}H_{13}F_2O$ ($[M + H]^+$) 211.0935, found 211.0947.

3.3.6. (E)-6,6-Difluoro-4,4-dimethyl-1-phenylhexa-1,5-dien-3-one (19c)

Compound **19c** was prepared by the method described for **19a** using CF_2Br_2 (1.68 g, 7.99 mmol), microwave-dried molecular sieves (4 Å) powder (0.60 g), THF (6.0 mL), $P(NMe_2)_3$ (2.60 g, 16.0 mmol), and **18c** (805 mg, 3.98 mmol). Purification by column chromatography on silica gel (AcOEt–hexane 1:20) gave **19c** (330 mg, 35%) as a white solid.

^1H NMR (500 MHz, $CDCl_3$) δ 1.36 (6H, s), 4.47 (1H, dd, J_{HF} = 28.0, 4.2 Hz), 7.07 (1H, d, J = 15.6 Hz), 7.32–7.38 (3H, m), 7.51–7.57 (2H, m), 7.74 (1H, d, J = 15.6 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 24.6, 43.9 (dd, J_{CF} = 3.7, 3.7 Hz), 83.7 (dd, J_{CF} = 23, 15 Hz), 120.6, 128.1, 128.6, 130.2, 134.4, 143.5, 155.7 (dd, J_{CF} = 294, 288 Hz), 199.4. ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 77.6 (1F, br d, J_{FF} = 42 Hz), 78.2 (1F, dd, J_{FF} = 42 Hz, J_{FH} = 28 Hz). IR (neat) 2974, 1734, 1687, 1608, 1329, 1225, 1134, 1061, 997, 764, 715, 685, 561 cm^{-1}. Anal. Calcd for $C_{14}H_{14}F_2O$: C, 71.17; H, 5.97%, found: C, 71.33; H, 6.20%.

3.3.7. 1,1-Difluoro-3,3-dimethyltridec-1-en-4-one (19d)

Compound **19d** was prepared by the method described for **19a** using CF_2Br_2 (3.72 g, 17.7 mmol), microwave-dried molecular sieves (4 Å) powder (1.77 g), THF (13 mL), $P(NMe_2)_3$ (5.77 g, 35.4 mmol), and **18d** (2.00 g, 8.85 mmol). The mixture was stirred for 1.5 h. Purification by column chromatography on silica gel (Et_2O–hexane 1:20) gave **19d** (1.58 g, 68%) as a white solid.

^1H NMR (500 MHz, $CDCl_3$) δ 0.88 (3H, t, J = 6.9 Hz), 1.26–1.31 (18H, m), 1.56 (2H, tt, J = 7.1, 7.1 Hz), 2.49 (2H, t, J = 7.1 Hz), 4.37 (1H, dd, J_{HF} = 27.9, 4.4 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 14.0, 22.6, 24.1, 24.9 (d, J_{CF} = 3 Hz), 29.2, 29.2, 29.4, 29.4, 31.8, 37.0, 45.1(dd, J_{CF} = 4, 4 Hz), 83.9 (dd, J_{CF} = 23, 15 Hz), 155.7 (dd, J_{CF} = 294, 287 Hz), 211.7. ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 76.9 (1F, dd, J_{FF} = 44 Hz, J_{FH} = 4 Hz), 78.2 (1F, dd, J_{FF} = 44 Hz, J_{FH} = 28 Hz). IR (neat) 2925, 2854, 1738, 1716, 1508, 1456, 1331, 1223, 1001,

771 cm^{-1}. HRMS (FAB): calcd for $C_{15}H_{27}F_2O$ ($[M + H]^+$) 261.2030, found 261.2049.

3.3.8. tert-Butyl 5,5-difluoro-3,3-dimethyl-2-oxopent-4-enoate (**19e**)

Compound **19e** was prepared by the method described for **19a** using CF_2Br_2 (6.82 g, 32.5 mmol), microwave-dried molecular sieves (4 Å) powder (3.88 g), THF (13 mL), $P(NMe_2)_3$ (9.61 g, 58.8 mmol), and **18e** (3.91 g, 19.5 mmol). Purification by column chromatography on silica gel (Et_2O–hexane 1:20) gave **19e** (1.13 g, 25%) as a white solid.

^1H NMR (500 MHz, $CDCl_3$) δ 1.42 (6H, s), 1.55 (9H, s), 4.44 (1H, dd, J_{HF} = 27.5, 3.8 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 24.6 (d, J_{CF} = 3 Hz), 27.7, 43.1 (dd, J_{CF} = 5, 3 Hz), 82.7 (dd, J_{CF} = 25, 15 Hz), 84.3, 156.0 (dd, J_{CF} = 294, 288 Hz), 162.5, 197.5 (dd, J_{CF} = 2, 2 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 78.1 (1F, dd, J_{FF} = 42 Hz, J_{FH} = 4 Hz), 78.2 (1F, dd, J_{FF} = 42 Hz, J_{FH} = 28 Hz). IR (neat) 2983, 1731, 1716, 1371, 1302, 1228, 1157, 1047, 1001, 841 cm^{-1}. Anal. Calcd for $C_{11}H_{16}F_2O_3$: C, 56.40; H, 6.88%. Found: C, 56.62; H, 7.12%.

3.3.9. 2-(2,2-Difluorovinyl)-2-methyl-3,4-dihydronaphthalen-1(2H)-one (**19f**)

Compound **19f** was prepared by the method described for **19a** using CF_2Br_2 (5.05 g, 24.1 mmol), microwave-dried molecular sieves (4 Å) powder (2.41 g), THF (20 mL), $P(NMe_2)_3$ (7.87 g, 28.2 mmol), and 2-methyl-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carbaldehyde (**18f**, 2.30 g, 12.1 mmol), prepared according to a reported procedure [33] from 2-hydroxymethylene-3,4-dihydro-2*H*-naphthalen-1-one [34]. The mixture was stirred at room temperature for 1.5 h. Purification by column chromatography on silica gel (AcOEt–hexane 1:10) gave **19f** (2.36 g, 88%) as a pale yellow oil.

^1H NMR (500 MHz, $CDCl_3$) δ 1.40 (3H, s), 2.14 (1H, ddd, J = 13.1, 6.3, 6.3 Hz), 2.22 (1H, ddd, J = 13.1, 6.3, 6.3 Hz), 3.00 (1H, dd, J = 6.3, 6.3 Hz), 3.00 (1H, dd, J = 6.3, 6.3 Hz), 4.58 (1H, dd, J_{HF} = 28.4, 4.4 Hz), 7.22 (1H, dd, J = 7.7, 1.1 Hz), 7.29 (1H, ddd, J = 7.7, 7.7, 1.1 Hz), 7.46 (1H, ddd, J = 7.7, 7.7, 1.1 Hz), 8.04 (1H, dd, J = 7.7, 1.1 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 22.4 (dd, J_{CF} = 2, 2 Hz), 25.4, 34.8 (dd, J_{CF} = 2, 2 Hz), 43.1 (dd, J_{CF} = 4, 4 Hz), 82.2 (dd, J_{CF} = 25, 15 Hz), 126.7, 128.2, 128.7, 130.9, 133.3, 142.9, 156.0 (dd, J_{CF} = 291, 285 Hz), 198.7. ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 77.4 (1F, dd, J_{FF} = 45 Hz, J_{FH} = 4 Hz), 78.4 (1F, dd, J_{FF} = 45 Hz, J_{FH} = 28 Hz). IR (neat) 2933, 1736, 1684, 1456, 1300, 1227, 1192, 889, 739 cm^{-1}. HRMS (FAB): calcd for $C_{13}H_{12}F_2O$ ($[M + H]^+$) 223.0935, found 223.0937.

3.3.10. 1,1-Difluoro-4,4-dimethoxy-3,3-dimethyl-1-phenylbut-1-ene (**22**)

Ketone **19a** (2.22 g, 10.6 mmol), trimethyl orthoformate (4.48 g, 42.2 mmol), and *p*-toluenesulfonic acid monohydrate (1.01 g, 5.3 mmol) were dissolved in MeOH (21 mL) and heated to reflux for 15 h. NaOMe (0.29 g, 5.3 mmol) was added through a solid addition funnel at 0 °C. The mixture was diluted with pentane (30 mL) and filtrated through a Celite pad. The organic layer was washed with water and brine, and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (NEt_3–AcOEt–hexane 1:5:100) to give 22 (2.17g, 80%) as a colorless oil.

^1H NMR (500 MHz, $CDCl_3$) δ 1.04 (3H, s), 1.05 (3H, s), 3.29 (6H, s), 4.65 (1H, dd, J_{HF} = 28.7, 7.0 Hz), 7.25 (1H, t, J = 7.2 Hz), 7.29 (2H, t, J = 7.2 Hz), 7.40 (2H, d, J = 7.2 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 24.9, 24.9, 41.8 (dd, J_{CF} = 4, 4 Hz), 51.3, 85.4 (dd, J_{CF} = 24, 12 Hz), 106.3 (dd, J_{CF} = 2, 2 Hz), 127.0, 127.6, 129.3, 138.1, 154.5 (dd, J_{CF} = 293, 281 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 75.1 (1F, dd, J_{FF} = 52 Hz, J_{FH} = 29 Hz), 76.1 (1F, dd, J_{FF} = 52 Hz, J_{FH} = 7 Hz). IR (neat) 1738, 1325, 1228, 1178, 1103, 1055, 985, 908, 758, 707 cm^{-1}. HRMS (FAB): calcd for $C_{14}H_{19}F_2O_2$ ($[M + H]^+$) 257.1353, found 257.1341.

3.3.11. (Z)-4-Fluoro-2,2-dimethyl-1-phenylbut-3-en-1-one (**23a**)

To a solution of **22** (207 mg, 0.81 mmol) in toluene (3 mL) was added sodium bis(2-methoxyethoxy)aluminum dihydride (Red-Al®, 0.12 mL, 3.3 M in toluene, 0.40 mmol) at 0 °C. After heating to reflux for 3 h, the reaction was quenched with phosphate buffer (pH 7) at 0 °C. The mixture was filtrated through a Celete pad, and organic materials were extracted with Et_2O three times. The combined extracts were washed with brine and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was dissolved in EtOH and treated with aqueous 12 M HCl (1.3 mL, 16 mmol). After stirring at room temperature for 10 min, $NaHCO_3$ (1.29 g, 15 mmol) and phosphate buffer (pH 7) were added at 0 °C. Organic materials were extracted with Et_2O three times. The combined extracts were washed with brine and dried over $MgSO_4$. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (AcOEt–hexane 1:20). Further purification was conducted by gel permeation chromatography (GPC, $CHCl_3$) to give **23a** (84 mg, 54%) as a colorless liquid.

^1H NMR (500 MHz, $CDCl_3$) δ 1.41 (6H, s), 5.76 (1H, dd, J_{HF} = 20.6 Hz, J = 11.4 Hz), 6.63 (1H, dd, J_{HF} = 83.7 Hz, J = 11.4 Hz), 7.39 (2H, t, J = 7.5 Hz), 7.47 (1H, t, J = 7.5 Hz), 7.85 (2H, d, J = 7.5 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 26.5, 45.6 (d, J_{CF} = 8 Hz), 118.3 (d, J_{CF} = 11 Hz), 128.0, 128.9, 131.7, 136.7, 149.7 (d, J_{CF} = 256 Hz), 203.7 (d, J_{CF} = 2 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 30.9 (dd, J_{FH} = 84, 21 Hz). IR (neat) 2978, 1736, 1678, 1254, 1169, 1076, 957, 920, 700 cm^{-1}. HRMS (FAB): calcd for $C_{12}H_{14}FO$ ($[M + H]^+$) 193.1029, found 193.1043.

3.3.12. 4,4-Dichloro-2,2-dimethyl-1-phenylbut-3-en-1-one (**23c**) [24]

To a solution of diethyl trichloromethylphosphonate (3.35 g, 13.1 mmol) [25] in THF (40 mL) was added butyllithium (8.23 mL, 1.6 M in hexane, 13.1 mmol) dropwise at −90 °C. After stirring for 1 h, **18a** (2.31 g, 13.1 mmol) [32] was added, and then the mixture was stirred at room temperature for 8 h. The reaction was quenched with phosphate buffer (pH 7), and organic materials were extracted with Et_2O three times. The

combined extracts were washed with water and brine, and dried over $MgSO_4$. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (Et_2O–hexane 1:10) to give **23c** (956 mg, 30%) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.48 (3H, s), 1.48 (3H, s), 6.38 (1H, s), 7.44 (2H, td, J = 7.7, 1.3 Hz), 7.54 (1H, tt, J = 7.7, 1.3 Hz), 7.9 (2H, dd, J = 7.7, 1.3 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 26.4, 26.4, 48.4, 121.9, 128.2, 129.1, 132.6, 134.5, 135.4, 201.0. IR (neat) 2979, 1682, 1446, 1242, 1165, 906, 849, 715 cm^{-1}. HRMS (FAB): calcd for $C_{12}H_{13}Cl_2O$ ($[M + H]^+$) 243.0343, found 243.0363.

3.3.13. 4,4-Dibromo-2,2-dimethyl-1-phenylbut-3-en-1-one (**23d**) [26]

To a solution of PPh_3 (4.23 g, 16.1 mmol) in CH_2Cl_2 (27 mL) was added CBr_4 (2.67 g, 8.05 mmol) through a solid addition funnel at 0 °C. The reaction mixture was stirred for 20 min at that temperature, and **18a** (946 mg, 5.37 mmol) [32] was added. After stirring at room temperature for 6 h, the reaction was quenched with water and hexane, and the mixture was filtrated through a Celite pad. Organic materials were extracted with AcOEt twice, and the combined extracts were dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (AcOEt–hexane 1:20) to give **23d** (1.28 g, 72%) as a pale yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.50 (3H, s), 1.50 (3H, s), 7.04 (1H, s), 7.44 (2H, t, J = 7.9 Hz), 7.54 (1H, tt, J = 7.9, 1.2 Hz), 7.98 (2H, dd, J = 7.9, 1.2 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 26.4, 26.4, 50.6, 90.3, 128.2, 129.2, 132.6, 134.5, 143.8, 200.7. IR (neat) 2981, 1676, 1446, 1240, 1163, 976, 874, 787, 710, 685 cm^{-1}. HRMS (FAB): calcd for $C_{12}H_{13}Br_2O$ ($[M + H]^+$) 330.9333, found 330.9351.

3.3.14. 4,4-Difluoro-2,2-dimethyl-1-phenylbut-3-en-1-one oxime (**20a**)

To a solution of **19a** (1.16 g, 5.5 mmol) in EtOH (10 mL) was added pyridine (1.2 g, 16 mmol) and hydroxyamine hydrochloride (NH_2OH·HCl, 0.72 g, 10 mmol). After the mixture was heated to reflux for 2 h, the reaction was quenched with phosphate buffer (pH 7) at room temperature. Organic materials were extracted with AcOEt three times. The combined extracts were washed with brine and aqueous 2 M HCl five times, and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by recrystalization from hexane to give **20a** (0.80 g, 64%) as white needles.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.34 (6H, dd, J = 1.7, 0.6 Hz), 4.29 (1H, dd, J_{HF} = 27.4, 5.4 Hz), 7.13 (2H, ddd, J = 6.7, 1.7, 1.7 Hz), 7.40–7.45 (3H, m), 7.90 (1H, s). ^{13}C NMR (126 MHz, $CDCl_3$) δ 26.9 (d, J_{CF} = 4 Hz), 38.6 (dd, J_{CF} = 5, 4 Hz), 84.9 (dd, J_{CF} = 23, 14 Hz), 127.8, 128.1, 128.3, 132.8, 155.4 (dd, J_{CF} = 294, 286 Hz), 163.8. ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 76.9 (1F, dd, J_{FF} = 45 Hz, J_{FH} = 5 Hz), 77.5 (1F, dd, J_{FF} = 45 Hz, J_{FH} = 27 Hz). IR (neat) 3255, 2978, 1739, 1452, 1331, 1225, 1130, 1016, 957, 771, 702 cm^{-1}. Anal. Calcd for $C_{12}H_{13}F_2NO$: C, 63.99; H, 5.82; N, 6.22%. Found: C, 63.74; H, 5.87; N, 6.11%. Crystal data. $C_{12}H_{13}F_2NO$, M = 225.23, monoclinic, a = 7.5652(18), b = 6.3060(15), c = 23.707(6) Å, U = 1121.4(5) Å^3, T = 120(2) K, space group $P2_1/c$, Z = 4, μ(Mo Kα) = 0.107 mm^{-1}, 6907 reflections measured, 2186 unique (R_{int} = 0.0158) which were used in all calculations. The final $wR(F^2)$ was 0.3643 (all data). The largest residual electron density hole was −1.338e Å^{-3}.

3.3.15. [1-(2,2-Difluorovinyl)cyclohexyl]phenylmethanone oxime (**20b**)

To a mixture of CF_2Br_2 (13 g, 63 mmol) and microwave-dried molecular sieves (4 Å) powder (6.4 g) in THF (60 mL) was added $P(NMe_2)_3$ (21 g, 0.13 mol) at −78 °C. The reaction mixture was stirred at that temperature for 30 min, and **18b** (6.9 g, 32 mmol) was added at room temperature. After stirring for 10 h, the reaction was quenched with phosphate buffer (pH 7). The mixture was extracted with AcOEt three times. The combined extracts were washed with brine and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was dissolved in EtOH (50 mL). Pyridine (5.9 g, 74 mmol) and NH_2OH·HCl (3.4 g, 49 mmol) were added, and the mixture was heated to reflux for 2 h. The reaction was quenched with phosphate buffer (pH 7) at room temperature. Organic materials were extracted with AcOEt three times, and the combined extracts were washed with brine and aqueous 2 M HCl five times, and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by recrystalization from hexane to give **20b** (5.4 g, 64%) as white needles.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.25 (1H, dtt, J = 11.6, 11.6, 3.1 Hz), 1.37–1.44 (2H, m), 1.53–1.69 (5H, m), 1.82 (2H, br d, J = 12.2 Hz), 4.07 (1H, dd, J_{HF} = 28.4, 5.2 Hz), 7.13 (2H, dm, J = 7.0 Hz), 7.38 (1H, tm, J = 7.0 Hz), 7.42 (2H, tm, J = 7.0 Hz), 8.28 (1H, s). ^{13}C NMR (126 MHz, $CDCl_3$) δ 22.3, 25.6, 34.4 (d, J_{CF} = 2 Hz), 42.4 (dd, J_{CF} = 4, 4 Hz), 82.8 (dd, J_{CF} = 24, 13 Hz), 127.9, 128.0, 128.2, 132.9, 155.6 (dd, J_{CF} = 294, 287 Hz) 163.5. ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 78.1 (1F, brd, J_{FF} = 42 Hz), 79.0 (1F, dd, J_{FF} = 42 Hz, J_{FH} = 28 Hz). IR (neat) 3244, 2931, 1736, 1333, 1221, 1182, 1163, 1001, 958, 900, 765, 705 cm^{-1}. HRMS (FAB): calcd for $C_{15}H_{18}F_2NO$ ($[M + H]^+$) 266.1356, found 266.1351.

3.3.16. (E)-6,6-Difluoro-4,4-dimethyl-1-phenylhexa-1,5-dien-3-one oxime (**20c**)

Compound **20c** was prepared by the method described for **20a** using **19c** (330 mg, 1.40 mmol), EtOH (3.0 mL), pyridine (0.33 g, 4.2 mmol), and NH_2OH·HCl (0.19 g, 2.8 mmol). The mixture was heated to reflux for 2 h. Purification by column chromatography on silica gel (hexane–AcOEt 5:1) gave **20c** (119 mg, 34%) as white needles.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.46 (6H, s), 4.43 (1H, dd, J_{HF} = 27.3, 4.5 Hz), 6.93 (1H, d, J = 16.9 Hz), 7.30 (1H, t, J = 7.4 Hz), 7.35 (2H, t, J = 7.4 Hz), 7.50 (2H, d, J = 7.4 Hz), 7.53 (1H, d, J = 16.9 Hz), 10.26 (1H, br s). ^{13}C NMR (126 MHz, $CDCl_3$) δ 27.7, 38.3 (dd, J_{CF} = 5, 3 Hz), 86.2 (dd, J_{CF} = 23, 14 Hz), 115.5, 127.1, 128.7, 128.9, 136.6, 139.2,

155.4 (dd, J_{CF} = 307, 287 Hz), 158.4. ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 76.3 (1F, dd, J_{FF} = 45 Hz, J_{FH} = 5 Hz), 77.3 (1F, dd, J_{FF} = 45 Hz, J_{FH} = 27 Hz). IR (neat) 3276, 2983, 1734, 1448, 1327, 1221, 1124, 955, 752, 690 cm^{-1}. Anal. Calcd for $C_{14}H_{15}F_2NO$: C, 66.92; H, 6.02; N, 5.57%. Found: C, 67.05; H, 6.26; N, 5.47%.

*3.3.17. 1,1-Difluoro-3,3-dimethyltridec-1-en-4-one oxime (**20d**)*

Compound **20d** was prepared by the method described for **20a** using **19d** (1.58 g, 6.06 mmol), EtOH (12 mL), pyridine (1.44 g, 18.2 mmol), and NH_2OH·HCl (842 mg, 12.1 mmol). Purification by column chromatography on silica gel (hexane–AcOEt 5:1) gave **20d** (1.35 g, 81%) as a colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (3H, t, J = 7.0 Hz), 1.24–1.37 (12H, m), 1.32 (6H, s), 1.57 (2H, tt, J = 8.1, 8.1 Hz), 2.25 (2H, t, J = 8.1 Hz), 4.21 (1H, dd, J_{HF} = 25.4, 7.4 Hz), 9.37 (1H, br s). ^{13}C NMR (126 MHz, $CDCl_3$) δ 14.1, 22.7, 26.3, 26.3, 27.0, 29.2, 29.3, 29.5, 30.4, 31.9, 38.9 (dd, J_{CF} = 4, 2 Hz), 85.0 (dd, J_{CF} = 22, 15 Hz), 155.6 (dd, J_{CF} = 294, 287 Hz), 164.8. ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 76.5 (1F, dd, J_{FF} = 46 Hz, J_{FH} = 7 Hz), 76.7 (1F, dd, J_{FF} = 46 Hz, J_{FH} = 25 Hz). IR (neat) 3297, 2924, 1736, 1331, 1221, 1128, 1001, 945, 721 cm^{-1}. HRMS (FAB): calcd for $C_{15}H_{28}F_2NO$ ($[M + H]^+$) 276.2139, found 276.2143.

*3.3.18. tert-Butyl 5,5-difluoro-2-hydroxyimino-3,3-dimethylpent-4-enoate (**20e**)*

Compound **20e** was prepared by the method described for **20a** using **19e** (1.13 g, 4.83 mmol), EtOH (14 mL), pyridine (1.15 g, 14.5 mmol), and NH_2OH·HCl (671 mg, 9.66 mmol). The combined extracts were washed with brine and aqueous 0.5 M HCl five times, and dried over Na_2SO_4. Purification by column chromatography on silica gel (hexane–AcOEt 5:1) gave **20e** (1.35 g, 71%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.39 (6H, s), 1.55 (9H, s), 4.33 (1H, dd, J_{HF} = 27.1, 4.9 Hz), 8.08 (1H, s). ^{13}C NMR (126 MHz, $CDCl_3$) δ 26.4 (d, J_{CF} = 4 Hz) 28.1, 36.2 (dd, J_{CF} = 6, 3 Hz), 84.0, 84.1 (dd, J_{CF} = 24, 14 Hz), 155.7 (dd, J_{CF} = 295, 286 Hz), 157.8, 162.5. ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 76.8 (1F, dd, J_{FF} = 44 Hz, J_{FH} = 5 Hz), 78.2 (1F, dd, J_{FF} = 44 Hz, J_{FH} = 27 Hz). IR (neat) 3452, 2983, 1732, 1371, 1302, 1227, 1159, 1128, 1078, 1005, 955, 841 cm^{-1}. Anal. Calcd for $C_{11}H_{17}F_2NO_3$: C, 53.01; H, 6.87; N, 5.62%. Found: C, 52.93; H, 6.87; N, 5.35%.

*3.3.19. 2-(2,2-Difluorovinyl)-2-methyl-3,4-dihydro-2H-naphthalen-1-one oxime (**20f**)*

Compound **20f** was prepared by the method described for **20a** using **19f** (2.36 g, 10.6 mmol), EtOH (32 mL), pyridine (10.1 g, 127 mmol), and NH_2OH·HCl (5.9 g, 85 mmol). The reaction mixture was heated to reflux for 10 h. Purification by column chromatography on silica gel (hexane–AcOEt 5:1) gave **20f** (1.35 g, 49%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) [major] δ 1.63 (3H, s), 1.81 (1H, ddd, J = 12.9, 7.5, 3.8 Hz), 1.99 (1H, ddd, J = 12.9, 8.6, 3.8 Hz), 2.71 (1H, ddd, J = 15.4, 7.5, 3.8 Hz), 2.78 (1H, ddd, J = 15.4, 8.6, 3.8 Hz), 4.63 (1H, dd, J_{HF} = 27.8, 4.9 Hz), 7.15 (1H, dd, J = 7.6, 0.7 Hz), 7.22 (1H, td, J = 7.6, 0.7 Hz), 7.27 (1H, td, J = 7.6, 1.3 Hz), 7.82 (1H, dd, J = 7.6, 1.3 Hz), 9.12 (1H, br s). [minor] δ 1.44 (3H, s), 1.96 (1H, ddd, J = 13.7, 8.2, 1.4 Hz), 2.10 (1H, ddd, J = 13.7, 5.3, 5.3 Hz,), 2.91–2.97 (2H, m), 4.33 (1H, dd, J_{HF} = 26.6, 5.9 Hz), 7.19 (1H, dd, J = 7.6, 0.7 Hz), 7.25 (1H, td, J = 7.6, 0.7 Hz), 7.31 (1H, td, J = 7.6, 1.3 Hz), 8.45 (1H, dd, J = 7.6, 1.3 Hz), 9.12 (1H, br s). ^{13}C NMR (126 MHz, $CDCl_3$) [major] δ 22.5, 26.7, 36.9 (dd, J_{CF} = 5, 3 Hz), 38.3 (dd, J_{CF} = 3, 3 Hz), 85.2 (dd, J_{CF} = 24, 14 Hz), 125.4 (d, J_{CF} = 6 Hz), 126.7, 128.0, 129.0, 131.6, 139.8, 155.1 (dd, J_{CF} = 292, 284 Hz), 157.0. [minor] δ 24.6 (dd, J_{CF} = 3, 3 Hz), 26.3, 36.2, 38.7 (dd, J_{CF} = 5, 3 Hz), 83.6 (dd, J_{CF} = 23, 14 Hz), 126.0, 126.9 (d, J_{CF} = 7 Hz), 128.7, 129.8, 131.2, 138.7, 155.7 (dd, J_{CF} = 293, 286 Hz), 156.0. ^{19}F NMR (471 MHz, $CDCl_3$) [major] δ_F 73.1 (1F, dd, J_{FF} = 50 Hz, J_{FH} = 5 Hz), 76.2 (1F, dd, J_{FF} = 50 Hz, J_{FH} = 28 Hz). [minor] δ_F 76.8 (1F, dd, J_{FF} = 44 Hz, J_{FH} = 6 Hz), 78.0 (1F, dd, J_{FF} = 44 Hz, J_{FH} = 27 Hz). IR (neat) 3452, 2935, 1736, 1456, 1323, 1182, 912, 852, 769, 731 cm^{-1}. HRMS (FAB): calcd for $C_{13}H_{14}F_2NO$ ($[M + H]^+$) 238.1043, found 238.1062.

*3.3.20. (Z)-4-Fluoro-2,2-dimethyl-1-phenylbut-3-en-1-one oxime (**24a**)*

Compound **24a** was prepared by the method described for **20a** using **23a** (156 mg, 0.81 mmol), EtOH (3 mL), pyridine (0.19 g, 2.4 mmol), and NH_2OH·HCl (0.11 g, 1.6 mmol). Purification by column chromatography on silica gel (hexane–AcOEt 5:1) gave **24a** (112 mg, 75%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.23 (6H, s), 5.49 (1H, dd, J_{HF} = 21.2 Hz, J = 11.3 Hz), 6.39 (1H, dd, J_{HF} = 84.3 Hz, J = 11.3 Hz), 7.11 (2H, d, J = 7.2 Hz), 7.36 (1H, t, J = 7.2 Hz), 7.40 (2H, t, J = 7.2 Hz), 9.37 (1H, br s). ^{13}C NMR (126 MHz, $CDCl_3$) δ 25.8, 39.5 (d, J_{CF} = 9 Hz), 118.4 (d, J_{CF} = 11 Hz), 127.8, 127.9, 128.2, 132.7, 149.3 (d, J_{CF} = 254 Hz), 164.0 (d, J_{CF} = 2 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 28.9 (dd, J_{FH} = 84, 21 Hz). IR (neat) 3267, 2976, 1739, 1670, 1078, 951, 924, 756, 702, 650 cm^{-1}. HRMS (FAB): calcd for $C_{12}H_{15}FNO$ ($[M + H]^+$) 208.1138, found 208.1141.

*3.3.21. 2,2-Dimethyl-1-phenylbut-3-en-1-one oxime (**24b**)*

Compound **24b** was prepared by the method described for **20a** using 2,2-dimethyl-1-phenylbut-3-en-1-one (**23b**, 203 mg, 1.2 mmol) [27], EtOH (2.3 mL), pyridine (0.28 g, 3.5 mmol), and NH_2OH·HCl (0.16 g, 2.3 mmol). Purification by thin-layer chromatography on silica gel (hexane–AcOEt 5:1) gave **24b** (193 mg, 88%) as white needles.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.20 (6H, s), 4.97 (1H, d, J = 17.4 Hz), 5.01 (1H, d, J = 10.6 Hz), 5.91 (1H, dd, J = 17.4, 10.6 Hz), 7.12 (2H, d, J = 6.8 Hz), 7.31 (1H, t, J = 6.8 Hz), 7.36 (2H, t, J = 6.8 Hz), 9.70 (1H, s). ^{13}C NMR (126 MHz, $CDCl_3$) δ 25.2, 43.1, 113.0, 127.7, 127.8, 127.9, 133.2, 143.8, 164.1. IR (neat) 3255, 2970, 1410, 1360, 1012, 968, 951, 918, 769, 717, 696 cm^{-1}. HRMS (FAB): calcd for $C_{12}H_{16}NO$ ($[M + H]^+$) 190.1232, found 190.1225.

*3.3.22. 4,4-Dichloro-2,2-dimethyl-1-phenylbut-3-en-1-one oxime (**24c**)*

Compound **24c** was prepared by the method described for **20a** using **23c** (971 mg, 4.00 mmol), EtOH (8 mL), pyridine (0.95 g, 12 mmol), and $NH_2OH{\cdot}HCl$ (0.56 g, 8.0 mmol). Purification by column chromatography on silica gel (hexane–AcOEt 5:1) gave **24c** (433 mg, 42%) as a colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.39 (6H, s), 5.90 (1H, s), 7.18 (2H, tm, J = 7.2 Hz), 7.39 (1H, tt, J = 7.2, 1.4 Hz), 7.43 (2H, tm, J = 7.2 Hz), 8.38 (1H, br s). ^{13}C NMR (126 MHz, $CDCl_3$) δ 26.3, 42.9, 122.1, 127.7, 128.2, 128.4, 132.9, 134.7, 162.0. IR (neat) 3261, 2978, 1608, 1385, 1271, 1014, 958, 906, 849, 742, 698, 660, 598 cm^{-1}. HRMS (FAB): calcd for $C_{12}H_{14}Cl_2NO$ ($[M + H]^+$) 258.0452, found 258.0450.

*3.3.23. 4,4-Dibromo-2,2-dimethyl-1-phenylbut-3-en-1-one oxime (**24d**)*

Compound **24d** was prepared by the method described for **20a** using **23d** (1.61 g, 4.87 mmol), EtOH (9.8 mL), pyridine (1.16 g, 14.6 mmol), and $NH_2OH{\cdot}HCl$ (678 mg, 9.76 mmol). Purification by column chromatography on silica gel (hexane–AcOEt 5:1) gave **24d** (1.01 g, 66%) as a pale yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.33 (6H, s), 6.49 (1H, s), 7.05 (1H, br s), 7.15 (2H, d, J = 8.1 Hz), 7.32 (1H, t, J = 8.1 Hz), 7.36 (2H, t, J = 8.1 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 26.6, 45.0, 90.0, 127.8, 128.2, 128.5, 132.9, 142.8, 161.4. IR (neat) 3240, 2974, 1460, 1443, 1016, 951, 883, 766, 694 cm^{-1}. HRMS (FAB): calcd for $C_{12}H_{14}Br_2NO$ ($[M + H]^+$) 345.9442, found 345.9428.

*3.3.24. 4,4-Difluoro-2,2-dimethyl-1-phenylbut-3-en-1-one O-pentafluorobenzoyloxime (**15a**)*

To a solution of oxime **20a** (0.80 g, 3.5 mmol) in CH_2Cl_2 (10 mL) were added NEt_3 (0.72 g, 7.1 mmol) and pentafluorobenzoyl chloride (C_6F_5COCl, 1.2 g, 5.3 mmol) at 0 °C. After the mixture was stirred for 15 min, the reaction was quenched with phosphate buffer (pH 7). Organic materials were extracted with CH_2Cl_2 three times, and the combined extracts were washed with brine and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (hexane–AcOEt 10:1) to give **15a** (1.4 g, 92%) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.48 (6H, d, J = 1.4 Hz), 4.38 (1H, dd, J_{HF} = 27.1, 5.0 Hz), 7.07–7.10 (2H, m), 7.39–7.41 (3H, m). ^{13}C NMR (126 MHz, $CDCl_3$) δ 26.6 (dd, J_{CF} = 4, 1 Hz), 39.8 (dd, J_{CF} = 6, 4 Hz), 84.1 (dd, J_{CF} = 25, 13 Hz), 106.9 (td, J_{CF} = 11, 4 Hz), 126.6, 128.1, 128.9, 131.8, 137.5 (ddddd, J_{CF} = 256, 14, 14, 6, 2 Hz), 143.2 (dtt, J_{CF} = 243, 17, 5 Hz), 145.3 (dddd, J_{CF} = 238, 15, 7, 4 Hz), 155.7 (dd, J_{CF} = 295, 287 Hz), 156.5, 174.2 (dd, J_{CF} = 4, 4 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 1.5 (2F, dddd, J_{FF} = 26, 20, 12, 5 Hz), 13.6 (1F, tt, J_{FF} = 20, 5 Hz), 24.3 (2F, dddd, J_{FF} = 26, 5, 5, 5 Hz), 78.4 (1F, dd, J_{FF} = 42 Hz, J_{FH} = 5 Hz), 77.5 (1F, dd, J_{FF} = 42 Hz, J_{FH} = 27 Hz). IR (neat) 1753, 1523, 1500, 1327, 1194, 1095, 1005, 931, 702 cm^{-1}. Anal. Calcd for $C_{19}H_{12}F_7NO_2$: C, 54.43; H, 2.88; N, 3.34%. Found: C, 54.45; H, 3.04; N, 3.33%.

*3.3.25. [1-(2,2-Difluorovinyl)cyclohexyl]phenylmethanone O-pentafluorobenzoyloxime (**15b**)*

Compound **15b** was prepared by the method described for **15a** using **20b** (4.2 g, 16 mmol), CH_2Cl_2 (40 mL), NEt_3 (3.2 g, 32 mmol), and C_6F_5COCl (5.5 g, 24 mmol). Purification by column chromatography on silica gel (hexane–AcOEt 10:1) gave **15b** (5.6 g, 78%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.34 (1H, dtt, J = 12.8, 10.5, 4.1 Hz), 1.46 (2H, ddddd, J = 13.5, 10.5, 10.5, 3.8, 3.4 Hz), 1.60 (1H, dtt, J = 12.8, 4.3, 3.8 Hz), 1.70 (2H, ddddd, J = 13.5, 4.5, 4.3, 4.1, 3.7 Hz), 1.81–1.90 (2H, m), 1.90–1.98 (2H, m), 4.14 (1H, dd, J_{HF} = 28.1, 4.8 Hz), 7.08–7.11 (2H, m), 7.37–7.40 (3H, m). ^{13}C NMR (126 MHz, $CDCl_3$) δ 22.2, 25.4, 34.2 (dd, J_{CF} = 3, 1 Hz), 43.8 (dd, J_{CF} = 4, 4 Hz), 82.0 (dd, J_{CF} = 24, 8 Hz), 107.0 (td, J_{CF} = 17, 2 Hz), 126.7, 128.0, 128.8, 131.8, 137.5 (ddddd, J_{CF} = 256, 16, 16, 5, 2 Hz), 143.2 (dtt, J_{CF} = 261, 13, 5 Hz), 145.1 (dddd, J_{CF} = 252, 16, 7, 4 Hz), 155.9 (dd. J_{CF} = 297, 288 Hz), 156.6, 173.6. ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 1.5 (2F, dddd, J_{FF} = 22, 20, 10, 5 Hz), 13.4 (1F, tt, J_{FF} = 22, 4 Hz), 24.4 (2F, dddd, J_{FF} = 20, 5, 5, 4 Hz), 79.6 (1F, br d, J_{FF} = 38 Hz), 80.6 (1F, dd, J_{FF} = 38 Hz, J_{FH} = 28 Hz). IR (neat) 1734, 1523, 1496, 1325, 1180, 1167, 995, 922, 891, 831, 731, 702, 696 cm^{-1}. HRMS (FAB): calcd for $C_{22}H_{17}F_7NO_2$ ($[M + H]^+$) 460.1148, found 460.1156.

*3.3.26. (E)-6,6-Difluoro-4,4-dimethyl-1-phenylhexa-1,5-dien-3-one O-pentafluorobenzoyloxime (**15c**)*

Compound **15c** was prepared by the method described for **15a** using **20c** (119 mg, 0.47 mmol), CH_2Cl_2 (2 mL), NEt_3 (95 mg, 0.94 mmol), and C_6F_5COCl (0.16 g, 0.71 mmol). Purification by thin-layer chromatography on silica gel (hexane–AcOEt 5:1) gave **15c** (189 mg, 87%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.54 (6H, s), 4.50 (1H, dd, J_{HF} = 27.1, 4.5 Hz), 6.83 (1H, d, J = 16.7 Hz), 7.31 (1H, d, J = 16.7 Hz), 7.35–7.41(3H, m), 7.48 (2H, dd, J = 7.6, 1.5 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 27.5, 39.3 (dd, J_{CF} = 5, 3 Hz), 85.6 (dd, J_{CF} = 24, 14 Hz), 107.3 (td, J_{CF} = 17, 3 Hz), 114.9, 127.3, 128.9, 129.8, 135.3, 137.7 (ddddd, J_{CF} = 256, 18, 13, 6, 3 Hz), 141.2, 143.3 (dtt, J_{CF} = 259, 13, 5 Hz), 145.3 (dddd, J_{CF} = 255, 17, 6, 3 Hz), 155.7 (dd, J_{CF} = 295, 287 Hz), 156.5, 174.2. ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 1.5 (2F, dddd, J_{FF} = 26, 21, 11, 5 Hz), 13.6 (1F, tt, J_{FF} = 21, 5 Hz), 24.3 (2F, dddd, J_{FF} = 26, 5, 5, 5 Hz), 77.5 (1F, dd, J_{FF} = 42 Hz, J_{FH} = 27 Hz), 78.4 (1F, dd, J_{FF} = 42 Hz, J_{FH} = 5 Hz). IR (neat) 1753, 1523, 1500, 1327, 1194, 1095, 1005, 931, 702 cm^{-1}. HRMS (FAB): calcd for $C_{21}H_{15}F_7NO_2$ ($[M + H]^+$) 446.0991, found 446.1003.

*3.3.27. 1,1-Difluoro-3,3-dimethyltridec-1-en-4-one O-pentafluorobenzoyloxime (**15d**)*

Compound **15d** was prepared by the method described for **15a** using **20d** (1.33 g, 4.84 mmol), CH_2Cl_2 (10 mL), NEt_3 (980 mg, 9.69 mmol), and C_6F_5COCl (1.68 g, 7.29 mmol). Purification by column chromatography on silica gel (hexane–AcOEt 10:1) gave **15d** (1.75 g, 77%) as a colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (3H, t, J = 7.0 Hz), 1.21–1.31 (10H, m), 1.35 (2H, tt, J = 7.3, 6.9 Hz), 1.43 (6H, s), 1.56 (2H, tt, J = 7.9, 7.3 Hz), 2.35 (2H, t, J = 7.9 Hz), 4.32 (1H,

dd, J_{HF} = 26.8, 5.1 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 14.0, 22.6, 26.1 (d, J_{CF} = 3 Hz), 27.0, 28.8, 28.9, 29.2, 29.3, 30.1, 31.8, 40.0 (dd, J_{CF} = 5, 3 Hz), 84.3 (dd, J_{CF} = 24, 14 Hz), 107.4 (td, J_{CF} = 17, 4 Hz), 137.7 (ddddd, J_{CF} = 256, 17, 15, 6, 1 Hz), 143.3 (dtt, J_{CF} = 261, 13, 5 Hz), 145.3 (dddd, J_{CF} = 255, 15, 8, 4 Hz), 155.8 (dd, J_{CF} = 295, 287 Hz), 156.7, 174.6. ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 1.8 (2F, dddd, J_{FF} = 26, 21, 11, 5 Hz), 13.7 (1F, tt, J_{FF} = 21, 5 Hz,), 24.4 (2F, dddd, J_{FF} = 26, 5, 5, 5 Hz), 77.8 (1F, dd, J_{FF} = 43 Hz, J_{FH} = 5 Hz), 78.2 (1F, dd, J_{FF} = 43 Hz, J_{FH} = 27 Hz). IR (neat) 2927, 1763, 1736, 1496, 1325, 1188, 997, 866 cm^{-1}. HRMS (FAB): calcd for $C_{22}H_{27}F_7NO_2$ ([M + H]$^+$) 470.1930, found 470.1928.

3.3.28. tert-Butyl 5,5-difluoro-2-pentafluorobenzoyloxyimino-3,3-dimethylpent-4-enoate (15e)

Compound **15e** was prepared by the method described for **15a** using **20e** (35.3 mg, 0.142 mmol), CH_2Cl_2 (2 mL), NEt_3 (28 mg, 0.28 mmol), and C_6F_5COCl (49 mg, 0.21 mmol). Purification by thin-layer chromatography on silica gel (hexane–AcOEt 5:1) gave **15e** (41 mg, 64%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.51 (9H, s), 1.52 (6H, br s), 4.40 (1H, dd, J_{HF} = 26.8, 4.4 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 26.3 (d, J_{CF} = 4 Hz), 27.8, 37.5 (dd, J_{CF} = 6, 3 Hz), 83.3 (dd, J_{CF} = 26, 14 Hz), 85.4, 107.4 (td, J_{CF} = 16, 4 Hz), 137.7 (ddddd, J_{CF} = 257, 16, 16, 5, 1 Hz), 143.6 (dtt, J_{CF} = 261, 14, 5 Hz), 145.4 (dddd, J_{CF} = 260, 17, 6, 4 Hz), 155.6, 156.0 (dd, J_{CF} = 298, 288 Hz), 160.3, 166.1. ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 2.0 (2F, dddd, J_{FF} = 28, 20, 12, 6 Hz), 14.9 (1F, tt, J_{FF} = 20, 5 Hz), 24.4 (2F, dddd, J_{FF} = 28, 6, 6, 5 Hz), 78.7 (1F, dd, J_{FF} = 40 Hz, J_{FH} = 4 Hz), 78.2 (1F, dd, J_{FF} = 40 Hz, J_{FH} = 27 Hz). IR (neat) 1732, 1496, 1327, 1182, 1157, 1066, 1003, 874 cm^{-1}. Anal. Calcd for $C_{18}H_{16}F_7NO_4$: C, 48.77; H, 3.64; N, 3.16%. Found: C, 48.85; H, 3.76; N, 2.99%.

3.3.29. 2-(2,2-Difluorovinyl)-2-methyl-3,4-dihydro-2H-naphthalen-1-one O-pentafluorobenzoyloxime (15f)

Compound **15f** was prepared by the method described for **15a** using **20f** (1.24 g, 5.2 mmol), CH_2Cl_2 (10 mL), NEt_3 (1.06 g, 10.5 mmol), and C_6F_5COCl (1.81 g, 7.9 mmol). The reaction mixture was stirred at 0 °C for 1 h, and purification by column chromatography on silica gel (hexane–AcOEt 10:1) gave **15f** (1.65 g, 72%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) [major] δ 1.59 (3H, s), 1.85 (1H, ddd, J = 13.3, 6.8, 3.7 Hz), 2.00 (1H, ddd, J = 13.3, 9.2, 3.8 Hz), 2.77 (1H, ddd, J = 16.0, 6.8, 3.8 Hz), 2.83 (1H, ddd, J = 16.0, 9.2, 3.7 Hz), 4.52 (1H, dd, J_{HF} = 27.0, 4.2 Hz), 7.20 (1H, d, J = 7.4 Hz), 7.37 (1H, td, J = 7.4, 1.5 Hz), 7.38 (1H, td, J = 7.4, 1.5 Hz), 8.14 (1H, d, J = 7.4 Hz). [minor] δ 1.53 (3H, s), 2.08 (1H, ddd, J = 15.1, 7.5, 0.9 Hz), 2.20 (1H, ddd, J = 15.1, 4.9, 4.9 Hz), 2.95–3.07 (2H, m), 4.44 (1H, dd, J_{HF} = 27.5, 4.4 Hz), 7.20–7.29 (3H, m), 7.95 (1H, d, J = 8.0 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) [major] δ 23.0, 26.1, 37.9 (dd, J_{CF} = 5, 2 Hz), 38.3 (dd, J_{CF} = 2, 2 Hz), 85.1 (dd, J_{CF} = 25, 14 Hz), 107.2 (td, J_{CF} = 17, 3 Hz), 125.6, 126.9, 127.0, 128.2, 131.1, 137.7 (ddddd, J_{CF} = 257, 18, 10, 4, 2 Hz), 141.0, 143.4 (dtt, J_{CF} = 260, 13, 4 Hz), 145.1 (ddddd, J_{CF} = 260, 18, 7, 3, 2 Hz), 155.2 (dd, J_{CF} = 292, 286 Hz), 156.1, 165.5. [minor] δ 24.1 (dd, J_{CF} = 2, 2 Hz), 26.0, 36.3, 39.8 (dd, J_{CF} = 5, 3 Hz), 82.5 (dd, J_{CF} = 24, 15 Hz), 107.2 (td, J_{CF} = 17, 3 Hz), 125.9, 128.7, 128.9, 131.0, 131.1, 137.7 (ddddd, J_{CF} = 257, 18, 10, 4, 2 Hz), 139.4, 143.4 (dtt, J_{CF} = 260, 13, 4 Hz), 145.1 (ddddd, J_{CF} = 260, 18, 7, 3, 2 Hz), 155.7 (dd, J_{CF} = 294, 288 Hz), 157.0, 165.9. ^{19}F NMR (471 MHz, $CDCl_3$) [major] δ_F 2.1 (2F, dddd, J_{FF} = 26, 21, 12, 6 Hz), 14.2 (1F, tt, J_{FF} = 21, 5 Hz), 24.3 (2F, dddd, J_{FF} = 26, 6, 6, 5 Hz), 74.1 (1F, br d, J_{FF} = 46 Hz), 77.7 (1F, dd, J_{FF} = 46 Hz, J_{FH} = 27 Hz). [minor] δ_F 1.8 (2F, dddd, J_{FF} = 26, 20, 11, 5 Hz), 13.7 (1F, tt, J_{FF} = 20, 4 Hz), 24.5 (2F, dddd, J_{FF} = 26, 5, 5, 4 Hz), 77.4 (1F, dd, J_{FF} = 43 Hz, J_{FH} = 4 Hz), 78.0 (1F, dd, J_{FF} = 43 Hz, J_{FH} = 28 Hz). IR (neat) 1750, 1525, 1496, 1325, 1194, 1005, 922, 872, 775, 739 cm^{-1}. HRMS (FAB): calcd for $C_{20}H_{13}F_7NO_2$ ([M + H]$^+$) 432.0835, found 432.0853.

3.3.30. (Z)-4-Fluoro-2,2-dimethyl-1-phenylbut-3-en-1-one O-pentafluorobenzoyloxime (21a)

Compound **21a** was prepared by the method described for **15a** using **24a** (112 mg, 0.54 mmol), CH_2Cl_2 (1.5 mL), NEt_3 (109 mg, 1.08 mmol), and C_6F_5COCl (166 mg, 0.72 mmol). Purification by thin-layer chromatography on silica gel (hexane–AcOEt 5:1) gave **21a** (132 mg, 61%) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.41 (6H, s), 5.59 (1H, dd, J_{HF} = 20.7 Hz, J = 11.3 Hz), 6.52 (1H, dd, J_{HF} = 83.6 Hz, J = 11.3 Hz), 7.10 (2H, dd, J = 7.6, 2.0 Hz), 7.37–7.42 (3H, m). ^{13}C NMR (126 MHz, $CDCl_3$) δ 25.5, 40.7 (d, J_{CF} = 10 Hz), 106.8 (td, J_{CF} = 16, 4 Hz), 117.4 (d, J_{CF} = 12 Hz), 126.7, 127.9, 128.8, 131.7, 137.5 (ddddd, J_{CF} = 255, 16, 14, 5, 2 Hz), 143.1 (dtt, J_{CF} = 246, 13, 5 Hz), 145.1 (dddd, J_{CF} = 259, 18, 7, 4 Hz), 150.1 (d, J_{CF} = 256 Hz), 156.4, 174.7 (d, J_{CF} = 3 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 1.5 (2F, dddd, J_{FF} = 26, 21, 12, 6 Hz), 13.6 (1F, tt, J_{FF} = 21, 4 Hz), 24.4 (2F, dddd, J_{FF} = 26, 6, 5, 4 Hz), 31.0 (1F, dd, J_{FH} = 84, 21 Hz). IR (neat) 1759, 1496, 1325, 1190, 1080, 1001, 926, 876, 700 cm^{-1}. HRMS (FAB): calcd for $C_{19}H_{14}F_6NO_2$ ([M + H]$^+$) 402.0929, found 402.0909.

3.3.31. 2,2-Dimethyl-1-phenylbut-3-en-1-one O-pentafluorobenzoyloxime (21b)

Compound **21b** was prepared by the method described for **15a** using **24b** (167 mg, 0.88 mmol), CH_2Cl_2 (2 mL), NEt_3 (0.18 g, 1.8 mmol), C_6F_5COCl (0.30 g, 1.3 mmol). Purification by thin-layer chromatography on silica gel (hexane–AcOEt 5:1) gave **21b** (0.30 g, 89%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.38 (6H, s), 5.13 (1H, d, J = 17.4 Hz), 5.18 (1H, dd, J = 10.6, 0.7 Hz), 6.00 (1H, dd, J = 17.4, 10.6 Hz), 7.08–7.11 (2H, m), 7.34–7.37 (3H, m). ^{13}C NMR (126 MHz, $CDCl_3$) δ 25.0, 44.4, 107.0 (td, J_{CF} = 17, 4 Hz), 114.4, 126.7, 127.7, 128.6, 132.2, 137.5 (ddddd, J_{CF} = 256, 17, 13, 6, 2 Hz), 142.5, 143.1 (dtt, J_{CF} = 260, 17, 5 Hz), 145.1 (dddd, J_{CF} = 259, 16, 8, 4 Hz), 156.5, 175.2. ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 1.4 (2F, dddd, J_{FF} = 19, 19, 13, 6 Hz), 13.3 (1F, tt, J_{FF} = 19, 5 Hz), 24.4 (2F, dddd, J_{FF} = 19, 6, 5, 4 Hz). IR (neat) 1761, 1651, 1522, 1496, 1325, 1190, 995, 922, 864, 706 cm^{-1}. HRMS (FAB): calcd for $C_{19}H_{15}F_5NO_2$ ([M + H]$^+$) 384.1023, found 384.1021.

*3.3.32. 4,4-Dichloro-2,2-dimethyl-1-phenylbut-3-en-1-one O-pentafluorobenzoyloxime (**21c**)*

Compound **21c** was prepared by the method described for **15a** using **24c** (231 mg, 0.891 mmol), CH_2Cl_2 (2 mL), NEt_3 (180 mg, 1.78 mmol), and C_6F_5COCl (307 mg, 1.33 mmol). The reaction mixture was stirred at 0 °C for 0.5 h, and purification by thin-layer column chromatography on silica gel (hexane–AcOEt 10:1) gave **21c** (262 mg, 65%) as a colorless liquid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.53 (6H, s), 5.94 (1H, s), 7.12–7,15 (2H, m), 7.37–7.42 (3H, m). ^{13}C NMR (126 MHz, $CDCl_3$) δ 26.3, 43.9, 106.9 (td, J_{CF} = 15, 4 Hz), 123.3, 126.6, 128.2, 129.0, 131.9, 133.3, 137.5 (ddddd, J_{CF} = 255, 17, 13, 5, 2 Hz), 143.1 (dtt, J_{CF} = 264, 17, 5 Hz), 145.1 (ddddd, J_{CF} = 254, 16, 8, 3, 2 Hz), 156.6, 172.4. ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 1.5 (2F, dddd, J_{FF} = 26, 21, 11, 5 Hz), 13.5 (1F, tt, J_{FF} = 21, 4 Hz), 24.4 (2F, dddd, J_{FF} = 26, 5, 5, 4 Hz). IR (neat) 1756, 1496, 1325, 1188, 995, 930, 870, 698 cm^{-1}. HRMS (FAB): calcd for $C_{19}H_{13}Cl_2F_5NO_2$ ([M + H]$^+$) 452.0244, found 452.0215.

*3.3.33. 4,4-Dibromo-2,2-dimethyl-1-phenylbut-3-en-1-one O-pentafluorobenzoyloxime (**21d**)*

Compound **21d** was prepared by the method described for **15a** using **24d** (1.11 g, 3.2 mmol), CH_2Cl_2 (6.4 mL), NEt_3 (0.65 g, 6.4 mmol), C_6F_5COCl (1.10 g, 4.8 mmol). Purification by column chromatography on silica gel (hexane–AcOEt 10:1) gave **21d** (1.42 g, 82%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.54 (6H, s), 6.58 (1H, s), 7.14–7.18 (2H, m), 7.24 (1H, tm, J = 6.7 Hz), 7.41 (2H, dd, J = 5.2, 1.9 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 26.1, 45.8, 91.1, 106.9 (td, J_{CF} = 16, 3 Hz), 126.6, 128.0, 128.9, 131.8, 137.4 (ddddd, J_{CF} = 255, 13, 11, 4, 1 Hz), 141.4, 143.0 (dtt, J_{CF} = 260, 13, 5 Hz), 145.0 (dddd, J_{CF} = 256, 15, 8, 4 Hz), 156.6, 171.8. ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 1.5 (2F, dddd, J_{FF} = 26, 20, 12, 6 Hz), 13.5 (1F, tt, J_{FF} = 20, 4 Hz), 24.4 (2F, dddd, J_{FF} = 26, 6, 5, 4 Hz). IR (neat) 1761, 1522, 1496, 1325, 1186, 995, 928, 858, 772, 708, 698 cm^{-1}. HRMS (FAB): calcd for $C_{19}H_{13}Br_2F_5NO_2$ ([M + H]$^+$) 539.9233, found 539.9225.

*3.3.34. 5-Fluoro-3,3-dimethyl-2-phenyl-3H-pyrrole (**16a**)*

O-Pentafluorobenzoyloxime **15a** (72 mg, 0.17 mmol), $Pd(PPh_3)_4$ (20 mg, 0.017 mmol), and PPh_3 (49 mg, 0.17 mmol) were dissolved in DMA (7 mL) and heated at 110 °C for 8 h. The reaction was quenched with phosphate buffer (pH 7) at room temperature, and organic materials were extracted with AcOEt three times. The combined extracts were washed with brine and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by thin-layer chromatography on silica gel (benzene–hexane 1:1) to give **16a** (27 mg, 71%) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.49 (6H, d, J = 1.2 Hz), 5.32 (1H, d, J_{HF} = 6.4 Hz), 7.44–7.48 (2H, m), 7.99–8.01 (3H, m). ^{13}C NMR (126 MHz, $CDCl_3$) δ 23.1 (d, J_{CF} = 3 Hz), 55.0, 106.4 (d, J_{CF} = 15 Hz), 128.1, 128.6, 130.8, 132.0 (d, J_{CF} = 1 Hz), 161.8 (d, J_{CF} = 261 Hz), 183.5 (d, J_{CF} = 11 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 47.8 (d, J_{FH} = 6 Hz). IR (neat) 3097, 3060, 2972, 1633, 1460, 1279, 1254, 1132, 1012, 945, 783, 702 cm^{-1}. HRMS (FAB): calcd for $C_{12}H_{13}FN$ ([M + H]$^+$) 190.1032, found 190.1038.

*3.3.35. 3-Fluoro-1-phenyl-2-azaspiro[4.5]deca-1,3-diene (**16b**)*

Compound **16b** was synthesized by the method described for **16a** using **15b** (87 mg, 0.19 mmol), $Pd(PPh_3)_4$ (23 mg, 0.019 mmol), PPh_3 (50 mg, 0.19 mmol), and DMA (10 mL). Purification by thin-layer chromatography on silica gel (benzene–hexane 1:1) gave **16b** (34 mg, 78%) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.38–1.58 (5H, m), 1.87–1.94 (3H, m), 2.13 (1H, td, J = 11.2 Hz, J_{HF} = 3.3 Hz), 2.13 (1H, td, J = 11.2 Hz, J_{HF} = 3.3 Hz), 5.86 (1H, d, J_{HF} = 6.3 Hz), 7.42–7.46 (3H, m), 8.03–8.07 (2H, m). ^{13}C NMR (126 MHz, $CDCl_3$) δ 24.8, 25.6, 32.6 (d, J_{CF} = 2 Hz), 61.4, 102.3 (d, J_{CF} = 15 Hz), 128.3, 128.5, 129.1, 130.7, 163.3 (d, J_{CF} = 261 Hz), 183.5 (d, J_{CF} = 11.5 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 48.6 (ddd, J_{FH} = 6, 3, 3 Hz). IR (neat) 2933, 1626, 1450, 1442, 1317, 1286, 1275, 1198, 997, 773, 758, 721, 688 cm^{-1}. HRMS (FAB): calcd for $C_{15}H_{17}FN$ ([M + H]$^+$) 230.1345, found 230.1336.

*3.3.36. (E)-5-Fluoro-3,3-dimethyl-2-styryl-3H-pyrrole (**16c**)*

Compound **16c** was synthesized by the method described for **16a** using **15c** (52 mg, 0.11 mmol), $Pd(PPh_3)_4$ (13 mg, 0.011 mmol), PPh_3 (30 mg, 0.11 mmol), and DMA (6 mL). The reaction mixture was heated at 110 °C for 1 h, and purification by thin-layer chromatography on silica gel (benzene–hexane 1:1) gave **33b** (19 mg, 76%) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.36 (3H, s), 1.37 (3H, s), 5.26 (1H, d, J_{HF} = 6.8 Hz), 6.91 (1H, d, J = 16.4 Hz), 7.35 (1H, tt, J = 7.2, 1.6 Hz), 7.39 (2H, tm, J = 7.2 Hz), 7.53 (1H, d, J = 16.4 Hz), 7.56 (2H, dd, J = 7.2, 1.6 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 22.3, 22.3, 54.3, 104.8 (d, J_{CF} = 15 Hz), 118.7 (d, J_{CF} = 2 Hz), 127.5, 128.9, 129.5, 135.7, 138.3, 162.6 (d, J_{CF} = 261 Hz), 184.0 (d, J_{CF} = 12 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 48.7 (d, J_{FH} = 7 Hz). IR (neat) 2968, 1628, 1618, 1292, 1132, 972, 754, 702 cm^{-1}. HRMS (FAB): calcd for $C_{14}H_{15}FN$ ([M + H]$^+$) 216.1189, found 216.1165.

*3.3.37. 5-Fluoro-3,3-dimethyl-2-nonyl-3H-pyrrole (**16d**)*

Compound **16d** was synthesized by the method described for **16a** using **15d** (149 mg, 0.32 mmol), $Pd(PPh_3)_4$ (37 mg, 0.032 mmol), PPh_3 (83 mg, 0.32 mmol), and DMA (16 mL). The reaction was quenched with saturated aqueous sodium bicarbonate at −10 °C, and organic materials were extracted with AcOEt three times at room temperature. The combined extracts were washed with brine and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by thin-layer chromatography on silica gel (deactivated by treatment with AcOEt–Et_3N 100:1, then dried) (NEt_3–benzene–hexane 1:50:50 and then NEt_3–AcOEt–hexane 1:10:90) gave **16d** (21 mg, 29%) as a yellow oil (**16d** was unstable under acidic conditions).

^{1}H NMR (500 MHz, $CDCl_3$) d 0.88 (3H, t, J = 6.8 Hz), 1.18–1.39 (12H, m), 1.27 (6H, s), 1.60 (2H, tt, J = 7.2, 7.2 Hz),

2.32 (2H, t, J = 7.2 Hz), 5.18 (1H, d, J_{HF} = 5.9 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) d 14.1, 22.4 (d, J_{CF} = 2 Hz), 22.6 (d, J_{CF} = 4 Hz), 28.6, 29.1, 29.1, 29.3, 29.4, 31.7, 34.4, 54.1 (d, J_{CF} = 2 Hz), 104.0 (d, J_{CF} = 15 Hz), 162.4 (d, J_{CF} = 261 Hz), 184.3 (d, J_{CF} = 12 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) d_F 48.3 (d, J_{FH} = 6 Hz). IR (neat) 2922, 2852, 1738, 1691, 1522, 1377, 1176, 1120, 1080, 721, 542 cm^{-1}. HRMS (FAB): calcd for $C_{15}H_{27}FN$ ([M+H]$^+$) 240.2128, found 240.2139.

*3.3.38. tert-Butyl 5-fluoro-3,3-dimethyl-3H-pyrrole-2-carboxylate (**16e**)*

Compound **16e** was synthesized by the method described for **16a** using **15e** (105 mg, 0.24 mmol), $Pd(PPh_3)_4$ (27 mg, 0.024 mmol), PPh_3 (62 mg, 0.24 mmol), and DMA (12 mL). Purification by thin-layer chromatography on silica gel (benzene–hexane 1:1) gave **16e** (7.1 mg, 14%) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.42 (6H, s), 1.59 (9H, s), 5.49 (1H, d, J_{HF} = 6.9 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 20.7 (d, J_{CF} = 3 Hz), 28.1, 56.1, 83.2, 111.2 (d, J_{CF} = 14 Hz), 159.1, 161.0 (d, J_{CF} = 267 Hz), 177.4 (d, J_{CF} = 9 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 49.6 (d, J_{FH} = 7 Hz). IR (neat) 3726, 1733, 1460, 1435, 1219, 1097, 955, 771, 692, 669, 523 cm^{-1}. HRMS (FAB): calcd for $C_{11}H_{17}FNO_2$ ([M + H]$^+$) 214.1243, found 214.1265.

*3.3.39. 2-Fluoro-3a-methyl-4,5-dihydro-3aH-benzo[g]indole (**16f**)*

Compound **16f** was synthesized by the method described for **16a** using **15f** (24 mg, 0.055 mmol), $Pd(PPh_3)_4$ (19 mg, 0.017 mmol), PPh_3 (15 mg, 0.055 mmol), and DMA (3 mL). Purification by thin-layer chromatography on silica gel (benzene-hexane 1:1) gave **16f** (5.2 mg, 47%) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.24 (3H, s), 1.78 (1H, ddd, J = 13.1, 12.9, 5.9 Hz), 2.24 (1H, ddd, J = 13.1, 5.7, 1.0 Hz), 2.93 (1H, ddd, J = 17.6, 5.9, 1.0 Hz), 3.14 (1H, ddd, J = 17.6, 12.9, 5.7 Hz), 5.34 (1H, d, J_{HF} = 6.8 Hz), 7.25 (1H, d, J = 7.5 Hz), 7.30 (1H, t, J = 7.5 Hz), 7.40 (1H, td, J = 7.5, 1.0 Hz), 7.94 (1H, dd, J = 7.5, 1.0 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ 17.9 (d, J_{CF} = 3 Hz), 25.9, 32.4 (d, J_{CF} = 3 Hz), 53.1 (d, J_{CF} = 2 Hz), 102.8 (d, J_{CF} = 15 Hz), 125.5, 126.8, 128.9, 129.0 (d, J_{CF} = 1 Hz), 131.3, 139.7, 164.2 (d, J_{CF} = 264 Hz), 185.6 (d, J_{CF} = 13 Hz). ^{19}F NMR (471 MHz, $CDCl_3$) δ_F 50.5 (d, J_{FH} = 7 Hz). IR (neat) 2929, 1684, 1616, 1464, 1281, 1248, 775, 739 cm^{-1}. HRMS (FAB): calcd for $C_{13}H_{13}FN$ ([M + H]$^+$) 202.1032, found 202.1048.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jfluchem.2005.12.023.

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