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Synthesis of Polycyclic Imines by Palladium-Catalyzed Domino Cyclization of Di- and Trienyl Ketone *O*-Pentafluorobenzoyloximes

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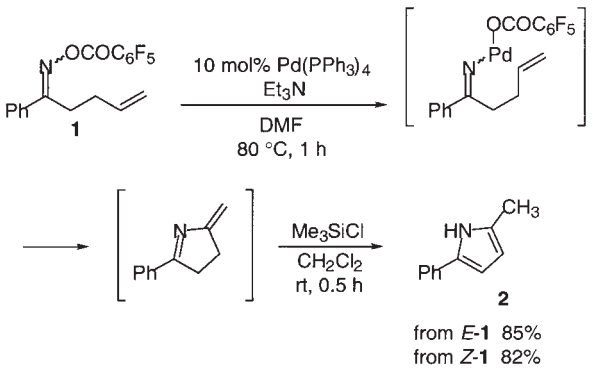
Various cyclic imines, such as spiro imines and a fused bicyclic imine, are synthesized from dienyl and trienyl ketone *O*-pentafluorobenzoyloximes by the domino amino-Heck reaction. Treatment of the oximes with a catalytic amount of $Pd(PPh_3)_4$ and triethylamine gives polycyclic imines in high yields via alkylideneaminopalladium(II) intermediates generated in situ by the oxidative addition of the oximes to the Pd(0) complex.

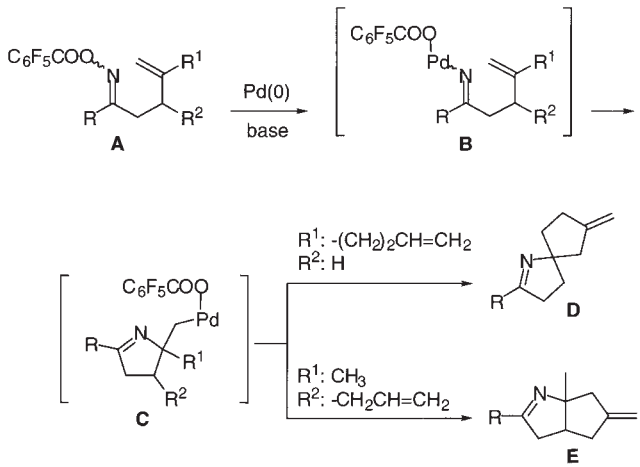
Oxidative addition of various sp^2 carbon–heteroatom bonds (sp^2C–X) to transition metals occurs to give alkenyl- and arylmetals,[1] which are widely used as active intermediates for carbon–carbon bond formation such as Mizoroki–Heck reaction[2] and other transition metal-catalyzed coupling reactions.[3] Recently, we found that the sp^2N–O bonds of γ,δ-unsaturated *O*-pentafluorobenzoyloximes are cleaved by oxidative addition to Pd(0) compounds to generate alkylideneaminopalladium(II) species,[4,5] which in turn add to the intramolecular olefinic moiety to yield various azaheterocycles (amino-Heck reaction).[4] Some representative examples are the syntheses of pyrroles,[4b,c] isoquinolines,[4d] pyridines,[4d] spiroimines,[4e] and 1-azaazulenes.[4f] This amino-Heck reaction is not affected by the geometry of oximes, probably due to the linear-like structures of the alkylideneaminometal species.[6] Both *E* and *Z* γ,δ-unsaturated ketone oximes **1** cyclize to pyrroles **2** in good yields (Eq. 1).[4b,c]



(1)

In continuation with our studies on the amino-Heck reaction of olefinic oxime derivatives, we expected that dienyloximes **A** could be utilized for the preparation of polycyclic imines by domino cyclization[7] as shown in Scheme 1. The skeleton of **D** is found in some bioactive natural products such as cephalotaxin.[8,9]

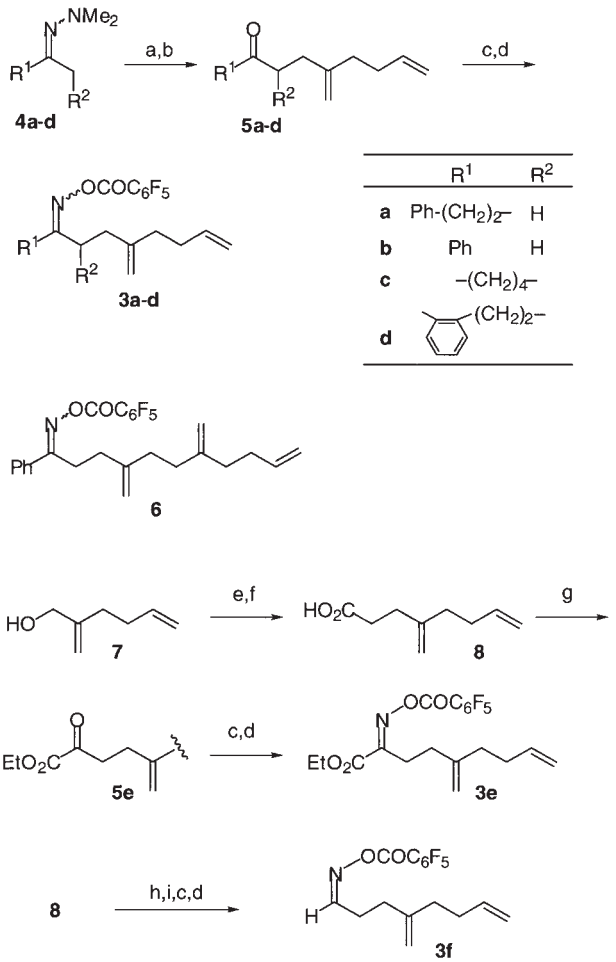
Recently, we communicated the preliminary results of the synthesis of spirocyclic imines by the palladium(0)-catalyzed cyclization of dienyl *O*-pentafluorobenzoyloximes.[4e] This paper describes full accounts of this domino amino-Heck reaction.



Scheme 1. Synthetic plan of spiro/fused imines by the domino amino-Heck reaction.

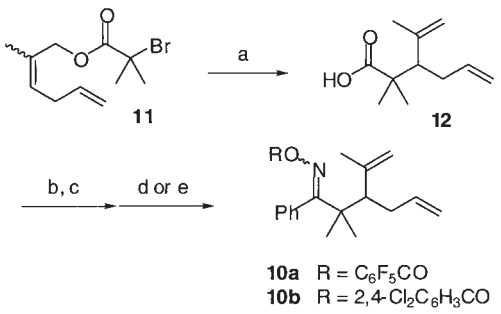
Results and Discussion

Preparation of Oximes for Domino Amino-Heck Reaction. Linear dienyl *O*-pentafluorobenzoyloximes **3a–e** were prepared for spiro imine synthesis as shown in Scheme 2. Aryl or alkyl ketone oximes **3a–d** were prepared by alkylation of *N*,*N*-dimethylhydrazones **4** with 2-bromomethyl-1,5-hexadiene,[7b] hydrolysis,[10,11] oximation, and *O*-pentafluorobenzoylation. Trienyl ketone *O*-pentafluorobenzoyloxime **6** was prepared in a similar way by alkylation with the corresponding trienyl chloride.[7b] Oxime of α-keto ester **3e** was prepared from 2-methylene-5-hexen-1-ol (**7**), which was converted to acid **8** by Johnson–Claisen rearrangement[12] and the successive hydrolysis. By the method of Hangauer Jr.,[13] acid **8** was transformed to α-keto ester **5e** and then to pentafluorobenzoyl oxime **3e**. Aldoxime **3f** was prepared from **8** by the transformation of carboxyl group to formyl group.



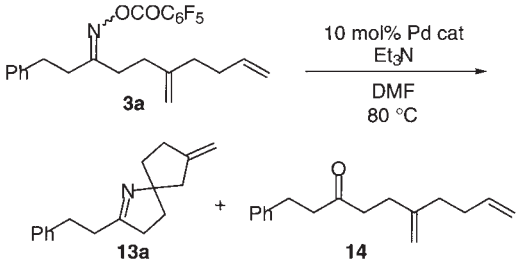
Scheme 2. Preparation of linear dienyl oximes **3**. a) LDA, THF, 0 °C, 1 h; 2-bromomethyl-1,5-hexadiene, −78 °C → rt, over night. b) NaOAc, AcOH, THF, water, rt, 3 h. c) $NH_2OH \cdot HCl$, pyridine, EtOH, rt, 1–3 h. d) C_6F_5COCl, Et_3N, CH_2Cl_2, 0 °C, 10–30 min. e) $CH_3C(OEt)_3$, $CH_3CH_2CO_2H$, 140 °C, 1.5 h. f) aq NaOH, MeOH, 0 °C, 45 min. g) 2 LDA, TMEDA, THF, rt, 4 h; $(EtOOC)_2$, −78 → −40 °C, 1.5 h; aq $NaHCO_3$. h) $NHMe(OMe) \cdot HCl$, $Me_2N(CH_2)_3–N=C=N–CH_2CH_3 \cdot HCl$, Et_3N, CH_2Cl_2, rt, over night. i) $LiAlH_4$, Et_2O, −78 °C, 20 min.

Branched dienyl oximes **10a** and **10b** were prepared for fused imine synthesis (Scheme 3). Ester **11**, which was prepared by esterification of 2-methyl-2,5-hexadien-1-ol[14] with 2-bromo-2-methylpropanoyl bromide, was converted to acid **12** by Reformatsky-Claisen rearrangement.[15] Acid **12** was treated with phenyllithium to give the corresponding phenyl ketone,[16] which was transformed to *O*-pentafluorobenzoyloxime **10a** and *O*-2,4-dichlorobenzoyloxime **10b**.



Scheme 3. Preparation of branched dienyl oximes **10**. a) Zn, TMSCl, CH_3CN, 90 °C, 10 h. b) PhLi, Et_2O, reflux, 20 min. c) $NH_2OH \cdot HCl$, pyridine, EtOH, 90 °C, 2 d. d) C_6F_5COCl, Et_3N, CH_2Cl_2, 0 °C, 15 min. e) 2,4-$Cl_2C_6H_3COCl$, Et_3N, CH_2Cl_2, 0 °C, 30 min.

Table 1. The Domino Amino-Heck Reaction of **3a**



Run	Pd cat	Base	Time/h	Yield/%[a]	
				13a	**14**
1	$Pd(PPh_3)_4$	Et_3N	11.5	60	34
2	$Pd(dba)_2$ + $n$$PPh_3$[b]	Et_3N	1–8	17–53	78–42
3	$Pd(PPh_3)_4$	DABCO	12	31	53

a) Isolated yield. b) $n = 2$, 4 or 6.

PPh_3 accelerated the reaction, the yield of the cyclized product **13a** was not improved but a larger amount of the ketone was obtained (run 2). Palladium(II) chloride complexes such as $PdCl_2[P(o\text{-tol})_3]_2$, $PdCl_2[P(c\text{-hex})_3]_2$, [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium [$PdCl_2$(dppf)], or [1,3′-bis(diphenylphosphino)propane]dichloropalladium [$PdCl_2$(dppp)] were not suitable for this cyclization. To improve the yield of **13a**, it was required to suppress the formation of ketone **14**. The ketone might be formed either by protonation of the initially formed alkylideneaminopalladium(II) complex **B** with the resulting ammonium salt ($Et_3NH^+ \cdot C_6F_5COO^-$) and/or contaminated water or by the reductive elimination from palladium hydride species (H–Pd–N=C$\langle$) that are generated by complexation of **B** and Et_3N and the successive β-hydrogen elimination.[17] Although 1,4-diazabicyclo[2.2.2]octane (DABCO) was used instead of Et_3N, the yield of **13a** was not improved and a large amount of ketone was formed (run 3).

The domino amino-Heck reaction was accelerated at a higher temperature (110 °C) and the yield of the spirocyclic imine **13a** was improved up to 70% (Table 2, run 1). Although the best yield was obtained with K_2CO_3 (runs 2–4), the yield was not reproducible (run 4). Therefore, Et_3N was used as a base for further studies. Cyclization proceeded more smoothly in polar aprotic solvents (runs 5, 6) than in non-polar solvent

Table 2. Optimization of Conditions of the Domino Amino-Heck Reaction of **3a** Using $Pd(PPh_3)_4$[a)]

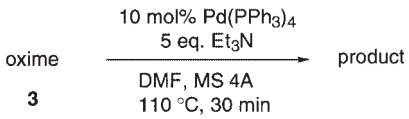
Run	Base (mol amt.)	Temp/°C	Solvent	Additive	Time/h	Yield/%[b)]	
						13a	**14**
1	Et_3N (5.0)	110	DMF	—	0.5	70	22
2	*t*-BuOK (2.0)	110	DMF	—	0.5	22	33
3	Cs_2CO_3 (2.0)	110	DMF	—	0.5	53	18
4	K_2CO_3 (2.0)	110	DMF	—	1	60–82	20–5
5	Et_3N (5.0)	110	DMA	—	0.5	70	22
6	Et_3N (5.0)	110	DMPU[c)]	—	0.5	53	18
7	Et_3N (5.0)	110	toluene	—	2	22	33
8	Et_3N (5.0)	reflux	CH_3CN	—	6.5	46	37
9	Et_3N (5.0)	110	DMF	MS 4A	0.5	77	trace

a) **3a**:$Pd(PPh_3)_4$ = 1:0.1. b) Isolated yield. c) DMPU = 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone.

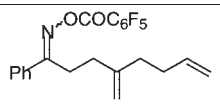
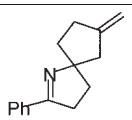
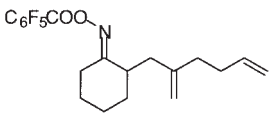
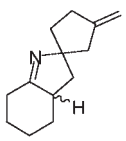
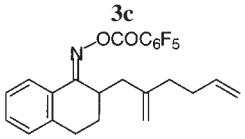
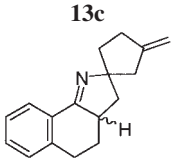
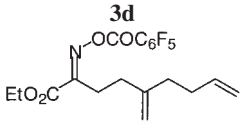
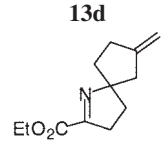
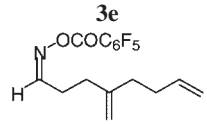
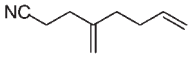
(run 7).

In the presence of molecular sieves 4A (MS 4A), the yield of the cyclized product **13a** was improved to 77% and the formation of ketone was almost suppressed (run 9). It seems that the molecular sieves trap trace amounts of moisture and acidic protons to prevent the protonolysis of the amino palladium species **B**.

Table 3. Spirocyclization of Various *O*-Pentafluorobenzoyloximes[a)]



3

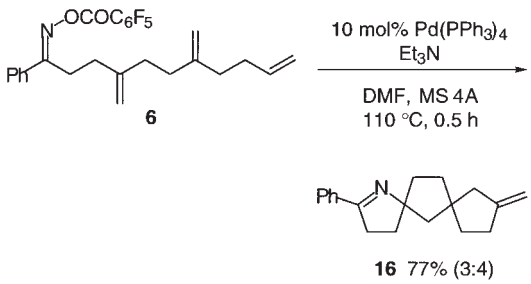
Run	Oxime	Product	Yield/%[b)]
1	 **3b**	 **13b**	82
2[c)]	 **3c**	 **13c**	64 (1:1)[d)]
3	 **3d**	 **13d**	80 (1:1)[d)]
4	 **3e**	 **13e**	76
5[e)]	 **3f**	 **15**	85

a) Reaction conditions: 10 mol% $Pd(PPh_3)_4$, 5 mol amt. Et_3N, DMF, MS 4A, 110 °C, 0.5 h. b) Isolated yield. c) The reaction carried out for 1 h. d) Diastereomer mixture. Determined by ^1H NMR. e) 60 °C, 20 min.

The scope of the palladium-catalyzed domino cyclization was then extended as shown in Table 3 under these reaction conditions: 10 mol% of $Pd(PPh_3)_4$ and 5 molar amounts of Et_3N in DMF in the presence of MS 4A at 110 °C.

Phenyl ketone oxime **3b** cyclized smoothly to **13b** in 82% yield (run 1). Cyclohexanone oxime derivative **3c** cyclized to give tricyclic imine **13c** as a 1:1 diastereomeric mixture in moderate yield (run 2). Similarly, tetracyclic imine **13d** was obtained in 80% yield by using tetralone oxime derivative **3d** (run 3). Cyclic imine having an ethoxycarbonyl group **13e** was also prepared from oxime of α-keto ester **3e** (run 4). Thus, keto oximes were successfully converted to spiro imines, whereas aldoxime **3f** did not cyclize and gave exclusively nitrile **15** by Beckmann fragmentation (run 5).

Further extension of the olefinic chain to a trienyl moiety resulted in the formation of tricyclic imine **16** (3:4 diastereomeric mixture) as shown in Eq. 2.

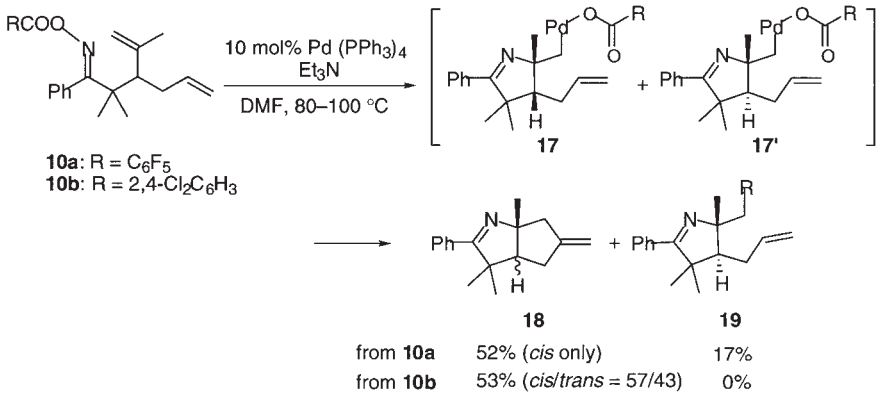


6 (2)

16 77% (3:4)

Fused mode cyclization also proceeded from branched dienyl oxime **10**. When *O*-pentafluorobenzoyl oxime **10a** was treated with $Pd(PPh_3)_4$ and Et_3N in DMF, *cis*-fused bicyclic product **18a** and monocyclic 2*H*-dihydopyrrole **19a** were obtained (Scheme 4). The monocyclic imine **19a** would be formed via the decarboxylation from intermediate **17′a** and the subsequent reductive elimination.[18] On the other hand, *O*-2,4-dichlorobenzoyloxime **10b** gave a *cis/trans* mixture of **18b** without forming **19b**, probably due to the hardness of decarboxylation of **17′b** rather than cyclization of **17′b** to give *trans*-**18**.

In conclusion, spiro imines and a fused bicyclic imine were



Scheme 4.

synthesized from dienyl or trienyl ketone *O*-pentafluorobenzoyl oximes by the domino amino-Heck reaction. The reaction proceeds by treatment with a catalytic amount of $Pd(PPh_3)_4$, Et_3N, and MS 4A via the formation of alkylideneaminopalladium(II) intermediates generated in situ by the oxidative addition of oximes to a Pd(0) complex.

Experimental

^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were recorded on Bruker Avance 500 and Bruker DRX 500 spectrometers in $CDCl_3$ using tetramethylsilane (for ^{1}H: $\delta = 0$) and $CDCl_3$ (for ^{13}C: $\delta = 77.0$) as an internal standard. IR spectra were recorded on a Horiba FT 300 spectrophotometer. High-resolution mass spectra were obtained with a JEOL JMS-700P mass spectrometer. Elemental analyses were carried out at The Elemental Analysis Laboratory, Department of Chemistry, Faculty of Science, The University of Tokyo. Flash column chromatography was performed on silica gel [Merck Silica gel 60, and Kanto Chemical Co., Inc. Silica gel 60N (spherical, neutral)]. *N*,*N*-Dimethylformamide (DMF) was distilled twice under reduced pressure from P_2O_5 initially and then from CaH_2, and stored over molecular sieves 4A under an argon atmosphere. Dichloromethane was distilled from P_2O_5, then from CaH_2, and stored over molecular sieves 4A. Triethylamine was distilled from CaH_2, and stored over molecular sieves 4A. $Pd(PPh_3)_4$ was prepared by the literature procedure.[19] Pentafluorobenzoyl chloride was purchased from Tokyo Chemical Industry Co., Ltd. and used without purification. Dehydrated THF and diethyl ether were purchased from Kanto Chemical Co.

General Procedure for the Preparation of Dienyl Ketones 5a–d and 4,7-Dimethylene-1-phenyl-10-undecen-1-one. Preparation Dienyl Ketone 5a Is Described below as a Typical Procedure: 4-Phenyl-2-butanone *N*,*N*-dimethylhydrazone (1.75 g, 9.2 mmol) was treated with LDA [from *n*-BuLi (1.6 M in hexane, 3.9 mL) and diisopropylamine (9.2 mL) in THF (25 mL)] at 0 °C and the mixture was stirred for 1 h under argon atmosphere. The reaction mixture was then cooled to −78 °C and the 2-bromomethyl-1,5-hexadiene (1.07 g, 6.2 mmol) in THF (4 mL) was added slowly. The reaction mixture was stirred continuously, warmed to room temperature overnight and quenched by adding an aqueous sat. NH_4Cl solution. The reaction mixture was then extracted with diethyl ether (×3), washed with water and brine, dried over anhydrous $MgSO_4$, and evaporated in vacuo to give crude alkylated hydrazone. To a mixture of acetic acid (3.4 mL, 69 mmol), sodium acetate (1.89 g, 13.9 mmol), water (0.5 mL), and THF (2.2 mL) was added the crude alkylated hydrazone, and the mixture was stirred at room temperature for 3 h. After the reaction was quenched by adding an aqueous NaOH solution at 0 °C, the mixture was extracted with ether (×3). The combined organic extracts were washed with water and brine, dried over anhydrous $MgSO_4$, and evaporated in vacuo. The residue was purified by a flash column chromatography [hexane/ethyl acetate = 95/5–90/10] to afford 0.54 g (55%) of dienyl ketone **5a**.

4,7-Dimethylene-1-phenyl-10-undecen-1-one for tricyclization was prepared in a similar way from the corresponding chloride[7b] and acetophenone *N*,*N*-dimethyl hydrazone.

6-Methylene-1-phenyl-9-decen-3-one (5a): Yellow oil; IR (KBr) 1716, 1643, 1604, 1496, 1454, 1365, 1282, 1187, 1091, 910, 748, 700 cm^{-1}; ^{1}H NMR δ 2.08 (t, $J = 7.5$ Hz, 2H), 2.16–2.20 (m, 2H), 2.27 (t, $J = 7.5$ Hz, 2H), 2.53 (t, $J = 7.5$ Hz, 2H), 2.74 (t, $J = 7.6$ Hz, 2H), 2.90 (t, $J = 7.7$ Hz, 2H), 4.67 (s, 1H), 4.74 (s, 1H), 4.95 (dd, $J = 10.2$ Hz, 1.5 Hz, 1H), 4.95 (dd, $J = 10.2$ Hz, 1.6 Hz, 1H), 5.01 (dd, $J = 17.1$ Hz, 1.6 Hz, 1H), 5.75–5.83 (m, 1H), 7.16–7.20 (m, 3H), 7.25–7.28 (t, $J = 7.4$ Hz, 2H); ^{13}C NMR δ 29.7, 29.8, 31.9, 35.6, 41.2, 44.3, 109.4, 114.6, 126.1, 128.3, 128.5, 138.2, 141.1, 147.7, 209.3; Anal. Found: C, 83.96; H, 8.98%. Calcd for $C_{17}H_{22}O$: C, 84.25; H, 9.15%.

4-Methylene-1-phenyl-7-octen-1-one (5b): Yellow oil; IR (KBr) 1689, 1643, 1596, 1581, 1448, 1355, 1278, 1205, 1180, 989, 906, 744, 690, 507 cm^{-1}; ^{1}H NMR δ 2.14–2.17 (m, 2H), 2.20–2.24 (m, 2H), 2.45 (t, $J = 7.7$ Hz, 2H), 3.12 (t, $J = 7.7$ Hz, 2H), 4.77 (s, 1H), 4.79 (s, 1H), 4.96 (d, $J = 10.5$ Hz, 1H), 5.02 (dd, $J = 17.0$ Hz, 1.6 Hz, 1H), 5.81 (ddt, $J = 17.0$, 10.5, 6.5 Hz, 1H), 7.45 (dd, $J = 7.2$, 8.5 Hz, 2H), 7.55 (t, 7.2 Hz, 1H), 7.96 (dd, $J = 8.5$ Hz, 1.5 Hz, 2H); ^{13}C NMR δ 30.1, 32.0, 35.7, 36.9, 109.4, 114.7, 128.0, 128.6, 133.0, 136.9, 138.2, 147.9, 199.7; Anal. Found: C, 83.84; H, 8.52%, Calcd for $C_{15}H_{18}O$: C, 84.06; H, 8.46%.

2-(2-Methylene-5-hexenyl)cyclohexanone (5c): Colorless oil; IR (KBr) 1712, 1641, 1448, 1338, 1313, 1224, 1128, 998, 908, 811, 636 cm^{-1}; ^{1}H NMR δ 1.26–1.34 (m, 1H), 1.60–1.73 (m, 2H), 1.87 (dd, $J = 14.8$, 8.8 Hz, 2H), 2.02–2.07 (m, 3H), 2.09–2.25 (m, 3 H), 2.29–2.35 (m, 1H), 2.39–2.49 (m, 2H), 2.61 (dd, $J = 14.8$, 4.8 Hz, 1H), 4.70 (s, 1H), 4.79 (s, 1H), 4.95 (d, $J = 7.1$ Hz, 1H), 5.02 (dd, $J = 17.1$, 1.6 Hz, 1H), 5.77–5.82 (m, 1H); ^{13}C NMR δ 24.8, 28.0, 31.9, 33.4, 35.2, 35.7, 42.0, 48.5, 110.8, 114.6, 138.3, 146.5, 212.8, Anal. Found: C, 81.17; H, 10.29%. Calcd for $C_{13}H_{20}O$: C, 81.19; H, 10.48%.

2-(2-Methylene-5-hexenyl)-3,4-dihydronaphthalene-1(2*H*)-one (5d): Colorless oil, IR (KBr) 1683, 1641, 1600, 1484, 1454,

1432, 1355, 1295, 1218, 1157, 1029, 998, 902, 773, 742, 669, 628 cm^{-1}; ^1H NMR δ 1.74–1.82 (m, 1H), 2.09 (dd, $J = 14.5$ Hz, 9.8 Hz, 1H), 2.13 (t, $J = 7.5$ Hz, 2H), 2.18–2.29 (m, 3H), 2.63 (ddd, $J = 15.1$, 10.2, 4.3 Hz, 1H), 2.87 (dd, $J = 14.5$, 3.9 Hz, 1H), 2.92–3.02 (m, 2H), 4.80 (s, 1H), 4.87 (s, 1H), 4.97 (dd, $J = 10.2$, 1.2 Hz, 1H), 5.04 (dd, $J = 17.1$, 1.6 Hz, 1H), 5.79–5.87 (m, 1H), 7.23 (d, $J = 7.6$ Hz, 1H), 7.29 (t, $J = 7.5$ Hz, 1H), 7.45 (dt, $J = 1.2$, 7.5 Hz, 1H), 8.03 (d, $J = 7.7$ Hz, 1H); ^{13}C NMR δ 27.7, 28.3, 31.8, 34.8, 36.1, 45.4, 111.6, 114.6, 126.5, 127.4, 128.7, 132.4, 133.1, 138.2, 144.0, 146.4, 199.8; Anal. Found: C, 84.75; H, 8.33%, Calcd for $C_{17}H_{20}O$: C, 84.95; H, 8.32%.

4,7-Dimethylene-1-phenyl-10-undecen-1-one: Colorless oil; IR (KBr) 1687, 1643, 1596, 1581, 1448, 1357, 1321, 1203, 1180, 1000, 985, 908, 889, 744, 690, 502 cm^{-1}; ^1H NMR δ 1.99 (t, $J =$ 7.5 Hz, 1H), 2.11–2.24 (m, 2H), 2.16–2.20 (m, 6H), 2.47 (t, $J = 7.5$ Hz, 2H), 3.13 (t, $J = 7.8$ Hz, 2H), 4.75 (s, 1H), 4.76 (s, 1H), 4.77 (s, 1H), 4.80 (s, 1H), 4.96 (d, $J = 10.5$ Hz, 1H), 5.03 (dd, $J = 17.2$, 1.5 Hz, 1H), 5.78–5.86 (m, 1H), 7.46 (t, $J = 7.7$ Hz, 2H), 7.56 (t, $J = 7.4$ Hz, 1H), 7.79 (d, $J = 7.4$ Hz, 2H); ^{13}C NMR δ 30.1, 32.0, 34.4, 34.7, 35.4, 36.9, 109.2, 109.3, 114.5, 128.0, 128.6, 133.0, 136.9, 138.4, 148.3, 148.7, 199.7; Anal. Found: C, 85.05; H, 8.93%, Calcd for $C_{19}H_{24}O$: C, 85.02; H, 9.01%.

Ethyl 5-Methylene-2-oxo-8-nonenoate (5e): A THF (5 mL) solution of 4-methylene-7-octenoic acid (1.15 g, 7.45 mmol) was added to a solution of TMEDA (2.6 mL, 17 mmol) and LDA [prepared from *n*-BuLi (1.62 M in hexane, 11.0 mL, 17.8 mmol) and diisopropylamine (2.6 mL, 19 mmol) in THF (10 mL)] in THF (15 mL) at 0 °C and the mixture was stirred for 4 h at room temperature. The mixture was transferred to a solution of diethyl oxalate (15 mL, 110 mmol) in THF (30 mL) at −78 °C, and the mixture was stirred for 30 min and warmed to −40 °C over 1 h. The reaction was quenched by pouring into sat. aqueous $NaHCO_3$, and the mixture was extracted with Et_2O (×3). The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc = 92/8) to afford ethyl 5-methylene-2-oxo-8-nonenoate **5e** (1.23 g, 55%). Colorless oil; IR (ZnSe) 3077, 2981, 2937, 1726, 1644, 1446, 1398, 1369, 1249, 1184, 1074, 1029, 910, 858 cm^{-1}; ^1H NMR δ 1.37 (t, $J = 7.1$ Hz, 3H), 2.09–2.14 (m, 2H), 2.16–2.23 (m, 2H), 2.36 (t, $J = 7.6$ Hz, 2H), 3.00 (t, $J = 7.6$ Hz, 2H), 4.33 (q, $J = 7.1$ Hz, 2H), 4.75 (s, 1H), 4.79 (s, 1H), 4.97 (d, $J = 10.2$ Hz, 1H), 5.03 (d, $J = 17.1$ Hz, 1H), 5.81 (ddt, $J = 17.1$, 10.2 Hz, 6.5 Hz, 1H); ^{13}C NMR δ 18.9, 32.8, 35.4, 38.8, 40.7, 63.6, 107.5, 111.8, 133.3, 141.4, 154.6, 184.9; HRMS (FAB$^+$) m/z 211.1342 [211.1334 Calcd for $C_{12}H_{19}O_3$, $(M + H)^+$].

3-Isopropenyl-2,2-dimethyl-1-phenyl-5-hexen-1-one: To a suspension of Zn dust (1.32 g, 20.1 mmol) and TMSCl (1.63 g, 15.0 mmol) in CH_3CN (15 mL) was added 2-methyl-2,5-hexadienyl 2-bromo-2-methylpropanoate (2.16 g, 8.25 mmol) at room temperature, and the mixture was stirred for 10 h at 90 °C. After cooling to room temperature, the mixture was filtered through a celite pad, and the filtrate was concentrated in vacuo. To the residue was added 1 M NaOH solution and the mixture was washed with Et_2O. The aqueous layer was acidified by adding aqueous HCl, and the mixture was extracted with EtOAc (×3). The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated in vacuo to afford crude 3-isopropenyl-2,2-dimethyl-5-hexenoic acid (1.35 g, 90%). To a solution of the crude acid (1.03 g, 5.68 mmol) in Et_2O was added PhLi (1.04 M in Et_2O, 11.0 mL, 11.4 mmol) at room temperature and the reaction mixture was heated to reflux and stirred for 20 min. The reaction was stopped by adding water, and the mixture was extracted with Et_2O (×3). The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc = 97/3) to afford 3-isopropenyl-2,2-dimethyl-1-phenyl-5-hexen-1-one (800 mg, 58%). 3-Isopropenyl-2,2-dimethyl-5-hexenoic acid (387 mg, 37%) was recovered from the alkali aqueous layer. Colorless oil; IR (ZnSe) 3070, 2975, 2940, 1716, 1670, 1637, 1471, 1446, 1384, 1375, 1238, 1174, 972, 910 cm^{-1}; ^1H NMR δ 1.28 (s, 3H), 1.30 (s, 3H), 1.73 (s, 3H), 2.05–2.12 (m, 1H), 2.23–2.29 (m, 1H), 2.88 (dd, $J = 12.4$, 3.2 Hz, 1H), 4.77 (s, 1H), 4.90 (d, 1H, $J = 10.2$ Hz), 4.94 (dd, $J = 17.0$, 1.6 Hz, 1H), 4.98 (brs, 1H), 5.61 (ddt, $J = 17.0$, 10.2, 6.9 Hz, 1H), 7.39 (dd, $J = 7.2$, 7.2 Hz, 2H), 7.45 (t, $J = 7.2$ Hz, 1H), 7.62 (d, $J = 7.2$ Hz, 2H); ^{13}C NMR δ 22.3, 23.1, 25.3, 33.8, 51.3, 52.5, 115.5, 115.8, 127.6, 128.0, 130.5, 137.0, 139.6, 143.9, 209.6; HRMS (FAB$^+$) m/z 243.1764 [243.1749 Calcd for $C_{17}H_{23}O$, $(M + H)^+$].

General Procedure for the Preparation of the Oxime Derivatives. Preparation of Dienyl Ketone Oxime 4a Is Described below as a Typical Procedure: An EtOH (30 mL) solution of dienyl ketone **5a** (1.37 g, 5.7 mmol), pyridine (0.70 mL, 8.5 mmol), hydroxylamine hydrochloride (0.53 g, 7.6 mmol) was stirred at room temperature for 1 h. The reaction mixture was quenched by adding H_2O and brine, and this was extracted with ethyl acetate. The combined organic fractions were washed with 2 M HCl, sat. aqueous $NaHCO_3$, and brine and dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by flash column chromatography to afford 1.41 g (97%) of oxime **4a** as a 1:1 mixture of *E* and *Z* isomers.

6-Methylene-1-phenyl-9-decen-3-one Oxime: $(E)/(Z) =$ 1/1 mixture; pale yellow oil; IR (KBr) 1643, 1604, 1496, 1454, 1299, 1166, 1078, 1031, 997, 962, 910, 748, 700, 555 cm^{-1}; ^1H NMR δ 2.01 (t, $J = 7.4$ Hz, 1H), 2.07–2.19 (m, 6H), 2.42–2.46 (m, 2H), 2.57 (dd, $J = 8.5$, 5.5 Hz, 1H), 2.78 (dd, $J = 16.5$, 10.0 Hz, 2H), 4.66 (s, 0.5 H), 4.68 (s, 0.5 H), 4.70 (s, 0.5 H), 4.71 (s, 0.5 H), 4.88 (dd, $J = 10.1$, 1.6 Hz, 1H), 4.96 (dd, $J = 17.1$, 1.8 Hz, 1H), 5.69–5.78 (m, 1H), 7.07–7.20 (m, 3H), 7.21 (t, $J = 7.6$ Hz, 2H), 8.46 (bs, 1H); ^{13}C NMR δ 26.5, 30.0, 31.5, 31.6, 31.9, 31.9, 32.3, 32.5, 33.0, 35.3, 35.4, 36.0, 109.7, 109.7, 114.6, 126.1, 126.1, 128.3, 128.4, 138.3, 141.3, 141.4, 147.9, 148.1, 160.7; Anal. Found: C, 79.04; H, 9.10; N, 5.34%. Calcd for $C_{17}H_{23}NO$: C, 79.33; H, 9.00; N, 5.44%.

(*E*)-4-Methylene-1-phenyl-7-octen-1-one Oxime: Yellow oil; IR (KBr) 1643, 1597, 1578, 1448, 1345, 1155, 1075, 989, 906, 744, 690 cm^{-1}; ^1H NMR δ 2.14–2.20 (m, 4H), 2.27 (t, $J = 8.1$ Hz, 2H), 2.94 (t, $J = 8.2$ Hz, 2H), 4.78 (s, 1H), 4.81 (s, 1H), 4.95 (d, $J = 10.2$ Hz, 1H), 5.01 (dd, $J = 17.5$, 1.3 Hz, 1H), 5.76–5.84 (m, 1H), 7.37–7.39 (m, 3H), 7.58–7.60 (m, 2H), 8.49 (bs, 1H); ^{13}C NMR δ 24.9, 31.9, 32.3, 35.3, 109.7, 114.6, 126.3, 128.7, 129.2, 135.6, 138.4, 148.2, 159.5; Anal. Found: C, 78.28; H, 8.41; N, 6.17%. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11%.

(*E*)-2-(2-Methylene-5-hexenyl)cyclohexanone Oxime: Colorless oil; IR (KBr) 1641, 1444, 1351, 1249, 1145, 997, 939, 908, 823, 767, 665 cm^{-1}; ^1H NMR δ 1.36–1.49 (m, 1H), 1.42–1.52 (m, 1H), 1.54–1.62 (m, 1H), 1.65–1.76 (m, 2H), 1.84 (ddd, $J = 4.3$, 8.1, 12.2 Hz, 1H), 2.05–2.09 (m, 3H), 2.15–2.22 (m, 2H), 2.26 (ddd, $J = 4.5$, 9.0, 14.0 Hz, 1H), 2.41 (ddd, $J = 13.5$, 8.5, 4.8 Hz, 1H), 2.47 (dd, $J = 13.8$, 5.4 Hz, 1H), 2.75–2.81 (m,

1H), 4.74 (s, 1H), 4.80 (s, 1H), 4.95 (dd, $J = 10.2$, 1.6 Hz, 1H), 5.02 (dd, $J = 17.2$, 1.7 Hz, 1H), 5.77–5.85 (m, 1H), 8.73 (bs, 1 H); ^{13}C NMR δ 23.3, 23.6, 26.1, 31.8, 32.0, 34.8, 37.5, 39.6, 111.3, 114.5, 138.4, 146.5, 162.7. Anal. Found: C, 75.14; H, 10.15; N, 6.72%, Calcd for $C_{13}H_{21}NO$: C, 15.31; H, 10.20; N, 6.75%.

(*E*)-2-(2-Methylene-5-hexenyl)-3,4-dihydronaphthalene-1-(2*H*)-one Oxime: White solid; IR (KBr) 1644, 1598, 1488, 1454, 1353, 1313, 1124, 1095, 1054, 1037, 964, 892, 767, 730, 665 cm^{-1}; ^{1}H NMR δ 1.78–1.92 (m, 2H), 2.13 (q, $J = 13.7$, 11.1 Hz, 1H), 2.20 (t, $J = 5.8$ Hz, 1H), 2.23–2.26 (m, 2H), 2.32 (m, 1H), 2.50 (dd, $J = 4.2$, 13.8 Hz,1H), 2.65 (td, $J = 16.7$, 4.0 Hz, 1H), 2.95 (ddd, $J = 17.1$, 11.9, 5.3 Hz, 1H), 3.74–3.79 (m, 1H), 4.80 (s, 1H), 4.85 (s, 1H), 4.97 (d, $J = 10.3$ Hz, 1H), 5.05 (dd, $J = 17.3$, 1.1 Hz, 1H), 5.81–5.89 (m, 1H), 7.15 (d, $J = 7.5$ Hz, 1H), 7.19 (t, $J = 7.4$ Hz, 1H), 7.27 (dt, $J = 7.6$, 1.0 Hz, 1H), 7.88 (d, $J = 7.5$ Hz, 1H), 9.23 (bs, 1H); ^{13}C NMR δ 23.9, 24.7, 29.5, 31.9, 34.4, 35.0, 111.9, 114.5, 124.4, 126.3, 128.9, 129.2, 129.9, 138.5, 138.7, 146.5, 158.2. Anal. Found: C, 79.68; H, 8.29; N, 5.42%. Calcd for $C_{17}H_{20}O$: C, 79.96; H, 8.28, N, 5.48%.

(*E*)-Ethyl 5-Methylene-2-oxo-8-nonenoate Oxime: Colorless oil; IR (ZnSe) 3255, 3075, 2981, 2935, 1720, 1641, 1473, 1442, 1373, 1299, 1187, 1124, 1018, 910, 892, 769 cm^{-1}; ^{1}H NMR δ 1.35 (t, 3H, $J = 7.2$ Hz), 2.15–2.25 (m, 4H), 2.25 (t, 2H, $J = 8.0$ Hz), 2.76 (t, 2H, $J = 8.0$ Hz), 4.30 (q, 2H, $J = 7.2$ Hz), 4.77 (s, 1H), 4.79 (s, 1H), 4.96 (d, 1H, $J = 10.2$ Hz), 5.03 (d, 1H, $J = 16.8$ Hz), 5.82 (ddt, 1H, $J = 16.8$, 10.2, 6.4 Hz); ^{13}C NMR δ 14.0, 23.5, 31.8, 31.9, 35.0, 61.7, 110.1, 114.6, 138.3, 147.7, 125.8, 163.4; HRMS (FAB$^+$) m/z 226.1472 [226.1443 Calcd for $C_{12}H_{20}NO_3$, $(M + H)^+$].

(*E*)-4,7-Dimethylene-1-phenyl-10-undecen-1-one Oxime: Colorless oil; IR (KBr) 1949, 1643, 1598, 1575, 1498, 1446, 1319, 1303, 1157, 1070, 998, 931, 890, 765, 694 cm^{-1}; ^{1}H NMR δ 2.10 (t, $J = 7.5$ Hz, 2H), 2.14–2.21 (m, 6H), 2.28 (t, $J = 8.2$ Hz, 2H), 2.96 (t, $J = 8.1$ Hz, 2H), 4.73 (s, 2H), 4.79 (s, 1H), 4.80 (s, 1H), 4.95 (dd, $J = 10.3$ Hz, 1.2 Hz, 1H), 5.02 (dd, $J = 17.2$, 1.7 Hz, 1H), 5.77–5.85 (m, 1H), 7.37–7.40 (m, 3H), 7.58–7.60 (m, 2H), 9.20 (bs, 1H); ^{13}C NMR δ 24.9, 31.9, 32.2, 34.3, 34.3, 35.4, 109.3, 109.5, 114.5, 126.3, 128.6, 129.2, 135.5, 138.4, 148.5, 148.7, 159.35. Anal. Found: C, 80.24; H, 8.75; N, 4.85%. Calcd for $C_{19}H_{25}NO$: C, 80.52; H, 8.75; N, 4.94%.

(*Z*)-3-Isopropenyl-2,2-dimethyl-1-phenyl-5-hexen-1-one Oxime: Colorless powder; IR (ZnSe) 3241, 2973, 1637, 1456, 1016, 950, 931, 771 cm^{-1}; ^{1}H NMR δ 1.06 (s, 3H), 1.19 (s, 3H), 1.68 (s, 3H), 2.23–2.33 (m, 2H), 2.37 (ddd, $J = 12.8$, 6.2, 1.1 Hz, 1H), 4.67 (s, 1H), 4.95 (s, 1H), 4.96 (d, $J = 10.1$ Hz, 1H), 5.04 (dd, $J = 16.6$, 1.4 Hz, 1H), 5.67 (ddt, $J = 16.6$, 10.1, 6.3 Hz, 1H), 7.10 (d, $J = 8.3$ Hz, 2H), 7.38 (t, $J = 7.3$ Hz, 1H), 7.43 (dd, $J = 7.2$, 8.4 Hz, 2H); ^{13}C NMR δ 20.6, 23.9, 26.7, 33.7, 43.9, 51.1, 115.2, 115.4, 127.7, 128.05, 128.09, 133.3, 137.4, 143.8, 166.1; Anal. Found: C, 79.14; H, 9.22; N, 5.27%. Calcd for $C_{19}H_{25}NO$: C, 79.33; H, 9.01; N, 5.44%.

General Procedure for the Preparation of *O*-Pentafluorobenzoyloxime Derivatives and *O*-2,4-Dichlorobenzoyloxime. Preparation Dienyl Ketone *O*-pentafluorobenzoyloxime 3a Is Described below as a Typical Procedure: To a solution of 6-methylene-1-phenyl-9-decen-3-one oxime (1.41 g, 5.5 mmol) and Et_3N (1.6 mL, 10.9 mmol) in CH_2Cl_2 (20 mL) at 0 °C was added C_6F_5COCl (1.6 g, 7.1 mmol) in CH_2Cl_2 (5 mL) and the mixture was stirred for 30 min. After water was added at 0 °C, the mixture was extracted with ether (×3). The combined organic layer was washed with water and brine and then dried over anhydrous $MgSO_4$. After the solvents were removed in vacuo, the residue was purified by flash column chromatography (hexane/ethyl acetate = 95/5) to give 2.29 g (95%) of a dienyl oxime *O*-pentafluorobenzoate **3a**. The *O*-2,4-dichlorobenzoyl oxime **10b** was prepared in a similar way by the reaction of 2,4-dichlorobenzoyl chloride instead of pentafluorobenzoyl chloride.

6-Methylene-1-phenyl-9-decen-3-one *O*-Pentafluorobenzoyloxime (3a): $(E)/(Z) = 1/1$ mixture; pale yellow oil; IR (KBr) 1760, 1650, 1523, 1506, 1454, 1417, 1326, 1189, 1091, 1002, 906, 862, 750, 700, 509 cm^{-1}; ^{1}H NMR δ 2.01 (t, $J = 7.4$ Hz, 1H), 2.07–2.19 (m, 6H), 2.42–2.46 (m, 2H), 2.57 (dd, $J = 8.5$, 5.5 Hz, 1H), 2.78 (dd, $J = 16.5$, 10.0 Hz, 2H), 4.66 (s, 0.5 H), 4.68 (s, 0.5 H), 4.70 (s, 0.5 H), 4.71 (s, 0.5 H), 4.88 (dd, $J = 10.1$, 1.6 Hz, 1H), 4.96 (dd, $J = 17.1$, 1.8 Hz, 1H), 5.69–5.78 (m, 1H), 7.07–7.20 (m, 3H), 7.21 (t, $J = 7.6$ Hz, 2H), 8.46 (bs, 1H); ^{13}C NMR δ 26.4, 29.9, 31.5, 31.6, 31.9, 31.9, 32.3, 32.5, 33.0, 35.3, 35.4, 36.0, 109.7, 109.7, 114.6, 126.1, 126.1, 128.3, 128.4, 138.3, 141.3, 141.4, 147.9, 148.1, 160.7; Anal. Found: C, 64.08; H, 5.04; N, 3.08%. Calcd for $C_{24}H_{22}F_5NO_2$: C, 63.85; H, 4.91; N, 3.10%.

(*E*)-4-Methylene-1-phenyl-7-octen-1-one *O*-Pentafluorobenzoyloxime (3b): White solid; IR (KBr) 1766, 1648, 1523, 1498, 1444, 1419, 1326, 1195, 1095, 1004, 946, 904, 865, 769, 694 cm^{-1}; ^{1}H NMR δ 2.11–2.14 (m, 4H), 2.27 (t, $J = 8.3$ Hz, 2H), 3.03 (t, $J = 8.3$ Hz, 2H), 4.78 (s, 1H), 4.80 (s, 1H), 4.91–4.97 (m, 2H), 5.70–5.79 (m, 1H), 7.44 (t, $J = 7.3$ Hz, 2H), 7.49 (t, $J = 7.3$ Hz, 1H), 7.74 (d, $J = 7.5$ Hz, 2H); ^{13}C NMR δ 27.5, 31.7, 32.7, 35.0, 107.0, 110.4, 114.6, 127.4, 127.6, 128.0, 128.6, 128.8, 131.1, 132.9, 136.7–136.9 (overlapped m), 137.9, 138.7–138.9, 142.4–142.5, 144.4–144.5, 146.4–146.5 (overlapped m), 146.9, 156.5, 168.4; Anal. Found: C, 62.29; H, 4.42; N, 3.38%, Calcd for $C_{22}H_{18}F_5NO_2$: C, 62.41; H, 4.28; N, 3.31%.

(*E*)-2-(2-Methylene-5-hexenyl)cyclohexanone *O*-Pentafluorobenzoyloxime (3c): Colorless oil; IR (KBr) 1752, 1652, 1523, 1508, 1448, 1419, 1326, 1197, 1141, 1093, 1002, 873, 759, 698 cm^{-1}; ^{1}H NMR δ 1.54–1.62 (m, 2H), 1.68–1.78 (m, 3H), 1.87–1.93 (m, 1H), 2.11 (t, $J = 7.5$ Hz, 2H), 2.15–2.25 (m, 3H), 2.52 (ddd, $J = 13.6$, 6.5 Hz, 6.5 Hz, 2H), 2.62–2.66 (m, 1H), 2.67–2.74 (m, 1H), 4.79 (s, 1H), 4.84 (s, 1H), 4.96 (d, $J = 10.1$ Hz, 1H), 5.03 (dd, $J = 17.1$, 1.45 Hz, 1H), 5.77–5.85 (m, 1H); ^{13}C NMR δ 22.6, 25.9, 26.4, 31.6, 31.8, 34.7, 37.2, 39.9, 107.5 (complex), 111.8, 114.6, 137.7 (d complex, $J = 254$ Hz), 138.2, 143.2 (d complex, $J = 258$ Hz), 145.3 (d complex, $J = 250$ Hz), 145.8, 156.9, 173.1, Anal. Found: C, 60.06; H, 5.11; N, 3.55%. Calcd for $C_{20}H_{20}F_5NO_2$: C, 59.84; H, 5.02, N, 3.48%.

(*E*)-2-(2-Methylene-5-hexenyl)-3,4-dihydronaphthalene-1(2*H*)-one *O*-Pentafluorobenzoyloxime (3d): White solid; IR (KBr) 1762, 1652, 1523, 1452, 1417, 1326, 1251, 1193, 1091, 1002, 946, 904, 865, 769, 730 cm^{-1}; ^{1}H NMR δ 1.87–1.95 (m, 2H), 2.02–2.13 (m, 4H), 2.20 (dd, $J = 14.0$, 10.5 Hz, 1H), 2.31 (dd, $J = 13.8$, 5.2 Hz, 1H), 2.71 (dt, $J = 16.7$, 4.0 Hz, 1H), 2.97 (ddd, $J = 17.3$, 11.6, 6.0 Hz, 1H), 3.65–3.70 (m, 1H), 4.77 (s, 1H), 4.84 (s, 1H), 4.87 (s, 2H), 4.91 (dd, $J = 8.2$, 1.4 Hz, 2H), 5.65–5.73 (m, 1H), 7.17 (d, $J = 7.7$ Hz, 1H), 7.23 (t, $J = 7.5$ Hz, 1H), 7.36 (dt, $J = 7.5$, 1.2 Hz, 1H), 8.15 (d, $J = 7.7$ Hz, 1H); ^{13}C NMR δ 24.0, 24.2, 31.7, 31.9, 34.1, 35.7, 107.4, 112.8, 114.5, 126.3, 126.5, 126.6, 127.5, 129.1, 131.4, 137.79 (d complex, $J = 255$ Hz), 137.80, 140.0, 143.4 (d complex, $J = 271$ Hz), 145.1, 145.2 (d complex, $J = 257$ Hz), 156.5, 166.5. Anal. Found: C, 63.87; H, 4.57; N, 3.16%. Calcd for $C_{24}F_5H_{20}NO_2$: C, 64.14; H, 4.48, N, 3.11%.

(*E*)-Ethyl 5-Methylene-2-oxo-8-nonenoate *O*-Pentafluorobenzoyloxime (3e): Colorless oil; IR (ZnSe) 3083, 2983, 2940, 1772, 1729, 1652, 1523, 1498, 1419, 1324, 1182, 1002, 906 cm^{-1}; ^1H NMR δ 1.40 (t, $J = 7.1$ Hz, 3H), 2.08–2.21 (m, 4H), 2.29 (t, $J = 7.9$ Hz, 2H), 2.88 (t, $J = 7.9$ Hz, 2H), 4.39 (q, $J = 7.1$ Hz, 2H), 4.79 (s, 1H), 4.81 (s, 1H), 4.94 (d, $J = 10.3$ Hz, 1H), 4.99 (d, $J = 16.8$ Hz, 1H), 5.82 (ddt, $J = 16.8$, 10.3, 6.4 Hz, 1H); ^{13}C NMR δ 13.9, 26.4, 31.7, 32.2, 34.8, 62.8, 106.0 (complex), 110.9, 114.6, 137.85, 137.86 (d complex, $J = 255$ Hz), 143.9 (d complex, $J = 261$ Hz), 145.7 (d complex, $J = 265$ Hz), 146.4, 155.5, 161.8, 162.3; HRMS (FAB^+) m/z 420.1204 [420.1234 Calcd for $C_{19}F_5H_{19}NO_4$, $(M + H)^+$].

(*E*)-4,7-Dimethylene-1-phenyl-10-undecen-1-one *O*-Pentafluorobenzoyloxime (6): Colorless oil; IR (KBr) 1760, 1650, 1604, 1521, 1506, 1455, 1417, 1324, 1197, 1091, 1002, 948, 865, 750, 698 cm^{-1}; ^1H NMR δ 2.04–2.10 (m, 4H), 2.12–2.18 (m, 4H), 2.28 (t, $J = 7.9$ Hz, 2H), 3.04 (t, $J = 8.2$ Hz, 2H), 4.66 (s, 1H), 4.70 (s, 1H), 4.77 (s, 1H), 4.80 (s, 1H), 4.95 (d, $J =$ 10.9 Hz, 1H), 5.01 (dd, $J = 17.1$, 1.5 Hz, 1H), 5.75–5.83 (m, 1H), 7.44 (t, $J = 7.4$ Hz, 2H), 7.49 (t, $J = 7.3$ Hz, 1H), 7.74 (d, $J = 7.2$ Hz, 2H); ^{13}C NMR δ 27.5, 31.9, 32.7, 34.0, 34.1, 35.3, 107.0 (complex), 109.1, 110.2, 114.5, 127.4, 128.8, 131.0, 133.0, 137.7 (d complex, $J = 242$ Hz), 138.2, 143.4 (d complex, $J = 246$ Hz), 145.4 (d complex, $J = 260$ Hz), 147.3, 148.4, 156.4, 168.3; Anal. Found: C, 65.70; H, 5.28; N, 2.94%. Calcd for $C_{24}H_{24}F_5NO_2$: C, 65.40; H, 5.06, N, 2.93%.

(*Z*)-3-Isopropenyl-2,2-dimethyl-1-phenyl-5-hexen-1-one *O*-Pentafluorobenzoyloxime (10a): Colorless oil; IR (ZnSe) 3083, 2979, 1758, 1650, 1521, 1496, 1324, 1189, 1093, 995, 923, 863 cm^{-1}; ^1H NMR δ 1.16 (s, 3H), 1.34 (s, 3H), 1.72 (s, 3H), 2.31–2.45 (m, 3H), 4.74 (s, 1H), 4.99 (d, $J = 10.2$ Hz, 1H), 5.01 (s, 1H), 5.07 (dd, $J = 17.1$, 1.5 Hz, 1H), 5.69 (ddt, $J = 17.1$, 10.2, 6.6 Hz, 1H), 7.03–7.07 (m, 2H), 7.35–7.41 (m, 3H); ^{13}C NMR δ 20.6, 23.8, 26.5, 33.8, 45.6, 51.1, 107.0 (complex), 115.6, 116.1, 126.4, 128.1, 132.4, 136.8, 136.9 (d complex, $J = 260$ Hz), 143.2 (d complex, $J = 255$ Hz), 143.3, 145.1 (d complex, $J = 255$ Hz), 177.1; HRMS (FAB^+) m/z 452.1642 [452.1649 Calcd for $C_{24}H_{23}F_5NO_2$, $(M + H)^+$].

(*Z*)-3-Isopropenyl-2,2-dimethyl-1-phenyl-5-hexen-1-one *O*-2,4-Dichlorobenzoyloxime (10b): Colorless oil; ^1H NMR δ 1.15 (s, 3H), 1.35 (s, 3H), 1.71 (s, 3H), 2.31–2.39 (m, 1H), 2.43–2.49 (m, 2H), 4.73 (s, 1H), 4.93 (d, $J = 10.0$ Hz, 1H), 4.99 (t, $J = 1.5$ Hz, 1H), 5.05 (dd, $J = 17.0$, 1.5 Hz, 1H), 5.68 (ddt, $J = 17.0$, 10.0, 6.5 Hz, 1H), 7.06–7.10 (m, 3H), 7.16 (d, $J =$ 8.0 Hz, 1H), 7.32 (d, $J = 2.0$ Hz, 1H), 7.34–7.40 (m, 3H); ^{13}C NMR δ 20.5, 23.9, 26.6, 33.8, 45.4, 51.0, 115.5, 116.0, 126.7, 126.8, 127.3, 128.1, 128.4, 130.8, 132.2, 133.2, 134.9, 136.9, 138.3, 143.4, 162.1, 176.3; HRMS (FAB^+) m/z 430.1341 [430.1341 Calcd for $C_{24}H_{26}Cl_2NO_2$, $(M + H)^+$].

General Procedure for Domino Amino-Heck Reaction. Spirocyclization of 3a Is Described below as a Typical Procedure: A DMF (4 mL) suspension of **5a** (102 mg, 0.20 mmol), $Pd(PPh_3)_4$ (26 mg, 0.020 mmol), triethylamine (0.20 mL, 1.1 mmol), and molecular sieves 4A (150 mg) under argon atmosphere was warmed to 110 °C and stirred for 30 min. After cooling to room temperature, the mixture was filtered through a celite pad. Water was added to the filtrate, and the mixture was extracted with Et_2O (×3). The combined extracts were washed with water (×2) and brine, dried over anhydrous $MgSO_4$, and evaporated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc = 95/5–90/10) to afford spiroimine **13a** (42 mg, 77%).

7-Methylene-2-phenethyl-1-azaspiro[4.4]non-1-ene (13a): Yellow oil; IR (KBr) 1641, 1604, 1496, 1454, 1428, 1311, 1085, 1031, 875, 750, 700 cm^{-1}; ^1H NMR δ 1.62 (ddd, $J = 12.5$, 7.3, 5.5 Hz, 1H), 1.71–1.79 (m, 2H), 1.93 (dd, $J = 8.5$, 12.0 Hz, 1H), 2.22 (d, $J = 15.5$ Hz, 1H), 2.34–2.40 (m, 1H), 2.46–2.49 (t, $J = 7.7$ Hz, 2H), 2.56 (dd, $J = 17.5$, 2.0 Hz, 2H), 2.63 (t, $J =$ 7.8 Hz, 2H), 2.90 (t, $J = 7.9$ Hz, 2H), 4.87 (s, 2H), 7.17 (d, $J =$ 7.2 Hz, 1H), 7.21 (d, $J = 7.2$ Hz, 2H), 7.27 (t, $J = 7.5$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 31.3, 32.9, 34.4, 35.4, 37.3, 39.0, 46.3, 82.1, 106.1, 125.7, 128.3, 128.3, 141.3, 150.9, 175.2; HRMS (FAB^+) m/z 240.1727 [240.1727 Calcd for $C_{17}H_{22}N$, $(M + H)^+$].

7-Methylene-2-phenyl-1-azaspiro[4.4]non-1-ene (13b): IR (KBr) 1660, 1614, 1575, 1494, 1448, 1428, 1340, 1299, 1240, 1178, 1074, 1029, 919, 875, 759, 692, 557 cm^{-1}; ^1H NMR δ 1.73 (ddd, $J = 12.5$, 7.5, 4.5 Hz, 1H), 1.91–1.96 (m, 2H), 2.09 (ddd, $J = 12.2$, 8.6, 3.6 Hz, 1H), 2.33 (d, $J = 15.9$ Hz, 1H), 2.39–2.46 (m, 1H), 2.62–2.67 (m, 1H), 2.71 (dd, $J = 15.8$, 1.9 Hz, 1H), 2.99 (t, $J = 7.5$ Hz, 2H), 4.91 (s, 2H), 7.37–7.40 (m, 3H), 7.82 (dd, $J = 7.3$, 1.8 Hz, 2H); ^{13}C NMR ($CDCl_3$); δ 31.4, 34.4, 34.9, 39.2, 46.5, 82.8, 106.1, 127.7, 128.3, 130.2 134.8, 151.0, 170.6. Anal. Found: C, 85.02; H, 8.17; N, 6.57%. Calcd for $C_{15}H_{17}N$: C, 85.26; H, 8.10; N, 6.62%.

3′,3′a,4′,5′,6′,7′-Hexahydro-3-methylenespiro[cyclopentane-1,2′-[2*H*]-indole] (13c): Diastereomer mixture (1:1): Colorless oil; IR (KBr) 1654, 1648, 1430, 1348 1309, 1276, 1166, 1083, 1029, 977, 873, 804 cm^{-1}; ^1H NMR δ 1.08–1.18 (m, 1H), 1.32–1.49 (m, 3H), 1.58–1.64 (m, 0.5 H), 1.67–1.86 (m, 2H), 1.93–2.02 (m, 1H), 2.03–2.27 (m, 4H), 2.27–2.42 (m, 2H), 2.49–2.78 (m, 3.5 H), 4.83–4.94 (m, 2H); ^{13}C NMR δ 25.28, 25.30, 26.7, 26.8, 31.26, 31.30, 31.9, 34.9, 35.0, 38.8, 40.6, 41.7, 41.9, 46.2, 47.9, 48.0, 48.2, 80.5, 80.6, 106.0, 106.1, 151.0, 177.1; HRMS (FAB^+) m/z 190.1562 [190.1596 Calcd for $C_{13}H_{20}N$, $(M + H)^+$].

3,3a,4,5-Tetrahydro-3′-methylenespiro[2*H*-benz[*g*]indole-2,1′-cyclopentane] (13d): Diastereomer mixture (1:1): Yellow oil; IR (KBr) 1658, 1619, 1602, 1569, 1481, 1459, 1430, 1355, 1342, 1274, 1247, 1153, 1074, 1029, 871, 767, 730, 663 cm^{-1}; ^1H NMR δ 1.48 (dd, $J = 19.8$, 8.8 Hz, 1H), 1.55–1.75 (m, 1.5 H), 1.77–1.83 (m, 1H), 2.19–2.45 (m, 5H), 2.56–2.70 (m, 1H), 2.85–3.06 (m, 3.5 H), 4.80–4.93 (m, 2H), 7.17 (d, $J = 7.6$ Hz, 1H), 7.22 (t, $J = 7.5$ Hz, 1H), 7.31 (t, $J = 7.4$ Hz, 1H), 8.10 (d, $J = 7.7$ Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 29.8, 29.9, 30.0, 31.3, 31.4, 37.1, 40.4, 42.2, 42.3, 44.5, 46.6, 46.7, 47.7, 80.9, 80.9, 105.9, 106.1, 126.1, 126.3, 128.7, 130.2, 130.3, 130.5, 140.8, 151.0, 151.1, 171.5. Anal. Found: C, 85.74; H, 8.11; N, 6.09%. Calcd for $C_{17}H_{19}N$: C, 86.02; H, 8.06, N, 5.90%.

Ethyl 7-Methylene-1-azaspiro[4.4]non-1-ene-2-carboxylate (13e): Colorless oil; IR (ZnSe) 2937, 1745, 1718, 1625, 1461, 1434, 1375, 1340, 1322, 1299, 1251, 1180, 1122, 1101, 1070, 1016, 954, 879 cm^{-1}; ^1H NMR δ 1.37 (t, $J = 7.0$ Hz, 3H), 1.67–1.74 (m, 1H), 1.84–1.94 (m, 2H), 2.13 (dt, $J = 12.4$, 8.8 Hz, 1H), 2.31 (d, $J = 16.0$ Hz, 1H), 2.35–2.44 (m, 1H), 2.57–2.64 (m, 1H), 2.76 (d, $J = 16.0$ Hz, 1H), 2.88 (t, $J = 7.0$ Hz, 2H), 4.35 (q, $J = 7.0$ Hz, 2H), 4.9 (bs, 2H); ^{13}C NMR δ 14.1, 31.2, 33.8, 35.3, 38.8, 46.1, 61.8, 84.1, 106.6, 149.9, 163.1, 165.8; HRMS (FAB^+) m/z 208.1337 [208.1338 Calcd for $C_{12}H_{18}NO_2$, $(M + H)^+$].

9-Methylene-2-phenyl-1-azadispiro[4.1.4.2]tridec-1-ene (16): Colorless oil; IR(KBr) 1658, 1614, 1575, 1494, 1448, 1428, 1342, 1305, 1176, 1014, 987, 917, 875, 759, 692, 665, 559 cm^{-1}; (major isomer) ^1H NMR ($CDCl_3$) δ 1.63–1.70 (m, 2H), 1.71–1.87 (m, 4H), 1.96–2.08 (m, 4H), 2.29 (s, 2H), 2.35 (t, $J = 8.2$ Hz, 2H), 2.92–2.96 (m, 2H), 4.83–4.86 (m, 2H), 7.36–7.40 (m, 3H), 7.81–

7.83 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 31.4, 34.9, 36.9, 37.7, 39.7, 40.1, 47.7, 50.0, 51.4, 83.3, 105.4, 127.6, 128.3, 130.1, 135.0, 152.8, 169.5; (minor isomer) ^{1}H NMR δ 1.60–1.81 (m, 6H), 1.84 (ddd, J = 12.8, 5.5, 7.6 Hz, 1H) 1.95–2.07 (m, 4H), 2.34–2.41 (m, 3H), 2.89–2.98 (m, 2H), 4.82 (s, 1H), 4.86 (s, 1H), 7.36–7.41 (m, 3H), 7.82 (dd, J = 7.7, 1.8 Hz, 2H); ^{13}C NMR δ 31.5, 34.9, 36.9, 37.8, 39.6, 40.0, 47.8, 50.0, 51.4, 109.3, 114.5, 127.6, 128.0, 128.6, 133.0, 152.5, 169.0. Anal. Found: C, 85.74; H, 8.69; N, 5.14%. Calcd for $C_{19}H_{23}N$: C, 85.98; H, 8.73, N, 5.27%.

3,3,6a-Trimethyl-5-methylene-2-phenyl-3,3a,4,5,6,6a-hexahydrocyclopenta[*b*]pyrrole (18a): Colorless oil; IR (ZnSe) 3056, 2964, 2927, 1668, 1602, 1571, 1502, 1467, 1442, 1386, 1004, 989, 881 cm^{-1}; ^{1}H NMR δ 1.15 (s, 3H), 1.40 (s, 3H), 1.51 (s, 3H), 2.14 (dd, J = 9.4, 4.7 Hz, 1H), 2.34 (dd, J = 15.4, 4.5 Hz, 1H), 2.39–2.46 (m, 2H), 2.59 (d, J = 15.4 Hz, 1H), 4.75 (s, 1H), 4.78 (s, 1H), 7.32–7.38 (m, 3H), 7.54–7.59 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 22.8, 28.4, 30.6, 36.2, 47.4, 53.2, 58.9, 80.3, 105.8, 128.0, 129.0, 135.5, 150.9, 177.2; HRMS (FAB$^+$) m/z 240.1752 [240.1752 Calcd for $C_{17}H_{22}N$, $(M + H)^+$].

3-Allyl-2,4,4-trimethyl-2-pentafluorophenylmethyl-5-phenyl-3,4-dihydro-2*H*-pyrrole (19a): Colorless oil, IR (ZnSe) 2975, 2931, 1654, 1641, 1608, 1573, 1520, 1502, 1375, 1301, 1178, 1122, 995, 970, 918, 775 cm^{-1}; ^{1}H NMR δ 1.18 (s, 3H), 1.21 (s, 3H), 1.37 (s, 3H), 1.89 (t, 1H, J = 7.5 Hz), 2.25–2.37 (m, 2H), 2.79 (d, 1H, J = 13.5 Hz), 3.15 (d, 1H, J = 13.5 Hz), 5.12 (dd, 1H, J = 9.9, 1.1 Hz), 5.21 (dd, 1H, J = 17.1, 1.4 Hz), 5.87 (ddt, 1H, J = 17.1, 9.9, 7.1 Hz), 7.34–7.40 (m, 3H), 7.63–7.67 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 21.5, 22.3, 28.0, 31.2, 36.0, 52.8, 56.2, 74.2, 112.3 (complex), 116.5, 127.9, 128.2, 129.5, 134.9, 137.4 (b), 137.4 (d complex, J = 249 Hz), 139.7 (d complex, J = 250 Hz), 142.6 (d complex, J = 240 Hz), 178.0; HRMS (FAB$^+$) m/z 408.1766 [408.1751 Calcd for $C_{23}H_{23}F_5N$, $(M + H)^+$].

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