Synthesis of Dihydropyrrole and Pyrrole Derivatives by Radical Cyclization of γ,δ-Unsaturated Ketone *O*-Acetyloximes

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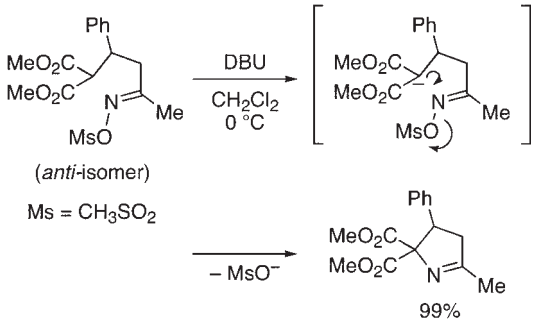
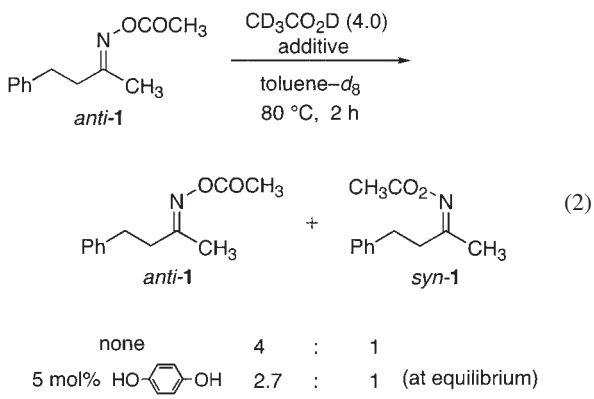
Treatment of γ,δ-unsaturated ketone *O*-acetyloximes with a catalytic amount of 1,5-naphthalenediol or hydroquinone, acetic acid, and 1,4-cyclohexadiene affords various dihydropyrrole and pyrrole derivatives via radical cyclization induced by one-electron reduction of the oximes.

Recently, we reported a new synthetic method of cyclic imines from oxime derivatives by the intramolecular S_N2-type substitution on the sp^2 nitrogen atom of oximes.[1] For instance, *O*-methylsulfonyloximes having an active methine group are converted to cyclic imines by treatment with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (Eq. 1).[1e,f] Due to the stereospecificity of S_N2 reaction, only *anti* isomers[2] of the oximes are converted to cyclic imines. This stereospecificity, however, causes a serious drawback in applying this reaction to organic synthesis, because it is quite hard to prepare oxime derivatives in a stereoselective manner.



(1)

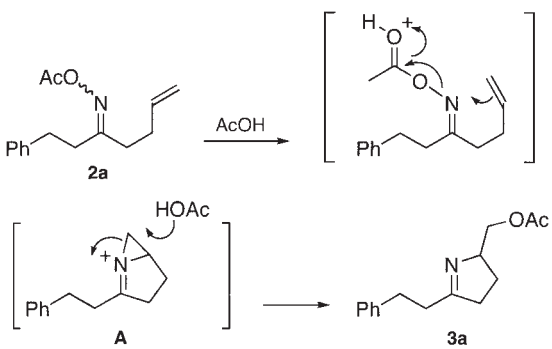
It was expected that the both stereoisomers of oxime derivatives could be employed for the cyclization if the *syn–anti* isomerization occurs under the cyclization conditions. Oximes themselves easily isomerize under acidic conditions,[3a] whereas *O*-substituted oximes usually don't isomerize under mild conditions.[3] We investigated the isomerization of *O*-acetyloximes and found that they could be isomerized by treatment with acetic acid, but very slowly. For example, though (*E*)-4-phenyl-2-butanone *O*-acetyloxime (**1**) isomerized at 80 °C, the isomerization had not attained equilibrium even after 2 h. It is noteworthy that the addition of a catalytic amount of hydroquinone accelerated the isomerization and the *syn*:*anti* ratio of 1:2.7 was attained at equilibrium, as shown in Eq. 2.



(2)

Based on these findings, intramolecular cyclization of γ,δ-unsaturated ketone *O*-acetyloxime **2a** was examined; we expected that 3,4-dihydro-2*H*-pyrroles **3a** would be formed by the nucleophilic substitution reaction of the acetoxy group of **2a** with the intramolecular olefinic moiety via the cationic intermediate **A**, as depicted in Scheme 1.

In fact, however, not only the nucleophilic cyclization product, 2-acetoxymethyl-3,4-dihydro-2*H*-pyrrole **3a**, but also unexpected 2-methyl-3,4-dihydro-2*H*-pyrrole **4a** was obtained (Eq. 3).



Scheme 1. Synthetic plan of 2*H*-pyrrol **3a** from *O*-acetyloxime **2a**.

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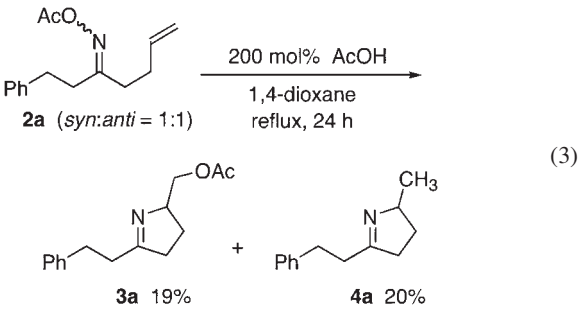


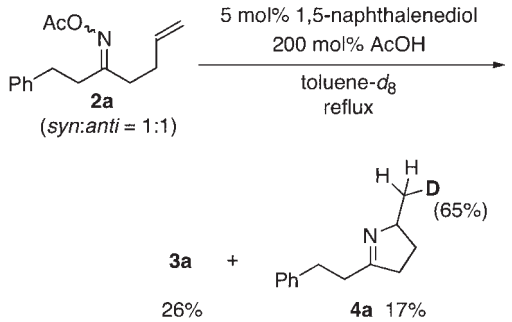
(3)

We have studied the formation of **4a**, and found a new synthetic method of 3,4-dihydro-2*H*-pyrroles, which was briefly reported as a communication.[4] This paper presents full accounts of the syntheses of 3,4-dihydro-2*H*-pyrroles and pyrrole derivatives from γ,δ-unsaturated ketone *O*-acetyloximes.

Results and Discussion

As we have explained in Eq. 2, addition of hydroquinone was effective for the isomerization of *O*-acetyloxime with acetic acid. We therefore examined the cyclization of **2a** in the presence or absence of hydroquinone derivatives; the results are summarized in Table 1. By treating **2a** with 2 molar amounts of acetic acid in refluxing 1,4-dioxane for 24 h, we obtained nucleophilic substitution product **3a** in 19% yield with 20% yield of 2-methyl-3,4-dihydro-2*H*-pyrrole **4a** (Entry 1). The addition of 1,4-cyclohexadiene as a radical trapping reagent improved the yield of imine **4a** to 29% (Entry 2). The reaction was finished within 6 h. The total yield of **3a** and **4a** was increased to 85–86% when a catalytic amount of hydroquinone or 1,5-naphthalenediol was added (Entries 3, 4). By the addition of 1,5-dimethoxynaphthalene, however, the yield of imine **4a** was not improved.

2-Methylcyclic imine **4a** could not be formed by the S_N2-type mechanism, but was supposed to be generated by radical cyclization. In fact, the reaction in toluene-d_8 without 1,4-cyclohexadiene gave the cyclic imine **4a** in 17% yield containing 65% deuterium in the methyl group along with 26% yield of **3a** (Eq. 4). In contrast, no cyclic imine containing deuterium was detected when a radical trapping reagent, 1,4-cyclohexadiene, was added.



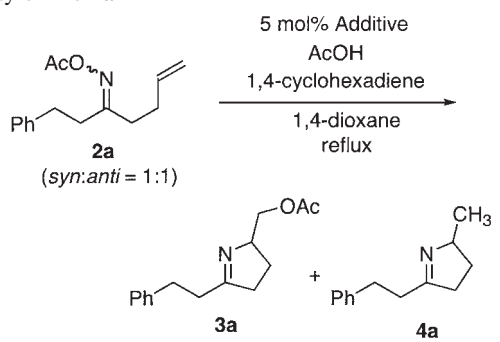
(4)

A plausible mechanism of the formation of **4a** by using 1,5-naphthalenediol is depicted in Scheme 2. One-electron transfer occurs from 1,5-naphthalenediol to **2a**, and the resulting radical **B** cyclizes to generate alkyl radical **C**, which abstracts hydrogen from 1,4-cyclohexadiene. The catalyst, 1,5-naphthalenediol, is regenerated from hydroxynaphthalenoxyl radical by hydrogen abstraction from 1,4-cyclohexadiene.

As shown in Table 2, various *O*-acetyloximes were cyclized by the treatment with a 5 mol% amount of 1,5-naphtalenediol, 2 molar amounts of acetic acid, and 10 molar amounts of 1,4-cyclohexadiene in refluxing 1,4-dioxane. By the reaction of *O*-acetyloxime **2** having an electron-rich olefinic moiety, acetoxymethyl derivative **3** was yielded as a major product (Entries 2, 3). In contrast, only radical cyclization products **4d** and **4e** were obtained from oximes **2d** and **2e**, which have an electron-deficient olefinic moiety (Entries 4, 5). The reaction of *O*-acetyloxime of phenyl ketone **2f** gave radical cyclization product **4f** exclusively (Entry 6). As oxime **2f** predominantly exist in the *syn* forms.[5] The nucleophilic attack of the alkenyl group was suppressed to give only radical cyclization products **4f**. *O*-pivaloyl oxime of α-keto ester **2g**[6] gave only radical cyclization product (Entry 7).

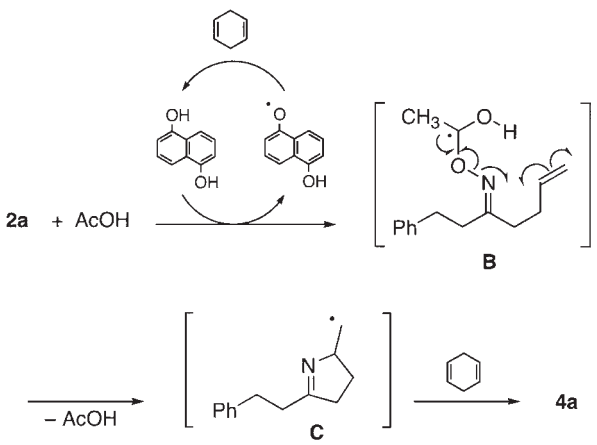
Next, this method was applied to the preparation of pyrroles from the *O*-acetyloximes having an alkynyl moiety. First, 1-phenyl-6-heptyn-3-one *O*-acetyloxime (**5a**) was treated with

Table 1. Influence of Additive in the Cyclization of *O*-Acetyloxime **2a**[a)]



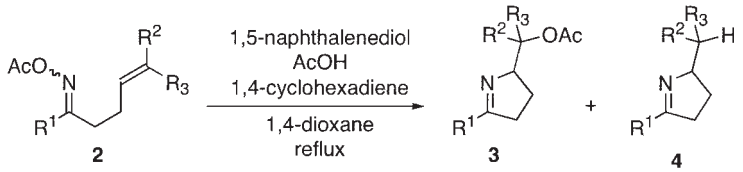
Entry	Additive	Time/h	Yield/%	
			3a	**4a**
1[b)]	none	24	19	20
2	none	24	12	29
3	hydroquinone	6	32	53
4	1,5-naphthalenediol	6	34	52
5	1,5-dimethoxynaphthalene	24	16	26

a) **2a**:AcOH:1,4-cyclohexadiene = 1:2:10. b) 1,4-Cyclohexadiene was not used.



Scheme 2. Plausible mechanism for formation of **4a**.

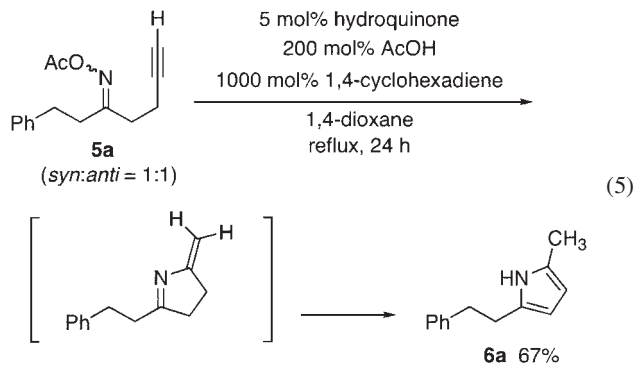
Table 2. Cyclization of Various *O*-Acetyloximes **2**[a)]



Entry	R^1	R^2	R^3		Time/h	Yield/%	
1	$PhCH_2CH_2$	H	H	(**2a**)[b)]	6	34 (**3a**)	52 (**4a**)
2	$PhCH_2CH_2$	Me	H	(**2b**)[b,c)]	6	67 (**3b**)[d)]	16 (**4b**)
3	$PhCH_2CH_2$	Me	Me	(**2c**)[b)]	6	72 (**3c**)	5 (**4c**)
4	$PhCH_2CH_2$	CN	H	(**2d**)[b)]	12	0 (**3d**)	69 (**4d**)
5	$PhCH_2CH_2$	CO_2Et	H	(**2e**)[e)]	12	0 (**3e**)	72 (**4e**)
6	Ph	H	H	(**2f**)[f)]	8	0 (**3f**)	75 (**4f**)
7[g)]	$Ph(CH_2)_3O_2C$	H	H	(**2g**)[h)]	6	0 (**3g**)	67 (**4g**)

a) Cyclization was carried out under the following conditions: 1,5-naphthalenediol (5 mol%), acetic acid (2 molar amounts), 1,4-cyclohexadiene (10 molar amounts). b) *syn*:*anti* = 1:1. c) The stereochemistry of olefin moiety was *E*:*Z* = 5:1. d) Diastereomer mixture (2:1). e) *syn*:*anti* = 1:2. f) Only *syn*-isomer was used. g) *O*-Pivaloyloxime was used instead of *O*-acetyloxime. h) Single isomer was used. The stereochemistry is unknown. See Ref. 7.

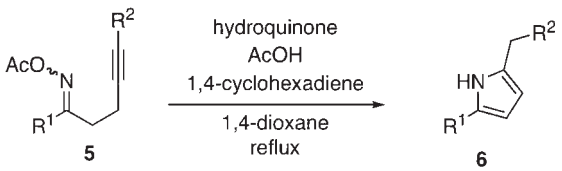
a catalytic amount of hydroquinone, acetic acid, and 1,4-cyclohexdiene; 2-methyl-5-phenethylpyrrole (**6a**) was obtained in 67% yield as a radical cyclization product without forming a S_N2-type reaction product (Eq. 5).



(5)

The preparation of pyrroles from various acetylenic *O*-acetyloximes **5** was examined as shown in Table 3. Both alkyl and aryl ketoxime having a terminal alkynyl group were converted to 2,5-disubstituted pyrroles in good yields (Entries 1 and 2). No significant influence was observed on the substituents of the alkyne moiety, except for the phenyl group. That is, acetylenic oximes having electron-donating or -withdrawing groups **5c** and **5d** gave the corresponding pyrroles **6c** and **6d** in 72% and 83% yields, respectively (Entries 3, 4).

Table 3. Cyclization of Various *O*-Acetyloximes **5**[a)]



Entry	R^1	R^2		Time/h	Yield/%
1	$PhCH_2CH_2$[b)]	H	(**5a**)	24	67 (**6a**)
2	Ph[c)]	H	(**5b**)	24	67 (**6b**)
3	Ph[c)]	Me	(**5c**)	24	72 (**6c**)
4	Ph[c)]	CO_2Et	(**5d**)	28	83 (**6d**)
5	Me[d)]	Ph	(**5e**)	6	32 (**6e**)

a) Cyclization was carried out under the following conditions: hydroquinone (5 mol%), acetic acid (2 molar amounts), 1,4-cyclohexadiene (10 molar amounts). b) *syn*:*anti* = 1:1. c) Only *syn*-isomer was used. d) Only *anti*-isomer was used.

The one-electron reduction of γ,δ-olefinic and acetylenic ketone *O*-acetyloximes with a catalytic amount of hydroquinone or 1,5-naphthalenediol leads to the cyclization to 3,4-dihydro-2*H*-pyrroles and pyrroles via a radical process. Several methods have been reported for radical cyclization of oxime derivatives.[8,9] For example, tributyltin hydride method,[9c,d] oxidation reaction,[9a,b] photochemical reaction,[9c,i,10] and Weinreb's method[9g] were used for radical cyclization of olefinic oxime derivatives via N–O bond dissociation. Zard et al. reported the radical cyclization of *O*-acetyloximes based on the reduction with an excess amount of nickel powder.[9f] The present reaction developed in this article would provide a catalytic method for the reductive cyclization of *O*-acetyloximes.

Experimental

General. ^{1}H NMR (500 MHz) spectra were recorded on a Bruker DRX 500 and a Bruker AVANCE 500 spectrometers in $CDCl_3$ using TMS ($\delta = 0.00$) as internal standard. ^{13}C NMR (125 MHz) spectra were recorded on Bruker DRX 500 and Bruker AVANCE 500 spectrometers in $CDCl_3$ using $CHCl_3$ ($\delta = 77.0$) as internal standard. IR spectra were recorded on a Horiba FT 300-S and Perkin Elmer SPECTRUM 1000 spectrophotometer on KBr (neat). High-resolution mass spectra were obtained with a JEOL JMS-700P mass spectrometer. The melting points were uncorrected. 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)), and preparative thin-layer chromatography was carried out using Wakogel B-5F. Dehydrated 1,4-dioxane was purchased from Kanto Chemical Co., Inc. and was used as freshly distilled from $LiAlH_4$ under an argon atmosphere. Hydroquinone and 1,5-naphthalenediol

were recrystallized from benzene and dried under reduced pressure. 1,4-Cyclohexadiene was purchased from Tokyo Chemical Industry Co., Ltd. and used without purification. Configurations of *O*-acetyloximes (*syn* or *anti*) were determined by the ^{13}C NMR of the *O*-acetyloximes or the corresponding oximes (*N*-hydroxy).[11]

Preparation of γ,δ-Unsaturated Ketone *O*-Acetyloximes. Experimental procedures for the preparation of γ,δ-unsaturated ketone *O*-acetyloximes are shown below as a typical example for the synthesis of 1-phenyl-6-hepten-3-one *O*-acetyloxime (**2a**).

To a solution of 1-phenyl-6-hepten-3-one oxime (760 mg, 3.74 mmol) and triethylamine (1.02 mL, 7.48 mmol) in dichloromethane (15 mL) was slowly added a solution of acetic anhydride (572 mg, 5.61 mmol) in dichloromethane (5 mL), and this mixture was stirred at room temperature for 12 h. After the reaction was quenched with sat. $NaHCO_3$, the mixture was extracted twice with dichloromethane. The combined extracts were washed with sat. $NaHCO_3$, and the dichloromethane solution was dried over anhydrous sodium sulfate. Dichloromethane was removed in vacuo, and the crude materials were purified by flash column chromatography (silica gel, hexane:ethyl acetate = 10:1) to give 1-phenyl-6-hepten-3-one *O*-acetyloxime (**2a**) (780 mg, 3.22 mmol, 93%).

Spectral Data for γ,δ-Unsaturated Ketone *O*-Acetyloximes. **1-Phenyl-6-hepten-3-one *O*-Acetyloxime (2a):** *E*:*Z* = 1:1 mixture; Colorless oil; IR (KBr) 3028, 1768, 1639, 1454, 1365, 1207, 999, 920, 748, 700 cm^{-1}; ^{1}H NMR δ 2.13 (3H, s), 2.24–2.39 (3H, m), 2.49–2.52 (1H, m), 2.63–2.70 (2H, m), 2.82–2.85 (1H, m), 2.89–2.92 (1H, m), 4.99–5.08 (2H, m), 5.74–5.84 (1H, m), 7.18–7.32 (5H, m); ^{13}C NMR δ 19.5, 19.6, 29.0, 29.8, 30.1, 31.4, 31.9, 32.3, 33.7, 36.0, 115.6, 115.8, 126.2, 126.4, 128.1, 128.2, 128.4, 128.5, 136.4, 136.6, 140.2, 140.6, 167.9, 168.0, 168.6, 168.7. Found: C, 73.46; H, 7.70; N, 5.77%. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71%.

1-Phenyl-6-octen-3-one *O*-Acetyloxime (2b): Diastereomer mixture (6*E*)-(*E*)-oxime:(6*E*)-(*Z*)-oxime:(6*Z*)-(*E*)-oxime:(6*Z*)-(*Z*)-oxime = 5:5:1:1; Colorless oil; IR (ZnSe) 3029, 2933, 1760, 1633, 1496, 1454, 1365, 1199, 1041, 1029, 998, 966, 925, 873, 748, 700 cm^{-1}; ^{1}H NMR δ 1.58–1.66 (m, 3H), 2.13 (s) and 2.14 (s) and 2.16 (s) and 2.17 (s) (3H), 2.17–2.30 (m, 2H), 2.30–2.35 (m, 1H), 2.43–2.48 (m, 1H), 2.61–2.72 (m, 2H), 2.80–2.86 (m, 1H), 2.87–2.94 (m, 1H), 5.30–5.57 (m, 2H), 7.17–7.23 (m, 3H), 7.26–7.32 (m, 2H); ^{13}C NMR (major two diastereomers) δ 17.80, 17.84, 19.63, 19.69, 28.8, 29.2, 29.7, 31.4, 32.0, 32.4, 34.4, 36.1, 126.2, 126.3, 126.4, 126.6, 128.15, 128.26, 128.48, 128.56, 129.0, 129.2, 140.3, 140.6, 168.3, 168.4, 168.7, 168.9. HRMS (FAB) Found *m*/*z* 260.1623. Calcd for $C_{16}H_{22}NO_2$, $(M + H)^+$ 260.1651.

7-Methyl-1-phenyl-6-octen-3-one *O*-Acetyloxime (2c): *E*:*Z* = 1:1 mixture; Colorless oil; IR (KBr) 2929, 1768, 1635, 1454, 1365, 1203, 998, 927, 750, 700 cm^{-1}; ^{1}H NMR δ 1.60 (1.5H, s), 1.61 (1.5H, s), 1.68 (1.5H, s), 1.69 (1.5H, s), 2.14 (1.5H, s), 2.19 (1.5H, s), 2.19–2.31 (3H, m), 2.40–2.43 (1H, m), 2.62–2.70 (2H, m), 2.82–2.85 (1H, m), 2.89–2.92 (1H, m), 5.07–5.11 (1H, m), 7.18–7.24 (3H, m), 7.28–7.32 (2H, m); ^{13}C NMR δ 17.6, 17.7, 19.7, 24.5, 24.9, 25.6, 29.8, 31.4, 32.1, 32.5, 34.5, 36.2, 122.3, 122.5, 126.3, 126.5, 128.2, 128.3, 128.5, 128.6, 133.0, 133.5, 140.4, 140.7, 168.4, 168.4, 168.6, 168.7. Found: C, 74.75; H, 8.46; N, 5.16%. Calcd for $C_{17}H_{23}NO_2$: C, 74.69; H, 8.48; N, 5.12%.

6-Acetyloxyimino-8-phenyl-2-octenenitrile (2d): *E*:*Z* = 1:1 mixture; Colorless oil; IR (KBr) 2933, 1768, 1760, 1633, 1454, 1367, 1203, 1000, 929, 748, 700 cm^{-1}; ^{1}H NMR δ 2.15 (1.5H, s), 2.18 (1.5H, s), 2.31–2.34 (1H, m), 2.37–2.43 (1H, m), 2.46–2.53 (2H, m), 2.63–2.73 (2H, m), 2.83–2.95 (2H, m), 5.29–5.36 (1H, m), 6.60–6.67 (1H, m), 7.16–7.36 (5H, m); ^{13}C NMR δ 19.5, 27.8, 28.9, 29.2, 31.5, 31.86, 31.90, 32.2, 32.7, 36.0, 31.7, 126.4, 126.6, 128.1, 128.2, 128.5, 128.6, 139.8, 140.1, 152.8, 153.5, 166.0, 146.0, 146.5, 166.0, 166.2, 168.3, 168.5. Found: C, 70.97; H, 6.83; N, 10.26%. Calcd for $C_{16}H_{18}N_2O_2$: C, 71.09; H, 6.71; N, 10.36%.

Ethyl 6-Acetyloxyimino-8-phenyl-2-octenoate (2e): *E*:*Z* = 1:1 mixture; Colorless oil; IR (KBr) 2981, 1766, 1718, 1657, 1454, 1367, 1268, 998, 927, 748, 700 cm^{-1}; ^{1}H NMR δ 1.27–1.30 (3H, m), 2.13 (3H, s), 2.37–2.43 (2H, m), 2.44–2.50 (1H, m), 2.53–2.55 (1H, m), 2.63–2.70 (2H, m), 2.83–2.86 (1H, m), 2.90–2.93 (1H, m), 4.16–4.21 (2H, m), 5.81–5.85 (1H, m), 6.88–6.93 (1H, m), 7.17–7.32 (5H, m); ^{13}C NMR δ 14.1, 19.6, 28.2, 31.7, 32.0, 32.3, 33.0, 36.0, 60.2, 60.3, 122.3, 122.5, 126.3, 126.5, 128.1, 128.2, 128.5, 128.6, 140.0, 140.3, 146.0, 146.5, 166.0, 166.2, 167.0, 167.0, 168.5, 168.5. Found: C, 67.87; H, 7.24; N, 4.47%. Calcd for $C_{18}H_{23}NO_2$: C, 68.12; H, 7.30; N, 4.41%.

1-Phenyl-4-penten-1-one (*E*)-*O*-Acetyloxime (2f): Colorless oil; IR (KBr) 2935, 1770, 1641, 1444, 1365, 1201, 998, 931, 771, 694 cm^{-1}; ^{1}H NMR δ 2.27 (3H, s), 2.30–2.34 (2H, m), 2.95 (2H, t, *J* = 7.9 Hz), 5.01–5.07 (2H, m), 5.78–5.86 (1H, m), 7.39–7.47 (3H, m), 7.69–7.71 (2H, m); ^{13}C NMR δ 20.0, 27.7, 30.6, 115.8, 127.3, 128.6, 130.5, 134.0, 136.5, 165.6, 169.0. Found: C, 71.88; H, 6.91; N, 6.45%. Calcd for $C_{13}H_{15}NO_2$: C, 71.87; H, 6.96; N, 6.45%.

3-Phenylpropyl (*E*)-Pivaloyloxyimino-5-hexenoate (2g): Colorless oil; IR (KBr) 2975, 1772, 1726, 1641, 1479, 1454, 1207, 1155, 1095, 1024, 920, 752, 700 cm^{-1}; ^{1}H NMR δ 1.32 (9H, s), 2.04–2.11 (2H, m), 2.31–2.35 (2H, m), 2.71–2.74 (2H, m), 2.76–2.79 (2H, m), 4.29–4.31 (2H, m), 4.98–5.09 (2H, m), 5.75–5.85 (1H, m), 7.18–7.20 (3H, m), 7.26–7.30 (2H, m); ^{13}C NMR δ 26.8, 27.1, 29.8, 30.3, 31.9, 38.7, 65.8, 116.3, 126.1, 128.36, 128.44, 136.0, 140.8, 159.4, 163.0, 173.9. Found: C, 69.42; H, 7.89; N, 3.86%. Calcd for $C_{20}H_{27}NO_4$: C, 69.54; H, 7.88; N, 4.05%.

1-Phenyl-6-heptyn-3-one *O*-Acetyloxime (5a): *E*:*Z* = 1:1 mixture; Colorless oil; IR (ZnSe) 3290, 2933, 1763, 1637, 1603, 1496, 1198, 999, 931, 885, 752, 698 cm^{-1}; ^{1}H NMR δ 1.98–2.02 (1H, m), 2.16 (3H, s), 2.43–2.49 (2H, m), 2.60–2.64 (2H, m), 2.69–2.74 (2H, m), 2.82–2.94 (2H, m), 7.17–7.23 (3H, m), 7.25–7.31 (2H, m); ^{13}C NMR δ 15.2, 15.5, 19.57, 19.64, 28.5, 31.6, 31.9, 32.2, 32.4, 33.3, 36.3, 37.5, 69.4, 69.8, 82.0, 82.5, 126.2, 126.5, 128.1, 128.5, 128.6, 140.0, 140.4, 166.65, 166.71, 168.6. Found: C, 74.02; H, 7.28; N, 5.70%. Calcd for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04; N, 5.76%.

1-Phenyl-4-pentyn-1-one (*E*)-*O*-Acetyloxime (5b): White needles, mp 73–74 °C; IR (ZnSe) 2958, 1770, 1699, 1392, 1329, 928, 760, 729 cm^{-1}; ^{1}H NMR δ 1.98 (1H, t, *J* = 2.7 Hz), 2.26 (3H, s), 2.45 (2H, dt, *J* = 2.7, 7.7 Hz), 3.08 (2H, t, *J* = 7.7 Hz), 7.38–7.44 (3H, m), 7.70–7.72 (2H, m); ^{13}C NMR δ 15.9, 19.8, 27.2, 69.7, 81.9, 127.3, 128.9, 130.6, 133.4, 164.0, 168.7. Found: C, 72.67; H, 6.29; N, 6.35%. Calcd for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09; N, 6.51%.

1-Phenyl-4-hexyn-1-one (*E*)-*O*-Acetyloxime (5c): Colorless oil; IR (ZnSe) 2917, 1766, 1703, 1444, 1190, 995, 931, 893, 768, 692 cm^{-1}; ^{1}H NMR δ 1.72 (3H, t, *J* = 2.5 Hz), 2.28 (3H, s), 2.40–2.44 (2H, m), 3.05 (2H, t, *J* = 7.7 Hz), 7.39–7.45 (3H, m), 7.73–7.74 (2H, m); ^{13}C NMR δ 3.32, 16.4, 19.8, 28.0, 76.96, 76.99,

127.4, 128.6, 130.6, 133.8, 164.7, 168.8. Found: C, 73.23; H, 6.77; N, 5.91%. Calcd for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11%.

Ethyl (*E*)-6-Acetyloxyimino-6-phenyl-2-hexynoate (5d): Colorless oil; IR (ZnSe) 2924, 2237, 1768, 1703, 1250, 1186, 1074, 1186, 1074, 769, 692 cm^{-1}; ^1H NMR δ 1.29 (3H, t, $J = 7.0$ Hz), 2.29 (3H, s), 2.62 (2H, t, $J = 7.4$ Hz), 3.16 (2H, t, $J = 7.4$ Hz), 4.21 (2H, q, $J = 7.0$ Hz), 7.43–7.46 (3H, m), 7.71–7.73 (2H, m); ^{13}C NMR δ 14.0, 16.2, 19.8, 26.2, 61.9, 74.1, 86.1, 127.2, 128.8, 130.9, 133.0, 153.3, 163.2, 168.5. Found: C, 66.95; H, 6.14; N, 4.77%. Calcd for $C_{16}H_{17}NO_4$: C, 66.89; H, 5.96; N, 4.88%.

6-Phenyl-5-hexyn-2-one (*E*)-*O*-Acetyloxime (5e): Colorless oil; IR (ZnSe) 2910, 1763, 1693, 1643, 1365, 1196, 999, 930, 756, 692 cm^{-1}; ^1H NMR δ 2.07 (3H, s), 2.18 (3H, s), 2.65 (2H, t, $J =$ 7.1 Hz), 2.71 (2H, t, $J = 7.1$ Hz), 7.27–7.38 (5H, m); ^{13}C NMR δ 15.6, 16.8, 19.6, 34.8, 81.8, 87.8, 123.4, 127.8, 128.1, 131.5, 164.6, 168.8. Found: C, 73.17; H, 6.84; N, 6.10%. Calcd for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11%.

General Procedure for the Synthesis of 3,4-Dihydro-2*H*-pyrroles and Pyrroles. Into a flask containing *O*-acetyloxime (**2a**) (254.3 mg, 1.04 mmol) in 1,4-dioxane (4 mL) was added hydroquinone (289 mg, 0.250 mmol), acetic acid (131 mg, 2.08 mmol) and 1,4-cyclohexadiene (0.984 mL, 10.4 mmol) at room temperature under an argon atmosphere. The mixture was immediately heated to reflux. After 6 h, the reaction was quenched with sat. Na_2CO_3. The mixture was extracted three times with ethyl acetate and the combined extracts were dried over anhydrous sodium sulfate. The solvent was removed in vacuo, and the crude product was purified by thin-layer chromatography (hexane:ethyl acetate = 1:1) to afford 2-acetoxymethyl-5-phenethyl-3,4-dihydro-2*H*-pyrrole (**3a**) (100 mg, 0.541 mmol) in 52% yield and 2-methyl-5-phenethyl-3,4-dihydro-2*H*-pyrrole (**4a**) (86.9 mg, 0.355 mmol) in 34% yield, respectively.

Spectral Data for 3,4-Dihydro-2*H*-pyrroles. 2-Acetoxymethyl-3,4-dihydro-5-phenethyl-2*H*-pyrrole (3a): Colorless oil; IR (neat) 2948, 1737, 1641, 1234, 1039, 752, 700 cm^{-1}; ^1H NMR δ 1.58 (1H, dddd, $J = 6.6$, 7.4, 10.0, 13.1 Hz), 2.03 (1H, dddd, $J = 5.1$, 8.0, 9.6, 13.1 Hz), 2.06 (3H, s), 2.45 (1H, m), 2.54 (1H, dddd, $J = 2.0$, 5.1, 10.0, 17.4 Hz), 2.68 (2H, t, $J =$ 8.2 Hz), 2.93 (2H, t, $J = 8.2$ Hz), 4.11 (1H, dd, $J = 5.9$, 11.0 Hz), 4.19 (1H, dd, $J = 4.9$, 11.0 Hz), 4.22–4.28 (1H, m), 7.16–7.20 (3H, m), 7.24–7.28 (2H, m); ^{13}C NMR δ 20.9, 25.4, 32.7, 35.3, 37.6, 67.2, 70.9, 126.0, 128.2, 128.4, 141.2, 171.0, 179.0. Found: C, 73.19; H, 7.89; N, 5.67%. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71%.

2-Methyl-5-phenethyl-3,4-dihydro-2*H*-pyrrole (4a):[9h] Colorless oil; IR (neat) 2960, 1643, 1603, 1496, 1454, 1288, 750, 700 cm^{-1}; ^1H NMR δ 1.24 (3H, d, $J = 6.8$ Hz), 1.30–1.39 (1H, m), 2.02–2.09 (1H, m), 2.41 (1H, ddd, $J = 8.7$, 8.7, 17.2 Hz), 2.47–2.54 (1H, m), 2.61 (2H, t, $J = 7.8$ Hz), 2.91 (2H, dt, $J = 4.5$, 7.8 Hz), 4.01–4.07 (1H, m), 7.15–7.20 (3H, m), 7.24–7.28 (2H, m); ^{13}C NMR δ 22.0, 30.6, 32.7, 35.3, 37.7, 67.7, 125.9, 128.2, 128.3, 141.4, 176.1.

2-(1-Acetoxyethyl)-5-phenethyl-3,4-dihydro-2*H*-pyrrole (3b): Diastereomer mixture (2:1); Pale yellow oil; IR (ZnSe) 2933, 1731, 1644, 1496, 1456, 1428, 1371, 1240, 1141, 1060, 1031, 937, 750, 700 cm^{-1}; ^1H NMR δ 1.23 (d, $J = 6.4$ Hz) and 1.24 (d, $J = 6.4$ Hz) (3H), 1.45–1.70 (m, 1H), 1.91–2.00 (m, 1H), 2.01 (s) and 2.04 (s) (3H), 2.39–2.54 (m, 2H), 2.62–2.73 (m, 2H), 2.87–2.98 (m, 2H), 4.07–4.16 (m, 1H), 4.97–5.06 (m, 1H), 7.18–7.24 (m, 3H), 7.26–7.30 (m, 2H); ^{13}C NMR ($*$ means major isomer) δ 16.5, *16.8, *21.33, 21.37, *24.2, 24.6, 32.6, *32.7, *35.3, *37.5, 37.8, 72.8, *72.9, 75.3, *76.0, 126.02, *126.06, *128.25, 128.28, 128.39, *128.41, *141.19, 141.27, *170.6, 170.7, 178.7, *178.9. HRMS (FAB) Found m/z 260.1643. Calcd for $C_{16}H_{22}NO_2$, $(M + H)^+$ 260.1651.

2-Ethyl-5-phenethyl-3,4-dihydro-2*H*-pyrrole (4b): Colorless oil; IR (ZnSe) 3025, 2958, 2921, 1644, 1602, 1496, 1454, 1428, 1376, 1315, 1270, 1078, 937, 750, 700 cm^{-1}; ^1H NMR δ 0.94 (3H, t, $J = 7.4$ Hz), 1.37–1.46 (2H, m), 1.71–1.80 (m, 1H), 1.98–2.05 (1H, m), 2.37–2.51 (2H, m), 2.64 (2H, t, $J = 6.3$ Hz), 2.87–2.97 (2H, m), 3.86–3.92 (1H, m), 7.17–7.23 (3H, m), 7.26–7.31 (2H, m); ^{13}C NMR δ 10.8, 18.0, 29.2, 32.8, 35.4, 37.4, 73.9, 126.0, 128.3, 128.4, 141.5, 176.38. HRMS (FAB) Found m/z 202.1593. Calcd for $C_{14}H_{20}N$, $(M + H)^+$ 202.1596.

2-(1-Acetoxy-1-methylethyl)-5-phenethyl-3,4-dihydro-2*H*-pyrrole (3c): Colorless oil; IR (neat) 2978, 2935, 1730, 1367, 1254, 700 cm^{-1}; ^1H NMR δ 1.35 (3H, s), 1.56 (3H, s), 1.66–1.71 (1H, m), 1.86–1.94 (1H, m), 1.95 (3H, s), 2.37–2.53 (2H, m), 2.63–2.73 (2H, m), 2.87–2.97 (2H, m), 4.27–4.34 (1H, m), 7.15–7.28 (5H, m); ^{13}C NMR δ 21.9, 22.4, 23.6, 32.7, 35.2, 37.7, 79.8, 83.8, 125.9, 128.2, 128.3, 141.2, 141.2, 170.4, 178.2. HRMS (FAB) Found m/z 274.1804. Calcd for $C_{17}H_{24}NO_2$, $(M + H)^+$ 274.1807.

2-Isopropyl-5-phenethyl-3,4-dihydro-2*H*-pyrrole (4c):[9h] Colorless oil; IR (neat) 1643, 1495, 1454, 750, 700 cm^{-1}; ^1H NMR δ 0.85 (3H, d, $J = 6.8$ Hz), 1.00 (3H, d, $J = 6.8$ Hz), 1.50–1.58 (1H, m), 1.85–1.95 (2H, m), 2.38–2.50 (2H, m), 2.69 (2H, t, $J = 8.0$ Hz), 2.94 (2H, t, $J = 8.0$ Hz), 3.80–3.86 (1H, m), 7.18–7.25 (3H, m), 7.28–7.33 (2H, m); ^{13}C NMR δ 18.0, 19.8, 24.8, 32.9, 35.3, 37.6, 78.3, 126.0, 128.3, 128.4, 141.4, 176.7.

2-Cyanomethyl-5-phenethyl-3,4-dihydro-2*H*-pyrrole (4d):[9h] Colorless oil; IR (neat) 2925, 2247, 1646, 1495, 1454, 1423, 1311, 1290, 754, 701 cm^{-1}; ^1H NMR δ 1.67–1.75 (1H, m), 2.18–2.26 (1H, m), 2.52–2.60 (1H, m), 2.62–2.77 (5H, m), 2.92–3.02 (2H, m), 4.25–4.31 (1H, m), 7.18–7.24 (3H, m), 7.28–7.33 (2H, m); ^{13}C NMR δ 24.4, 27.7, 32.5, 35.1, 38.2, 67.9, 117.8, 126.1, 128.2, 128.5, 140.9, 179.8.

2-(Ethoxycarbonyl)methyl-5-phenethyl-3,4-dihydro-2*H*-pyrrole (4e):[9h] Colorless oil; IR (neat) 2935, 1734, 1643, 1495, 1373, 1315, 1261, 1180, 1028, 752, 702 cm^{-1}; ^1H NMR δ 1.26 (3H, t, $J = 7.2$ Hz), 1.48–1.57 (1H, m), 2.10–2.20 (1H, m), 2.33 (1H, dd, $J = 8.7$, 15.4 Hz), 2.44–2.60 (2H, m), 2.64 (2H, t, $J = 8.0$ Hz), 2.80 (1H, dd, $J = 5.6$, 15.4 Hz), 2.92 (2H, t, $J = 8.0$ Hz), 4.16 (2H, q, $J = 7.2$ Hz), 4.35–4.41 (1H, m), 7.19–7.24 (3H, m), 7.28–7.32 (2H, m); ^{13}C NMR δ 14.2, 28.5, 32.6, 35.3, 37.7, 41.0, 60.3, 68.8, 126.0, 128.2, 128.4, 141.2, 171.9, 177.8.

2-Methyl-5-phenyl-3,4-dihydro-2*H*-pyrrole (4f):[9d] Colorless oil; IR (neat) 3058, 2962, 2866, 1614, 1576, 1495, 1448, 1340, 1018, 906 cm^{-1}; ^1H NMR δ 1.36 (3H, d, $J = 6.8$ Hz), 1.56 (1H, dddd, $J = 7.3$, 7.5, 9.9, 12.6 Hz), 2.25 (1H, dddd, $J = 4.8$, 7.3, 9.7, 12.6 Hz), 2.88 (1H, dddd, $J = 2.0$, 7.5, 9.7, 17.0 Hz), 3.06 (1H, dddd, $J = 2.0$, 4.8, 9.9, 17.0 Hz), 4.25–4.33 (1H, m), 7.37–7.42 (3H, m), 7.83–7.86 (2H, m); ^{13}C NMR δ 22.1, 30.7, 35.2, 68.4, 127.6, 128.4, 130.2, 134.7, 171.8.

2-Methyl-5-(3-phenylpropyloxycarbonyl)-3,4-dihydro-2*H*-pyrrole (4g): Colorless oil; IR (neat) 1743, 1720, 1454, 1251, 1126, 1030, 750, 700 cm^{-1}; ^1H NMR δ 1.37 (3H, d, $J = 6.9$ Hz), 1.45–1.56 (1H, m), 2.05–2.12 (2H, m), 2.16–2.24 (1H, m), 2.70–2.79 (3H, m), 2.87–2.95 (1H, m), 4.25–4.37 (3H, m), 7.17–7.22 (3H, m), 7.25–7.31 (2H, m); ^{13}C NMR δ 21.4, 29.9,

30.0, 32.1, 35.6, 65.2, 69.8, 126.0, 128.33, 128.42, 140.9, 163.0, 166.8. Found: C, 73.52; H, 7.87; N, 5.49%. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71%.

Spectral Data for Pyrroles. 2-Methyl-5-phenethylpyrrole (6a):[12] Yellow oil; IR (ZnSe) 3367, 2924, 1601, 1593, 1512, 1452, 1038, 748, 698 cm^{-1}; ^1H NMR δ 2.21 (3H, s), 2.87–2.92 (4H, m), 5.77–5.81 (2H, m), 7.20–7.22 (3H, m), 7.29–7.32 (2H, m), 7.48 (1H, brs); ^{13}C NMR δ 12.9, 29.7, 36.2, 105.1, 105.5, 123.3, 126.0, 126.1, 128.3, 128.3, 130.5, 141.7.

2-Methyl-5-phenylpyrrole (6b):[12] Yellow oil; IR (ZnSe) 3398, 2916, 1603, 1510, 1213, 904, 746, 727, 687 cm^{-1}; ^1H NMR δ 2.32 (3H, s), 5.95 (1H, br s), 6.39 (1H, br s), 7.15 (1H, t, $J = 7.3$ Hz), 7.32 (2H, m), 7.42 (2H, m), 8.09 (1H, brs); ^{13}C NMR δ 13.2, 106.1, 107.9, 123.3, 125.6, 128.8, 129.0, 130.7, 132.9.

2-Ethyl-5-phenylpyrrole (6c):[12] Yellow oil; IR (ZnSe) 3390, 2966, 1604, 1514, 1333, 1205, 1039, 912, 750, 690 cm^{-1}; ^1H NMR δ 1.29 (3H, t, $J = 7.6$ Hz), 2.68 (2H, q, $J = 7.6$ Hz), 5.98 (1H, br s), 6.42 (1H, br s), 7.16 (1H, t, $J = 7.3$ Hz), 7.33 (2H, dt, $J = 7.5$, 7.3 Hz), 7.43 (2H, t, $J = 7.5$ Hz), 8.13 (1H, brs); ^{13}C NMR δ 13.6, 21.0, 106.0, 106.2, 123.4, 125.4, 128.8, 130.6, 133.0, 135.6.

Ethyl (5-phenyl-2-pyrrolyl)acetate (6d):[12] Yellow oil; IR (ZnSe) 3371, 2981, 1716, 1616, 1512, 1221, 1151, 1026, 750, 690 cm^{-1}; ^1H NMR δ 1.27 (3H, t, $J = 7.1$ Hz), 3.68 (2H, s), 4.17 (2H, q, $J = 7.1$ Hz), 6.06 (1H, br s), 6.40 (1H, br s), 7.16 (1H, t, $J = 7.3$ Hz), 7.32 (2H, dd, $J = 7.3$, 7.6 Hz), 7.44 (2H, d, $J = 7.6$ Hz), 9.06 (1H, brs); ^{13}C NMR δ 14.1, 33.3, 61.2, 105.8, 109.1, 123.6, 124.5, 125.9, 128.7, 132.1, 132.7, 171.2.

2-Benzyl-5-methylpyrrole (6e):[13] Yellow oil; IR (ZnSe) 3228, 2922, 1766, 1603, 1496, 1454, 1369, 1203, 1038, 914, 746, 698 cm^{-1}; ^1H NMR δ 2.19 (3H, s), 3.91 (2H, s), 5.78 (1H, m), 5.84 (1H, m), 7.21–7.24 (3H, m), 7.29–7.32 (2H, m), 7.47 (1H, brs); ^{13}C NMR δ 13.0, 34.2, 105.7, 106.5, 126.3, 127.0, 128.5, 128.6, 129.2, 139.8.

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