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Synthesis of Isoxazoline/Cyclic Nitrone-Featured Methylenes Using Unsaturated Ketoximes: A Dual Role of TEMPO

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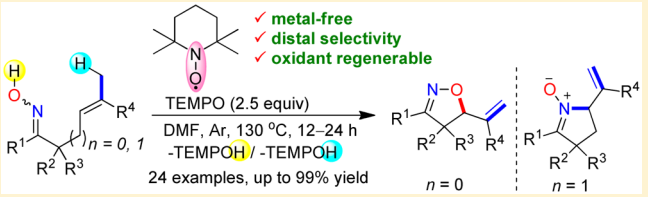
Supporting Information

ABSTRACT: A novel, metal-free, and regioselective approach for the synthesis of isoxazoline/cyclic nitrone-featured methylenes has been developed by the reaction of readily accessible β,γ- and γ,δ-unsaturated ketoximes with TEMPO via tandem iminoxyl radical-promoted cyclization/TEMPO-mediated Cope-like elimination, respectively. This protocol utilizes commercially available TEMPO as the iminoxyl radical initiator as well as the β-hydrogen acceptor in the Cope-like elimination.



Olefins are one of the simplest and most useful functional groups in organic chemistry considering their versatile transformations in organic synthesis. Consequently, the preparation of olefins has been extensively studied. Among a wide variety of synthetic methodologies, the Heck reaction has become a famous and powerful tool for the preparation of multisubstituted olefins, but it is difficult to obtain terminal ones.[1] Thus, the synthesis of terminal olefins has attracted more and more attention from organic chemists. In 2012, for instance, Baran reported a radical-based simple and efficient approach to produce terminal olefin by a "portable desaturase".[2] In 2014, Nishikata developed a general and convenient method to synthesize methylenes utilizing a copper-amine catalytic system.[3] Despite some efforts that have been made,[4] the advancement is far from the demand, and much remains to be explored. Herein, we wish to report a novel, metal-free, and regioselective iminoxyl radical-involved protocol for the synthesis of isoxazoline/cyclic nitrone-featured methylenes by the reaction of β,γ- and γ,δ-unsaturated ketoximes with nitroxide TEMPO[5] (2,2,6,6-tetramethyl-1-piperidinyloxy), respectively.

Among various methylenes, those tethered onto five-membered heterocycles are ubiquitous structural motifs in organic chemistry. They not only serve as valuable building blocks but also present in many natural products. For example, compound **I** is an important intermediate for the synthesis of paliclavine;[6] compounds **II** and **III** are natural products (+)-nodulisporic acid A and B (Figure 1).[7] In this context, the protocol presents a facile and efficient method for the synthesis of structurally important isoxazoline/cyclic nitrone-featured methylenes as well a tandem C−O(N)/C=C bond formation via iminoxyl radical[8]-promoted dichotomous cyclization[9] followed by a Cope-like elimination. Significantly, in such a protocol, TEMPO serves as both the iminoxyl radical initiator and the β-hydrogen acceptor in the Cope-like elimination (Scheme 1).

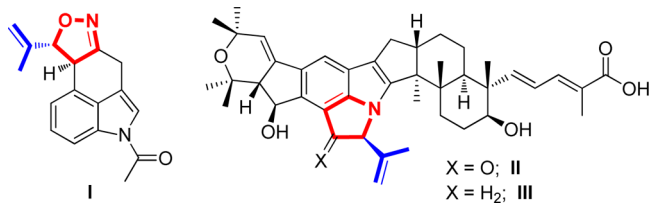
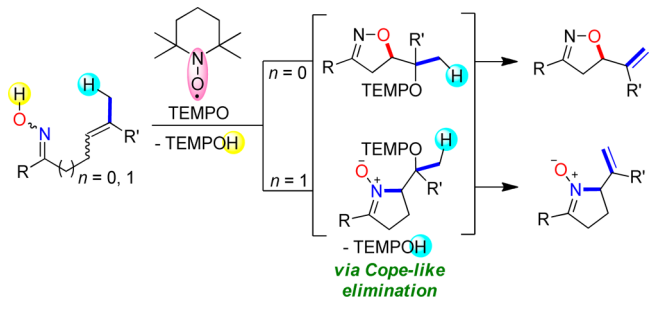


Figure 1. Heterocycle featured methylenes in natural product.

Scheme 1. TEMPO-Mediated Regioselective Synthesis of Isoxazoline/Cyclic Nitrone-Featured Methylenes



We commenced our studies by stirring β,γ-unsaturated ketoxime **1a** with TEMPO (2.5 equiv) in DMF under an argon atmosphere at 130 °C for 12 h. To our delight, the cascade cyclization/elimination sequence took place, and the desired isoxazoline-featured methylene **2a** was obtained in 91% yield (Table 1). To explore the effect of solvent polarity on the reaction, nonpolar solvent toluene was tested in the reaction, and **2a** was also obtained in 90% yield (Table 1). To examine the scope of the present protocol, a variety of β,γ-unsaturated

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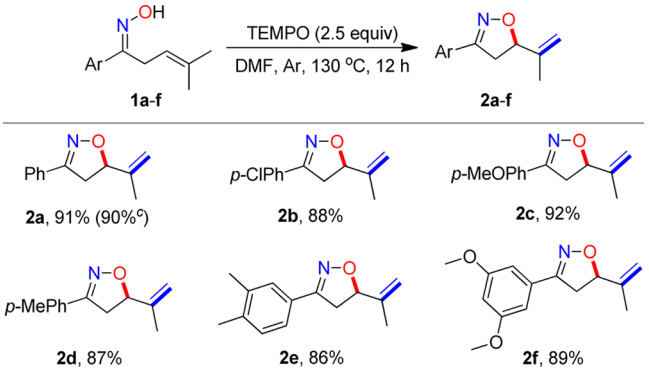
Table 1. Scope of β,γ-Unsaturated Ketoximes[a,b]



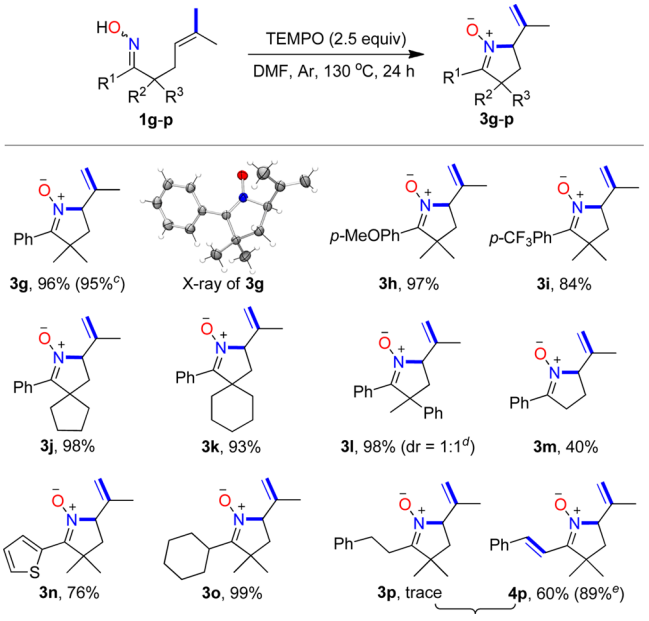
[a]All reactions run with 0.3 M in DMF using ketoximes **1** (0.3 mmol) and TEMPO (2.5 equiv) at 130 °C for 12 h. [b]Isolated yields. [c]Toluene was used as the solvent.

ketoximes were employed in the reaction, and the results are summarized in Table 1. 4-Phenyl with a range of electronic properties substituted β,γ-unsaturated ketoximes were all tolerated well in the reaction, affording isoxazoline-featured methylenes (**2b–d**) in excellent yields. When the phenyl-bearing multisubstituent such as 3,4-dimethyl or 3,5-dimethoxyl was incorporated in the ketoximes, as in the cases of **1e** and **1f**, the reaction took place smoothly as well, giving rise to the corresponding products **2e** and **2f** in 86% and 89% yields, respectively.

Next, we shifted our attention to γ,δ-unsaturated counterparts to see if the latter could also undergo the 5-*exo*-trig N-radical cyclization[10] to form cyclic nitrones, as we previously observed.[9] Indeed, as shown in Table 2, cyclic nitrone-featured methylenes **3** were obtained in excellent yields. On the other side, the O atom-involved 1,5-H shift, which happens under other circumstances,[8e] was not detected in the present cases, since it is much less advantageous than the N-radical-involved 5-*exo*-trig cyclization. Phenyl with a range of electronic properties substituted γ,δ-unsaturated ketoximes participated well in the reaction to produce the desired cyclic nitrone-featured methylenes (**3g–i**) in excellent yields. Notably, the tandem reaction could be easily carried out on a gram scale without difficulty, as demonstrated in the case of **3g**. When the cyclopentane or cyclohexane moiety was merged into the γ,δ-unsaturated ketoxime at the α-position, the reaction delivered cyclic nitrone-featured methylenes **3j** or **3k** as spiro-compound in excellent yields. When the ketoxime-bearing methyl and phenyl groups at the α-position were involved in the reaction, the product **3l** was formed as a mixture of diastereomers in a ratio of 1:1. When the *gem*-dimethyl group was removed from the substrate, the yield of the corresponding product **3m** was sharply decreased to 40%. Thiophene incorporated ketoxime also reacted with TEMPO to afford the desired product **3n** in good yield. In addition, alkyl substituents such as cyclohexyl and phenethyl incorporated ketoximes **1o** and **1p** were also allowed to react with TEMPO to further investigate the applicability of the reaction. To our delight, ketoxime **1o** was transformed smoothly to the corresponding product **3o** in nearly quantitative yield. Surprisingly, when ketoxime **1p** was involved in the reaction, the unexpected double-olefin-containing product **4p** was obtained in 60% yield accompanied by a trace amount of the normal product **3p**. Apparently, the product **4p** was generated from the overoxidative dehydrogenation of **3p** by TEMPO. By using a stoichiometric amount of TEMPO (5 equiv), the yield of **4p** was remarkably increased to 89%.

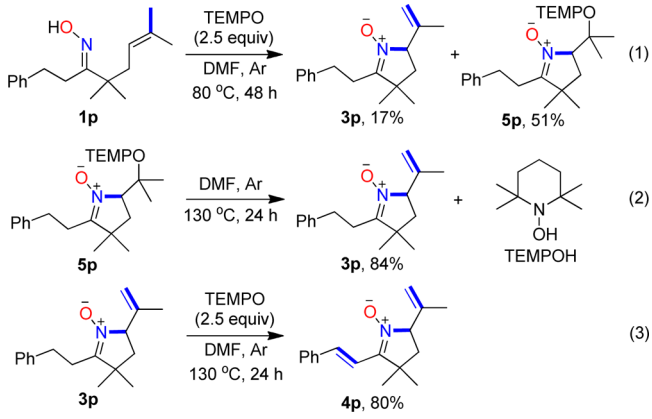
To access the rationalization of the formation of **4p** and the insight into the mechanism of the protocol, some control experiments were carried out as shown in Scheme 2.

Table 2. Scope of γ,δ-Unsaturated Ketoximes[a,b]



[a]All reactions run with 0.3 M in DMF using **1** (0.3 mmol) and TEMPO (2.5 equiv) at 130 °C for 24 h. [b]Isolated yields. [c]Ketoxime **1g** (5 mmol) was used, and the corresponding product **3g** was obtained in 1.09 g. [d]The diastereomer radio was determined by ^{1}H NMR spectroscopy. [e]TEMPO (5 equiv) was used.

Scheme 2. Control Experiments



Interestingly, when compound **1p** was allowed to react with TEMPO under the same conditions at 80 °C, the reaction gave the TEMPO-trapped cyclic nitrone **5p** in 51% yield along with the normal product cyclic nitrone-featured methylene **3p** in 17% yield and the aforementioned unexpected product **4p** unfound (Scheme 2, eq 1). Heating of compound **5p** at 130 °C gave the TEMPOH eliminated product **3p** via a Cope-like elimination (Scheme 2, eq 2). The treatment of **3p** with TEMPO at 130 °C provided **4p** in 80% yield (Scheme 2, eq 3). These results not only indicated that **4p** was formed definitely via further oxidative dehydrogenation of the phenylethane

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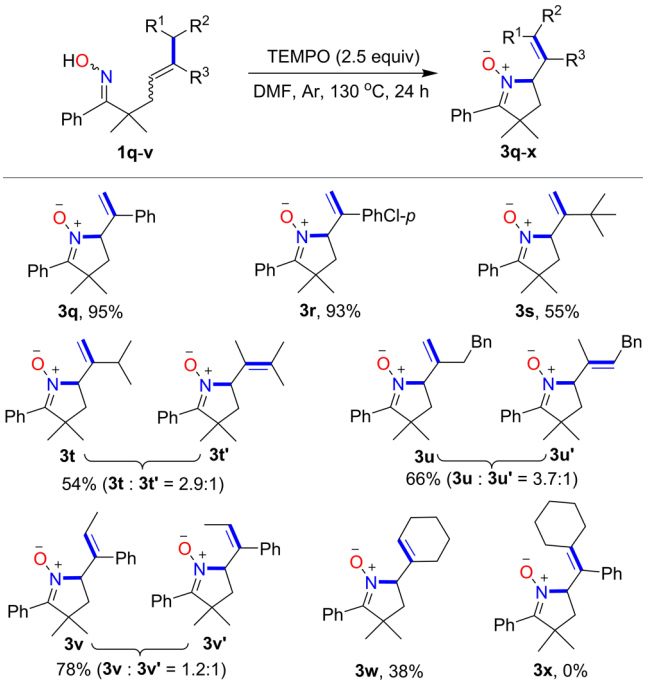
moiety[11] of **3p** by TEMPO under high temperature but also revealed that the TEMPO-trapped product was the key intermediate for the subsequent Cope-like TEMPOH elimination.

Although the methylenation of symmetric dimethyl alkenes was achieved successfully, comparable results were also obtained with other olefin moieties as shown in Table 3. The

Table 3. Scope of Alkene Moieties[a,b,c]

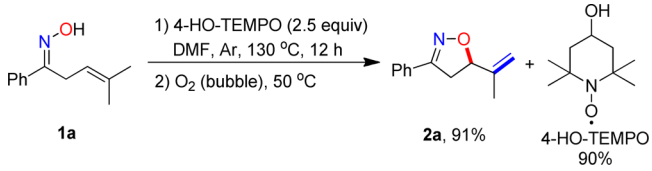


[a]All reactions run with 0.3 M in DMF using **1** (0.3 mmol) and TEMPO (2.5 equiv) at 130 °C for 24 h. [b]Isolated yields. [c]The configuration of **3v** was determined by a X-ray single-crystal study.

methylenation of unsymmetrical olefins bearing such as phenyl, *p*-Cl-phenyl, and *t*-butyl in the alkene moiety gave the corresponding methylenes (**3q**–**s**) in moderate to excellent yields. When ketoxime-bearing *i*-propyl in the alkene moiety was utilized in the reaction, the products methylene **3t** and methanediylylidene **3t′** were obtained in a ratio of 2.9:1. A similar selectivity of *β*-hydrogen elimination was also observed in the case of **1u**, in which phenethyl group was incorporated in the alkene moiety, resulting in the methylenation product **3u** and the methination product **3u′** in a ratio of 3.7:1. This selectivity suggested that the elimination was governed almost entirely by the number of hydrogen atoms at the various *β*-positions and preferred to produce the less-substituted alkene, which is consistent with the Cope elimination. Moreover, ketoxime involving ethyl in the olefin moiety also participated swimmingly in the reaction and provided the cyclic nitrone-featured methines **3v** and **3v′** as the separable *cis*–*trans* isomers in a combined yield of 78%. When the olefin moiety was incorporated in 1,1′-cyclohexane, as in the case of **1w**, the reaction afforded the product **3w** in 38% yield. Unfortunately, compound **1x** was inert to transform to **3x**, and it was recovered in the reaction.

It is noteworthy that the oxidant TEMPO was reduced to TEMPOH as a stoichiometric byproduct in the reaction. As we know, TEMPOH can be autoxidized quantitatively to the corresponding TEMPO by O_2 or air. Therefore, recycling of TEMPO can be realized from economic and environmental points of view. However, the recovery of TEMPO was difficult because of its high volatility. Therefore, the oxidation of *β*,*γ*-unsaturated ketoxime **1a** was repeated with less volatile 4-HO-TEMPO. After completion of the oxidation, the reaction mixture was treated with O_2 to recover 4-HO-TEMPO. Remarkably, the product **2a** was achieved in 91% yield along with 4-HO-TEMPO in 90% yield (Scheme 3). Eventually, O_2

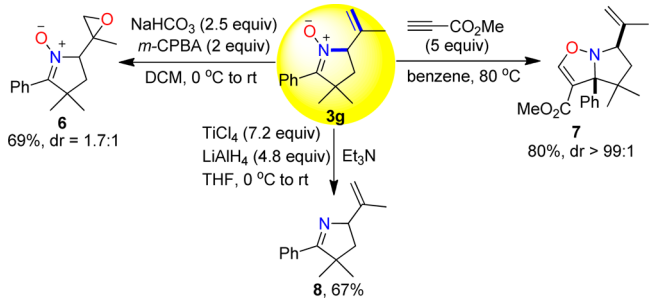
Scheme 3. 4-HO-TEMPO Regeneration



acts as a terminal oxidant, and the aminoxyl radical was lightly recovered in high yield rendering this protocol attractive for industrial and sustainable chemistry.

Besides the importance of the cyclic nitrone scaffold in pharmacophore and 1,3-dipolar cycloaddition, the formation of compound **3** involves terminal alkene formation which is of great synthetic value in multitransformation for important organic intermediates. As in the case of **3g**, methylene moiety can be converted to epoxide under the conditions of *meta*-chloroperoxybenzoic acid (*m*-CPBA) and $NaHCO_3$, delivering product **6** in 69% yield. In addition, **3g** could also be used as 1,3-dipole to react with methyl propiolate to yield heterocyclic-fused compound **7** in 80% yield as a single diastereomer. Furthermore, reductive deoxygenation of **3g** under the conditions $TiCl_4$ and $LiAlH_4$ gave the corresponding pyrroline-feature methylene **8** in 67% yield (Scheme 4).

Scheme 4. Follow-Up Transformations



Based on the experimental results and the aforementioned control experiments, a proposed mechanism for the TEMPO-mediated iminoxyl radical-involved methylenation is drawn in Figure 2. Ketoximes are first initiated to iminoxyl radicals by TEMPO via a hydrogen-atom transfer process, which serve as *σ* radicals with the single electronic spin delocalized on both the O atom and the N atom (resonance structures **IV** and **V**). The iminoxyl radicals subsequently undergo fast O atom/N atom 5-*exo*-trig cyclization depending on the position of the alkenes to yield the deuterogenic C-centered radicals **VI** and **VII**, which are trapped immediately by TEMPO to produce the intermediates **VIII** and **IX**, respectively. Finally, the latter undergoes Cope-like elimination by losing TEMPOH via a five-centered cyclic transition state to give the desired products **2** and **3**, respectively.[12]

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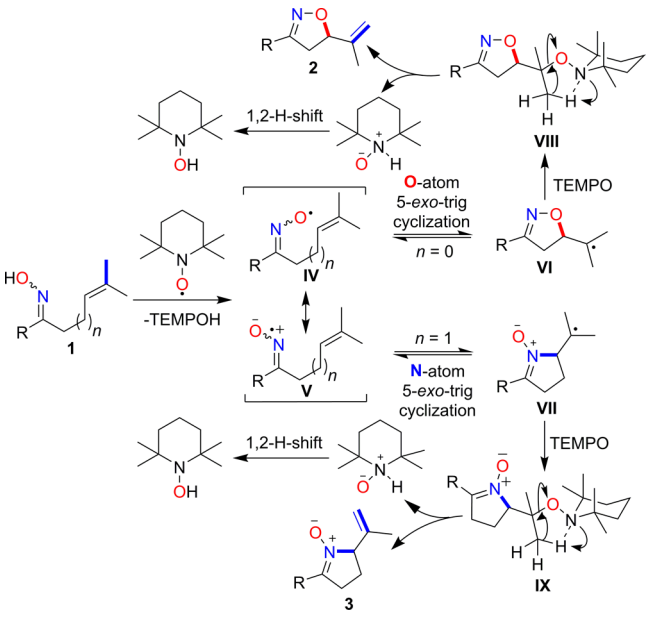

Figure 2. Proposed mechanism.

In summary, we have demonstrated a novel, metal-free, and regioselective approach for the synthesis of isoxazoline/cyclic nitrone-featured methylenes by the reaction of β,γ- and γ,δ-unsaturated ketoximes with TEMPO via iminoxyl radical-promoted cyclization, followed instantly by β-hydrogen elimination. In this protocol, TEMPO plays a dual role: one as the iminoxyl radical initiator and the other as an acceptor of β-hydrogen in the Cope-like elimination. Further studies on the iminoxyl radical-promoted reaction are in progress in our laboratory.

EXPERIMENTAL SECTION

General Methods. All reagents were purchased from commercial suppliers and used without further purification. Flash chromatography was carried out with silica gel (200−300 mesh). Analytical TLC was performed with silica gel GF254 plates, and the products were visualized by UV detection. Melting points were determined without correction on a digital melting point apparatus. ^{1}H NMR and ^{13}C NMR (400 and 100 MHz, respectively) spectra were recorded in $CDCl_3$. Chemical shifts (δ) are reported in ppm using TMS as internal standard, and spin−spin coupling constants (J) are given in Hz. The high-resolution mass spectra (HRMS) were measured on an electrospray ionization (ESI) apparatus using a time-of-flight (TOF) mass spectrometry. Data collections for crystal structure were performed at room temperature (293 K) using MoKα radiation on a diffractometer.

General Procedure for the Synthesis of Unsaturated Ketoximes 1a−1x. To a solution of the corresponding unsaturated ketone (1 equiv) in ethanol were added pyridine (4 equiv) and hydroxylamine hydrochloride (4 equiv) at room temperature. The mixture was heated to reflux for 2 h and concentrated in vacuo. Then the mixture was extracted with ethyl acetate, and the combined organic layers were washed with water and brine, dried with Na_2SO_4, filtered, and concentrated in vacuo. The crude material was purified by flash chromatography on silica gel to afford the corresponding unsaturated ketoxime.

*(E)-4-Methyl-1-phenylpent-3-en-1-one oxime (**1a**).* Colorless oil; (850 mg, 90% yield); R_f = 0.25 (hexanes/ethyl acetate 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.73 (brs, NO*H*, 1H), 7.58−7.61 (m, 2H), 7.36−7.37 (m, 3H), 5.17 (t, J = 6.8 Hz, 1H), 3.54 (d, J = 6.8 Hz, 2H), 1.72 (s, 3H), 1.68 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 158.2, 135.8, 134.2, 129.1, 128.4, 126.4, 118.1, 26.0, 25.6, 18.0; ESI-HRMS: m/z Calcd for $C_{12}H_{15}NO + H^+$: 190.1226, found 190.1228.

*(E)-1-(4-Chlorophenyl)-4-methylpent-3-en-1-one oxime (**1b**).* Colorless oil; (948 mg, 85% yield); R_f = 0.20 (hexanes/ethyl acetate 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.62 (brs, NO*H*, 1H), 7.50−7.54 (m, 2H), 7.32−7.35 (m, 2H), 5.10−5.14 (m, 1H), 3.50 (d, J = 6.8 Hz, 2H), 1.71 (s, 3H), 1.68 (d, J = 0.8 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 157.5, 135.2, 134.6, 134.2, 128.7, 127.8, 117.6, 25.9, 25.6, 18.0; ESI-HRMS: m/z Calcd for $C_{12}H_{14}ClNO + H^+$: 224.0837, found 224.0839.

*(E)-1-(4-Methoxyphenyl)-4-methylpent-3-en-1-one oxime (**1c**).* Colorless oil; (898 mg, 82% yield); R_f = 0.18 (hexanes/ethyl acetate 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.83 (brs, NO*H*, 1H), 7.55 (d, J = 8.8 Hz, 2H), 6.90 (d, J = 8.8 Hz, 2H), 5.14−5.17 (m, 1H), 3.82 (s, 3H), 3.51 (d, J = 6.8 Hz, 2H), 1.73 (s, 3H), 1.68 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 160.4, 157.9, 134.1, 128.3, 127.8, 118.3, 113.8, 55.3, 25.8, 25.7, 18.0; ESI-HRMS: m/z Calcd for $C_{13}H_{17}NO_2 + H^+$: 220.1332, found 220.1333.

*(E)-4-Methyl-1-(p-tolyl)pent-3-en-1-one oxime (**1d**).* Colorless oil; (873 mg, 86% yield); R_f = 0.23 (hexanes/ethyl acetate 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.67 (brs, NO*H*, 1H), 7.49 (d, J = 8.0 Hz, 2H), 7.17 (d, J = 7.6 Hz, 2H), 5.14−5.16 (m, 1H), 3.52 (d, J = 6.4 Hz, 2H), 2.35 (s, 3H), 1.72 (s, 3H), 1.67 (d, J = 0.8, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 158.1, 139.1, 134.1, 133.0, 129.2, 126.3, 118.2, 25.9, 25.6, 21.2, 18.0; ESI-HRMS: m/z Calcd for $C_{13}H_{17}NO + H^+$: 204.1383, found 204.1385.

*(E)-1-(3,4-Dimethylphenyl)-4-methylpent-3-en-1-one oxime (**1e**).* Pale yellow oil; (922 mg, 85% yield); R_f = 0.22 (hexanes/ethyl acetate 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.25 (brs, NO*H*, 1H), 7.38 (s, 1H), 7.32 (d, J = 7.6 Hz, 1H), 7.12 (d, J = 7.6 Hz, 1H), 5.16 (t, J = 6.8 Hz, 1H), 3.51 (d, J = 6.8 Hz, 2H), 2.27 (s, 3H), 2.26 (s, 3H), 1.73 (s, 3H), 1.68 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 158.4, 137.8, 136.6, 133.9, 133.4, 129.7, 127.6, 123.9, 118.3, 25.9, 25.6, 19.8, 19.6, 18.0; ESI-HRMS: m/z Calcd for $C_{14}H_{19}NO + H^+$: 218.1539, found 218.1537.

*(E)-1-(3,5-Dimethoxyphenyl)-4-methylpent-3-en-1-one oxime (**1f**).* Colorless oil; (1021 mg, 82% yield); R_f = 0.13 (hexanes/ethyl acetate 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.62 (brs, NO*H*, 1H), 6.77 (d, J = 2.0 Hz, 2H), 6.48 (t, J = 2.0 Hz, 1H), 5.14−5.18 (m, 1H), 3.79 (s, 6H), 3.49 (d, J = 7.2 Hz, 2H), 1.72 (s, 3H), 1.68 (d, J = 0.8 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 160.6, 158.1, 137.8, 134.0, 118.1, 104.6, 101.4, 55.3, 26.1, 25.6, 17.9; ESI-HRMS: m/z Calcd for $C_{14}H_{19}NO_3 + H^+$: 250.1438, found 250.1439.

*(Z)-2,2,5-Trimethyl-1-phenylhex-4-en-1-one oxime (**1g**).* White solid; (4389 mg, 95% yield); mp 134−135 °C; R_f = 0.22 (hexanes/ethyl acetate 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.90 (s, NO*H*, 1H), 7.34−7.43 (m, 3H), 7.11−7.12 (m, 2H), 5.18 (t, J = 6.0 Hz, 1H), 2.10 (d, J = 6.4 Hz, 2H), 1.72 (s, 3H), 1.53 (s, 3H), 1.10 (s, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 165.7, 133.7, 133.6, 128.0, 127.9, 127.6, 120.2, 40.9, 38.2, 26.0, 25.8, 18.0; ESI-HRMS: m/z Calcd for $C_{15}H_{21}NO + H^+$: 232.1696, found 232.1697.

*(Z)-1-(4-Methoxyphenyl)-2,2,5-trimethylhex-4-en-1-one oxime (**1h**).* White solid; (1109 mg, 85% yield); mp 148−149 °C; R_f = 0.17 (hexanes/ethyl acetate 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.84 (s, NO*H*, 1H), 7.05 (d, J = 8.4 Hz, 2H), 6.95 (d, J = 8.8 Hz, 2H), 5.17 (t, J = 6.8 Hz, 1H), 3.82(s, 3H), 2.08 (d, J = 6.8 Hz, 2H), 1.72 (s, 3H), 1.54 (s, 3H), 1.10 (s, 6H), 1.33−1.41 (m, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 165.5, 159.1, 133.6, 128.9, 125.5, 120.2, 113.5, 55.1, 41.0, 38.3, 26.0, 25.8, 18.1; ESI-HRMS: m/z Calcd for $C_{16}H_{23}NO_2 + H^+$: 262.1802, found 262.1803.

*(Z)-2,2,5-Trimethyl-1-(4-(trifluoromethyl)phenyl)hex-4-en-1-one oxime (**1i**).* White solid; (1345 mg, 90% yield); mp 148−149 °C; R_f = 0.12 (hexanes/ethyl acetate 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.68 (s, NO*H*, 1H), 7.67 (d, J = 8.0 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 5.17 (t, J = 6.8 Hz, 1H), 2.09 (d, J = 7.2 Hz, 2H), 1.73 (s, 3H), 1.54 (s, 3H), 1.12 (s, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 164.8, 137.5, 134.2, 130.1 (q, $^2J_{C,F}$ = 32.2 Hz), 128.2, 125.0 (q, $^3J_{C,F}$ = 4.0 Hz), 124.0 (q, $^1J_{C,F}$ = 271.6 Hz), 119.8, 40.9, 38.3, 26.0, 25.8, 18.1; ESI-HRMS: m/z Calcd for $C_{16}H_{20}F_3NO + H^+$: 300.1570, found 300.1568.

*(Z)-(1-(3-Methylbut-2-en-1-yl)cyclopentyl) (phenyl)methanone oxime (**1j**).* White solid; (1144 mg, 89% yield); mp 117−119 °C; R_f = 0.24 (hexanes/ethyl acetate 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ

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8.40 (s, NO*H*, 1H), 7.33−7.42 (m, 3H), 7.13−7.15 (m, 2H), 5.20 (t, *J* = 6.4 Hz, 1H), 2.13 (d, *J* = 6.4 Hz, 2H), 1.92−1.98 (m, 2H), 1.73 (s, 3H), 1.63−1.70 (m, 4H), 1.54 (s, 3H), 1.44−1.51 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 164.0, 134.1, 133.3, 128.0, 127.9, 127.4, 120.8, 52.8, 35.1, 25.9, 23.3, 18.1; ESI-HRMS: *m*/*z* Calcd for $C_{17}H_{23}NO$ + H^+: 258.1852, found 258.1853.

*(Z)-(1-(3-Methylbut-2-en-1-yl)cyclohexyl) (phenyl)methanone oxime (**1k**).* White solid; (1219 mg, 90% yield); mp 152−153 °C; R_f = 0.25 (hexanes/ethyl acetate 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (brs, NO*H*, 1H), 7.33−7.42 (m, 3H), 7.11−7.14 (m, 2H), 5.20−5.24 (m, 1H), 2.14 (d, *J* = 6.4 Hz, 2H), 1.74−1.78 (m, 5H), 1.59 (s, 3H), 1.53−1.57 (m, 2H), 1.45−1.48 (m, 3H), 1.33−1.41 (m, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 164.0, 133.5, 133.4, 127.9, 127.8, 127.6, 119.8, 44.0, 35.6, 33.8, 26.1, 26.0, 22.3, 18.2; ESI-HRMS: *m*/*z* Calcd for $C_{18}H_{25}NO$ + H^+: 272.2009, found 272.2011.

*(E)-2,5-Dimethyl-1,2-diphenylhex-4-en-1-one oxime (**1l**).* White solid; (879 mg, 60% yield); mp 135−136 °C; R_f = 0.22 (hexanes/ethyl acetate 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41 (s, NO*H*, 1H), 7.30−7.38 (m, 4H), 7.16−7.27 (m, 4H), 6.64−6.66 (m, 2H), 5.01 (t, *J* = 6.8 Hz, 1H), 2.60−2.71 (m, 2H), 1.65 (s, 3H), 1.51 (s, 3H), 1.40 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 164.1, 143.8, 133.9, 133.2, 128.2, 128.0, 127.9, 127.6, 127.2, 126.6, 120.1, 48.3, 37.2, 26.0, 23.2, 18.1; ESI-HRMS: *m*/*z* Calcd for $C_{20}H_{23}NO$ + H^+: 294.1852, found 294.1850.

*(E)-5-Methyl-1-phenylhex-4-en-1-one oxime (**1m**).* Pale yellow oil; (964 mg, 95% yield); R_f = 0.23 (hexanes/ethyl acetate 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.54 (brs, NO*H*, 1H), 7.59−7.62 (m, 2H), 7.37−7.40 (m, 3H), 5.18 (t, *J* = 7.2 Hz, 1H), 2.83 (t, *J* = 7.6 Hz, 2H), 2.24−2.30 (m, 2H), 1.66 (s, 3H), 1.57 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 159.5, 135.8, 132.7, 129.1, 128.5, 126.3, 123.2, 26.6, 25.6, 24.8, 17.6; ESI-HRMS: *m*/*z* Calcd for $C_{13}H_{17}NO$ + H^+: 204.1383, found 204.1381.

*(Z)-2,2,5-Trimethyl-1-(thiophen-2-yl)hex-4-en-1-one oxime (**1n**).* White solid; (995 mg, 84% yield); mp 101−103 °C; R_f = 0.18 (hexanes/ethyl acetate 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.11 (s, NO*H*, 1H), 7.44−7.45 (m, 1H), 7.07−7.11 (m, 3H), 5.10−5.14 (m, 1H), 2.21 (d, *J* = 7.2 Hz, 2H), 1.71 (d, *J* = 0.8 Hz, 3H), 1.54 (s, 3H), 1.20 (s, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 159.1, 133.9, 130.7, 127.8, 126.8, 126.3, 120.0, 41.5, 38.6, 26.1, 26.0, 18.0; ESI-HRMS: *m*/*z* Calcd for $C_{13}H_{19}NOS$ + H^+: 238.1260, found 238.1262.

*(E)-1-Cyclohexyl-2,2,5-trimethylhex-4-en-1-one oxime (**1o**).* White solid; (474 mg, 40% yield); mp 115−117 °C; R_f = 0.24 (hexanes/ethyl acetate 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.32 (s, NO*H*, 1H), 5.09 (t, *J* = 7.2 Hz, 1H), 2.29−2.38 (m, 2H), 2.20−2.26 (m, 1H), 2.14−2.15 (m, 2H), 1.74−1.77 (m, 2H), 1.71 (s, 3H), 1.64−1.66 (m, 1H), 1.60 (s, 3H), 1.49−1.52 (m, 2H), 1.14−1.33 (m, 3H), 1.07 (s, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 167.1, 133.2, 120.6, 41.8, 40.8, 37.8, 27.2, 27.0, 26.0, 24.9, 18.0; ESI-HRMS: *m*/*z* Calcd for $C_{15}H_{27}NO$ + H^+: 238.2165, found 238.2167.

*(E)-4,4,7-Trimethyl-1-phenyloct-6-en-3-one oxime (**1p**).* White solid; (1062 mg, 82% yield); mp 56−58 °C; R_f = 0.23 (hexanes/ethyl acetate 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.43 (brs, NO*H*, 1H), 7.26−7.32 (m, 4H), 7.18−7.22 (m, 1H), 5.08 (t, *J* = 7.2 Hz, 1H), 2.90−2.94 (m, 2H), 2.56−2.61 (m, 2H), 2.18 (d, *J* = 7.2 Hz, 2H), 1.71 (s, 3H), 1.60 (s, 3H), 1.14 (s, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 165.5, 142.4, 133.6, 128.4, 128.2, 125.9, 120.1, 41.2, 38.3, 32.0, 28.5, 25.9, 25.1, 18.0; ESI-HRMS: *m*/*z* Calcd for $C_{17}H_{25}NO$ + H^+: 260.2009, found 260.2007.

*(1Z,4E)-2,2-Dimethyl-1,5-diphenylhex-4-en-1-one oxime (**1q**).* White solid; (1172 mg, 80% yield); mp 99−101 °C; R_f = 0.23 (hexanes/ethyl acetate 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (s, NO*H*, 1H), 7.37−7.43 (m, 5H), 7.30−7.35 (m, 2H), 7.22−7.25 (m, 1H), 7.12−7.13 (m, 2H), 5.86 (t, *J* = 6.8 Hz, 1H), 2.35 (d, *J* = 7.2 Hz, 2H), 1.98 (s, 3H), 1.21 (s, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 165.8, 144.0, 136.8, 133.4, 128.2, 128.1, 128.0, 127.7, 126.7, 125.8, 124.3, 41.1, 39, 26.0, 16.3; ESI-HRMS: *m*/*z* Calcd for $C_{20}H_{23}NO$ + H^+: 294.1852, found 294.1855.

*(1Z, 4Z/E)-5-(4-Chlorophenyl)-2,2-dimethyl-1-phenylhex-4-en-1-one oxime (**1r**; Z/E Mixture 1/3).* White solid; (1390 mg, 85% yield); R^1_f = 0.22, R^2_f = 0.20 (hexanes/ethyl acetate 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.22 (s, NO*H*, 1H), 9.20 (s, NO*H*, 1H) 7.01−7.43 (m, 18H), 5.80 (t, *J* = 6.4 Hz, 1H), 5.56 (t, *J* = 6.0 Hz, 1H), 2.31 (d, *J* = 7.2 Hz, 2H), 2.09 (d, *J* = 6.8 Hz, 2H), 2.01 (s, 3H), 1.92 (s, 3H), 1.18 (s, 6H), 1.04 (s, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 165.2, 165.0, 142.3, 140.3, 137.3, 135.8, 133.4, 133.3, 132.3, 132.2, 129.3, 128.2, 128.0, 128.0, 127.94, 127.92, 127.6, 127.5, 127.0, 124.6, 123.7, 41.0, 40.6, 38.93, 38.87, 26.0, 25.95, 25.7, 16.2; ESI-HRMS: *m*/*z* Calcd for $C_{20}H_{22}ClNO$ + H^+: 328.1463, found 328.1464.

*(1Z,4E)-2,2,5,6,6-Pentamethyl-1-phenylhept-4-en-1-one oxime (**1s**).* White solid; (1160 mg, 85% yield); mp 114−115 °C; R_f = 0.21 (hexanes/ethyl acetate 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.06 (s, NO*H*, 1H), 7.33−7.42 (m, 3H), 7.10−7.12 (m, 2H), 5.27 (m, 1H), 2.09 (d, *J* = 6.8 Hz, 2H), 1.52 (s, 3H), 1.11 (s, 6H), 1.04 (s, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 165.5, 145.2, 133.7, 127.9, 127.8, 127.6, 116.7, 41.0, 38.2, 36.4, 29.1, 25.8, 13.1; ESI-HRMS: *m*/*z* Calcd for $C_{18}H_{27}NO$ + H^+: 274.2165, found 274.2166.

*(1Z,4Z/E)-2,2,5,6-Tetramethyl-1-phenylhept-4-en-1-one oxime (**1t**; Z/E Mixture 1/5).* White solid; (1114 mg, 86% yield); R^1_f = 0.23, R^2_f = 0.21 (hexanes/ethyl acetate 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 (brs, NO*H*, 1H), 8.12 (brs, NO*H*, 1H) 7.34−7.43 (m, 6H), 7.10−7.12 (m, 4H), 5.23 (t, *J* = 7.2 Hz, 1H), 5.11 (t, *J* = 6.8 Hz, 1H), 2.71 (sep, *J* = 6.8 Hz, 1H), 2.28 (sep, *J* = 6.8 Hz, 1H), 2.14 (d, *J* = 7.2 Hz, 2H), 2.11 (d, *J* = 6.8 Hz, 2H), 1.64 (s, 3H), 1.50 (s, 3H), 1.12 (s, 12H), 1.01 (s, 3H), 0.99 (s, 3H), 0.94 (s, 3H), 0.92 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 166.0, 165.9, 143.2, 142.6, 133.6, 133.5, 128.0, 127.92, 127.89, 127.6, 119.3, 117.7, 40.9, 40.5, 37.9, 37.2, 37.1, 28.6, 25.9, 25.8, 21.5, 20.5, 18.2, 13.6; ESI-HRMS: *m*/*z* Calcd for $C_{17}H_{25}NO$ + H^+: 260.2009, found 260.2011.

*(1Z,4Z/E)-2,2,5-Trimethyl-1,7-diphenylhept-4-en-1-one oxime (**1u**; Z/E Mixture 1/3).* White solid; (1284 mg, 80% yield); R^1_f = 0.24, R^2_f = 0.22 (hexanes/ethyl acetate 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.74 (brs, NO*H*, 2H), 7.34−7.40 (m, 6H), 7.22−7.28 (m, 4H), 7.12−7.18 (m, 7H), 7.05−7.10 (m, 3H), 5.18−5.23 (m, 2H), 2.72 (t, *J* = 8.0 Hz, 2H), 2.61 (t, *J* = 8.0 Hz, 2H), 2.32 (t, *J* = 8.4 Hz, 2H), 2.23 (t, *J* = 8.8 Hz, 2H), 2.09 (d, *J* = 6.8 Hz, 2H), 2.01 (d, *J* = 6.8 Hz, 2H), 1.76 (s, 3H), 1.57 (s, 3H), 1.07 (s, 6H), 1.05 (s, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 165.73, 165.66, 142.2, 136.7, 133.53, 133.50, 128.4, 128.3, 128.2, 128.0, 127.90, 127.87, 127.6, 125.7, 125.6, 121.3, 120.8, 41.6, 40.8, 40.5, 38.0, 37.7, 34.6, 34.2, 34.0, 25.8, 25.7, 23.6, 16.5; ESI-HRMS: *m*/*z* Calcd for $C_{22}H_{27}NO$ + H^+: 322.2165, found 322.2168.

*(1Z,4Z/E)-2,2-Dimethyl-1,5-diphenylhept-4-en-1-one oxime (**1v**; Z/E Mixture 1/4).* White solid; (1274 mg, 83% yield); R^1_f = 0.23, R^2_f = 0.21 (hexanes/ethyl acetate 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (brs, NO*H*, 1H), 7.68 (brs, NO*H*, 1H) 7.02−7.44 (m, 20H), 5.70 (t, *J* = 7.2 Hz, 1H), 5.53 (t, *J* = 7.2 Hz, 1H), 2.46 (q, *J* = 7.2 Hz, 2H), 2.37 (q, *J* = 7.2 Hz, 2H), 2.35 (d, *J* = 7.2 Hz, 2H), 2.08 (d, *J* = 6.8 Hz, 2H), 1.20 (s, 6H), 1.05 (s, 6H), 0.97 (t, *J* = 7.6 Hz, 3H), 0.93 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 165.8, 144.9, 143.5, 143.1, 133.4, 128.4, 128.2, 128.1, 128.0, 127.98, 127.95, 127.9, 127.7, 127.58, 126.63, 126.4, 126.3, 123.9, 121.5, 40.8, 40.6, 38.7, 38.4, 32.5, 26.1, 26.0, 23.2, 13.2, 13.1; ESI-HRMS: *m*/*z* Calcd for $C_{21}H_{25}NO$ + H^+: 308.2009, found 308.2007.

*(Z)-4-Cyclohexylidene-2,2-dimethyl-1-phenylbutan-1-one oxime (**1w**).* White solid; (1070 mg, 79% yield); mp 148−149 °C; R_f = 0.25 (hexanes/ethyl acetate 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.70 (s, NO*H*, 1H), 7.34−7.43 (m, 3H), 7.12−7.14 (m, 2H), 5.12 (t, *J* = 6.8 Hz, 1H), 2.11−2.13 (m, 4H), 2.03−2.06 (m, 2H), 1.45−1.52 (m, 6H), 1.10 (s, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 165.8, 141.9, 133.6, 128.0, 127.9, 127.7, 116.8, 40.8, 37.4, 37.2, 28.9, 28.6, 27.5, 26.9, 25.8; ESI-HRMS: *m*/*z* Calcd for $C_{18}H_{25}NO$ + H^+: 272.2009, found 272.2012.

*(1Z,4Z)-5-Cyclohexyl-2,2-dimethyl-1,5-diphenylpent-4-en-1-one oxime (**1x**).* White solid; (1462 mg, 81% yield); mp 151−153 °C; R_f = 0.23 (hexanes/ethyl acetate 10:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.83 ((s, NO*H*, 1H), 7.31−7.39 (m, 3H), 7.17−7.27 (m, 3H), 7.04−7.06 (m, 2H), 6.98−7.00 (m, 2H), 5.47 (t, *J* = 6.8 Hz, 1H), 2.14−2.20 (m, 1H), 1.96 (d, *J* = 6.8 Hz, 2H), 1.71−1.77 (m, 4H), 1.62−1.65 (m, 1H), 1.18−1.26 (m, 2H), 1.07−1.16 (m, 3H), 1.02 (s, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 165.3, 149.0, 141.4, 133.5, 128.8, 127.9, 127.8,

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127.7, 127.6, 126.1, 120.5, 46.4, 40.6, 38.6, 32.4, 26.7, 26.2, 26.0; ESI-HRMS: m/z Calcd for $C_{25}H_{31}NO + H^+$: 362.2478, found 362.2479.

General Experimental Procedure. A 30 mL oven-dried sealed tube was charged with ketoximes **1** (0.3 mmol), TEMPO (0.75 mmol, 2.5 equiv), and DMF (1 mL). The tube was then sealed, and the mixture was stirred for 12−24 h at 130 °C under argon. Upon completion of the reaction, the mixture was diluted with EtOAc. Organic layer was washed with saturated brine solution five times and dried over anhydrous $MgSO_4$. The solvent was then removed under vacuum. The residue was purified with chromatography column on silica gel using mixtures of ethyl acetate and hexanes to give the corresponding products **2** or **3**. The identity and purity of the product were confirmed by ^1H and ^{13}C NMR spectroscopic analysis.

*3-Phenyl-5-(prop-1-en-2-yl)-4,5-dihydroisoxazole (**2a**).* Pale yellow oil; (51 mg, 91% yield); R_f = 0.32 (hexanes/ethyl acetate 20:1); ^1H NMR (400 MHz, $CDCl_3$): δ 7.65−7.69 (m, 2H), 7.40−7.42 (m, 3H), 5.11−5.18 (m, 2H), 4.94 (s, 1H), 3.47 (dd, J = 16.8 Hz, J = 11.2 Hz, 1H), 3.17 (dd, J = 16.8 Hz, J = 8.4 Hz, 1H), 1.78 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 156.0, 142.6, 129.9, 129.4, 128.6, 126.5, 113.3, 84.3, 39.1, 16.8; ESI-HRMS: m/z Calcd for $C_{12}H_{13}NO + H^+$: 188.1070, found 188.1069.

*3-(4-Chlorophenyl)-5-(prop-1-en-2-yl)-4,5-dihydroisoxazole (**2b**).* Pale yellow solid; (58 mg, 88% yield); mp 88−90 °C; R_f = 0.30 (hexanes/ethyl acetate 20:1); ^1H NMR (400 MHz, $CDCl_3$): δ 7.60 (d, J = 8.4 Hz, 2H), 7.37 (d, J = 8.4 Hz, 2H), 5.11−5.19 (m, 2H), 4.95 (s, 1H), 3.43 (dd, J = 16.8 Hz, J = 11.2 Hz, 1H), 3.13 (dd, J = 16.4 Hz, J = 8.8 Hz, 1H), 1.77 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 155.2, 142.4, 135.9, 128.9, 128.0, 127.8, 113.5, 84.6, 39.0, 16.9; ESI-HRMS: m/z Calcd for $C_{12}H_{12}ClNO + H^+$: 222.0680, found 222.0682.

*3-(4-Methoxyphenyl)-5-(prop-1-en-2-yl)-4,5-dihydroisoxazole (**2c**).* White solid; (60 mg, 92% yield); mp 55−57 °C; R_f = 0.14 (hexanes/ethyl acetate 20:1); ^1H NMR (400 MHz, $CDCl_3$): δ 7.61 (d, J = 8.8 Hz, 2H), 6.92 (d, J = 8.8 Hz, 2H), 5.10−5.14 (m, 2H), 4.93 (s, 1H), 3.83 (s, 3H), 3.43 (dd, J = 16.8 Hz, J = 11.2 Hz, 1H), 3.13 (dd, J = 16.4 Hz, J = 8.4 Hz, 1H), 1.77 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 161.0, 155.6, 142.8, 128.1, 122.1, 114.1, 113.2, 84.1, 55.3, 39.4, 16.9; ESI-HRMS: m/z Calcd for $C_{13}H_{15}NO_2 + H^+$: 218.1176, found 218.1175.

*5-(Prop-1-en-2-yl)-3-(p-tolyl)-4,5-dihydroisoxazole (**2d**).* White solid; (52 mg, 87% yield); mp 58−60 °C; R_f = 0.32 (hexanes/ethyl acetate 20:1); ^1H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, J = 8.4 Hz, 2H), 7.20 (d, J = 8.0 Hz, 2H), 5.10−5.16 (m, 2H), 4.93 (s, 1H), 3.44 (dd, J = 16.4 Hz, J = 10.8 Hz, 1H), 3.14 (dd, J = 16.8 Hz, J = 8.4 Hz, 1H), 2.34 (s, 3H), 1.77 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 156.0, 142.8, 140.2, 129.3, 126.7, 126.5, 113.2, 84.2, 39.3, 21.4, 16.9; ESI-HRMS: m/z Calcd for $C_{13}H_{15}NO + H^+$: 202.1226, found 202.1227.

*3-(3,4-Dimethylphenyl)-5-(prop-1-en-2-yl)-4,5-dihydroisoxazole (**2e**).* Pale yellow oil; (55 mg, 86% yield); R_f = 0.29 (hexanes/ethyl acetate 20:1); ^1H NMR (400 MHz, $CDCl_3$): δ 7.48 (s, 1H), 7.36−7.38 (m, 1H), 7.15 (d, J = 7.6 Hz, 1H), 5.10−5.15 (m, 2H), 4.93 (s, 1H), 3.44 (dd, J = 16.4 Hz, J = 10.8 Hz, 1H), 3.14 (dd, J = 16.8 Hz, J = 8.4 Hz, 1H), 2.28 (s, 6H), 1.77 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 156.1, 142.8, 138.9, 137.0, 129.9, 127.7, 127.0, 124.2, 113.2, 84.1, 39.4, 19.70, 19.66, 16.9; ESI-HRMS: m/z Calcd for $C_{14}H_{17}NO + H^+$: 216.1383, found 216.1384.

*3-(3,5-Dimethoxyphenyl)-5-(prop-1-en-2-yl)-4,5-dihydroisoxazole (**2f**).* Pale yellow oil; (66 mg, 89% yield); R_f = 0.30 (hexanes/ethyl acetate 10:1); ^1H NMR (400 MHz, $CDCl_3$): δ 6.82 (d, J = 2.4 Hz, 2H), 6.50 (s, 1H), 5.10−5.17 (m, 2H), 4.94 (s, 1H), 3.81 (s, 6H), 3.42 (dd, J = 16.8 Hz, J = 11.2 Hz, 1H), 3.12 (dd, J = 16.8 Hz, J = 8.4 Hz, 1H), 1.77 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 160.8, 156.1, 142.6, 131.2, 113.3, 104.6, 102.2, 84.5, 55.4, 39.1, 16.8; ESI-HRMS: m/z Calcd for $C_{14}H_{17}NO_3 + H^+$: 248.1281, found 248.1283.

*4,4-Dimethyl-5-phenyl-2-(prop-1-en-2-yl)-3,4-dihydro-2H-pyrrole 1-Oxide (**3g**).* Colorless solid; (66 mg, 96% yield; 1090 mg, 95%); mp 109−111 °C; R_f = 0.19 (hexanes/ethyl acetate 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ 7.93−7.96 (m, 2H), 7.36−7.46 (m, 3H), 5.15 (s, 1H), 5.14 (s, 1H), 4.79 (t, J = 8.8 Hz, 1H), 2.18 (dd, J = 13.2 Hz, J = 8.4 Hz, 1H), 1.98 (dd, J = 13.2 Hz, J = 9.2 Hz, 1H), 1.83 (s, 3H), 1.44 (s, 3H), 1.38 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 148.5, 140.7, 129.4, 128.9, 128.2, 128.1, 117.0, 43.3, 40.5, 27.9, 27.3, 16.47; ESI-HRMS: m/z Calcd for $C_{15}H_{19}NO + H^+$: 230.1539, found 230.1541.

*5-(4-Methoxyphenyl)-4,4-dimethyl-2-(prop-1-en-2-yl)-3,4-dihydro-2H-pyrrole-1-oxide (**3h**).* Colorless solid; (75 mg, 97% yield); mp 128−130 °C; R_f = 0.15 (hexanes/ethyl acetate 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, J = 8.8 Hz, 2H), 6.95 (d, J = 8.0 Hz, 2H), 5.13 (s, 2H), 4.75 (t, J = 8.8 Hz, 1H), 3.83 (d, J = 0.8 Hz, 3H), 2.15 (dd, J = 12.8 Hz, J = 8.4 Hz, 1H), 1.94 (dd, J = 12.4 Hz, J = 9.2 Hz, 1H), 1.82 (s, 3H), 1.45 (s, 3H), 1.41 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 160.1, 147.8, 140.9, 129.7, 121.3, 116.8, 113.5, 76.4, 55.1, 43.2, 40.7, 28.1, 27.4, 16.5; ESI-HRMS: m/z Calcd for $C_{16}H_{21}NO_2 + H^+$: 260.1645, found 260.1646.

*4,4-Dimethyl-2-(prop-1-en-2-yl)-5-(4-(trifluoromethyl)phenyl)-3,4-dihydro-2H-pyrrole 1-Oxide (**3i**).* Colorless solid; (75 mg, 84% yield); mp 134−136 °C; R_f = 0.42 (hexanes/ethyl acetate 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ 8.11 (d, J = 8.0 Hz, 2H), 7.69 (d, J = 8.4 Hz, 2H), 5.16 (s, 2H), 4.81 (t, J = 8.8 Hz, 1H), 2.22 (dd, J = 13.2 Hz, J = 8.4 Hz, 1H), 2.02 (dd, J = 12.8 Hz, J = 9.2 Hz, 1H), 1.83 (s, 3H), 1.46 (s, 3H), 1.40 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 146.8, 140.3, 132.5, 130.9 (q, $^2J_{C,F}$ = 32.2 Hz), 128.4, 125.2 (q, $^3J_{C,F}$ = 4.0 Hz), 123.7 (q, $^1J_{C,F}$ = 272.6 Hz), 117.4, 77.1, 43.2, 40.6, 27.8, 27.2, 16.4; ESI-HRMS: m/z Calcd for $C_{16}H_{18}F_3NO + H^+$: 298.1413, found 298.1415.

*1-Phenyl-3-(prop-1-en-2-yl)-2-azaspiro[4.4]non-1-ene 2-Oxide (**3j**).* White solid; (75 mg, 98% yield); mp 98−100 °C; R_f = 0.19 (hexanes/ethyl acetate 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ 7.89−7.91 (m, 2H), 7.36−7.45 (m, 3H), 5.13 (s, 2H), 4.75 (t, J = 8.4 Hz, 1H), 2.26 (dd, J = 12.4 Hz, J = 8.0 Hz, 1H), 2.09−2.16 (m, 1H), 1.89−2.03 (m, 1H), 1.92 (dd, J = 12.8 Hz, J = 8.4 Hz, 1H), 1.84 (s, 3H), 1.70−1.80 (m, 5H), 1.63−1.67 (m, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 147.3, 140.8, 129.3, 128.8, 128.2, 128.1, 116.7, 77.3, 53.7, 40.7, 37.7, 37.2, 24.6, 24.3, 16.7; ESI-HRMS: m/z Calcd for $C_{17}H_{21}NO + H^+$: 256.1696, found 256.1697.

*1-Phenyl-3-(prop-1-en-2-yl)-2-azaspiro[4.5]dec-1-ene 2-Oxide (**3k**).* Pale yellow solid; (75 mg, 93% yield); mp 131−133 °C; R_f = 0.19 (hexanes/ethyl acetate 1:2); ^1H NMR (400 MHz, $CDCl_3$): δ 7.63−7.65 (m, 2H), 7.37−7.46 (m, 3H), 5.14 (s, 1H), 5.12 (s, 1H), 4.77 (t, J = 8.4 Hz, 1H), 2.44 (dd, J = 13.2 Hz, J = 8.8 Hz, 1H), 1.87 (dd, J = 13.2 Hz, J = 8.4 Hz, 1H), 1.84 (s, 3H), 1.58−1.74 (m, 7H), 1.43−1.54 (m, 1H), 1.31−1.43 (m, 1H), 1.06−1.16 (m, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 149.7, 141.0, 129.4, 129.2, 128.7, 128.3, 116.7, 76.7, 47.8, 35.6, 34.5, 33.4, 25.0, 22.3, 21.8, 16.5; ESI-HRMS: m/z Calcd for $C_{18}H_{23}NO + H^+$: 270.1852, found 270.1854.

*4-Methyl-4,5-diphenyl-2-(prop-1-en-2-yl)-3,4-dihydro-2H-pyrrole 1-Oxide (**3l**).* Pale yellow solid; (86 mg, 98% yield); R_f = 0.52 (hexanes/ethyl acetate 1:1); dr =1.6:1 (a nonseparable mixture of two diastereomers); ^1H NMR (400 MHz, $CDCl_3$): δ 8.13−8.15 (m, 2H, dia.2), 7.89−7.92 (m, 2H, dia.1), 7.20−7.40 (m, 16H), 5.13−5.20 (m, 4H), 4.90−4.94 (m, 1H, dia.2), 4.84 (t, J = 8.8 Hz, 1H, dia.1), 2.38 (dd, J = 13.2 Hz, J = 8.4 Hz, 2H), 2.17−2.28 (m, 2H), 1.90 (s, 3H, dia.2), 1.88 (s, 6H), 1.77 (s, 3H, dia.1); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 146.6, 146.5, 146.4, 146.1, 140.6, 140.4, 129.60, 129.55, 129.1, 128.9, 128.5, 128.4, 128.3, 128.05, 127.99, 127.9, 127.1, 126.8, 126.0, 125.3, 118.2, 117.9, 77.8, 50.7, 50.1, 43.9, 42.7, 26.1, 23.6, 16.4; ESI-HRMS: m/z Calcd for $C_{20}H_{21}NO + H^+$: 292.1696, found 292.1697.

*5-Phenyl-2-(prop-1-en-2-yl)-3,4-dihydro-2H-pyrrole 1-Oxide (**3m**).* Pale yellow solid; (24 mg, 40% yield); mp 99−101 °C; R_f = 0.31 (hexanes/ethyl acetate 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ 8.38−8.40 (m, 2H), 7.40−7.48 (m, 3H), 5.10 (s, 2H), 4.76−4.80 (m, 1H), 3.15 (dd, J = 8.0 Hz, J = 6.8 Hz, 2H), 2.36−2.46 (m, 1H), 2.03−2.11 (m, 1H), 1.77 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 141.2, 140.1, 130.2, 129.3, 128.4, 127.3, 116.4, 81.0, 29.3, 22.2, 16.8; ESI-HRMS: m/z Calcd for $C_{13}H_{15}NO + H^+$: 202.1226, found 202.1227.

*4,4-Dimethyl-2-(prop-1-en-2-yl)-5-(thiophen-2-yl)-3,4-dihydro-2H-pyrrole 1-Oxide (**3n**).* Colorless solid; (54 mg, 76% yield); mp 110−112 °C; R_f = 0.35 (hexanes/ethyl acetate 1:1); ^1H NMR (400 MHz, $CDCl_3$): δ 7.68−7.69 (m, 1H), 7.49−7.50 (m, 1H), 7.18 (s, 1H), 5.14 (s, 1H), 5.12 (s, 1H), 4.77 (t, J = 8.4 Hz, 1H), 2.25 (dd, J =

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12.8 Hz, J = 9.2 Hz, 1H), 2.01 (dd, J = 12.4 Hz, J = 8.8 Hz, 1H), 1.76 (s, 3H), 1.62 (s, 3H), 1.51 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 145.0, 140.5, 129.8, 128.3, 126.6, 126.0, 117.2, 75.4, 42.8, 40.5, 28.5, 27.3, 16.6; ESI-HRMS: m/z Calcd for $C_{13}H_{17}NOS + H^+$: 236.1104, found 236.1102.

*5-Cyclohexyl-4,4-dimethyl-2-(prop-1-en-2-yl)-3,4-dihydro-2H-pyrrole 1-Oxide (**3o**).* Colorless oil; (70 mg, 99% yield); R_f = 0.18 (hexanes/ethyl acetate 1:4); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.06 (s, 1H), 5.04 (s, 1H), 4.58 (t, J = 8.4 Hz, 1H), 2.46−2.52 (m, 1H), 2.12−2.27 (m, 2H), 2.06 (dd, J = 13.2 Hz, J = 8.8 Hz, 1H), 1.74−1.82 (m, 3H), 1.67−1.71 (m, 4H), 1.56−1.60 (m, 2H), 1.26−1.30 (m, 6H), 1.21 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 156.1, 140.9, 116.3, 76.0, 43.3, 38.9, 36.6, 26.9, 26.7, 26.13, 26.10, 26.0, 25.7, 25.4, 16.2; ESI-HRMS: m/z Calcd for $C_{15}H_{25}NO + H^+$: 236.2009, found 236.2010.

*4,4-Dimethyl-5-phenethyl-2-(prop-1-en-2-yl)-3,4-dihydro-2H-pyrrole 1-Oxide (**3p**).* Pale yellow oil; (13 mg, 17% yield); R_f = 0.40 (CH_2Cl_2/CH_3OH 20:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26−7.30 (m, 4H), 7.17−7.21 (m, 1H), 5.10−5.11 (m, 2H), 4.62 (t, J = 8.8 Hz, 1H), 2.95−3.09 (m, 2H), 2.73−2.80 (m, 1H), 2.46−2.54 (m, 1H), 2.07 (dd, J = 13.2 Hz, J = 8.8 Hz, 1H), 1.73−1.79 (m, 4H), 1.08 (s, 3H), 1.06 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 153.4, 141.2, 140.6, 128.5, 128.4, 126.2, 117.0, 76.1, 42.6, 38.8, 30.1, 27.1, 26.6, 26.2, 16.5; ESI-HRMS: m/z Calcd for $C_{17}H_{23}NO + H^+$: 258.1852, found 258.1854.

*(E)-4,4-Dimethyl-2-(prop-1-en-2-yl)-5-styryl-3,4-dihydro-2H-pyrrole 1-Oxide (**4p**).* Pale yellow oil; (68 mg, 89% yield); R_f = 0.43 (hexanes/ethyl acetate 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.34 (d, J = 16.4 Hz, 1H), 7.54 (d, J = 7.6 Hz, 2H), 7.27−7.37 (m, 3H), 6.80 (d, J = 16.4 Hz, 1H), 5.13 (s, 1H), 5.11 (s, 1H), 4.68 (t, J = 8.0 Hz, 1H), 2.13 (dd, J = 12.8 Hz, J = 8.4 Hz, 1H), 1.89 (dd, J = 13.2 Hz, J = 8.8 Hz, 1H), 1.77 (s, 3H), 1.42 (s, 3H), 1.34 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 147.9, 140.8, 136.9, 136.8, 128.8, 128.7, 127.2, 117.0, 113.8, 76.3, 41.8, 39.2, 28.1, 27.5, 16.6; ESI-HRMS: m/z Calcd for $C_{17}H_{21}NO + H^+$: 256.1696, found 256.1697.

*4,4-Dimethyl-5-phenethyl-2-(2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)propan-2-yl)-3,4-dihydro-2H-pyrrole 1-Oxide (**5p**).* Pale yellow oil; (63 mg, 51% yield); R_f = 0.58 (CH_2Cl_2/CH_3OH 20:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25−7.30 (m, 4H), 7.18−7.21 (m, 1H), 4.37 (t, J = 8.4 Hz, 1H), 2.95 (t, J = 8.0 Hz, 2H), 2.66−2.73 (m, 1H), 2.42−2.49 (m, 1H), 2.04−2.10 (m, 2H), 1.83 (s, 3H), 1.45−1.49 (m, 5H), 1.30−1.32 (m, 2H), 1.25 (s, 3H), 1.16 (s, 3H), 1.08−1.09 (m, 8H), 1.07 (s, 3H), 1.06 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 154.7, 141.2, 128.4, 128.3, 126.0, 79.1, 59.3, 59.2, 40.8, 40.7, 40.6, 36.0, 34.4, 34.0, 30.0, 27.2, 26.7, 26.5, 24.1, 21.4, 20.9, 20.4, 16.9; ESI-HRMS: m/z Calcd for $C_{26}H_{42}N_2O_2 + H^+$: 415.3319, found 415.3322.

*4,4-Dimethyl-5-phenyl-2-(1-phenylvinyl)-3,4-dihydro-2H-pyrrole 1-Oxide (**3q**).* Colorless solid; (83 mg, 95% yield); mp 99−101 °C; R_f = 0.29 (hexanes/ethyl acetate 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95−7.97 (m, 2H), 7.28−7.48 (m, 8H), 5.57 (s, 1H), 5.52 (s, 1H), 5.15 (t, J = 8.0 Hz, 1H), 2.25 (dd, J = 12.8 Hz, J = 8.8 Hz, 1H), 1.90 (dd, J = 12.8 Hz, J = 7.2 Hz, 1H), 1.38 (s, 3H), 1.19 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 149.1, 145.5, 138.6, 129.5, 129.0, 128.4, 128.3, 128.2, 127.8, 127.5, 118.3, 76.3, 43.6, 41.1, 28.0, 27.7; ESI-HRMS: m/z Calcd for $C_{20}H_{21}NO + H^+$: 292.1696, found 292.1697.

*2-(1-(4-Chlorophenyl)vinyl)-4,4-dimethyl-5-phenyl-3,4-dihydro-2H-pyrrole 1-Oxide (**3r**).* Pale yellow solid; (91 mg, 93% yield); mp 98−100 °C; R_f = 0.32 (hexanes/ethyl acetate 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93−7.95 (m, 2H), 7.38−7.47 (m, 3H), 7.28−7.35 (m, 4H), 5.55 (s, 1H), 5.54 (s, 1H), 5.12 (t, J = 8.4 Hz, 1H), 2.24 (dd, J = 12.8 Hz, J = 8.8 Hz, 1H), 1.85 (dd, J = 12.8 Hz, J = 7.6 Hz, 1H), 1.38 (s, 3H), 1.19 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 149.2, 144.3, 136.9, 133.6, 129.5, 128.9, 128.7, 128.4, 128.2, 128.0, 119.4, 76.0, 43.5, 40.9, 27.7, 27.6; ESI-HRMS: m/z Calcd for $C_{20}H_{20}ClNO + H^+$: 326.1306, found 326.1307.

*2-(3,3-Dimethylbut-1-en-2-yl)-4,4-dimethyl-5-phenyl-3,4-dihydro-2H-pyrrole 1-Oxide (**3s**).* Pale yellow oil; (45 mg, 55% yield); R_f = 0.41 (hexanes/ethyl acetate 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00−8.02 (m, 2H), 7.36−7.45 (m, 3H), 5.30 (s, 1H), 5.00 (s, 1H), 4.85 (t, J = 8.4 Hz, 1H), 2.38 (dd, J = 12.8 Hz, J = 8.0 Hz, 1H), 1.93 (dd, J = 12.8 Hz, J = 8.8 Hz, 1H), 1.47 (s, 3H), 1.40 (s, 3H), 1.18 (s, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 156.5, 148.8, 129.4, 129.0, 128.2, 128.1, 109.2, 71.3, 46.9, 43.4, 35.8, 28.8, 28.3, 27.6; ESI-HRMS: m/z Calcd for $C_{18}H_{25}NO + H^+$: 272.2009, found 272.2008.

*4,4-Dimethyl-2-(3-methylbut-1-en-2-yl)-5-phenyl-3,4-dihydro-2H-pyrrole 1-Oxide (**3t**).* Pale yellow solid; (31 mg, 40% yield); mp 93−95 °C; R_f = 0.39 (hexanes/ethyl acetate 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95−7.97 (m, 2H), 7.36−7.45 (m, 3H), 5.20 (s, 1H), 5.14 (s, 1H), 4.75 (t, J = 8.4 Hz, 1H), 2.32−2.39 (m, 1H), 2.26 (dd, J = 12.8 Hz, J = 8.4 Hz, 1H), 1.98 (dd, J = 13.2 Hz, J = 8.4 Hz, 1H), 1.41 (s, 3H), 1.40 (s, 3H), 1.18 (d, J = 6.8 Hz, 3H), 1.15 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 152.4, 148.4, 129.4. 129.1, 128.2, 111.8, 75.6, 43.5, 42.6, 31.1, 28.1, 27.6, 23.1, 22.6; ESI-HRMS: m/z Calcd for $C_{17}H_{23}NO + H^+$: 258.1852, found 258.1853.

*4,4-Dimethyl-2-(3-methylbut-2-en-2-yl)-5-phenyl-3,4-dihydro-2H-pyrrole 1-Oxide (**3t′**).* Pale yellow oil; (11 mg, 14% yield); R_f = 0.31 (hexanes/ethyl acetate 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94−7.96 (m, 2H), 7.35−7.44 (m, 3H), 5.28−5.32 (m, 1H), 2.10 (dd, J = 12.8 Hz, J = 7.6 Hz, 1H), 1.82−1.88 (m, 1H), 1.81 (d, J = 1.2 Hz, 3H), 1.77 (s, 3H), 1.68 (s, 3H), 1.47 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 148.3, 131.9, 129.3, 129.2, 128.2, 123.7, 72.1, 43.0, 40.4, 27.9, 27.2, 21.4, 20.2, 11.9; ESI-HRMS: m/z Calcd for $C_{17}H_{23}NO + H^+$: 258.1852, found 258.1853.

*4,4-Dimethyl-5-phenyl-2-(4-phenylbut-1-en-2-yl)-3,4-dihydro-2H-pyrrole-1-oxide (**3u**).* Pale yellow solid; (50 mg, 52% yield); mp 83−85 °C; R_f = 0.32 (hexanes/ethyl acetate 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92−7.94 (m, 2H), 7.37−7.44 (m, 3H), 7.17−7.30 (m, 5H), 5.27 (s, 1H), 5.25 (s, 1H), 4.80 (t, J = 8.8 Hz, 1H), 2.92−3.00 (m, 1H), 2.82−2.89 (m, 1H), 2.45−2.53 (m, 1H), 2.31−2.39 (m, 1H), 2.17 (dd, J = 13.2 Hz, J = 8.4 Hz, 1H), 1.93 (dd, J = 12.8 Hz, J = 8.8 Hz, 1H), 1.41 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 148.5, 144.5, 141.8, 129.5, 128.9, 128.4, 128.3, 128.24, 128.18, 125.9, 115.2, 76.8, 43.4, 41.0, 33.8, 32.0, 27.9, 27.3; ESI-HRMS: m/z Calcd for $C_{22}H_{25}NO + H^+$: 320.2009, found 320.2007.

*4,4-Dimethyl-5-phenyl-2-(4-phenylbut-2-en-2-yl)-3,4-dihydro-2H-pyrrole-1-oxide (**3u′**).* Pale yellow-green oil; (13 mg, 14% yield); R_f = 0.39 (hexanes/ethyl acetate 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93−7.95 (m, 2H), 7.36−7.46 (m, 3H), 7.26−7.31 (m, 2H), 7.17−7.23 (m, 3H), 5.78 (t, J = 7.2 Hz, 1H), 4.77 (t, J = 8.8 Hz, 1H), 3.45−3.56 (m, 2H), 2.16 (dd, J = 12.8 Hz, J = 8.0 Hz, 1H), 2.00 (dd, J = 13.2 Hz, J = 10 Hz, 1H), 1.79 (s, 3H), 1.43 (s, 3H), 1.38 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 148.6, 140.3, 132.0, 131.0, 129.5, 129.1, 128.45, 128.40, 128.28, 128.26, 126.0, 78.4, 43.2, 40.7, 34.2, 28.0, 27.1, 10.8; ESI-HRMS: m/z Calcd for $C_{22}H_{25}NO + H^+$: 320.2009, found 320.2010.

*(E)-4,4-Dimethyl-5-phenyl-2-(1-phenylprop-1-en-1-yl)-3,4-dihydro-2H-pyrrole-1-oxide (**3v**).* Pale yellow solid; (39 mg, 43% yield); mp 97−99 °C; R_f = 0.25 (hexanes/ethyl acetate 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79−7.81 (m, 2H), 7.34−7.44 (m, 5H), 7.25−7.30 (m, 3H), 6.01 (q, J = 6.8 Hz, 1H), 4.91 (t, J = 8.4 Hz, 1H), 2.12 (dd, J = 13.2 Hz, J = 9.2 Hz, 1H), 1.82 (dd, J = 13.2 Hz, J = 8.0 Hz, 1H), 1.64 (d, J = 6.8 Hz, 3H), 1.31 (s, 3H), 0.83 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 148.9, 137.9, 136.1, 130.4, 130.0, 129.3, 129.2, 128.22, 128.18, 127.3, 78.7, 43.1, 39.5, 28.1, 27.4, 14.9; ESI-HRMS: m/z Calcd for $C_{21}H_{23}NO + H^+$: 306.1852, found 306.1854.

*(Z)-4,4-Dimethyl-5-phenyl-2-(1-phenylprop-1-en-1-yl)-3,4-dihydro-2H-pyrrole-1-oxide (**3v′**).* Pale yellow solid; (32 mg, 35% yield); mp 76−78 °C; R_f = 0.30 (hexanes/ethyl acetate 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91−7.93 (m, 2H), 7.37−7.46 (m, 3H), 7.23−7.32 (m, 5H), 6.05 (q, J = 6.8 Hz, 1H), 5.50 (t, J = 8.8 Hz, 1H), 2.10 (dd, J = 12.8 Hz, J = 8.0 Hz, 1H), 1.98 (d, J = 6.8 Hz, 3H), 1.86 (dd, J = 13.2 Hz, J = 9.6 Hz, 1H), 1.44 (s, 3H), 1.00 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 148.7, 140.4, 137.1, 132.1, 129.4, 129.1, 128.6, 128.3, 128.12, 128.06, 127.1, 69.9, 43.2, 39.9, 27.6, 27.4, 13.9; ESI-HRMS: m/z Calcd for $C_{21}H_{23}NO + H^+$: 306.1852, found 306.1853.

*2-(Cyclohex-1-en-1-yl)-4,4-dimethyl-5-phenyl-3,4-dihydro-2H-pyrrole 1-Oxide (**3w**).* Pale yellow solid; (31 mg, 38% yield); mp 123−125 °C; R_f = 0.22 (hexanes/ethyl acetate 1:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93−7.96 (m, 2H), 7.35−7.44 (m, 3H), 5.84 (s, 1H), 4.67 (t, J = 8.4 Hz, 1H), 2.06−2.21 (m, 3H), 1.95−2.02 (m, 3H), 1.68−

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1.75 (m, 3H), 1.51−1.59 (m, 1H), 1.42 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 148.1, 133.7, 129.3, 129.2, 128.7, 128.25, 128.19, 43.1, 40.5, 28.0, 27.4, 25.2, 22.6, 22.3, 22.2; ESI-HRMS: m/z Calcd for $C_{18}H_{23}NO + H^+$: 270.1852, found 270.1855.

Epoxidation of 3g To Synthesize Compound 6. To a solution of **3g** (0.3 mmol) in DCM (2 mL) were slowly added $NaHCO_3$ (0.75 mmol) and *m*-CPBA (0.3 mmol) at 0 °C. The reaction mixture was slowly allowed to warm to rt for 8 h. The reaction mixture was cooled to 0 °C again, and additional *m*-CPBA (0.3 mmol) was added. The reaction mixture was slowly allowed to warm to rt for another 8 h, then quenched by saturated Na_2SO_3 solution. The organic phase was extracted with ethyl acetate. The combined organic layers were washed with saturated $NaHCO_3$ solution followed by brine and dried over $MgSO_4$, After removal of the solvent under reduced pressure, the crude material was purified by silica gel column chromatography (CH_2Cl_2/CH_3OH 20:1) to afford the product **6** (51 mg) in 69% yield.

*4,4-Dimethyl-2-(2-methyloxiran-2-yl)-5-phenyl-3,4-dihydro-2H-pyrrole 1-Oxide (**6**).* Colorless oil; (51 mg, 69% yield); dr =1.7:1 (a nonseparable mixture of two diastereomers); R_f = 0.31 (CH_2Cl_2/CH_3OH 20:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88−7.90 (m, 2H, dia.2), 7.80−7.82 (m, 2H, dia.1), 7.40−7.45 (m, 6H), 4.35 (t, J = 8.0 Hz, 1H, dia.1), 3.96 (t, J = 8.8 Hz, 1H, dia.2), 3.11 (d, J = 4.4 Hz, 1H, dia.1), 3.03 (d, J = 4.4 Hz, 1H, dia.2), 2.92 (d, J = 4.4 Hz, 1H, dia.2), 2.76 (d, J = 4.4 Hz, 1H, dia.1), 2.10−2.24 (m, 3H), 1.95−2.02 (m, 1H, dia.1), 1.54 (s, 3H, dia.1), 1.44 (s, 6H, dia.2), 1.40 (s, 6H, dia.1), 1.38 (s, 3H, dia.2); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 150.5, 150.4, 129.8, 129.7, 129.4, 128.6, 128.4, 128.33, 128.29, 128.2, 75.3, 74.2, 56.4, 56.0, 55.9, 51.9, 43.59, 43.55, 37.6, 37.3, 28.0, 27.9, 27.8, 27.2, 19.7, 15.0; ESI-HRMS: m/z Calcd for $C_{15}H_{19}NO_2 + H^+$: 246.1489, found 246.1491.

Intermolecular [3 + 2] Cycloaddition of 3g with Methyl Propiolate To Synthesize Compound 7. The compound **3g** (0.2 mmol) was mixed with methyl propiolate (1 mmol) in benzene (1 mL) and was heated for 24 h at 80 °C. After removal of solvent, the residue was purified by silica gel chromatography (hexanes/EtOAc 20:1) to give the product 7 (50 mg) in 80% yield as a single diastereoisomer.

Methyl(3aS,6R*)-4,4-dimethyl-3a-phenyl-6-(prop-1-en-2-yl)-3a,4,5,6-tetrahydropyr-rolo[1,2-b]isoxazole-3-carboxylate (**7**).* Pale yellow oil; (50 mg, 80% yield); R_f = 0.41 (hexanes/ethyl acetate 20:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83−7.85 (m, 2H), 7.45 (s, 1H), 7.28−7.31 (m, 2H), 7.19−7.22 (m, 1H), 5.25 (s, 1H), 4.99 (s, 1H), 3.88 (dd, J = 12.4 Hz, J = 5.6 Hz, 1H), 3.77 (s, 3H), 1.92 (s, 3H), 1.75 (t, J = 12.4 Hz, 1H), 1.62 (dd, J = 12.4 Hz, J = 5.6 Hz, 1H), 1.37 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 166.2, 155.9, 145.2, 143.8, 127.7, 127.0, 126.6, 112.1, 111.6, 83.3, 71.2, 51.4, 44.8, 43.7, 27.8, 27.3, 19.2; ESI-HRMS: m/z Calcd for $C_{19}H_{23}NO_3 + H^+$: 314.1751, found 314.1750.

Deoxygenation of 3g To Synthesize Compound 8. $TiCl_4$ (2.16 mmol) was slowly added with stirring to dry THF (5 mL) under argon at 0 °C. To the resulting yellow solution was slowly added $LiAlH_4$ (1.44 mmol). The resulting black mixture was stirred at room temperature for 15 min, and then triethylamine (13.5 mmol) was added. The black mixture was then poured into a solution of **3g** (0.3 mmol) in dry THF (4 mL). The mixture was stirred for 30 min at room temperature, and then water (3.7 mL) was added. The mixture was filtered. The filtrate was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and evaporated under reduced pressure. The resulting pale yellow oil was purified by chromatography (hexanes/EtOAc 20:1) to give a pale yellow oil product **8** (43 mg) in 67% yield.

*4,4-Dimethyl-5-phenyl-2-(prop-1-en-2-yl)-3,4-dihydro-2H-pyrrole (**8**).* Pale yellow oil; (43 mg, 67% yield); R_f = 0.28 (hexanes/ethyl acetate 20:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74−7.76 (m, 2H), 7.35−7.38 (m, 3H), 5.02 (s, 1H), 4.86 (s, 1H), 4.51 (t, J = 8.0 Hz, 1H), 2.13 (dd, J = 12.4 Hz, J = 7.2 Hz, 1H), 1.81 (s, 3H), 1.74 (dd, J = 12.4 Hz, J = 8.8 Hz, 1H), 1.39 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 179.6, 147.0, 134.7, 129.4, 128.0, 127.9, 110.0, 72.3, 50.4, 47.3, 27.0, 25.8, 19.8; ESI−HRMS: m/z Calcd for $C_{15}H_{19}N + H^+$: 214.1590, found 214.1591.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00180.

^{1}H NMR and ^{13}C NMR spectra for all substrates and products (PDF)

Crystallographic data for **3g** (CIF)

Crystallographic data for **3v** (CIF)

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Notes

The authors declare no competing financial interest.

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