Formal γ-C(sp^3)–H Activation of Ketones via Microwave-Promoted and Iminyl-Radical-Mediated 1,5-Hydrogen Atom Transfer

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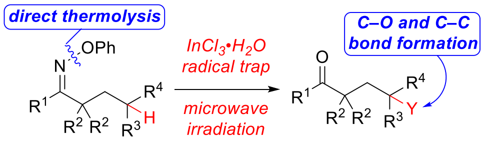


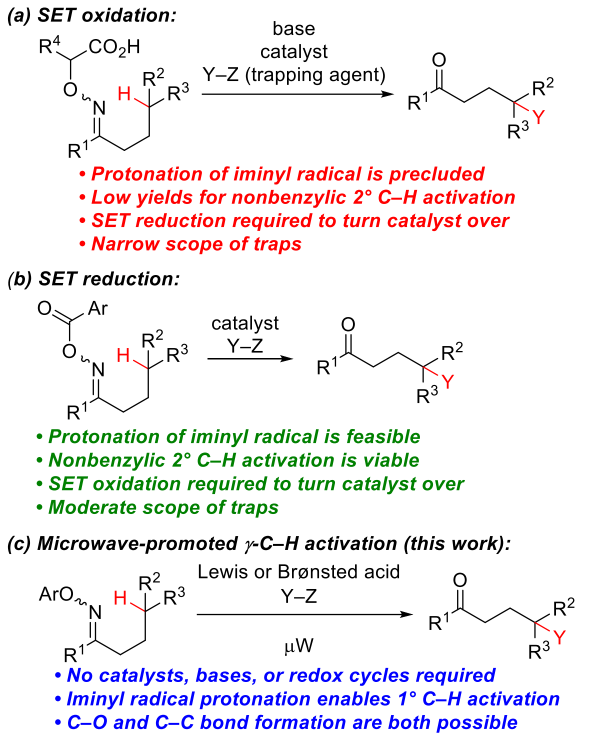
ABSTRACT. Microwave irradiation of *O*-phenyloximes triggers N–O homolysis and 1,5-hydrogen atom transfer (HAT), resulting in formal γ-C–H functionalization of ketones after trapping of the radical intermediate and in situ imine hydrolysis. The Lewis acid $InCl_3 \cdot H_2O$ facilitated HAT, enabling functionalization of benzylic and nonbenzylic 2° carbon atoms. Functionalization of 1° carbons was feasible but afforded low yields, requiring $ClCH_2CO_2H$ instead of $InCl_3 \cdot H_2O$ as an additive. C–O and C–C bond formation could both be accomplished by this method.

The chemistry of the carbonyl group is central to the field of organic synthesis. Nucleophilic additions to carbonyl carbons, reactions of electrophiles at enolate α-carbons, and conjugate additions of nucleophiles to the β-carbon atoms of enones and enoates are among the most ubiquitous and fundamental transformations. However, processes that functionalize the γ-carbon of a carbonyl compound are considerably less common.[1] Mohr's polarity-matched additions of electrophilic radicals to electron-rich dienol ethers constitute a notable advance in this area.[2]

In 2018, Leonori[3] and Studer[4] accomplished the formal γ-functionalization of ketones via iminyl-radical-mediated 1,5-hydrogen atom transfer (HAT). The iminyl radicals were generated from α-imino-oxy acids by deprotonation, single-electron transfer (SET) oxidation of the resulting carboxylate, and decarboxylative fragmentation. After a thermodynamically favored 1,5-HAT, functionalization of the resulting carbon-centered radical and hydrolysis of the NH imine delivered the ketone products (Scheme 1a). While this work is a milestone in ketone γ-C–H functionalization chemistry, the need for base precludes the use of acid to protonate the iminyl radical intermediate. Iminium ions have significantly higher N–H BDE values than neutral imines, rendering HAT processes involving protonated iminyl radicals more favorable than those employing neutral iminyl radicals.[3,5] Thus, the inability to utilize protonated iminyl radicals limits the scope of these base-promoted, SET-oxidation-dependent reactions to the functionalization of 3° and benzylic 2° carbons.[3,4] Additionally, catalyst turnover requires reduction of an intermediate or the final adduct, thereby restricting the types of viable trapping agents.

The development of analogous processes that rely on SET reduction instead of oxidation to produce iminyl radicals[6] has permitted the use of Lewis or Brønsted acids to promote 1,5-HAT. As a result, nonbenzylic 2° carbons can be activated in some cases (Scheme 1b).[6c,6d] However, catalyst turnover requires SET oxidation of the adduct. Thus, only traps that afford readily oxidizable adducts can be employed. Clearly, the generation of iminyl radicals by methods that do not rely on SET would increase the scope of HAT-mediated γ-C–H activation.[7]

Scheme 1. Comparison of HAT Methods Using Iminyl Radicals

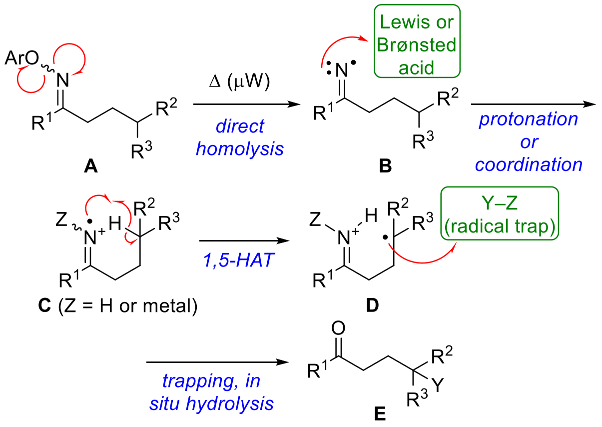


In 2007, Walton reported that the weak N–O bond of *O*-phenyloximes (BDE = ca. 35 kcal/mol)[8] could be cleaved by microwave irradiation, producing iminyl radicals that subsequently undergo 5-*exo*-*trig* and 5-*exo*-*dig* cyclizations.[9] Inspired by this seminal work that does not rely on SET, we began to explore the utility of thermally generated iminyl radicals. Our first contribution to this area involved the synthesis of 2-acylpyrroles via microwave-promoted 5-*exo*-*dig* iminyl radical cyclization followed by TEMPO trapping.[10] We subsequently constructed functionalized nitriles by means of microwave-promoted fragmentations of 4- and 5-membered cyclic iminyl radicals.[11] Recently, we generated a variety of pyrrolines via 5-*exo*-*trig* iminyl radical cyclizations. The latter reactions could be triggered by either microwave irradiation or conventional heating.[12] The lack of SET events and redox cycles has enabled a broad range of radical traps to be employed in both the fragmentations and the cyclizations.

We recognized that application of microwave-promoted iminyl radical chemistry to the γ-C–H functionalization of ketones could potentially expand the scope of radical traps and/or substrates compared to protocols that rely on SET oxidation and reduction. Herein, we report our investigations in this area, which have revealed that the ability to employ an acid in these base- and catalyst-free reactions enables participation of a range of substrates, including those possessing 1° γ-carbon atoms (Scheme 1c).

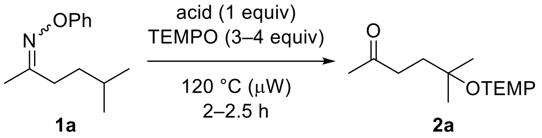
We hypothesized that the proposed γ-C–H functionalization would follow the pathway outlined in Scheme 2. Microwave irradiation of *O*-aryloxime **A** would induce N–O homolysis, furnishing iminyl radical **B**. Subsequent protonation of **B** or coordination to a Lewis acid would afford **C**, which should exhibit an enhanced propensity to engage in 1,5-HAT as described above.[3,5] Intramolecular abstraction of a γ-H atom by the *N*-centered radical would then provide alkyl radical **D**, which upon capture by a radical trapping agent and in situ iminium hydrolysis would be transformed into γ-functionalized ketone **E**.

Scheme 2. Proposed Mechanism



We commenced our efforts by selecting *O*-phenyloxime **1a** as the test substrate and TEMPO as the radical trap (Table 1). We elected to trigger iminyl radical formation via microwave irradiation rather than conventional heating due to the rapid rates inherent to this technique.[9–12] Reactions performed without additives were low-yielding and afforded complex mixtures, so we evaluated the use of Brønsted or Lewis acids. Various carboxylic acids promoted γ-C–H activation (entries 1–5), with chloroacetic acid delivering the best yield of ketone **2a** (entry 3). However, we shifted our focus to $InCl_3 \cdot H_2O$[6h] upon finding that this Lewis acid furnished **2a** in an improved yield (entry 6). A survey of solvents (entries 7–12) revealed the combination of $InCl_3 \cdot H_2O$ and $PhCF_3$–*i*PrOH–H_2O 23:1:1 to be optimal (entry 12). This solvent system caught our attention based on reports that it forms a single phase at elevated temperatures.[13] Finally, we note that formation of TEMPO-containing ketone **2a** in each of the reactions shown in Table 1 provides strong evidence supporting the radical mechanism presented in Scheme 2.

Table 1. Optimization of Reaction Conditions



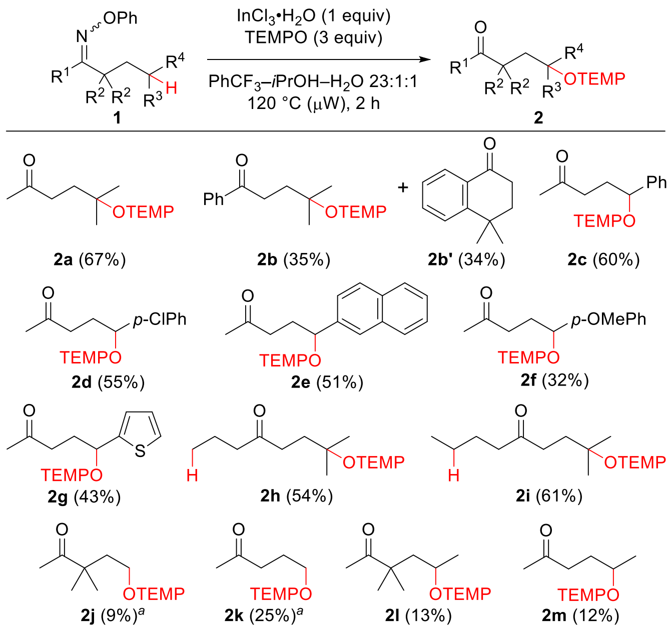
entry	acid	solvent	% yield[a]
1	CH_3CO_2H	CH_3CN	23
2	CH_3CO_2H[b]	CH_3CN	28
3	$ClCH_2CO_2H$[b]	CH_3CN	45
4	Cl_2CHCO_2H[b]	CH_3CN	38
5	Cl_3CCO_2H[b]	CH_3CN	19
6	$InCl_3{\cdot}H_2O$	CH_3CN–THF 2:1	49
7	$InCl_3{\cdot}H_2O$	CH_3OH	30
8	$InCl_3{\cdot}H_2O$	CH_3CN–CH_3OH 25:1	40
9	$InCl_3{\cdot}H_2O$	$PhCF_3$–THF–CH_3CN 4:2:1	38
10	$ClCH_2CO_2H$	$PhCF_3$–CH_3CN 25:1	40
11	$InCl_3{\cdot}H_2O$	$PhCF_3$–*i*PrOH–H_2O 8:1:1	58
12	$InCl_3{\cdot}H_2O$	$PhCF_3$–*i*PrOH–H_2O 23:1:1	67

[a] Isolated yield. [b] 2 equiv of acid was used.

The scope of the ketone γ-C–H functionalization was explored by subjecting several *O*-phenyloximes **1** to the optimal reaction conditions (Scheme 3). The substrates were constructed in one step by pyridine-mediated condensation of ketones with $PhONH_2{\cdot}HCl$.[14] Most *O*-phenyloximes were obtained as inconsequential mixtures of *E*- and *Z*-isomers that converged to a single iminyl radical after N–O homolysis. Benzoyl-containing substrate **1b** furnished a 1:1 mixture of adduct **2b** and tetralone **2b'**, indicating that cyclization of the intermediate radical onto the neighboring aromatic ring[5,15] is competitive with TEMPO trapping. Phenyl-substituted oxime ether **1c** delivered γ-functionalized ketone **2c** in good yield, demonstrating the viability of 2° benzylic radicals as intermediates in this reaction. Other aryl- and heteroaryl-substituted oxime ethers were also useful substrates, furnishing ketones **2d**–**2g** in fair to good yields. Ketone **2d** bearing an electron-poor aryl group was produced in a higher yield than ketone **2f** bearing an electron-rich aryl group. Aliphatic ketones **2h** and **2i** were obtained in good yields despite the presence of two types of γ-hydrogens in substrates **1h** and **1i**. These results indicate that the 1,5-HAT step is selective for generating 3° radicals in preference to 1° (e.g., **2h**) or 2° (e.g., **2i**) radicals.

Substrates possessing nonbenzylic 2° γ-carbons underwent the γ-C–H functionalization, albeit with low yields (e.g., **2l** and **2m**). Initial attempts to functionalize 1° γ-carbons using the standard conditions afforded products derived from TEMPO trapping at the α-carbon, indicating that $InCl_3$-promoted 1,5-HAT to furnish a 1° radical is too slow to compete with intermolecular hydrogen atom abstraction that generates a resonance-stabilized radical. Fortunately, chloroacetic acid was able to mediate the desired 1,5-HAT, delivering adducts **2j** and **2k** via the intermediacy of a 1° radical. This result suggests that chloroacetic acid is a stronger activator than $InCl_3$ for iminyl-radical-mediated 1,5-HAT. However, the low yields of these reactions as well as the modest yields observed with chloroacetic acid in the optimization studies of substrate **1a** (Table 1) hint at the existence of undesired competitive pathways and byproducts in the Brønsted-acid-promoted transformations. Moreover, attempts to purify ketones **2j** and **2k** were thwarted by their decomposition on various stationary phases (i.e., SiO_2 and neutral, basic, or acidic alumina). Further advances are clearly required for microwave-promoted and iminyl-radical-mediated γ-C–H functionalization at 1° and nonbenzylic 2° carbons to become a synthetically useful process. However, comparable protocols that rely on SET chemistry are known to fail with substrates bearing a 1° γ-carbon.[6b,6c,16]

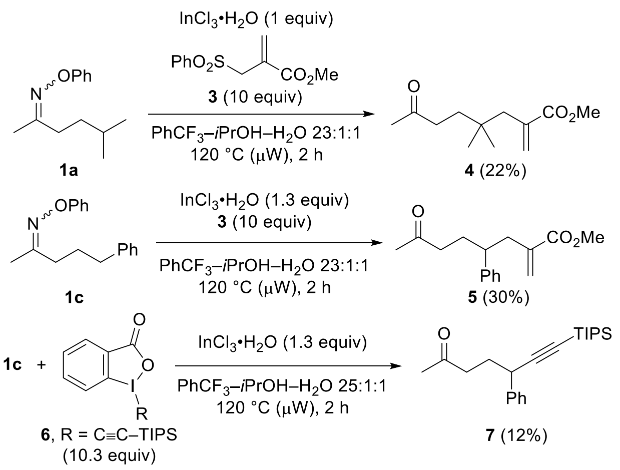
Scheme 3. Scope of *O*-Phenyloxime Substrates



[a] $ClCH_2CO_2H$ (2 equiv) was used instead of $InCl_3{\cdot}H_2O$, and CH_3CN was employed as the solvent. The yield was calculated by ^1H NMR of the crude reaction mixture with 1,3,5-trimethoxybenzene as internal standard.

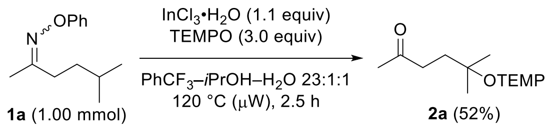
To determine if C–C bonds could be forged by this method, we examined the microwave-promoted γ-C–H functionalization with allylsulfone **3**[17] and benziodoxolone **6**[18] as radical traps (Scheme 4). Unlike TEMPO, these traps are closed-shell species that undergo radical addition to a π bond followed by elimination of a radical from the resulting adduct. The reactions of *O*-phenyloximes **1a** and **1c** required ten equivalents of these radical traps to afford adducts **4**, **5**, and **7**. The low yields of these transformations can be attributed to the inferior trapping ability of **3** and **6** relative to TEMPO permitting unwanted side reactions of the alkyl radical intermediates. Although the yields are currently not synthetically useful, these results demonstrate the possibility of merging microwave-promoted and iminyl-radical-mediated 1,5-HAT with C–C bond formation.

Scheme 4. γ-C–C Bond Formation



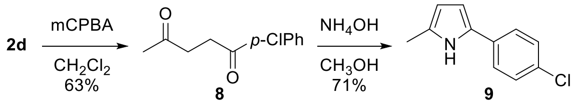
The γ-C–H functionalization could be performed on a preparative scale. Subjection of ca. 1 mmol of **1a** to the standard reaction conditions furnished ketone **2a** in 52% yield (Scheme 5). Although the yield is moderately lower than the corresponding smaller-scale reaction reported in Scheme 2, this result is nonetheless within the realm of synthetic utility.

Scheme 5. Preparative Scale Reaction



The products of this reaction are amenable to further transformation. For example, treatment of ketone **2d** with mCPBA caused oxidative cleavage of the OTEMP group,[19] delivering 1,4-ketone **8**. Exposure of **8** to NH_4OH[20] afforded pyrrole **9**. Other possibilities such as reductive N–O cleavage[21] and OTEMP elimination[22] can also be envisioned.

Scheme 6. Transformation of Adduct



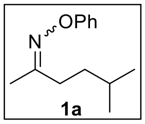
In conclusion, we have demonstrated that *O*-phenyloximes can undergo microwave-promoted N–O homolysis followed by 1,5-HAT, delivering the products of a formal γ-C(sp^3)–H ketone activation.

$InCl_3 \cdot H_2O$ was beneficial in most cases, presumably due to its ability to coordinate iminyl radicals and increase their reactivity to hydrogen atom abstraction. Chloroacetic acid enables generation of 1° radicals by this process, a feat that has not been achieved with SET-dependent iminyl radical chemistry that often precludes the use of acidic promoters. Both C–O and C–C bond formation could be accomplished by using TEMPO, an allylsulfone, and a benziodoxolone as radical traps. The reactions are rapid and involve simple experimental protocols. Although more work is necessary for some yields to reach synthetically useful levels, we believe that the potential of this method justifies further investigation.[23]

EXPERIMENTAL SECTION

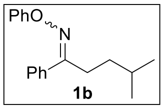
General Details. Pyridine was dried by passage through a solvent drying system employing activated alumina cylinders. Flash chromatography was carried out using 230 mesh silica gel. ^1H NMR spectra were obtained on Varian or Bruker 500 MHz spectrometers, with chloroform (7.27 ppm) as internal reference. Signals are reported as follows: s (singlet), d (doublet), t (triplet), q (quartet), sext (sextet), dd (doublet of doublets), ddd (doublet of doublet of doublets), br s (broad singlet), m (multiplet). Coupling constants are reported in hertz (Hz). ^{13}C NMR spectra were obtained on Varian or Bruker spectrometers operating at 125 MHz, with chloroform (77.23 ppm) as internal. Infrared spectra were obtained on an FT-IR spectrometer. Mass spectral data were obtained using ESI mass spectrometry. Microwave-promoted reactions were carried out by irradiating sealed reaction mixtures inside a CEM Discover SP microwave reactor that was set at 200 W. Reactions employing conventional heating were performed in an oil bath.

General procedure for synthesis of *O*-phenyloximes. A solution of ketone (0.28–2.08 mmol) in anhydrous pyridine (2.5–4 mL) at rt under Ar was treated with $PhONH_2 \cdot HCl$[14] (2 equiv). The resulting mixture was stirred at 40 °C for 24 h, then diluted with H_2O (3 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with sat aq $CuSO_4$ (3 × 6 mL), dried (Na_2SO_4), and concentrated *in vacuo*. Flash chromatography afforded *O*-phenyloximes **1a–1m**.


1a

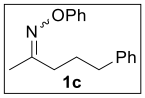
5-Methylhexan-2-one *O*-phenyl oxime (1a). 5-Methylhexan-2-one (150 µL, 122 mg, 1.07 mmol) was subjected to the General Procedure described above with anhydrous pyridine (3.0 mL) and $PhONH_2$•HCl (271 mg, 1.86 mmol, 1.7 equiv). The reaction time was 48 h instead of 24 h, the mixture was diluted with 6 mL of H_2O, and the extraction and washing were performed with 50 mL of EtOAc and sat aq $CuSO_4$, respectively. Flash chromatography (SiO_2, 2 × 15 cm, 1–4 % EtOAc in hexanes gradient elution) afforded **1a** (208.6 mg, 1.02 mmol, 95%) as a yellow oil that was a 2.9:1 mixture of diastereomers. ^{1}H NMR ($CDCl_3$, 500 MHz, data for major diastereomer) δ 7.21 (t, *J* = 7.9 Hz, 2H), 7.09 (d, *J* = 8.1 Hz, 2H), 6.90 (t, *J* = 7.3 Hz, 1H), 2.24 (t, *J* = 7.9 Hz, 2H), 1.95 (s, 3H), 1.57–1.47 (m, 1H), 1.42–1.33 (m, 2H), 0.86 (d, *J* = 6.6 Hz, 6H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz, data for major diastereomer) δ 161.8, 159.5, 129.2 (2C), 121.7, 114.6 (2C), 35.2, 33.9, 27.8, 22.4 (2C), 14.8; IR (film) ν_{max} 3064, 2956, 2869, 1643, 1592, 1489, 1368, 1214, 1071, 1023 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{13}H_{19}NOH$ 206.1539; Found 206.1536.

The following signals from the minor diastereomer were resolved in the ^{1}H NMR spectrum and were used to calculate the diastereomeric ratio: δ 2.42 (t, *J* = 8.1 Hz, 2H; corresponds to 2.24 ppm signal in major diastereomer), 1.91 (s, 3H; corresponds to 1.95 ppm signal in major diastereomer).


1b

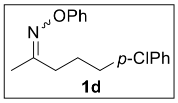
4-Methyl-1-phenylpentan-1-one *O*-phenyl oxime (1b). 4-Methylvalerophenone (52.0 µL, 50.5 mg, 0.286 mmol) was subjected to the General Procedure described above with anhydrous pyridine (3 mL) and $PhONH_2$•HCl (84.0 mg, 0.577 mmol, 2.0 equiv). Flash chromatography (SiO_2, 2 × 14.5 cm, 2–2.5% EtOAc in hexanes elution) afforded **1b** (53.9 mg, 0.202 mmol, 70%) as a yellow oil that was a 2.9:1 mixture of diastereomers: ^{1}H NMR ($CDCl_3$, 500 MHz, data for major diastereomer) δ 7.77–7.74 (m, 2H), 7.43–7.40 (m, 3H), 7.33 (t, *J* = 7.9 Hz, 2H), 7.30–7.27 (m, 3H), 2.94 (t, *J* = 8.2 Hz, 2H), 1.72–1.62 (m, 1H), 1.53–1.50 (m, 2H), 0.97 (d, *J* = 6.6 Hz, 6H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz, data for major diastereomer) δ 162.1, 159.6, 135.2, 129.6, 129.3 (2C), 128.6 (2C), 126.7 (2C), 122.0, 114.7 (2C), 35.6, 28.4, 25.4, 22.4 (2C); IR (film) ν_{max} 3060, 2956, 2927, 2869, 1687, 1594, 1468, 1216 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{18}H_{21}NOH$ 268.1696; Found 268.1693.

The following signals from the minor diastereomer were resolved in the ^{1}H NMR spectrum and were used to calculate the diastereomeric ratio: δ 2.68 (t, *J* = 7.9 Hz, 2H; corresponds to 2.94 ppm signal in major diastereomer), 1.45–1.40 (m, 2H; corresponds to 1.53–1.50 ppm signal in major diastereomer), 0.91 (d, *J* = 6.6 Hz, 6H; corresponds to 0.97 ppm signal in major diastereomer).


1c

5-Phenylpentan-2-one *O*-phenyl oxime (1c). 5-Phenylpentan-2-one[24] (90.0 mg, 0.555 mmol) was subjected to the General Procedure described above with anhydrous pyridine (3 mL) and $PhONH_2$•HCl (160.8 mg, 1.105 mmol, 2.0 equiv). Flash chromatography (SiO_2, 2 × 14.5 cm, 5% EtOAc in hexanes elution) afforded **1c** (140.5 mg, 0.555 mmol, quant.) as a brown oil that was a 3.2:1 mixture of diastereomers: ^{1}H NMR ($CDCl_3$, 500 MHz, data for major diastereomer) δ 7.29 (t, *J* = 7.9 Hz, 4H), 7.22–7.13 (m, 5H), 6.98 (t, *J* = 7.3 Hz, 1H), 2.69 (t, *J* = 7.7 Hz, 2H), 2.36 (t, *J* = 7.6 Hz, 2H), 2.03 (s, 3H), 1.97–1.87 (m, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz, data for both diastereomers) δ 161.0 (major) and 161.8 (minor), 159.5 (major) and 159.4 (minor), 141.8 (major) and 141.6 (minor), 129.2 (2C), 128.5 (2C), 128.4 (2C), 125.9, 121.6, 114.6 (2C), 35.4 (major) and 35.8 (minor), 35.3 (major) and 29.6 (minor), 27.9 (major) and 27.4 (minor), 14.9 (major) and 20.0 (minor); IR (film) ν_{max} 3084, 2963, 2918, 2815, 1596, 1473, 1272, cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{17}H_{19}NOH$ 254.1539; Found 254.1542.

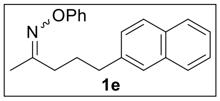
The following signals from the minor diastereomer were resolved in the ^{1}H NMR spectrum and were used to calculate the diastereomeric ratio: δ 2.55 (t, *J* = 7.9 Hz, 2H; corresponds to 2.36 ppm signal in major diastereomer), 2.00 (s, 3H; corresponds to 2.03 ppm signal in major diastereomer).



1d

5-(4-Chlorophenyl)pentan-2-one *O*-phenyl oxime (1d). 5-(4-Chlorophenyl)pentan-2-one[25] (116 mg, 0.590 mmol) was subjected to the General Procedure described above with anhydrous pyridine (4 mL) and $PhONH_2$•HCl (177 mg, 1.22 mmol, 2.1 equiv). The mixture was diluted with 4 mL of H_2O, and the extraction and washing were performed with 15 mL of EtOAc and 10 mL of sat aq $CuSO_4$, respectively. Flash chromatography (SiO_2, 2 × 14.5 cm, 1.5–2.5% EtOAc in hexanes elution) afforded **1d** (148 mg, 0.514 mmol, 87%) as a yellow oil that was a 3.1:1 mixture of diastereomers: ^1H NMR ($CDCl_3$, 500 MHz, data for major diastereomer) δ 7.30 (t, J = 8.0 Hz, 2H), 7.27–7.24 (m, 2H), 7.16 (d, J = 7.8 Hz, 2H), 7.13 (d, J = 8.2 Hz, 2H), 6.99 (t, J = 7.3 Hz, 1H), 2.66 (t, J = 7.6 Hz, 2H), 2.34 (t, J = 7.6 Hz, 2H), 2.03 (s, 3H), 1.95–1.84 (m, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz, data for both diastereomers) δ 160.8 (major) and 161.5 (minor), 159.5 (major) and 159.3 (minor), 140.2 (major) and 140.0 (minor), 131.6 (major) and 131.7 (minor), 129.8 (2C), 129.2 (2C), 128.5 (2C), 121.7, 114.5 (2C), 35.2 (major) and 35.0 (minor), 34.6 (major) and 29.4 (minor), 27.7 (major) and 27.3 (minor), 14.9 (major) and 20.0 (minor); IR (film) ν_{max} 3405, 2952, 1592, 1490, 1158 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{17}H_{18}ClNOH$ 288.1150; Found 288.1147.

The following signals from the minor diastereomer were resolved in the ^1H NMR spectrum and were used to calculate the diastereomeric ratio: δ 2.53 (t, J = 7.9 Hz, 2H; corresponds to 2.66 ppm signal in major diastereomer), 2.00 (s, 3H; corresponds to 2.03 ppm signal in major diastereomer).

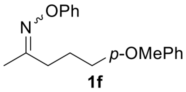


1e

5-(Naphthalen-2-yl)pentan-2-one *O*-phenyl oxime (1e). 5-(Naphthalen-2-yl)pentan-2-one[25] (120 mg, 0.565 mmol) was subjected to the General Procedure described above with anhydrous pyridine (4 mL) and $PhONH_2$•HCl (180 mg, 1.24 mmol, 2.2 equiv). The mixture was diluted with 4 mL of H_2O, and the extraction and washing were performed with 15 mL of EtOAc and 10 mL of sat aq $CuSO_4$, respectively. Flash chromatography (SiO_2, 2 × 14.5 cm, 2.5–3.5% EtOAc in hexanes elution) afforded **1e** (171.5 mg, 0.565 mmol, quantitative) as a yellow oil that was a 3.5:1 mixture of diastereomers: ^1H NMR

(CDCl$_3$, 500 MHz, data for major diastereomer) δ 7.81 (d, *J* = 7.8 Hz, 1H), 7.79 (d, *J* = 8.6 Hz, 1H), 7.64 (s, 1H), 7.47–7.40 (m, 2H), 7.32–7.27 (m, 3H), 7.19–7.13 (m, 3H), 6.98 (t, *J* = 7.3 Hz, 1H), 2.86 (t, *J* = 7.6 Hz, 2H), 2.39 (t, *J* = 7.6 Hz, 2H), 2.06 (s, 3H), 2.05–1.96 (m, 2H); ^{13}C{^{1}H} NMR (CDCl$_3$, 125 MHz, data for both diastereomers) δ 161.0 (major) and 161.8 (minor), 159.4 (major) and 158.5 (minor), 139.2 (major) and 139.0 (minor), 133.6, 132.0, 129.2 (2C), 128.0, 127.6, 127.4, 127.3 (major) and 127.2 (minor), 126.6 (major) and 126.5 (minor), 125.9, 125.2, 121.7, 114.6 (2C), 35.4 (major) and 35.9 (minor), 27.7 (major) and 27.3 (minor), 21.9 (major) and 20.0 (minor), 14.9 (major) and 16.2 (minor); IR (film) ν_{max} 3054, 2926, 2858, 1591, 1489, 1368, 1214, 1158, 1071 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{21}H_{21}NOH$ 304.1696; Found 304.1693.

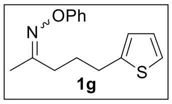
The following signal from the minor diastereomer was resolved in the ^{1}H NMR spectrum and was used to calculate the diastereomeric ratio: δ 2.59 (t, *J* = 7.8 Hz, 2H; corresponds to 2.39 ppm signal in major diastereomer).



1f

5-(4-Methoxyphenyl)pentan-2-one *O*-phenyl oxime (1f). 5-(4-Methoxyphenyl)pentan-2-one[26] (107 mg, 0.557 mmol) was subjected to the General Procedure described above with anhydrous pyridine (3 mL) and PhONH$_2$•HCl (162.2 mg, 1.114 mmol, 2.0 equiv). The extraction and washing were performed with 15 mL of EtOAc and 10 mL of sat aq CuSO$_4$, respectively. Flash chromatography (SiO$_2$, 2 × 14.5 cm, 2–3.5% EtOAc in hexanes elution) afforded **1f** (157.7 mg, 0.557 mmol, quantitative) as a yellow oil that was a 3.5:1 mixture of diastereomers: ^{1}H NMR (CDCl$_3$, 500 MHz, data for major diastereomer) δ 7.29 (t, *J* = 7.8 Hz, 2H), 7.17 (dd, *J* = 8.7, 1.9 Hz, 2H), 7.12 (d, *J* = 8.6 Hz, 2H), 6.98 (t, *J* = 7.3 Hz, 1H), 6.84 (d, *J* = 8.6 Hz, 2H), 3.79 (s, 3H), 2.63 (t, *J* = 7.6 Hz, 2H), 2.34 (t, *J* = 7.6 Hz, 2H), 2.06 (s, 3H), 1.93–1.83 (m, 2H); ^{13}C{^{1}H} NMR (CDCl$_3$, 125 MHz, data for both diastereomers) δ 161.1 (major) and 161.9 (minor), 159.5 (major) and 159.4 (minor), 157.8 (major) and 158.5 (minor), 133.8 (major) and 133.6 (minor), 129.4 (2C), 129.2 (2C), 121.7, 114.6 (2C), 113.8 (2C), 55.3, 35.4, 34.4 (major) and 34.8 (minor), 28.1 (major) and 27.7 (minor), 14.9 (major) and 20.0 (minor); IR (film) ν_{max} 3064, 2920, 1591, 1512, 1488, 1250, 1214, 1158 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{18}H_{21}NO_2H$ 284.1645; Found 284.1638.

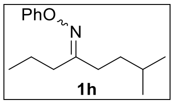
The following signals from the minor diastereomer were resolved in the ^{1}H NMR spectrum and were used to calculate the diastereomeric ratio: δ 2.54 (t, *J* = 7.9 Hz, 2H; corresponds to 2.34 ppm signal in major diastereomer), 2.02 (s, 3H; corresponds to 2.06 ppm signal in major diastereomer).



1g

5-(Thiophen-2-yl)pentan-2-one *O*-phenyl oxime (1g). 5-(Thiophen-2-yl)pentan-2-one[27] (109 mg, 0.648 mmol) was subjected to the General Procedure described above with anhydrous pyridine (3 mL) and $PhONH_2$•HCl (194.8 mg, 1.338 mmol, 2.1 equiv). The mixture was diluted with 4 mL of H_2O, and the extraction and washing were performed with 15 mL of EtOAc and 10 mL of sat aq $CuSO_4$, respectively. Flash chromatography (SiO_2, 2 × 14.5 cm, 2–3.5% EtOAc in hexanes elution) afforded **1g** (164.6 mg, 0.635 mmol, 98%) as a yellow oil that was a 2.6:1 mixture of diastereomers: ^{1}H NMR ($CDCl_3$, 500 MHz, data for major diastereomer) δ 7.29 (t, *J* = 7.6 Hz, 2H), 7.17 (d, *J* = 8.3 Hz, 2H), 7.14 (d, *J* = 5.6 Hz, 1H), 6.99 (t, *J* = 7.3 Hz, 1H), 6.93 (dd, *J* = 5.0, 3.4 Hz, 1H), 6.82 (d, *J* = 3.2 Hz, 1H), 2.92 (t, *J* = 7.5 Hz, 2H), 2.39 (t, *J* = 7.6 Hz, 2H), 2.04 (s, 3H), 2.02–1.93 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz, data for both diastereomers) δ 160.7 (major) and 161.4 (minor), 159.5 (major) and 159.3 (minor), 144.5 (major) and 144.4 (minor), 129.2 (2C), 126.8, 124.5, 123.2, 121.7, 114.6 (2C), 35.2, 29.3 (major) and 29.4 (minor), 28.1 (major) and 27.8 (minor), 14.9 (major) and 20.0 (minor); IR (film) ν_{max} 3069, 2930, 1644, 1488, 1368, 1212 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{15}H_{17}NOSH$ 260.1104; Found 260.1109.

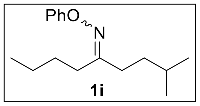
The following signal from the minor diastereomer was resolved in the ^{1}H NMR spectrum and was used to calculate the diastereomeric ratio: δ 2.58 (t, *J* = 7.9 Hz, 2H; corresponds to 2.39 ppm signal in major diastereomer).



1h

7-Methyloctan-4-one *O*-phenyl oxime (1h). 7-Methyloctan-4-one[28] (51.0 mg, 0.359 mmol) was subjected to the General Procedure described above with anhydrous pyridine (3 mL) and PhONH$_2$•HCl (104.4 mg, 0.717 mmol, 2.0 equiv). Flash chromatography (SiO$_2$, 2 × 14.5 cm, 2.5% EtOAc in hexanes elution) afforded **1h** (62.2 mg, 0.267 mmol, 74%) as a yellowish-brown oil: ^{1}H NMR (CDCl$_3$, 500 MHz) δ 7.29 (dd, *J* = 8.6, 7.4 Hz, 2H), 7.16 (d, *J* = 8.8 Hz, 2H), 6.97 (t, *J* = 7.3 Hz, 1H), 2.48–2.43 (m, 2H), 2.33–2.27 (m, 2H), 1.68–1.57 (m, 3H), 1.52–1.41 (m, 2H), 0.99 (t, *J* = 7.4 Hz, 3H), 0.94 (d, *J* = 6.6 Hz, 6H); ^{13}C{^{1}H} NMR (CDCl$_3$, 125 MHz) δ 165.3, 159.6, 129.2 (2C), 121.5, 114.6 and 114.5 (2C), 36.2, 35.2 and 34.9, 32.3 and 30.7, 28.3 and 27.9, 22.4 and 22.3 (2C), 19.6 and 19.5, 14.4 and 13.9; IR (film) ν_{max} 3064, 2959, 2871, 1591, 1489, 1219 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{15}H_{23}NOH$ 234.1852; Found 234.1850.

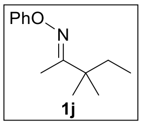
Compound **1h** was obtained as a mixture of diastereomers as evidenced by ^{13}C NMR spectroscopy; however, the lack of resolution between the diastereomers in the ^{1}H NMR spectrum prevented accurate determination of the dr. The ^{13}C NMR spectrum suggested an approximate dr of 1:1.



1i

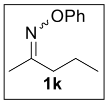
2-Methylnonan-5-one *O*-phenyl oxime (1i). 2-Methylnonan-5-one[6f] (51.5 mg, 0.330 mmol) was subjected to the General Procedure described above with anhydrous pyridine (3 mL) and PhONH$_2$•HCl (97.6 mg, 0.670 mmol, 2.0 equiv). Flash chromatography (SiO$_2$, 2 × 14.5 cm, 7.5–10% EtOAc in hexanes elution) afforded **1i** (69.5 mg, 0.281 mmol, 85%) as a yellowish-brown oil: ^{1}H NMR (CDCl$_3$, 500 MHz) δ 7.29 (dd, *J* = 8.7, 7.3 Hz, 2H), 7.15 (d, *J* = 8.7 Hz, 2H), 6.97 (t, *J* = 7.3 Hz, 1H), 2.49–2.44 (m, 2H), 2.33–2.29 (m, 2H), 1.66–1.55 (m, 3H), 1.54–1.35 (m, 4H), 0.97–0.93 (m, 9H); ^{13}C{^{1}H} NMR (CDCl$_3$, 125 MHz) δ 165.4, 159.6, 129.2 (2C), 121.5, 114.6 and 114.5 (2C), 35.2 and 34.9, 33.9 and 32.2, 28.5, 28.4 and 28.3, 28.2 and 27.9, 22.9 and 22.5, 22.4 and 22.3 (2C), 13.9 and 13.8; IR (film) ν_{max} 3064, 2956, 2870, 1592, 1489, 1216 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{16}H_{25}NOH$ 248.2009; Found 248.2006.

Compound **1i** was obtained as a mixture of diastereomers as evidenced by ^{13}C NMR spectroscopy; however, the lack of resolution between the diastereomers in the ^{1}H NMR spectrum prevented accurate determination of the dr. The ^{13}C NMR spectrum suggested an approximate dr of 1:1.



1j

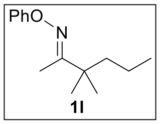
3,3-Dimethylpentan-2-one *O*-phenyl oxime (1j). 3,3-Dimethylpentan-2-one (52.0 µL, 42.1 mg, 0.369 mmol) was subjected to the General Procedure described above with anhydrous pyridine (3 mL) and PhONH$_2$•HCl (128.4 mg, 0.864 mmol, 2.3 equiv). Flash chromatography (SiO$_2$, 2 × 14.5 cm, 5–10% EtOAc in hexanes gradient elution) afforded **1j** (75.9 mg, 0.370 mmol, quant.) as a yellowish-brown oil that was a single diastereomer: ^{1}H NMR (CDCl$_3$, 500 MHz) δ 7.29 (dd, *J* = 8.7, 7.3 Hz, 2H), 7.18 (d, *J* = 8.8 Hz, 2H), 6.97 (t, *J* = 7.3 Hz, 1H), 1.97 (s, 3H), 1.54 (q, *J* = 7.5 Hz, 2H), 1.17 (s, 6H), 0.82 (t, *J* = 7.5 Hz, 3H); ^{13}C{^{1}H} NMR (CDCl$_3$, 125 MHz) δ 166.0, 159.8, 129.2 (2C), 121.4, 114.4 (2C), 41.2, 32.9, 25.2 (2C), 11.1, 9.0; IR (film) ν_{max} 3061, 2953, 2868, 1591, 1489, 1214 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{13}H_{19}NOH$ 206.1539; Found 206.1536.



1k

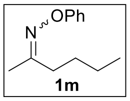
Pentan-2-one *O*-phenyl oxime (1k). 2-Pentanone (185 µL, 149 mg, 1.73 mmol) was subjected to the General Procedure described above with anhydrous pyridine (4 mL) and PhONH$_2$•HCl (491.5 mg, 3.376 mmol, 2.0 equiv). Flash chromatography (SiO$_2$, 2 × 14.5 cm, 0–2% EtOAc in hexanes gradient elution) afforded **1k** (271.6 mg, 1.532 mmol, 89%) as a dark-brown oil that was a 3.0:1 mixture of diastereomers: ^{1}H NMR (CDCl$_3$, 500 MHz, data for major diastereomer) δ 7.29 (t, *J* = 8.0 Hz, 2H), 7.16 (d, *J* = 7.8 Hz, 2H), 6.98 (t, *J* = 7.3 Hz, 1H), 2.29 (t, *J* = 7.6 Hz, 2H), 2.03 (s, 3H), 1.67–1.57 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (CDCl$_3$, 125 MHz, data for major diastereomer) δ 161.4, 159.5, 129.2 (2C), 121.6, 114.6 (2C), 37.8, 19.6, 14.6, 13.7; IR (film) ν_{max} 3063, 2954, 2865, 1590, 1432, 1215 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{11}H_{15}NOH$ 178.1226; Found 178.1217.

The following signals from the minor diastereomer were resolved in the ^{1}H NMR spectrum and were used to calculate the diastereomeric ratio: δ 2.50 (t, *J* = 7.8 Hz, 2H; corresponds to 2.29 ppm signal in major diastereomer), 1.99 (s, 3H; corresponds to 2.03 ppm signal in major diastereomer).



1l

3,3-Dimethylhexan-2-one *O*-phenyl oxime (1l). 3,3-Dimethylhexan-2-one (160 µL, 134 mg, 1.05 mmol) was subjected to the General Procedure described above with anhydrous pyridine (5 mL) and PhONH$_2$•HCl (298 mg, 2.05 mmol, 2.0 equiv). Flash chromatography (SiO$_2$, 2 × 14.5 cm, 1.5–2.5% EtOAc in hexanes gradient elution) afforded **1l** (192.5 mg, 0.878 mmol, 84%) as a yellowish-brown oil that was a single diastereomer: ^{1}H NMR (CDCl$_3$, 500 MHz) δ 7.29 (t, *J* = 7.9 Hz, 2H), 7.17 (d, *J* = 8.2 Hz, 2H), 6.97 (t, *J* = 7.3 Hz, 1H), 1.97 (s, 3H), 1.48–1.44 (m, 2H), 1.27–1.20 (m, 2H), 1.18 (s, 6H), 0.90 (t, *J* = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (CDCl$_3$, 125 MHz) δ 166.2, 159.8, 129.2 (2C), 121.4, 114.4 (2C), 42.8, 41.0, 25.6 (2C), 18.0, 14.7, 11.2; IR (film) ν_{max} 3064, 2959, 2871, 1707, 1590, 1430, 1215 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^{+}$ Calcd for $C_{14}H_{21}NOH$ 220.1696; Found 220.1701.

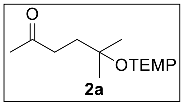


1m

Hexan-2-one *O*-phenyl oxime (1m). 2-Hexanone (257 µL, 209 mg, 2.08 mmol) was subjected to the General Procedure described above with anhydrous pyridine (4 mL) and PhONH$_2$•HCl (506.3 mg, 3.478 mmol, 1.7 equiv). Flash chromatography (SiO$_2$, 2 × 14.5 cm, 0–5% EtOAc in hexanes elution) afforded **1m** (385.9 mg, 2.02 mmol, 97%) as a dark-brown oil that was a 3.0:1 mixture of diastereomers: ^{1}H NMR (CDCl$_3$, 500 MHz, data for major diastereomer) δ 7.29 (t, *J* = 8.0 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 6.97 (t, *J* = 7.3 Hz, 1H), 2.31 (t, *J* = 7.7 Hz, 2H), 2.03 (s, 3H), 1.61–1.52 (m, 2H), 1.39 (sext, *J* = 7.4 Hz, 2H), 0.95 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (CDCl$_3$, 125 MHz, data for major diastereomer) δ 161.6, 159.5, 129.2 (2C), 121.6, 114.6 (2C), 35.5, 28.4, 22.3, 14.7, 13.8; IR (film) ν_{max} 3065, 2960, 2932, 1632, 1590, 1490, 1237, 1215 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^{+}$ Calcd for $C_{12}H_{17}NOH$ 192.1383; Found 192.1378.

The following signals from the minor diastereomer were resolved in the ^{1}H NMR spectrum and were used to calculate the diastereomeric ratio: δ 2.51 (t, *J* = 7.8 Hz, 2H; corresponds to 2.31 ppm signal in major diastereomer), 1.99 (s, 3H; corresponds to 2.03 ppm signal in major diastereomer).

General procedure for microwave-promoted γ-C–H functionalization. An oven-dried cylindrical microwave reaction vessel was charged with *O*-phenyloxime **1** (0.10–0.17 mmol), TEMPO (0.30–0.52 mmol), $InCl_3 \cdot H_2O$ (0.10–0.17 mmol), $PhCF_3$ (2.3 mL), 2-propanol (100 μL), and H_2O (100 μL). The reaction vessel was sealed with a Teflon cap that was equipped with a high-pressure release mechanism, and the mixture was subjected to microwave irradiation (200 W), raising the temperature from rt to 120 °C during a 1-minute period. The reaction temperature was monitored by a non-contact infrared sensor and kept constant at 120 °C for 2 h. The mixture was then allowed to cool to rt and was concentrated *in vacuo*. Flash chromatography afforded adducts **2a–2m**.

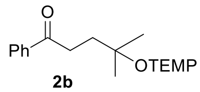


2a

5-Methyl-5-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)hexan-2-one (2a). *O*-Phenyloxime **1a** (25.0 mg, 0.122 mmol) was subjected to the General Procedure described above with TEMPO (58.0 mg, 0.371 mmol, 3.0 equiv), $InCl_3 \cdot H_2O$ (27.5 mg, 0.124 mmol, 1.0 equiv), $PhCF_3$ (2.3 mL), 2-propanol (100 μL), and H_2O (100 μL). Flash chromatography (SiO_2, 0.9 × 13.5 cm, 1.5–3.0% EtOAc in hexanes gradient elution) afforded **2a** (21.9 mg, 0.0813 mmol, 67%) as a light-yellow oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.58 (t, *J* = 8.2 Hz, 2H), 2.11 (s, 3H), 1.78 (t, *J* = 8.2 Hz, 2H), 1.49 (br s, 4H), 1.40–1.36 (m, 2H), 1.18 (s, 6H), 1.03 (s, 6H), 1.00 (s, 6H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 209.8, 77.7, 59.2 (2C), 40.8 (2C), 38.8, 37.1, 34.7 (2C), 30.1, 26.9 (2C), 20.8 (2C), 17.1; IR (film) ν_{max} 3054, 2930, 2852, 1718, 1467, 1363, 1158, 1131 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{31}NO_2H$ 270.2428; Found 270.2432.

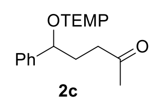
Preparative-scale Synthesis of 2a. *O*-Phenyloxime **1a** (205.6 mg, 1.00 mmol) was subjected to the General Procedure described above with TEMPO (472.8 mg, 3.03 mmol, 3.0 equiv), $InCl_3 \cdot H_2O$ (238.0

mg, 1.08 mmol, 1.1 equiv), $PhCF_3$ (9.4 mL), 2-propanol (300 μL), and H_2O (300 μL), and a 2.5 h reaction time. Flash chromatography (SiO_2, 3 × 19 cm, 0.5–3.0% Et_2O in hexanes gradient elution) afforded **2a** (139.1 mg, 0.516 mmol, 52%) as a light-yellow oil.



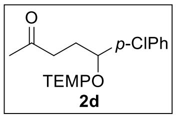
2b

4-Methyl-1-phenyl-4-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)pentan-1-one (2b). *O*-Phenyloxime **1b** (29.0 mg, 0.108 mmol) was subjected to the General Procedure described above with TEMPO (52.8 mg, 0.338 mmol, 3.1 equiv), $InCl_3{\cdot}H_2O$ (25.0 mg, 0.113 mmol, 1.0 equiv), $PhCF_3$ (2.3 mL), 2-propanol (100 μL), and H_2O (100 μL). Flash chromatography (SiO_2, 0.9 × 13.5 cm, 1.5–3% Et_2O in hexanes gradient elution) afforded a mixture of **2b** (12.6 mg, 0.0380 mmol, 35%) and tetralone **2b'**[15b] (6.4 mg, 0.0367 mmol, 34%) as a light-yellow oil. Additional purification afforded an analytical sample of **2b**: ^1H NMR ($CDCl_3$, 500 MHz) δ 8.02 (d, *J* = 7.8 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 3.20 (t, *J* = 8.1 Hz, 2H), 2.02 (t, *J* = 8.1 Hz, 2H), 1.60–1.52 (m, 4H, partially obscured by H_2O), 1.48–1.45 (m, 2H), 1.33 (s, 6H), 1.12 (s, 6H), 1.10 (s, 6H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 201.1, 132.9, 128.5 (2C), 128.1 (2C), 114.7, 77.9, 59.2 (2C), 40.8 (2C), 37.7, 34.7 (2C), 33.5, 27.1 (2C), 20.8 (2C), 17.1; IR (film) ν_{max} 2924, 2850, 2285, 1687, 1596, 1448, 1376, 1116, 1071 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{21}H_{33}NO_2H$ 332.2584; Found 332.2576.



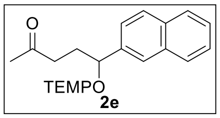
2c

5-Phenyl-5-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)pentan-2-one (2c). *O*-phenyloxime **1c** (24.3 mg, 0.0959 mmol) was subjected to the General Procedure described above with TEMPO (45.7 mg, 0.292 mmol, 3.0 equiv), $InCl_3{\cdot}H_2O$ (22.0 mg, 0.0995 mmol, 1.0 equiv), $PhCF_3$ (2.3 mL), 2-propanol (100 μL), and H_2O (100 μL). Flash chromatography (SiO_2, 0.9 × 13.5 cm, 10–20% EtOAc in hexanes gradient elution) afforded **2c** (18.2 mg, 0.0573 mmol, 60%) as a light-yellow oil: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.31 (t, *J* = 7.4 Hz, 2H), 7.27–7.22 (m, 3H), 4.65 (dd, *J* = 9.2, 3.9 Hz, 1H), 2.36–2.30 (m, 1H), 2.19 (t, *J* = 7.6 Hz, 2H), 2.12–2.04 (m, 1H), 2.02 (s, 3H), 1.54–1.43 (m, 4H), 1.38–1.31 (m, 2H), 1.30 (s, 3H), 1.17 (s, 3H), 1.00 (s, 3H), 0.56 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 208.5, 142.9, 128.0 (2C), 127.6 (2C), 127.2, 86.2, 59.9, 59.6, 40.4 (2C), 39.5, 34.4, 34.0, 29.9, 29.7, 20.3 (2C), 17.1; IR (film) ν_{max} 3002, 2927, 2851, 2360, 1719, 1584, 1413, 1360, 1257, 1113 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{20}H_{31}NO_2H$ 318.2428; Found 318.2430.



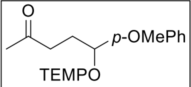
2d

5-(4-Chlorophenyl)-5-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)pentan-2-one (2d). *O*-phenyloxime **1d** (30.0 mg, 0.104 mmol) was subjected to the General Procedure described above with TEMPO (49.6 mg, 0.317 mmol, 3.0 equiv), $InCl_3·H_2O$ (28.0 mg, 0.127 mmol, 1.2 equiv), $PhCF_3$ (2.3 mL), 2-propanol (100 μL), and H_2O (100 μL). Flash chromatography (SiO_2, 0.9 × 13.5 cm, 7.5–25% Et_2O in hexanes gradient elution) afforded **2d** (20.0 mg, 0.0568 mmol, 55%) as a colorless oil: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.29 (d, *J* = 8.4 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 4.64 (dd, *J* = 9.2 Hz, 4.0 Hz, 1H), 2.34–2.28 (m, 1H), 2.17 (t, *J* = 7.6 Hz, 2H), 2.07–2.00 (m, 1H), 2.03 (s, 3H) 1.51–1.42 (m, 4H), 1.37–1.32 (m, 2H), 1.25 (s, 3H), 1.16 (s, 3H), 0.99 (s, 3H), 0.55 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 208.1, 141.4, 132.9, 128.9 (2C), 128.2 (2C), 85.5, 60.4 (2C), 40.4, 39.3, 34.1, 31.9, 30.0, 29.6, 22.7, 20.3 (2C), 17.1; IR (film) ν_{max} 3027, 2927, 2858, 1693, 1592, 1490, 1456, 1368, 1264, 1213, 1091 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{20}H_{30}ClNO_2H$ 352.2038; Found 352.2032.



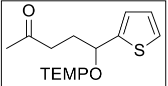
2e

5-(Naphthalen-2-yl)-5-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)pentan-2-one (2e). *O*-Phenyloxime **1e** (30.2 mg, 0.0995 mmol) was subjected to the General Procedure described above with TEMPO (48.0 mg, 0.307 mmol, 3.1 equiv), $InCl_3·H_2O$ (28.0 mg, 0.127 mmol, 1.3 equiv), $PhCF_3$ (2.3 mL), 2-propanol (100 μL), and H_2O (100 μL). Flash chromatography (SiO_2, 0.9 × 13.5 cm, 10–12.5% Et_2O in hexanes gradient elution) afforded **2e** (18.8 mg, 0.0512 mmol, 51%) as a colorless oil: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.85–7.81 (m, 3H), 7.66 (s, 1H), 7.50–7.44 (m, 3H), 4.81 (dd, *J* = 9.1, 3.9 Hz, 1H), 2.43–2.38 (m, 1H), 2.20–2.12 (m, 3H), 1.98 (s, 3H), 1.54–1.45 (m, 4H), 1.38–1.30 (m, 2H), 1.35 (s, 3H), 1.21 (s, 3H), 1.01 (s, 3H), 0.52 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 208.4, 140.3, 133.0, 132.8, 127.98, 127.93, 127.7, 126.5, 126.0, 125.7, 125.4, 86.5, 60.0, 59.6, 40.4 (2C), 39.5, 34.4, 34.2, 29.9, 29.6, 20.3 (2C), 17.1; IR (film) ν_{max} 3054, 2925, 2850, 1718, 1657, 1461, 1374, 1360, 1132 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{24}H_{33}NO_2H$ 368.2584; Found 368.2576.



2f

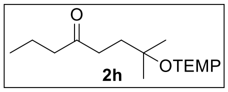
5-(4-Methoxyphenyl)-5-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)pentan-2-one (2f). *O*-Phenyloxime **1f** (31.5 mg, 0.111 mmol) was subjected to the General Procedure described above with TEMPO (53.8 mg, 0.344 mmol, 3.1 equiv), $InCl_3 \cdot H_2O$ (25.2 mg, 0.114 mmol, 1.0 equiv), $PhCF_3$ (2.3 mL), 2-propanol (100 µL), and H_2O (100 µL). Flash chromatography (SiO_2, 0.9 × 13.5 cm, 10–20% EtOAc in hexanes gradient elution) afforded **2f** (12.5 mg, 0.0360 mmol, 32%) as a creamy-white oil: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.17 (d, *J* = 8.6 Hz, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 4.58 (dd, *J* = 9.6, 4.1 Hz, 1H), 3.80 (s, 3H), 2.38–2.30 (m, 1H), 2.20–2.15 (m, 2H), 2.06–1.98 (m, 1H) 2.02 (s, 3H), 1.50–1.41 (m, 4H), 1.37–1.29 (m, 2H), 1.29 (s, 3H), 1.16 (s, 3H), 0.99 (s, 3H), 0.55 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 208.5, 158.7, 135.0, 128.8 (2C), 113.3 (2C), 85.6, 60.0, 59.5, 55.2, 40.4 (2C), 39.8, 34.4, 34.1, 29.9, 29.6, 20.3 (2C), 17.2; IR (film) ν_{max} 2967, 2928, 2849, 1716, 1610, 1512, 1463, 1360, 1247, 1174, 1036 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{33}NO_3H$ 348.2533; Found 348.2541.



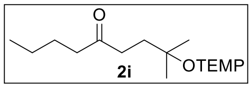
2g

5-((2,2,6,6-Tetramethylpiperidin-1-yl)oxy)-5-(thiophen-2-yl)pentan-2-one (2g). *O*-Phenyloxime **1g** (38.6 mg, 0.149 mmol) was subjected to the General Procedure described above with TEMPO (71.7 mg, 0.459 mmol, 3.1 equiv), $InCl_3 \cdot H_2O$ (36.0 mg, 0.163 mmol, 1.1 equiv), $PhCF_3$ (2.3 mL), 2-propanol (100 µL), and H_2O (100 µL). Flash chromatography (SiO_2, 0.9 × 13.5 cm, 7.5–10% EtOAc in hexanes gradient elution) afforded **2g** (20.8 mg, 0.0643 mmol, 43%) as a yellow oil: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.24 (dd, *J* = 5.0, 0.9 Hz, 1H), 6.94 (dd, *J* = 4.9, 3.5 Hz, 1H), 6.91 (dd, *J* = 3.4, 1.0 Hz, 1H), 4.92 (dd, *J* = 9.5, 4.5 Hz, 1H), 2.46–2.39 (m, 1H), 2.35–2.32 (m, 2H), 2.10–2.03 (m, 1H), 2.07 (s, 3H), 1.50–1.42 (m, 4H), 1.39–1.33 (m, 2H), 1.27 (s, 3H), 1.15 (s, 3H), 1.02 (s, 3H), 0.63 (s, 3H);

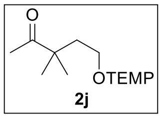
$^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 208.2, 146.3, 126.1, 125.7, 124.6, 81.0, 60.2, 59.6, 40.4 (2C), 39.9, 34.3, 32.9, 30.1, 30.0, 20.4, 20.3, 17.2; IR (film) ν_{max} 2921, 2850, 1721, 1591, 1461, 1218, 1063, 1130 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{29}NO_2SH$ 324.1992; Found 324.1988.



2h **7-Methyl-7-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)octan-4-one (2h).** *O*-Phenyloxime **1h** (26.9 mg, 0.115 mmol) was subjected to the General Procedure described above with TEMPO (54.9 mg, 0.351 mmol, 3.0 equiv), $InCl_3·H_2O$ (27.2 mg, 0.123 mmol, 1.1 equiv), $PhCF_3$ (2.3 mL), 2-propanol (100 μL), and H_2O (100 μL). Flash chromatography (SiO_2, 0.9 × 13.5 cm, 1.5–2.0% Et_2O in hexanes gradient elution) afforded **2h** (18.4 mg, 0.0619 mmol, 54%) as a brown oil: ^1H NMR ($CDCl_3$, 500 MHz) δ 2.61 (t, *J* = 8.2 Hz, 2H), 2.42 (t, *J* = 7.4 Hz, 2H), 1.84 (t, *J* = 8.2 Hz, 2H), 1.62 (sext, *J* = 7.4 Hz, 2H), 1.55–1.48 (m, 2H), 1.47–1.38 (m, 4H), 1.26 (s, 6H), 1.10 (s, 6H), 1.06 (s, 6H), 0.92 (t, *J* = 7.4 Hz, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 212.1, 77.7, 59.2 (2C), 44.9, 40.8 (2C), 37.7, 37.1, 34.7 (2C), 26.9 (2C), 20.7 (2C), 17.5, 17.1, 13.8; IR (film) ν_{max} 2965, 2927, 2872, 1714, 1376, 1363, 1132 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{35}NO_2H$ 298.2741; Found 298.2748.

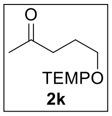


2i **2-Methyl-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)nonan-5-one (2i).** *O*-Phenyloxime **1i** (27.3 mg, 0.110 mmol) was subjected to the General Procedure described above with TEMPO (53.4 mg, 0.342 mmol, 3.1 equiv), $InCl_3·H_2O$ (25.3 mg, 0.114 mmol, 1.0 equiv), $PhCF_3$ (2.3 mL), 2-propanol (100 μL), and H_2O (100 μL). Flash chromatography (SiO_2, 0.9 × 13.5 cm, 1.75–2.5% Et_2O in hexanes gradient elution) afforded **2i** (21.1 mg, 0.0677 mmol, 61%) as a brown oil: ^1H NMR ($CDCl_3$, 500 MHz) δ 2.62 (t, *J* = 8.2 Hz, 2H), 2.44 (t, *J* = 7.5 Hz, 2H), 1.84 (t, *J* = 8.2 Hz, 2H), 1.60–1.55 (m, 2H), 1.54–1.47 (m, 2H), 1.47–1.40 (m, 4H), 1.32 (sext, *J* = 7.5 Hz, 2H), 1.26 (s, 6H), 1.10 (s, 6H), 1.07 (s, 6H), 0.91 (t, *J* = 7.3 Hz, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 212.2, 77.7, 59.2 (2C), 42.7, 40.8 (2C), 37.7, 37.1, 34.7 (2C), 26.9 (2C), 26.2, 22.4, 20.7 (2C), 17.1, 13.9; IR (film) ν_{max} 3007, 2957, 2931, 1715, 1466, 1376, 1258, 1132 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M+H]$^+$ Calcd for $C_{19}H_{37}NO_2H$ 312.2897; Found 312.2891.



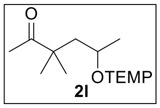
2j

3,3-Dimethyl-5-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)pentan-2-one (2j). An oven-dried reaction vessel was charged with *O*-phenyloxime **1j** (64.0 mg, 0.312 mmol), TEMPO (147.6 mg, 0.945 mmol, 3.0 equiv), $ClCH_2COOH$ (59.7 mg, 0.632 mmol, 2.0 equiv), and CH_3CN (5 mL). The reaction vessel was then sealed, and the mixture was subjected to microwave irradiation (200 W) at 120 °C for 2 h, then cooled to rt and concentrated *in vacuo*. This afforded 230 mg of a crude mixture as a light-yellow oil. A ^{1}H NMR spectrum of this mixture with 1,3,5-trimethoxybenzene as an internal standard revealed that 7.4 mg of **2j** (0.0275 mmol, 9%) was present. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.36 (t, J = 7.4 Hz, 2H), 2.08 (t, J = 7.4 Hz, 2H), 2.03 (s, 3H), 1.63–1.54 (m, 4H), 1.34 (s, 3H), 1.34–1.31 (m, 2H), 1.29 (s, 6H), 1.18 (s, 6H), 1.09 (s, 3H); HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{16}H_{31}NO_2H$ 270.2439; Found 270.2439.

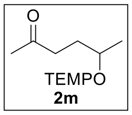


2k

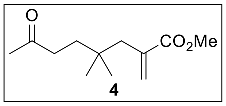
5-((2,2,6,6-Tetramethylpiperidin-1-yl)oxy)pentan-2-one (2k). An oven-dried reaction vessel was charged with *O*-phenyloxime **1k** (67.3 mg, 0.380 mmol), TEMPO (178.4 mg, 1.142 mmol, 3.0 equiv), $ClCH_2COOH$ (71.8 mg, 0.760 mmol, 2.0 equiv), and CH_3CN (5 mL). The reaction vessel was then sealed, and the mixture was subjected to microwave irradiation (200 W) at 120 °C for 2 h, then cooled to rt and concentrated *in vacuo*. This afforded 270 mg of a crude mixture as a light-yellow oil. A ^{1}H NMR spectrum of this mixture with 1,3,5-trimethoxybenzene as an internal standard revealed that 23.1 mg of **2k** (0.0957 mmol, 25%) was present. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.39 (t, J = 7.0 Hz, 2H), 2.10 (t, J = 7.7 Hz, 2H), 2.03 (s, 3H), 1.88–1.83 (m, 2H), 1.63–1.58 (m, 4H), 1.52 (s, 6H), 1.44–1.39 (m, 2H), 1.26 (s, 6H); HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{14}H_{27}NO_2H$ 242.2115; Found 242.2127.



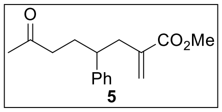
3,3-Dimethyl-5-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)hexan-2-one (2l). *O*-phenyloxime **1l** (33.9 mg, 0.155 mmol) was subjected to the General Procedure described above with TEMPO (74.5 mg, 0.477 mmol, 3.1 equiv), $InCl_3{\cdot}H_2O$ (35.0 mg, 0.158 mmol, 1.0 equiv), $PhCF_3$ (2.3 mL), 2-propanol (100 μL), and H_2O (100 μL). Flash chromatography (SiO_2, 0.9 × 13.5 cm, 1–1.75% EtOAc in hexanes gradient elution) afforded **2l** (5.7 mg, 0.0201 mmol, 13%) as a light-yellow oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.04–3.98 (m, 1H), 2.20 (s, 3H), 2.02 (dd, *J* = 14.6, 8.7 Hz, 1H), 1.53 (dd, *J* = 14.5, 3.0 Hz, 1H), 1.47–1.36 (m, 4H), 1.33–1.27 (m, 2H), 1.19 (d, *J* = 6.6 Hz, 3H), 1.18 (s, 3H), 1.15 (s, 3H), 1.10 (s, 3H), 1.08 (s, 3H), 1.04 (s, 3H), 0.99 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 213.0, 74.6, 60.3, 60.1, 47.8, 46.6, 40.6, 40.2, 34.1, 26.9 (2C), 25.2, 23.8 (2C), 21.0, 20.9, 17.3; IR (film) ν_{max} 2958, 2926, 2871, 1721, 1590, 1413, 1375, 1162, 1071 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{17}H_{33}NO_2H$ 284.2584; Found 284.2578.



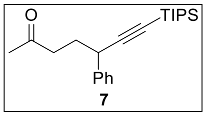
5-((2,2,6,6-Tetramethylpiperidin-1-yl)oxy)hexan-2-one (2m). *O*-phenyloxime **1m** (30.7 mg, 0.161 mmol) was subjected to the General Procedure described above with TEMPO (76.1 mg, 0.487 mmol, 3.0 equiv), $InCl_3{\cdot}H_2O$ (36.0 mg, 0.163 mmol, 1.0 equiv), $PhCF_3$ (2.3 mL), 2-propanol (100 μL), and H_2O (100 μL). Flash chromatography (SiO_2, 0.9 × 13.5 cm, 4–7.5% EtOAc in hexanes gradient elution) afforded **2m** (5.1 mg, 0.020 mmol, 12%) as a light-yellow oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.92 (sext, *J* = 6.2 Hz, 1H), 2.57–2.52 (m, 2H), 2.17 (s, 3H), 1.86–1.71 (m, 2H), 1.48–1.40 (m, 4H), 1.33–1.27 (m, 2H), 1.16 (d, *J* = 6.4 Hz, 3H), 1.10 (s, 9H), 1.05 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 209.2, 77.2 (obscured by solvent), 60.2, 59.1, 40.3, 40.2, 40.0, 34.4, 30.3, 29.9, 20.5, 20.4, 19.8 (2C), 17.3; IR (film) ν_{max} 3052, 2923, 2851, 1721, 1596, 1461, 1376, 1130 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{15}H_{29}NO_2H$ 256.2271; Found 256.2280.



Methyl 4,4-dimethyl-2-methylene-7-oxooctanoate (4). An oven-dried reaction vessel was charged with *O*-phenyloxime **1a** (33.2 mg, 0.162 mmol), methyl 2-((phenylsulfonyl)methyl)acrylate (**3**, 388.5 mg, 1.62 mmol, 10 equiv), $InCl_3{\cdot}H_2O$ (35.7 mg, 0.161 mmol, 1.0 equiv), $PhCF_3$ (4.6 mL), 2-propanol (200 μL), and H_2O (200 μL). The reaction vessel was then sealed, and the mixture was subjected to microwave irradiation (200 W) at 120 °C for 2 h, then cooled to rt and concentrated *in vacuo*. Flash chromatography (SiO_2, 0.9 × 13.5 cm, 8–20% EtOAc in hexanes gradient elution) afforded **4** (7.6 mg, 0.0358 mmol, 22%) as a light-yellow oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.20 (s, 1H), 5.49 (s, 1H), 3.74 (s, 3H), 2.44 (t, *J* = 8.2 Hz, 2H), 2.28 (s, 2H), 2.16 (s, 3H), 1.48 (t, *J* = 8.2 Hz, 2H), 0.83 (s, 6H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 209.4, 168.6, 138.0, 127.8, 51.9, 42.3, 38.9, 35.3, 33.5, 30.0, 26.3 (2C); IR (film) ν_{max} 3396, 2921, 2851, 2359, 2342, 1652, 1591, 1496, 1375, 1261, 1214, 1103 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{12}H_{20}O_3H$ 213.1485; Found 213.1478.

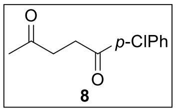


Methyl 2-methylene-7-oxo-4-phenyloctanoate (5). An oven-dried reaction vessel was charged with *O*-phenyloxime **1c** (25.0 mg, 0.0987 mmol), methyl 2-((phenylsulfonyl)methyl)acrylate (**3**, 237 mg, 0.986 mmol, 10.0 equiv), $InCl_3{\cdot}H_2O$ (28.2 mg, 0.127 mmol, 1.3 equiv), $PhCF_3$ (3.5 mL), 2-propanol (150 μL), and H_2O (150 μL). The reaction vessel was then sealed, and the mixture was subjected to microwave irradiation (200 W) at 120 °C for 2 h, then cooled to rt and concentrated *in vacuo*. Flash chromatography (SiO_2, 0.9 × 13.5 cm, 15–20% EtOAc in hexanes gradient elution) afforded **5** (7.7 mg, 0.0296 mmol, 30%) as a light yellow oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.29–7.26 (m, 2H), 7.19 (t, *J* = 7.4 Hz, 1H), 7.10 (d, *J* = 7.0 Hz, 2H), 6.05 (s, 1H), 5.32 (s, 1H), 3.71 (s, 3H), 2.81–2.75 (m, 1H), 2.66 (dd, *J* = 13.8, 6.3 Hz, 1H), 2.54 (dd, *J* = 13.9, 8.4 Hz, 1H), 2.34–2.20 (m, 2H), 2.03 (s, 3H), 2.03–1.98 (m, 1H), 1.85–1.77 (m, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 208.8, 167.6, 143.6, 138.2, 128.5 (2C), 127.7 (2C), 127.0, 126.5, 51.8, 44.1, 41.7, 39.7, 30.0, 29.4; IR (film) ν_{max} 3404, 2923, 2850, 2359, 1717, 1635, 1437, 1306, 1201, 1140, 1101 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{16}H_{20}O_3H$ 261.1485; Found 261.1482.



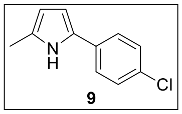
7

5-Phenyl-7-(triisopropylsilyl)hept-6-yn-2-one (7). An oven-dried reaction vessel was charged with *O*-phenyloxime **1c** (17.2 mg, 0.0679 mmol), 1-[(triisopropylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one[18] (**6**, 298.6 mg, 0.6970 mmol, 10.3 equiv), $InCl_3·H_2O$ (19.4 mg, 0.0877 mmol, 1.3 equiv), $PhCF_3$ (3.7 mL), 2-propanol (150 µL), and H_2O (150 µL). The reaction vessel was then sealed, and the mixture was subjected to microwave irradiation (200 W) at 120 °C for 2 h, then cooled to rt and concentrated *in vacuo*. Flash chromatography (SiO_2, 0.9 × 13.5 cm, 10–20% EtOAc in hexanes gradient elution) afforded **7** (2.8 mg, 0.0082 mmol, 12%) as a light yellow oil: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.39 (d, *J* = 7.3 Hz, 2H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.24 (t, *J* = 7.3 Hz, 1H), 3.80 (dd, *J* = 8.7, 5.4 Hz, 1H), 2.71 (ddd, *J* = 17.7, 9.1, 6.7 Hz, 1H), 2.56 (ddd, *J* = 17.7, 9.0, 5.2 Hz, 1H), 2.13 (s, 3H), 2.11–2.06 (m, 1H), 1.94–1.86 (m, 1H), 1.12–1.02 (m, 21H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 208.4, 141.2, 128.4 (2C), 127.4 (2C), 126.8, 108.9, 84.2, 40.9, 37.7, 32.4, 30.1, 18.7 (6C), 11.3 (3C); IR (film) ν_{max} 3396, 2923, 2853, 2361, 1717, 1593, 1489, 1456, 1367, 1158 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{22}H_{34}OSiH$ 343.2452; Found 343.2460.



8

1-(4-Chlorophenyl)pentane-1,4-dione (8). A solution of ketone **2d** (26.0 mg, 0.0739 mmol) and mCPBA (ca. 75% purity, 29.4 mg, 22.0 mg mCPBA, 0.127 mmol, 1.7 equiv) in CH_2Cl_2 (4.5 mL) was stirred at rt for 1.5 h. The reaction was quenched by the addition of sat aq $Na_2S_2O_8$ (1 mL) and extracted with CH_2Cl_2 (2 × 20 mL). The combined organic layers were washed with sat aq Na_2CO_3 (2 × 10 mL) and concentrated *in vacuo*. Flash chromatography (SiO_2, 0.9 × 13.5 cm, 35–50% EtOAc in hexanes gradient elution) afforded **8** (9.9 mg, 0.0470 mmol, 64%) as a colorless oil. Spectral data were identical to the previously reported data.[29]



2-(4-Chlorophenyl)-5-methyl-1*H*-pyrrole (9). A solution of 1,4-diketone **8** (9.9 mg, 0.0470 mmol) and aqueous NH_3 (ca. 30% NH_3, 200 µL, 3.5 mmol, 75 equiv) in CH_3OH (1.5 mL) was stirred at 45 °C for 28 h. The mixture was then filtered through Na_2SO_4 (washed with 20 mL of CH_2Cl_2) and concentrated *in vacuo*. This afforded **9** (6.4 mg, 0.0334 mmol, 71%) as a light-yellow oil. Spectral data were identical to the previously reported data.[30]

Data Availability Statement. The data underlying this study are available in the published article and its online supporting information.

Supporting Information Available. Copies of ^{1}H and ^{13}C NMR spectra for all new compounds, and copies of ^{1}H NMR spectra for known compounds **8** and **9**. This material is available free of charge via the Internet at http://pubs.acs.org.

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