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Photoredox Synthesis of Arylhydroxylamines from Carboxylic Acids and Nitrosoarenes

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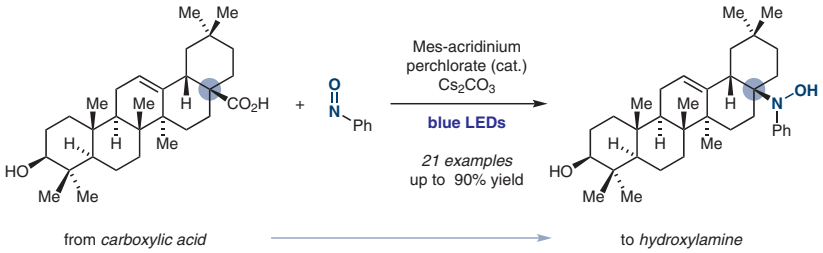

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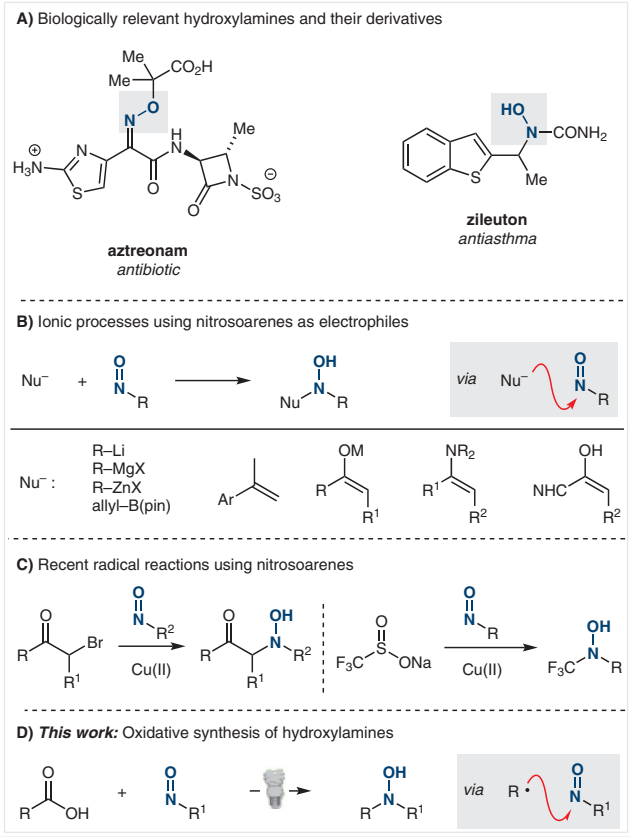
Abstract Hydroxylamines are found in biologically active compounds and serve as building blocks for the preparation of nitrogen-containing molecules. Here the direct conversion of carboxylic acids into the corresponding alkylhydroxylamines using organo-photoredox catalysis is reported. The process relies in the generation of alkyl radicals via photoinduced oxidation-decarboxylation and their following reaction with nitrosoarenes. We have successfully applied this method to the late-stage modification of complex and biologically active acids and applied it in novel radical cascade processes.

Key words hydroxylamines, radical addition, nitrosoarenes, late-stage functionalization, radical cascade, photoredox

Hydroxylamines and their derivatives are a privileged class of compounds with applications spanning from active pharmaceutical ingredients and agrochemicals to versatile building blocks for the synthesis of complex molecules (Scheme 1, A).[1] Despite this relevance, their preparation can still be troublesome and the development of novel strategies able to selectively introduce the hydroxylamine functionality on structurally complex molecules under mild reaction conditions is a relevant goal.

Visible-light photoredox catalysis is now an established and powerful technique to perform single-electron transfer (SET)[2] reactions under mild conditions.[3] In particular, the ability of harvesting carboxylic acids for the generation of sp^3-C-radicals by oxidative decarboxylation has enabled the development of many C–C and C–X (X = F, N_3, S…) bond-forming processes.[4]

Owing to our ongoing interest in the preparation of hydroxylamine derivatives as nitrogen-radical precursors,[5] we wondered if a visible-light-mediated protocol for their direct assembly from simple feedstock chemicals could be developed. In particular, we were interested in the possibility of using carboxylic acids as source of sp^3-C-radicals and to exploit them in the reaction with nitrosoarenes.[6] Such an approach would be complementary to the more established



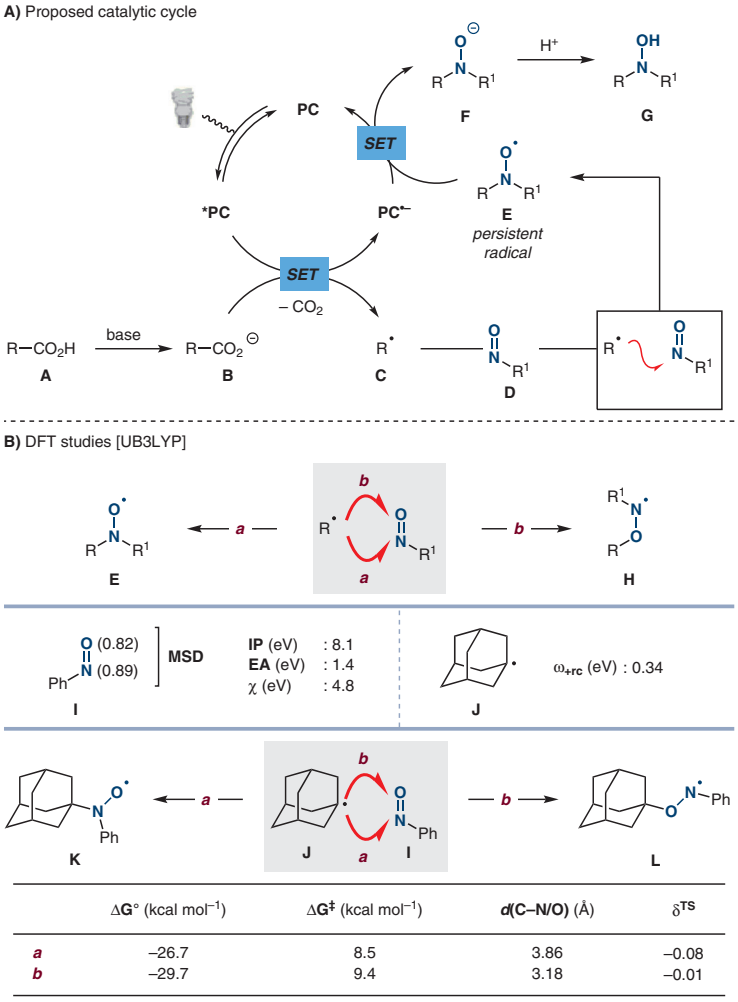
Scheme 1 Relevance of hydroxylamines, previous ionic and radical approaches using nitrosoarenes, and this work

ionic pathways where nitrosoarenes are used as electrophiles in conjunction with organometallic reagents,[7] enolates,[8] and enamine[9]/NHC[10]-based catalytic systems (Scheme 1, B).[11] Furthermore, the preparation of hydroxylamines via radical addition onto nitrosoarenes has been considerably overlooked and only few protocols are available.[12] Most notably, de Alaniz[13] and Selander[14] have recently developed Cu(II)-catalyzed protocols for the coupling of nitrosoarenes with radical deriving from α-bromocarbonyls and sodium triflinate, respectively (Scheme 1, C).

In this paper, we describe the development of the first approach for the generation of hydroxylamines from readily available carboxylic acids and its use in the functionalization of complex and biologically active molecules (Scheme 1, D).

At the outset, we envisioned a catalytic cycle starting with the visible-light-promoted excitation of a photocatalyst and the following oxidative SET decarboxylation of acid **A** upon in situ deprotonation **A** → **B** (Scheme 2, A).[4] This step would deliver the C-radical **C** that would react with a nitrosoarene **D** forging the required C–N bond and delivering the persistent nitroxyl radical **E**.[15] At this point, we speculated that the final hydroxylamine **G** could be obtained by reductive SET of **E** with the reduced photoredox catalyst (to give **F**) and protonation.

In order to obtain information regarding the feasibility of our proposed process, preliminary DFT studies were conducted (Scheme 2, B). We were in fact concerned about the potential addition of the C-radical at both the N (path ***a*** – to give **E**) and the O atom (path ***b*** – to give **H**) of the nitrosoarene, an issue frequently encountered in ionic processes.[7a,8c] We started by characterizing nitrosobenzene **I** in terms of electron donor properties by calculating its adiabatic ionization potential (IP), electron affinity (EA), and absolute electronegativity (χ_{DB}).[16] These values are in line with **I** being a competent radical acceptor. The preferred site of radical attack was then assessed by calculating the N and O atom Mulliken spin densities (MSDs) in the triplet state ($\pi\pi^*$).[16] According to this study, **I** should display a slight



Scheme 2 Proposed photoredox cycle and computational studies on the reaction of nitrosobenzene **I** with the adamantyl radical **J**

preference for the reaction at the N-atom owing to its higher MSD. Further support for this reactivity was obtained upon determination of the activation parameters for the reaction of **I** with the adamantyl radical **J** (nucleophilic radical; ω_{+rc} = 0.34).[17] According to our study both radical pathways (***a***: attack at the N-atom and ***b***: attack at the O-atom) are very exergonic but there is a slight preference for path ***a***, which would support our proposed process.[16] The very low $|\delta^{TS}|$ values also indicate that these radical additions are not influenced very much by polar effects in the transition state and should be predominantly enthalpy controlled.[18]

To assess our working hypothesis, the reaction of adamantane carboxylic acid (**1a**) and nitrosobenzene was investigated using various photoredox catalysts (Figure 1) and bases in CH_2Cl_2 (0.05 M) at room temperature. As illustrated in Table 1, we were pleased to find out that using mesityl acridinium perchlorate **2a** (Fukuzumi's acridinium, $E^*_{1/2}$ = +2.06 V vs SCE)[19] as the photoredox catalyst and Cs_2CO_3 as the base under blue LEDs irradiation, the product **3a** was obtained in good yield (Table 1, entry 1). We then changed the stoichiometry of the reaction (entries 2–4) and found out that a slight excess of nitrosobenzene (2.0 equiv with respect to **1a**) was optimum, providing **3a** in 90% yield (entry 3). Other bases were evaluated and while K_2CO_3 gave **3a** in a useful 62% yield (entry 5); 2,6-lutidine was not compatible and completely suppressed the reactivity (entry 6). We also tried to run the reaction under more concentrated conditions (entries 7 and 8) but this was detrimental. Other photocatalysts **2b–d** were screened but they generally provided **3a** in considerably lower efficiency (if any) (entries 9–11). Lastly, control experiments confirmed the requirement for base, light, and **2a** (entries 12–14).

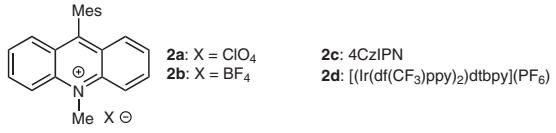
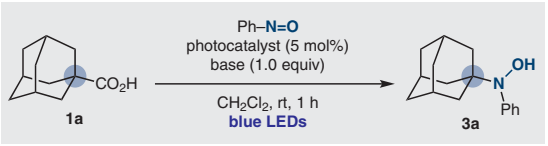


Figure 1 Photoredox catalysts used

With the optimized reaction conditions in hand, the scope of the process using nitrosobenzene and a series of structurally different carboxylic acids was evaluated (Scheme 3). In general, tertiary carboxylic acids worked well and provided the desired hydroxylamines **3b–g** in good yields. This approach tolerated several functional groups like alkyl halides, terminal olefins, carbamates and was effective for accessing C-3 and C-4 aminopiperidines, which are a frequent structural motif in many commercially available drugs (e.g., the antidiabetic alogliptin and the opioid analgesic sufentanil). Secondary carboxylic acids were tried next but unfortunately the use of a secondary mono-benzylic **3h** and a primary alkylic **3i** was not possible, thus representing the limitation of the strategy. Lastly,

Table 1 Optimization of the Visible Light-Mediated Synthesis of Hydroxylamine **3a** from Carboxylic Acid **1a**



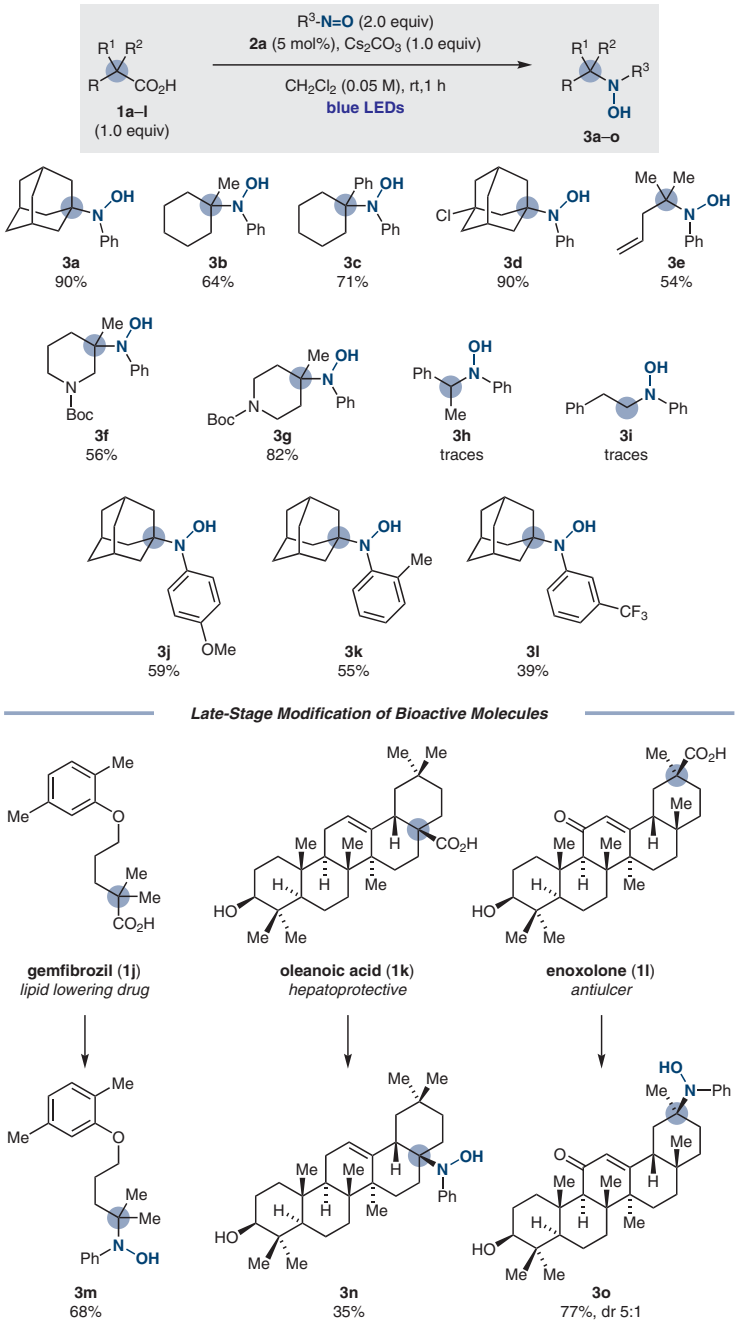
Entry	PC[a]	**1a**/PhNO	Base	[M]	Yield (%)
1	**2a**	1:1	Cs_2CO_3	0.05	58
2	**2a**	1:1.1	Cs_2CO_3	0.05	72
3	**2a**	1:2	Cs_2CO_3	0.05	90
4	**2a**	2:1	Cs_2CO_3	0.05	70
5	**2a**	1:2	K_2CO_3	0.05	62
6	**2a**	1:2	2,6-lutidine	0.05	–
7	**2a**	1:2	Cs_2CO_3	0.1	50
8	**2a**	1:2	Cs_2CO_3	0.2	36
9	**2b**	1:2	Cs_2CO_3	0.05	75
10	**2c**[b]	1:2	Cs_2CO_3	0.05	–
11	**2d**[c]	1:2	Cs_2CO_3	0.05	–
12	**2a**	1:2	Cs_2CO_3	0.05	–
13[b]	**2a**	1:2	Cs_2CO_3	0.05	–
14	–	1:2	Cs_2CO_3	0.05	–

[a] Photoredox catalyst.
[b] 1,2,3,5-Tetrakis(carbazol-9-yl)-4,6-dicyanobenzene.
[c] [Ir[dF(CF$_3$)ppy]$_2$(dtbpy)]PF$_6$ [[4,4′-bis(1,1-dimethylethyl)-2,2′-bipyridine-N^1,$N^{1'}$]bis[3,5-difluoro-2-[5-(trifluoromethyl)-2-pyridinyl-*N*]phenyl-C]iridium(III) hexafluorophosphate].
[d] The reaction was carried out in the dark.

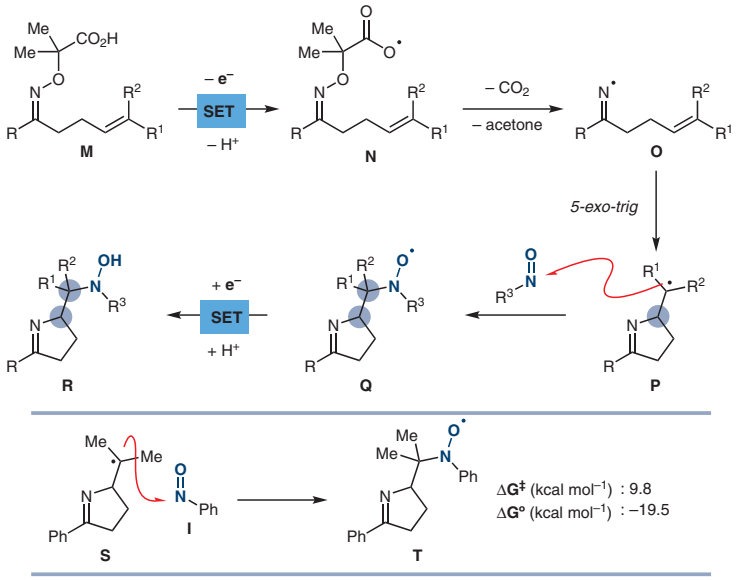
we evaluated the use of functionalized nitrosoarenes in conjunction with adamantine carboxylic acid (**1a**) and found them compatible. Both electron-rich **3j** and *ortho*-substituted **3k** derivatives reacted well. Substrates containing an electron-withdrawing CF_3-group **3l** could also be employed, albeit in lower yield.

We were particularly keen in showcasing the utility of the methodology by using high-value and structurally complex carboxylic acids in order to provide access to the corresponding hydroxylamines. As reported in Scheme 3, this approach was successfully used to modify the blockbuster drug gemfibrozil (**1j** → **3m**), which is used to lower lipid levels. Furthermore, we were able to selectively introduce the hydroxylamine functionality on the core of the highly complex hepatoprotective oleanoic acid (**1k** → **3n**) and the antiulcer drug enoxolone (**1l** → **3o**). Overall, these examples show that the methodology can be used as a late-stage modification techniques, which tolerates redox active functionalities such as electron rich aromatics (which could undergo SET oxidation), enones (which can be photo-excited upon visible-light irradiation as demonstrated by Lectka)[20] as well as free hydroxyl groups.

We then decided to evaluate if this radical decarboxylative process could be part of a cascade sequence leading to the concomitant formation of two C–N bond across an olefin. We have recently developed a divergent photoredox imino-functionalization strategy for the assembly of polyfunctionalized pyrroline-based heterocycles.[5b] Specifically, we envisaged a cascade process starting with the SET oxidation-fragmentation of the oxime **M** (Scheme 4). This would deliver an iminyl radical **O** (**M** → **N** → **O**) that would undergo fast 5-*exo*-*trig* cyclization resulting in the C-radical **P**. At this point, radical attack onto the nitrosoarene and SET reduction and protonation of the persistent nitroxyl radical **Q** would enable the formation of **R**. Also in this case, we have evaluated the key radical reaction between nitrosobenzene **I** and the Ph-dimethyl-substituted C-radical **S** (to give **T**) by DFT and found it feasible.[16]

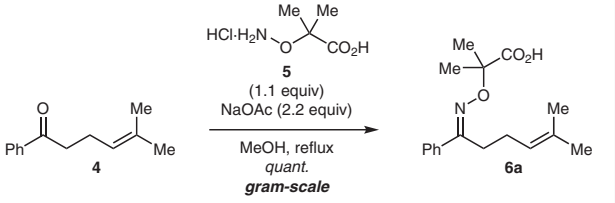


Scheme 3 Scope of the process for the synthesis of hydroxylamines **3**



Scheme 4 Proposed cascade for the imino-hydroxylamination of olefins via iminyl radicals and preliminary DFT studies

The implementation of this strategy was assessed using the oxime **6a**, which was prepared by condensation of the ketone **4** with commercially available 2-(aminooxy)-2-methylpropanoic acid (**5**) on a gram-scale (Scheme 5).



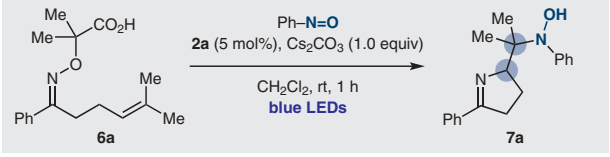
Scheme 5 Preparation of oxime **6a** from ketone **5**

As illustrated in Table 2, we were pleased to find out that by irradiating (blue LEDs) a solution of **6a** and nitrosobenzene (1:2) using **2a** as the photoredox catalyst, Cs_2CO_3 as the base in CH_2Cl_2 (0.1 M), the product **7a** was obtained in 48% (Table 2, entry 1). In this case however, increasing the amount of nitrosobenzene with respect to **6a** was detrimental (entries 2 and 3) and eventually a ratio of 1:1.1 (entry 4) and a reaction concentration of 0.05 M were identified to be optimum for this transformation (entry 5). Also in this case control experiments confirmed the requirement for base, **2a**, and blue LEDs for irradiation (entries 6–8).

With this optimized conditions in hand, other iminyl radical precursors were tested (Scheme 6). We were able to engage substrate containing pyridine **6b** and ester **6c** functionalities giving access to pyrrolines **7b** and **7c** that can be used for the preparation of nicotine and proline analogues. Interestingly, in this case we were able to engage a secondary α-ester radical **7d** in the cascade cyclization-functionalization reaction.

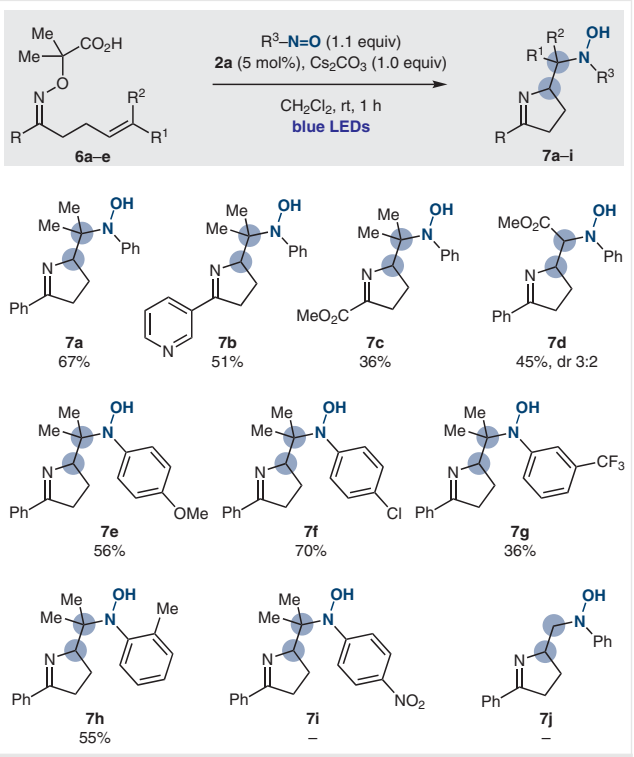
Other nitrosoarenes were compatible with the process as shown by the formation of products **7a–h** in good to moderate yields. Also in this case, the use of highly electron poor nitrosoarene **7i** as well as the trapping primary C-radicals (e.g., following cyclization onto a terminal olefin **7j**) was not possible representing the limit of the strategy. Overall, this cascade process generates molecules contain-

Table 2 Optimization of the Imino-Hydroxylamination Cascade Using Oxime **6a**



Entry	**6a**/PhNO	[M]	Yield (%)
1	1:2	0.1	48
2	1:3	0.1	26
3	1:4	0.1	16
4	1:2	0.05	53
5	1:1.1	0.05	60
6	1:1.1	0.05	67
7[a]	1:1.1	0.05	–
8[b]	1:1.1	0.05	–
9[c]	1:1.1	0.05	–

[a] The reaction was run in the dark.
[b] The reaction was run without **2a**.
[c] The reaction was run without Cs_2CO_3.



Scheme 6 Scope of the process for the synthesis of hydroxylamines **7**

ing two nitrogen functionalities, imine and hydroxylamines, which can be orthogonally functionalized and further modified.

In conclusion we have developed a photoredox decarboxylative approach for the formation of hydroxylamines and demonstrated its application in late-stage functionalizations and radical imino-hydroxylamination cascades.

All required fine chemicals were used directly without purification, unless stated otherwise. All air and moisture sensitive reactions were carried out under N_2 atmosphere using standard Schlenk manifold technique. ^1H and ^{13}C NMR spectra (abbreviations: M = major; m = minor) were acquired at various field strengths as indicated and were referenced to $CHCl_3$(7.27 and 77.0 ppm for ^1H and ^{13}C, respectively). High-resolution mass spectra were obtained using a JEOL JMS-700 spectrometer or a Fissions VG Trio 2000 quadrupole mass spectrometer. Spectra were obtained using electron impact ionization (EI) and chemical ionization (CI) techniques, or positive electrospray (ES). IR spectra were recorded using a JASCO FT/IR 410 spectrophotometer or using an ATI Mattson Genesis Seris FTIR spectrometer as evaporated films or liquid films. Flash column chromatography was performed using Merck Silica Gel 60 (40–63 µm). All the reactions were conducted in CEM 10 mL glass microwave tube using the EvoluChem PhotoRedOx Box.

The syntheses of the precursor ketones and oximes **6a–e** are described in the Supporting Information.

Hydroxylamines 3a–o; General Procedure 1 (GP1)

A dry tube equipped with a stirring bar was charged with the carboxylic acid **1a–l** (0.2 mmol, 1.0 equiv), **2a** (4.0 mg, 10 µmol, 5 mol%), Cs_2CO_3 (66 mg, 0.1 mmol, 1.0 equiv), and the requisite nitrosoarene (0.4 mmol, 2.0 equiv). The tube was capped with a Supelco aluminum crimp seal with septum (PTFE/butyl) and it was evacuated and refilled with N_2(3 ×). CH_2Cl_2 (anhydrous and degassed by bubbling through with N_2 for 20 min; 4.0 mL) was added. The N_2 inlet was then removed and the cap sealed with parafilm. The mixture was stirred at r.t. for 1 h in front of blue LEDs. The tube was opened to air and the mixture was diluted with CH_2Cl_2 (5 mL) and brine (5 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried ($MgSO_4$), filtered, and evaporated. Purification by column chromatography on silica gel gave **3a–o**.

N-[(3*s*,5*s*,7*s*)-Adamantan-1-yl]-*N*-phenylhydroxylamine (3a)

Following GP1, 1-adamantanecarboxylic acid (**1a**; 36 mg, 0.2 mmol) gave **3a** (44 mg, 90%) as a brown solid, purified by column chromatography (CH_2Cl_2).

IR (film): 2905, 2850, 1595, 1486, 1451, 1357, 1306, 1209, 1209, 1103, 1074 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 7.21 (4 H, dt, *J* = 15.4, 7.7 Hz), 7.10 (1 H, t, *J* = 7.0 Hz), 6.58 (1 H, br s), 2.04 (2 H, br s), 1.77–1.71 (6 H, d, *J* = 2.0 Hz), 1.57 (6 H, q, *J* = 12.0 Hz).

^{13}C NMR ($CDCl_3$, 101 MHz): δ = 147.9, 127.3, 125.1, 124.9, 60.5, 38.5, 36.5, 29.4.

MS (EI): *m*/*z* = 227 (MH – OH), 170, 135, 107.

HRMS (ASAP): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{22}NO$: 244.1696; found: 244.1691.

N-(1-Methylcyclohexyl)-*N*-phenylhydroxylamine (3b)

Following GP1, 1-methyl-1-cyclohexanecarboxylic acid (**1b**; 28 mg, 0.2 mmol) gave **3b** (26 mg, 64%) as a brown solid, purified by column chromatography (pentane/CH_2Cl_2 1:1).

IR (film): 2925, 2857, 2361, 1596, 1487, 1449, 1372, 1120, 1028 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 7.33 (2 H, br d, *J* = 7.8 Hz), 7.28 (2 H, t, *J* = 7.8 Hz), 7.17 (1 H, t, *J* = 7.1 Hz), 1.73–1.65 (3 H, m), 1.58–1.51 (3 H, m), 1.42–1.27 (4 H, m), 1.09 (3 H, s).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 128.6, 127.4, 125.8, 124.3, 34.4, 29.4, 25.44, 22.3, 17.5.

MS (EI): *m*/*z* = 205 [M]$^+$, 189, 146, 109.

HRMS (HESI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{20}NO$: 206.1539; found: 206.1540.

N-Phenyl-*N*-(1-phenylcyclohexyl)hydroxylamine (3c)

Following GP1, 1-phenylcyclohexane-1-carboxylic acid (**1c**; 41 mg, 0.2 mmol) gave **3c** (38 mg, 71%) as an orange solid, purified by column chromatography (pentane/CH_2Cl_2 1:1).

IR (film): 2929, 2861, 1593, 1484, 1456, 1447, 1204, 1152, 1037 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 7.32–7.11 (5 H, m), 7.15–6.99 (3 H, m), 6.71 (2 H, d, *J* = 7.6 Hz), 5.98 (1 H, br s), 2.41 (2 H, d, *J* = 12.6 Hz), 1.90 (2 H, t, *J* = 11.7 Hz), 1.66 (2 H, d, *J* = 9.5 Hz), 1.49 (1 H, d, *J* = 4.7 Hz), 1.39–1.12 (3 H, m).

^{13}C NMR ($CDCl_3$, 101 MHz): δ = 148.6, 138.0, 129.1, 127.5, 127.1, 126.9, 125.1, 124.9, 68.1, 33.4, 26.1, 22.7.

MS (EI): *m*/*z* = 267 [MH – OH], 251, 208, 182, 159.

HRMS (HESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{22}NO$: 268.1696; found: 268.1699.

N-[(1*r*,3*s*,5*R*,7*S*)-3-Chloroadamantan-1-yl]-*N*-phenylhydroxylamine (3d)

Following GP1, 3-chloroadamantane-1-carboxylic acid (**1d**; 43 mg, 0.2 mmol) gave **3d** (50 mg, 90%) as a brown solid, purified by column chromatography (pentane/CH_2Cl_2 1:1).

IR (film): 2913, 2859, 1595, 1487, 1450, 1349, 1328, 1303, 1204, 1154, 1074 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.25 (2 H, t, *J* = 7.5 Hz), 7.17 (2 H, d, *J* = 7.7 Hz), 7.13 (1 H, t, *J* = 7.2 Hz), 6.93 (1 H, br s), 2.21 (1 H, br s), 1.97 (4 H, q, *J* = 12.0 Hz), 1.72 (2 H, d, *J* = 11.7 Hz), 1.68 (2 H, q, *J* = 11.7 Hz), 1.58–1.37 (2 H, m).

^{13}C NMR ($CDCl_3$, 101 MHz): δ = 147.4, 127.7, 125.7, 124.8, 68.5, 63.4, 47.8, 46.7, 37.2, 34.5, 31.5.

MS (EI): *m*/*z* = 261 [MH – OH], 227 (MH – OH – Cl), 204, 170, 133.

HRMS (HESI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{21}NO$: 278.1306; found: 278.1304.

N-(2-Methylbut-3-en-2-yl)-*N*-phenylhydroxylamine (3e)

Following GP1, 2,2-dimethylpent-4-enoic acid (**1e**; 26 mg, 0.2 mmol) gave **3e** (21 mg, 54%) as an orange solid, purified by column chromatography (CH_2Cl_2).

IR (film): 3070, 2976, 2933, 1639, 1596, 1487, 1450, 1382, 1362, 1260, 1230, 1206, 1151, 1077, 1027 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.31–7.23 (4 H, m), 7.19–7.08 (1 H, m), 5.93 (1 H ddt, *J* = 15.8, 10.9, 7.4 Hz), 5.79 (1 H, br s), 5.08 (1 H, d, *J* = 1.4 Hz), 5.07–4.99 (1 H, m), 2.34 (2 H, d, *J* = 7.3 Hz), 1.08 (6 H, s).

^{13}C NMR ($CDCl_3$, 101 MHz): δ = 149.2, 135.6, 127.6, 125.2, 124.8, 117.2, 63.0, 43.6, 23.2.

MS (EI): *m*/*z* = 190 [M]$^+$, 150, 133, 109.

HRMS (HESI): *m*/*z* [M + Na]$^+$ calcd for $C_{12}H_{17}NONa$: 213.1124; found: 213.1125.

tert-Butyl 3-[Hydroxy(phenyl)amino]-3-methylpiperidine-1-carboxylate (3f)

Following GP1, 1-*N*-Boc-3-methylpiperidine-3-carboxylic acid (**1f**; 49 mg, 0.2 mmol) gave **3f** (34 mg, 56%) as a brown solid, purified by column chromatography (CH_2Cl_2).

IR (film): 3350, 2975, 2359, 1692, 1661, 1597, 1488, 1453, 1425, 1392, 1365, 1284, 1161, 1087 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ (rotamers) = 7.26 (4 H, m), 7.15 (1 H s), 7.12–7.07 (1 H, m), 4.35 (0.8 H, d, *J* = 13.8 Hz), 4.02 (0.8 H d, *J* = 12.9 Hz), 3.78–3.70 (0.2 H, m), 3.57 (0.2 H, br s), 3.32–3.17 (0.4 H, m), 2.88 (0.8 H, t, *J* = 12.2 Hz), 2.65 (0.8 H, d, *J* = 13.9 Hz), 2.15 (0.8 H, q, *J* = 12.2 Hz), 1.93 (0.2 H, br s), 1.68 (1.2 H, d, *J* = 13.3 Hz), 1.47 (9 H, s), 1.43–1.28 (2 H, m), 0.94 (3 H, m).

^{13}C NMR ($CDCl_3$, 101 MHz): δ (rotamers) = 157.2 (M), 154.9 (m), 149.3 (M), 148.8 (m), 127.8 (M + m), 125.4 (m), 125.0 (M), 124.5 (m), 124.4 (M), 80.2 (M + m), 61.6 (m), 61.1 (M), 53.1 (M + m), 46.3 (M), 44.3 (m), 34.9 (M), 34.4 (m), 28.6 (M + m), 21.7 (M), 21.6 (m), 17.3 (M), 16.7 (m).

MS (EI): *m*/*z* = 290 [MH – OH], 217, 190, 160, 132.

HRMS (HESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{27}N_2O_3$: 307.2016; found: 307.2016.

tert-Butyl 4-[Hydroxy(phenyl)amino]-4-methylpiperidine-1-carboxylate (3g)

Following GP1, 1-*N*-Boc-4-methylpiperidine-4-carboxylic acid (**1g**; 49 mg, 0.2 mmol) gave **3g** (50 mg, 82%) as a brown oil, purified by column chromatography (CH_2Cl_2 → CH_2Cl_2/MeOH 99:1.)

IR (film): 3390, 2973, 2929, 1692, 1669, 1596, 1486, 1425, 1391, 1366, 1348, 1279, 1262, 1245, 1153, 1125, 1092, 1026 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ (rotamers) = 7.31–7.21 (4 H, m), 7.19–7.11 (1 H, m), 3.78 (2 H, br s), 3.18–3.04 (2 H, m), 1.94–1.74 (2 H, m,), 1.57–1.37 (11 H, m), 1.09 (3 H, s).

^{13}C NMR ($CDCl_3$, 101 MHz): δ (rotamers) = 154.9, 148.6, 127.7, 125.5, 124.8, 79.4, 61.2, 34.8, 31.0, 28.5, 17.3.

MS (EI): *m*/*z* = 290 [MH – OH]$^+$, 233, 189, 141.

HRMS (HESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{27}N_2O_3$: 307.2016; found: 307.2018.

N-[(3*s*,5*s*,7*s*)-Adamantan-1-yl]-*N*-(4-methoxyphenyl)hydroxylamine (3j)

Following GP1, 1-adamantanecarboxylic acid (**1a**; 36 mg, 0.2 mmol) gave **3j** (32 mg, 59%) as a red solid, purified by column chromatography (CH_2Cl_2 → CH_2Cl_2/MeOH 99.5:0.5).

IR (film): 2905, 2850, 1502, 1454, 1298, 1245, 1210, 1182, 1106, 1034 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.11 (2 H, d, *J* = 8.2 Hz), 6.78 (2 H, d, *J* = 8.2 Hz), 3.82 (3 H, s), 2.05 (3 H, s), 1.74 (6 H, s), 1.59 (6 H, q, *J* = 12.1 Hz).

^{13}C NMR ($CDCl_3$, 101 MHz): δ = 156.3, 140.1, 125.3, 111.8, 59.6, 54.7, 44.7, 37.8, 35.8, 35.34 30.0, 28.7.

MS (EI): *m*/*z* = 257 (MH – OH), 242 (M – OMe), 214, 200, 163, 135.

HRMS (ASAP): *m*/*z* [M]$^+$ calcd for $C_{17}H_{23}NO_2$: 273.1723; found: 273.1726.

N-[(3*s*,5*s*,7*s*)-Adamantan-1-yl]-*N*-(*o*-tolyl)hydroxylamine (3k)

Following GP1, 1-adamantanecarboxylic acid (**1a**; 36 mg, 0.2 mmol) gave **3k** (28 mg, 55%) as a red solid, purified by column chromatography (pentane/CH_2Cl_2 3:1 → 1:1).

IR (film): 2905, 2850, 1487, 1452, 1356, 1307, 1103, 1080 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.48 (1 H, d, *J* = 8.0 Hz), 7.18 (1 H, t, *J* = 7.5 Hz), 7.14 (1 H, d, *J* = 7.3 Hz), 7.08 (1 H, t, *J* = 7.3 Hz), 5.11 (1 H, br s), 2.32 (3 H, s), 2.06 (3 H, s, br), 1.83 (6 H, br s).

^{13}C NMR ($CDCl_3$, 101 MHz): δ = 147.1, 135.1, 130.1, 127.0, 125.6, 125.3, 61.5, 38.2, 36.7, 29.5, 19.1.

MS (EI): *m*/*z* = 257 [M]$^+$, 241, 184, 135.

HRMS (ASAP): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{24}NO$: 258.1852; found: 258.1845.

N-[(3*s*,5*s*,7*s*)-Adamantan-1-yl]-*N*-[3-(trifluoromethyl)phenyl]-hydroxylamine (3l)

Following GP1, 1-adamantanecarboxylic acid (**1a**; 36 mg, 0.2 mmol) gave **3l** (24 mg, 39%) as an orange solid, purified by column chromatography (pentane/CH_2Cl_2 2:1 → 1:1).

IR (film): 2907, 2853, 1439, 1325, 1306, 1164, 1068, 1123, 1094, 1068 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.41 (1 H, s), 7.30 (4 H, m), 6.55 (1 H, br s), 2.08 (3 H, br s), 1.75 (6 H, s), 1.63 (3 H, d, *J* = 11.6 Hz), 1.55 (3 H, d, *J* = 11.5 Hz).

^{13}C NMR ($CDCl_3$, 101 MHz): δ = 148.5, 129.8 (q, *J* = 31.9, 31.3 Hz), 127.9, 127.7, 124.0 (q, *J* = 273.1 Hz), 121.7, 121.4, 60.8, 38.4, 36.4, 29.3.

^{19}F NMR ($CDCl_3$, 376 MHz): δ = –62.5.

MS (EI): *m*/*z* = 311 $[M]^+$, 295, 275, 238, 135.

HRMS (ASAP): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{21}F_3NO$: 312.1570; found: 312.1566.

N-[5-(2,5-Dimethylphenoxy)-2-methylpentan-2-yl]-*N*-phenylhydroxylamine (3m)

Following GP1, gemfibrozil (**1j**; 50 mg, 0.2 mmol) gave **3m** (42 mg, 68%) as a brown solid, purified by column chromatography (CH_2Cl_2).

IR (film): 2923, 1615, 1585, 1508, 1486, 1451, 1413, 1384, 1361, 1284, 1264, 1208, 1156, 1129, 1077, 1046, 1002 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.26–7.21 (4 H, m), 7.15–7.07 (1 H, m), 7.00 (1 H, d, *J* = 7.4 Hz), 6.66 (1 H, d, *J* = 7.4 Hz), 6.60 (1 H, br s), 3.86 (2 H, t, *J* = 6.3 Hz), 2.32 (3 H, s), 2.16 (3 H, s), 1.95–1.77 (2 H, m), 1.78–1.62 (2 H, m), 1.08 (6 H, s).

^{13}C NMR ($CDCl_3$, 101 MHz): δ = 157.0, 149.3, 136.4, 130.3, 127.6, 125.1, 124.7, 123.5, 120.6, 112.1, 68.3, 62.8, 35.6, 24.5, 23.0, 21.4, 15.8.

MS (EI): *m*/*z* = 296 [M – OH], 282, 204, 160, 135.

HRMS (HESI): *m*/*z* $[M + Na]^+$ calcd for $C_{20}H_{26}NO_2Na$: 335.1856; found: 335.1860.

N-[(4a*S*,6a*S*,6b*R*,8a*S*,12a*S*,12b*R*,14b*S*)-2,2,6a,6b,9,9,12a-Heptamethyl-1,3,4,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicen-4a(2*H*)-yl]-*N*-phenylhydroxylamine (3n)

Following GP1, oleanoic acid (**1k**; 91 mg, 0.2 mmol) gave **3n** (36 mg, 35%) as a red solid, purified by column chromatography (CH_2Cl_2).

IR (film): 2945, 1486, 1463, 1386, 1364, 1263, 1028 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.42–7.33 (2 H, d, *J* = 7.7 Hz), 7.26 (2 H, t, *J* = 7.7 Hz), 7.08 (1 H, t, *J* = 7.3 Hz), 5.21 (1 H, t, *J* = 3.4 Hz), 4.76 (1 H, br s), 3.32–3.13 (1 H, m), 2.49 (1 H, d, *J* = 13.0 Hz), 2.26–2.15 (1 H, m), 2.16–2.04 (1 H, m), 2.05–1.88 (2 H, m), 1.82–1.69 (2 H, m), 1.68–1.54 (7 H, m), 1.53–1.46 (2 H, m), 1.45–1.40 (2 H, m), 1.39–1.29 (2 H, m), 1.28–1.24 (2 H, m), 1.21 (3 H, s), 1.17–1.09 (2 H, m), 1.05 (3 H, s), 1.02 (3 H, s), 0.96 (3 H, s), 0.83 (3 H, s), 0.81 (3 H, s), 0.62 (3 H, s).

^{13}C NMR ($CDCl_3$, 101 MHz): δ = 149.6, 146.2, 127.5, 124.3, 124.2, 122.5, 79.1, 65.4, 55.3, 53.5, 48.3, 48.0, 43.0, 42.0, 39.6, 38.8, 38.4, 37.2, 37.1, 35.4, 32.6, 32.8, 30.8, 28.3, 27.3, 26.6, 26.4, 24.4, 23.9, 23.7, 23.6, 18.4, 17.6, 15.7, 15.3.

MS (EI): *m*/*z* = 410, 406, 395, 392.

HRMS (HESI): *m*/*z* $[M + H]^+$ calcd for $C_{35}H_{54}NO_2$: 520.4149; found: 520.4157.

(2*S*,4a*S*,6a*S*,6b*R*,8a*R*,10*S*,12a*S*,12b*R*,14b*R*)-10-Hydroxy-2-[hydroxy(phenyl)amino]-2,4a,6a,6b,9,9,12a-heptamethyl-1,3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,14b-octadecahydropicen-13(2*H*)-one (3o)

Following GP1, enoxolone (glycyrrhetinic acid, **1l**; 91 mg, 0.2 mmol) gave **3o** (82 mg, 77%) as an orange solid, purified by column chromatography (CH_2Cl_2 → CH_2Cl_2/MeOH 98:2); dr = 5:1.

IR (film): 3351, 2927, 1651, 1486, 1455, 1386, 1260, 1206, 1112, 1037 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ (diastereomers) = 7.24 (4 H, m), 7.13 (1 H, t, *J* = 6.9 Hz), 5.63 (0.2 H, d), 5.55 (0.8 H, s), 3.23 (1 H, dd, *J* = 10.6, 5.6 Hz), 2.79 (1 H, dt, *J* = 13.5, 3.5 Hz), 2.16–1.98 (2 H, m), 1.86–1.72 (2 H, m), 1.74–1.55 (8 H, m), 1.49–1.32 (5 H, m), 1.33 (3 H, s), 1.12 (7 H, m), 1.09 (3 H, s), 1.01 (3 H, s), 0.95 (2 H, m), 0.86–0.68 (6 H, m).

^{13}C NMR ($CDCl_3$, 126 MHz): δ (diastereomers) = 199.8 (m), 199.7 (M), 169.8 (m), 168.8 (M), 149.4 (m), 147.7 (M), 127.8 (M), 127.7 (m), 127.3 (m), 127.1 (M), 125.0 (M), 124.4 (M + m), 123.5 (m), 78.3 (m), 78.2 (M), 63.3 (M), 61.8 (m), 61.6 (m), 61.2 (M), 54.5 (m), 54.4 (M), 47.4 (M), 45.8 (m), 44.8 (M + m), 42.9 (m), 42.7 (M), 41.4 (m), 39.3 (M), 38.7 (M + m), 38.6 (M + m), 36.6 (M + m), 36.3 (M), 35.4 (m), 32.5 (m), 32.3 (M), 32.2 (M + m), 31.7 (M), 31.2 (m), 29.1 (M), 28.1 (m), 27.8 (M + m), 27.7 (M + m), 27.6 (M + m), 26.8 (M), 26.4 (m), 26.0 (m), 25.8 (M), 22.9 (M), 22.8 (m), 18.2 (M), 17.0 (M + m), 16.4 (m), 15.8 (M + m), 15.1 (M + m).

MS (EI): *m*/*z* = 515 (M – OH_2), 424 (M–H – NOHPh), 257, 216, 175, 135, 91.

HRMS (ASAP): *m*/*z* $[M + H]^+$ calcd for $C_{35}H_{52}NO_3$: 534.3942; found: 534.3949.

Hydroxylamines 7; General Procedure 2 (GP2)

A dry tube equipped with a stirring bar was charged with the carboxylic acid **6a–d** (0.1 mmol, 1.0 equiv), **2a** (2.0 mg, 5 µmol, 5 mol%), Cs_2CO_3 (33 mg, 0.1 mmol, 1.0 equiv), and the requisite nitrosoarene (0.11 mmol, 1.1 equiv). The tube was capped with a Supelco aluminum crimp seal with septum (PTFE/butyl) and it was evacuated and refilled with N_2(3 ×). CH_2Cl_2 (anhydrous and degassed by bubbling through with N_2 for 20 min) (2.0 mL) was added. The N_2 inlet was then removed and the cap sealed with parafilm. The mixture was stirred at r.t. for 1 h in front of blue LEDs. The tube was opened to air and the mixture was diluted with CH_2Cl_2 (5 mL) and brine (5 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried ($MgSO_4$), filtered, and evaporated. Purification by column chromatography on silica gel gave **7a–h**.

N-Phenyl-*N*-[2-(5-phenyl-3,4-dihydro-2*H*-pyrrol-2-yl)propan-2-yl]hydroxylamine (7a)

Following GP2, **6a** (58 mg, 0.2 mmol) gave **7a** (39 mg, 67%) as a brown solid, purified by column chromatography (CH_2Cl_2 → CH_2Cl_2/MeOH 99.8:0.2).

IR (film): 3212, 2978, 1618, 1596, 1576, 1486, 1448, 1342, 1168, 1063 cm^{-1}.

^{1}H NMR ($CDCl_3$, 101 MHz): δ = 7.89 (2 H, dd, *J* = 8.0, 1.4 Hz), 7.49–7.39 (5 H, m), 7.30 (2 H, t, *J* = 7.9 Hz), 7.13 (1 H, t, *J* = 7.3 Hz), 4.37 (1 H, t, *J* = 8.2 Hz), 3.04 (1 H, dddd, *J* = 16.8, 10.3, 3.0, 2.5 Hz), 2.83 (1 H, dtd, *J* = 11.6, 9.5, 2.3 Hz), 2.07 (1 H, dddd, *J* = 11.3, 9.8, 8.0, 3.3 Hz), 1.85–1.74 (1 H, (m), 1.27 (3 H, s), 1.11 (3 H, s).

^{13}C NMR ($CDCl_3$, 101 MHz): δ = 173.3, 149.2, 133.5, 131.2, 128.7, 129.0, 127.8, 125.2, 125.0, 78.6, 65.1, 34.1, 25.4, 25.1, 18.2.

MS (EI): *m*/*z* = 278 (MH – OH), 170, 144, 134, 77.

HRMS (APCI): *m*/*z* $[M + H]^+$ calcd for $C_{19}H_{22}N_2O$: 294.1727; found: 294.1725.

N-Phenyl-*N*-{2-[5-(pyridin-3-yl)-3,4-dihydro-2*H*-pyrrol-2-yl]-propan-2-yl}hydroxylamine (7b)

Following GP2, **6b** (29 mg, 0.1 mmol) gave **7b** (15 mg, 51%) as a brown oil, purified by column chromatography (CH_2Cl_2 → CH_2Cl_2/MeOH 99.5:0.5).

IR (film): 2979, 1620, 1594, 1485, 1413, 1377, 1358, 1342, 1168, 1071, 1026 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 9.00 (1 H, d, *J* = 2.2 Hz), 8.70 (1 H, dd, *J* = 4.8, 1.7 Hz), 8.25 (1 H, dt, *J* = 7.9, 2.0 Hz), 7.41–7.35 (3 H, m), 7.33–7.24 (2 H, m), 7.15–7.10 (1 H, m), 4.43 (1 H, tt, *J* = 8.2, 2.4 Hz), 3.05 (1 H, dddd, *J* = 17.3, 10.4, 3.5, 2.3 Hz), 2.93–2.79 (1 H, m), 2.11 (1 H, dddd, *J* = 13.2, 9.8, 8.0, 3.5 Hz), 1.87 (1 H, ddt, *J* = 13.1, 10.3, 8.6 Hz), 1.24 (3 H, s), 1.08 (3 H, s).

^{13}C NMR ($CDCl_3$, 101 MHz): δ = 171.1, 151.8, 149.3, 149.1, 135.0, 129.4, 127.8, 125.1, 125.1, 123.6, 79.0, 65.3, 34.2, 25.1, 23.9, 18.3.

MS (EI): *m*/*z* = 279 (MH – OH), 236, 171, 147, 134, 118, 91, 77.

HRMS (ASAP): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{22}N_3O$: 296.1757; found: 296.1758.

Methyl 2-{2-[Hydroxy(phenyl)amino]propan-2-yl}-3,4-dihydro-2*H*-pyrrole-5-carboxylate (7c)

Following GP2, **6c** (54 mg, 0.2 mmol) gave **7c** (20 mg, 36%) as a brown oil, purified by column chromatography (CH_2Cl_2 → CH_2Cl_2/MeOH 99.5:0.5).

IR (film): 2952, 1723, 1596, 1488, 1439, 1325, 1243, 1167, 1111 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 7.29 (4 H, m), 7.13 (1 H, t, *J* = 6.7 Hz), 6.45 (1 H, br s), 4.55 (1 H, tt, *J* = 8.2, 2.8 Hz), 3.88 (3 H, s), 2.92 (1 H, ddt, *J* = 17.7, 10.4, 3.4 Hz), 2.83–2.69 (1 H, m), 2.10–2.00 (1 H, m), 1.94 (1 H, dq, *J* = 13.4, 8.6 Hz), 1.23 (3 H, s), 0.96 (3 H, s).

^{13}C NMR ($CDCl_3$, 101 MHz): δ = 167.8, 163.2, 149.0, 127.8, 125.3, 125.1, 124.0, 80.5, 65.5, 52.8, 35.6, 24.3, 21.5, 19.2.

MS (EI): *m*/*z* = 260 (MH – OH), 185, 134, 77.

HRMS (ASAP): *m*/*z* $[M + H]^+$ calcd for $C_{15}H_{21}N_2O_3$: 277.1547; found: 277.1547.

Methyl 2-[Hydroxy(phenyl)amino]-2-(5-phenyl-3,4-dihydro-2*H*-pyrrol-2-yl)acetate (7d)

Following GP2, **6d** (34 mg, 0.2 mmol) gave **7d** (29 mg, 45%) as a brown oil, purified by column chromatography (CH_2Cl_2 → CH_2Cl_2/MeOH 99.5:0.5); dr = 3:2.

IR (film): 3059, 2950, 1737, 1614, 1597, 1578, 1520, 1489, 1447, 1434, 1342, 1259, 1197, 1155 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 7.85–7.79 (2 H, m), 7.48–7.36 (4 H, m), 7.32–7.27 (1 H, m), 7.14 (0.8 H, d, *J* = 7.9 Hz), 7.09 (1.2 H, d, *J* = 7.8 Hz), 7.00–6.87 (1 H, m), 4.97–4.88 (1 H, m), 4.48 (0.6 H, d, *J* = 6.4 Hz), 4.33 (0.4 H, d, *J* = 7.4 Hz), 3.72 (1.2 H, s), 3.71 (1.8 H, s), 3.11 (1 H, dddd, *J* = 19.8, 10.2, 4.2, 2.2 Hz), 3.03–2.92 (1 H, m), 2.40–2.31 (1 H, m), 2.09–1.96 (1 H, m).

^{13}C NMR ($CDCl_3$, 101 MHz): δ = 174.7 (M), 174.3 (m), 171.8 (m), 171.1 (M), 151.2 (M), 150.9 (m), 134.0 (m), 133.8 (M), 130.9 (M), 130.8 (m), 129.0 (m), 128.8 (M), 128.5 (M), 128.4 (m), 127.9 (M), 127.9 (m), 121.8 (m), 121.5 (M), 115.3 (M + m), 72.9 (m), 72.2 (M), 71.6 (M), 70.7 (m), 52.1 (M), 52.0 (m), 35.4 (M), 35.0 (m), 26.7 (M), 26.5 (m).

MS (EI): *m*/*z* = 308 (MH – OH), 249, 145, 104, 77.

HRMS (APCI): *m*/*z* $[M + H]^+$ calcd for $C_{19}H_{21}N_2O_3$: 325.1547; found: 325.1534.

N-(4-Methoxyphenyl)-*N*-[2-(5-phenyl-3,4-dihydro-2*H*-pyrrol-2-yl)propan-2-yl]hydroxylamine (7e)

Following GP2, **6a** (29 mg, 0.1 mmol) gave **7e** (18 mg, 56%) as a brown oil, purified by column chromatography (CH_2Cl_2 → CH_2Cl_2/MeOH 99.5:0.5).

IR (film): 3285, 2970, 1615, 1502, 1463, 1447, 1342, 1296, 1245, 1160, 1033 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 7.91 (2 H, d, *J* = 6.8 Hz), 7.52–7.44 (3 H, m), 7.37 (2 H, d, *J* = 8.8 Hz), 6.86 (2 H, d, *J* = 8.8 Hz), 4.41 (1 H, t, *J* = 8.1 Hz), 3.82 (3 H, s), 3.06 (1 H, ddt, J = 16.4, 10.4, 2.8 Hz), 2.92–2.79 (1 H, m), 2.15–2.03 (1 H, m), 1.90–1.73 (1 H, m), 1.26 (3 H, s), 1.08 (3 H, s).

^{13}C NMR ($CDCl_3$, 101 MHz): δ = 173.3, 157.1, 142.0, 133.5, 131.1, 128.6, 128.0, 126.5, 113.0, 78.5, 65.1, 55.5, 34.2, 25.3, 24.7, 18.0.

MS (EI): *m*/*z* = 308 (MH – OH), 265, 164, 115, 91.

HRMS (ASAP): *m*/*z* $[M]^+$ calcd for $C_{20}H_{24}N_2O_2$: 324.1832; found: 324.1836.

N-(4-Chlorophenyl)-*N*-[2-(5-phenyl-3,4-dihydro-2*H*-pyrrol-2-yl)propan-2-yl]hydroxylamine (7f)

Following GP2, **6a** (29 mg, 0.1 mmol) gave **7f** (23 mg, 70%) as a brown oil, purified by column chromatography (CH_2Cl_2 → CH_2Cl_2/MeOH 99.5:0.5).

IR (film): 3184, 2977, 1618, 1576, 1482, 1448, 1379, 1360, 1343, 1169, 1090, 1011 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 9.27 (1 H, br s), 7.87 (2 H, d, *J* = 7.4 Hz), 7.46 (3 H, m), 7.33 (2 H, d, *J* = 8.6 Hz), 7.25 (2 H, d, *J* = 8.7 Hz), 4.33 (1 H, t, *J* = 6.8 Hz), 3.09–2.99 (1 H, m), 2.84 (1 H, m), 2.12–2.03 (1 H, m), 1.84–1.72 (1 H, m), 1.22 (3 H, s), 1.10 (3 H, s).

^{13}C NMR ($CDCl_3$, 101 MHz): δ = 173.7, 147.9, 133.4, 131.4, 130.2, 128.8, 128.1, 127.9, 126.5, 78.7 (br), 65.3, 34.2 (br), 25.4, 25.0, 18.0.

MS (EI): *m*/*z* = 312 (MH – OH), 269, 169, 145, 91.

HRMS (HESI): *m*/*z* $[M + Na]^+$ calcd for $C_{19}H_{21}ClN_2ONa$: 351.1235; found: 351.1241.

N-[2-(5-Phenyl-3,4-dihydro-2*H*-pyrrol-2-yl)propan-2-yl]-*N*-[3-(trifluoromethyl)phenyl]hydroxylamine (7g)

Following GP2, **6a** (29 mg, 0.1 mmol) gave **7g** (13 mg, 36%) as a brown oil, purified by column chromatography (CH_2Cl_2).

IR (film): 2979, 1616, 1576, 1439, 1381, 1362, 1326, 1281, 1163, 1119, 1095, 1068 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 7.88 (2 H, d, *J* = 7.4 Hz), 7.65 (1 H, s), 7.57 (1 H, d, *J* = 7.4 Hz), 7.47 (3 H, m), 7.39 (2 H, m), 4.34 (1 H, br s), 3.11–3.01 (1 H, m), 2.86 (1 H, m), 2.15–2.06 (1 H, m), 1.79 (1 H, m), 1.23 (3 H, s), 1.13 (3 H, s).

^{13}C NMR ($CDCl_3$, 101 MHz): δ = 173.9, 145.0, 133.3, 131.5, 130.3 (q, *J* = 32.1 Hz), 128.8, 128.4, 128.2, 128.1, 124.3 (q, *J* = 272.7 Hz), 121.8 (q, *J* = 3.8 Hz), 121.6 (q, *J* = 3.7 Hz), 79.0, 65.6, 34.3, 25.3, 24.8, 17.8.

^{19}F NMR ($CDCl_3$, 376 MHz): δ = –63.9.

MS (EI): *m*/*z* = 346 (MH – OH), 345, 327, 202, 186, 145, 91.

HRMS (ASAP): *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{22}F_3N_2O$: 363.1679; found: 363.1679.

N-[2-(5-Phenyl-3,4-dihydro-2*H*-pyrrol-2-yl)propan-2-yl]-*N*-(*o*-tolyl)hydroxylamine (7h)

Following GP2, **6a** (29 mg, 0.1 mmol) gave **7h** (17 mg, 55%) as a brown solid, purified by column chromatography (CH_2Cl_2 → CH_2Cl_2/MeOH 99.5:0.5).

IR (film): 2979, 1616, 1576, 1487, 1447, 1376, 1342, 1168, 1063, 1027 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.89 (2 H, d, *J* = 6.9 Hz), 7.70 (1 H, d, *J* = 7.9 Hz), 7.45 (3 H, m), 7.19 (2 H, d, *J* = 8.1 Hz), 7.10 (1 H, t, *J* = 7.3 Hz), 4.62 (1 H, t, *J* = 8.1 Hz), 3.06 (1 H, ddt, *J* = 16.2, 10.2, 2.7 Hz), 2.95–2.85 (1 H, m), 2.45 (3 H, s), 2.20–2.06 (1 H, m), 1.93–1.81 (1 H, m), 1.27 (3 H, s), 0.95 (3 H, s).

^{13}C NMR ($CDCl_3$, 101 MHz): δ = 173.2, 147.9, 135.7, 133.7, 131.0, 130.3, 128.6, 128.0, 126.7, 125.7, 80.1 (br), 66.2, 34.4, 25.2, 22.4, 19.2, 17.1 (br).

MS (EI): *m*/*z* = 292 (MH – OH), 186, 148, 115, 91.

HRMS (ASAP): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{24}N_2O$: 308.1883; found: 308.1887.

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Supporting Information

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