Metal-free, photosensitized oxyimination of unactivated alkenes with bifunctional oxime carbonates

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The 1,2-aminoalcohol motif is one of the most prevalent structural components found in high-value organic molecules including pharmaceuticals and natural products. Generally, their preparation requires pre-functionalised substrates and manipulations of one functional group at a time to achieve the desired regioisomer. Herein, we describe a metal-free photosensitisation protocol for the installation of both amine and alcohol functionalities into alkene feedstocks in a single step. This approach is enabled by the identification of oxime carbonate as a suitable bifunctional source of both oxygen- and nitrogen-centred radicals for addition across alkenes with complementary regioselectivity compared to Sharpless aminohydroxylation. Use of orthogonal protection for amine and alcohol functionalities enables direct synthetic diversifications of one functional handle without influencing the other. With the use of readily available starting materials, convergent synthesis and mild reaction conditions, this process is well suited for use in various synthetic endeavors.

The vicinal aminoalcohol motif is one of the most abundant structural units in natural products, pharmaceuticals, agrochemicals and privileged ligands.[1-3] Synthetic routes to this motif rely typically on multistep, iterative manipulations of functional groups to introduce both amine and alcohol functionalities in their desired positions.[4-6] Usually transition metal-catalysed directed β-C–H functionalisation of alcohols or amines offers a synthetic alternative with the necessity of a preinstalled directing group.[7-10] Nevertheless, all these approaches involve manipulation of one functional group at a time (Fig. 1a). By comparison, aminohydroxylation of alkenes is the most straightforward yet powerful approach for the synthesis of 1-amino-2-alcohols allowing simultaneous introduction of both functionalities into the molecule in a single step, as pioneered by Sharpless.[11,12] The generality of this approach however is often plagued by poor regioselectivity and the need for *N*-haloamides.[13] The use of a similar concept to synthesise 2-amino-1-alcohol skeleton requires a complete regioselectivity switch and remains a challenge to date (Fig. 1b).[14,15] So far, transient N-centred radical initiated aminohydroxylation strategy has been exploited in different intramolecular cyclisation context through ingenious substrate design to generate 2-amino-1-alcohol framework.[16-19] Clearly, lack of substrate generality and intramolecular nature of these transformations obviates there widespread use. In this regard, Yoon has elegantly utilized high strain of oxaziridine ring in aminal synthesis with analogous regioselectivity.[20-22] However, the requirement for initial radical attack by the alkene substrate to the copper-activated oxaziridine limits the use of unactivated alkenes in this aminohydroxylation approach. Alternatively, a two-step aziridination of alkene followed by nucleophilic ring opening can also deliver a similar regioselective outcome.[23-25] However, low nucleophilicity of alcohols poses a significant challenge.

Radical-radical cross coupling may offer possibilities to address this issue via intermolecular oxyamination pathway, where in an alternative mechanistic scenario, first an oxygen-centred radical can attack the alkene followed by introduction of the amine functionality (Fig. 1b). Ideally, homolytic cleavage of a N–O bond, followed by addition of the resulting radicals to an olefin in desired regioselectivity would be the most direct approach towards the synthesis of 2-amino-1-alcohols.[26] Until now, the N–O bond has been mainly used as a source of transient N-centred radicals in different intermolecular amino-functionalisation reactions.[27-30] In sharp contrast, generation of O-centred radicals from N–O bonds for their use in olefin addition reactions is less explored.[31] Evidently, the generation of both N- and O-centred radicals for use in regioselective oxyamination of alkenes has yet been reported. Notwithstanding, concomitant generation of both N- and O-centred radicals can introduce numerous problems connected to the potentially unproductive side reactions stemming from mono-functionalisation, non-selective difunctionalisation and dimerisation. Furthermore, control over the reactivity of both N- and O-centred radicals is crucial for ensuring high regioselectivity in alkene addition.

Based on recent reports from the group of Cho and our laboratory on the use of oxime esters of carboxylic acids as the source of both C- and N-centred radicals, we hypothesised whether such a strategy could be effectively used to generate both N- and O-centred radicals with different reactivity.[32,33] If successful, then regioselective addition of the oxygen-centred radicals, followed by radical-radical coupling could serve as a direct route to the valuable 2-amino-1-alcohol core.

Seeking to address this challenge, we herein introduce oxime carbonates as bifunctional sources of both O- and N-centred radicals through organo-photosensitized homolysis of the N–O bond. Simultaneously, both amine and alcohol functionalities can be introduced through the regioselective addition of these O- and N-centred radicals over the unactivated C–C double bonds in one step (Fig. 1c). The 2-amino-1-alcohols obtained represent fundamentally important building blocks in synthetic chemistry that could be readily diversified. Significantly, the judicious use of complementary carbonate and iminyl protecting groups for O- and N-functionalities readily allows direct synthetic manipulation of one functional group without affecting the other.

Results

Reaction development. Seeking to develop an efficient oxyamination strategy for alkenes, the key challenge was the development of a simple, practical bifunctional reagent amenable to the simultaneous generation of both O- and N-centred radicals at an equal rate but with different reactivity. In most cases, competing high reactivity can be observed for different O- and N-centred radicals. To circumvent this, our initial effort relied on the identification of a suitable N-centred radical with a sufficiently long lifetime to allow preferential addition of the O-centred radical to the alkene in first place to ensure high regioselectivity. Based on the preferential addition of the alkyl radical to styrenes (1.3×10^5 s^{-1}) compared to the N-centred iminyl radical during our previous study,[33] we anticipated that such iminyl radicals with longer lifetimes might be suitable candidates to address the issue of regioselectivity.[35] Nevertheless, exploiting such a unique reactivity pattern of benzophenone-based iminyl radicals in our oxyamination context was uncharted territory. In accordance with our initial hypothesis, we rationalised that a benzophenone-based oxime ester of acetic acid (**2a**) could be a good starting point since triplet sensitisation of such esters (E_T = 45.4 kcal mol^{-1}) should be a thermodynamically favoured process for most of the commonly used photocatalysts.[36] For this purpose, 1-octene (**1**, E_T > 75 kcal mol^{-1}) was selected as an unactivated reaction partner that would be unable to interact with the photocatalyst.[37]

Consequently, we chose [Ir(dF(CF_3)ppy)$_2$(dtbbpy)](PF_6) (**3**, dF(CF_3)ppy = 2-(2,4-difluorophenyl)-5-trifluoromethylpyridine, dtbbpy = 4,4′-di-*tert*-butyl-2,2′-bipyridine) as the preferred photocatalyst for our initial studies owing to its high triplet energy (60.1 kcal mol^{-1}) and excited state lifetime (τ = 2.3 μs).[38] The desired oxyimination product was not observed since the kinetically favoured concerted fragmentation/decarboxylation from **2a** poses a significant challenge for the successful generation of O-centred radicals (Fig. 2a).[39,40] Likewise, the use of benzoic acid derived **2b** was also not successful to overcome this issue.[41] Aiming to prevent such a decarboxylation pathway, *n*-pentanol derived benzophenone oxime ether **2c** was next considered owing to its computed low triplet energy (41.8 kcal mol^{-1}). Despite the thermodynamic feasibility of energy transfer, no reactivity was observed under photosensitized conditions. This suggests that the ester functionality was a prerequisite for the successful cleavage of the N–O bond.[42] Therefore, to find the perfect balance between reactivity while minimizing the rate of decarboxylation, different oxime-based esters were evaluated. While phosphate ester **2d** and carbamate **2e** failed to provide the desired reactivity, different carbonate esters showed promising outcomes. Despite successful sensitisation, aryl carbonate ester **2f** was susceptible to decarboxylation as observed by GC/MS. Remarkably, when alkyl carbonate esters **2g** and **2h** were employed, good yields of the desired oxyimination product **4** were observed. Surprisingly, the reactivity of such alkoxycarbonyloxyl radicals has not yet been utilised for synthetic purposes regardless of their slow decarboxylation rate (3.8×10^3 s^{-1}).[43,44] Further modification of the alkyl group by introducing *tert*-butyl group showed diminished reactivity (**2i**).

Next, aiming to improve our catalytic system, we first confirmed the interaction between the photocatalyst **3** and the oxime carbonate **2h** through a luminescence quenching studies (Fig. 2b). Then, to understand the nature of their interaction, a systematic variation of a series of photocatalysts with different properties was performed (Fig. 2c). Importantly, photocatalysts with similar redox properties to **3** did not necessarily lead to product formation (Fig. 2c entry 2). In contrast, the product yield was directly correlated with the triplet energy of the photocatalyst with a cut-off near 49 kcal mol^{-1}, which is consistent with a triplet-triplet energy transfer (TTEnT) mechanism.[45] Guided by this observation, when we replaced **3** by thioxanthone (**5**) as a cheap and readily available organo-photosensitizer,[46] almost identical reactivity was observed under similar reaction conditions just by adjusting the irradiation wavelength to 405 nm (Fig. 2c entry 7). Importantly, with this set of reaction conditions, now the overall method does not require any metal or additives and uses mild and greener reaction conditions in a highly atom economic and redox neutral fashion. Furthermore, a reaction parameter-based sensitivity screening was performed to identify the critical reaction parameters detrimental to reproducibility (Supplementary Tables 1 and 2).[47] Notably, the reaction was sensitive towards low light intensity and high oxygen concentration, while solvent moisture content, concentration or temperature fluctuations had only minimal effect on the yield of **4** (Fig. 2d).

Reaction scope. Once the optimized conditions were identified, we systematically investigated the substrate scope of our method by employing different alkenes. A wide range of alkenes could be successfully transformed into the target products in good yields and excellent regioselectivity (Fig. 3). Styrene derivatives with different electron donating as well as withdrawing groups present at the 4-position of the aromatic ring readily underwent oxyimination (**6**-**12**). Substitutions at different positions of the aromatic ring in styrenes were tolerated without difficulties (**12**-**14**). Sterically hindered 2,4,6-trimethyl styrene participated smoothly to deliver the corresponding oxyimination product **14**. Unactivated terminal alkenes containing simple alkyl chains as well as different functionalities successfully delivered the oxyimination products in moderate yields (**4**, **16**-**20**). In all cases, the carbonate group first attacked the terminal position of the alkene ensuring an orthogonal selectivity in comparison to Sharpless' aminohydroxylation.[48] Next, a series of disubstituted alkenes were evaluated in our

oxyimination conditions. Different symmetrical as well as unsymmetrical 1,2-disubstituted olefins gave their desired products in respectable yields (**21**-**26**). In these cases, the regioselectivity of oxyimination was guided by the stability of the radical after the addition of the O-radical to the alkene. Fascinatingly, successful dearomatization of a benzothiophene skeleton was achieved by employing this oxyimination protocol (**24**, **25**). The anti-geometry between the carbonate and iminyl functionality was confirmed from the crystal structure of **24** (Supplementary Figure 11). This further supports the proposed initial attack of the alkoxycarbonyloxyl radical to the alkene followed by the radical-radical cross coupling with the iminyl radical from the opposite, sterically accessible side. As a consequence, high diastereoselectivity was observed for different cyclic alkenes (**21**, **22**, **24**, **25**, **26**). Furthermore, six different 1,1-disubstituted alkenes were investigated in order to synthesise 2-amino-1-alcohols with a tertiary alkylamine centre (**27**-**32**). Sterically demanding 1,1-diphenylethylene and methallyltrimethylsilane were accommodated under the oxyimination conditions (**28**, **30**). Remarkably, tetrahydropyran and cyclohexane rings with exocylic double bond were successfully used to construct tertiary alkylamine **29** and **32**.

The generality of this oxyimination reaction was further evaluated by exploring a series of six different trisubstituted alkenes (**33**-**38**). Despite high steric demand, all of them reacted fruitfully under the similar conditions. In perhaps the most impressive feat, tetrasubstituted carbon centres carrying either iminyl (**33**, **36**) or carbonate functionalities (**34**, **35**, **37**, **38**) were built successfully through the thoughtful choice of acceptor alkenes. Tetrasubstituted alkenes were however found to be unreactive. Subsequently, the efficiency of other bifunctional reagents was evaluated with styrene (**39**-**43**). Notably, side products originating from 1,5-hydrogen atom transfer (HAT) by the alkoxycarbonyloxyl radical were not observed when *n*-hexyl and cyclohexyl based carbonate esters were used (**41**, **42**). 4,4'-Difluorobenzophenone-derived oxime carbonate **43** was also found to be effective for oxyimination despite lower efficiency. We next probed a range of complex alkenes substrates amenable to our reaction conditions to demonstrate the suitability of our protocol for late stage use. Chiral auxiliary (1*S*)-(–)-camphanic acid and naturally occurring diprogulic acid derived alkenes reacted smoothly to deliver **44** and **46**. Natural products such as camphene and menthol derivatives also provided the desired products in good to moderate yields (**45**, **47**). Predictably, terminal enol ether reacted preferably against sterically inaccessible internal double bond to produce **48**.

Synthetic utility. The synthetic convenience of our oxyimination method for easy scale-up was first demonstrated through a large scale (1.5 g scale) synthesis of **6a** (Fig. 4a). Next, the application of this oxyimination strategy was demonstrated through the diversifications of either one or both the functional handles in different synthetic transformations (Fig. 4a). Benzophenone imines are known as the synthetic equivalents to ammonia and they are often employed in various cross coupling reactions.[49,50] The benzophenone group can be instantly removed by acidic hydrolysis to provide the unprotected amine in nearly quantitative yield (**49**).[49] Utilising the carbonate functionality in the β-position, 2-oxazolidone derivative **50** was prepared.[51] Both the iminyl and carbonate protecting groups can be easily removed by successful acidic and basic hydrolysis for the synthesis of free 2-amino-1-alcohol **51**.[52] In a similar manner, basic-only hydrolysis can remove the carbonate functionality to generate the free alcohol without affecting the iminyl group (**52**). Importantly, the carbonate functionality can be used as a leaving group to install perfluoroaryl ethers (**53**).[53] Secondary amines can be accessed through the reduction of the iminyl group with simultaneous removal of the carbonate protecting group in presence of $LiAlH_4$ as the reducing agent (**54**).[54] Furthermore, the utility of this method in 2-amino-1-alcohol synthesis was demonstrated by the synthesis of (±) Leucinol and (±) Isoleucinol starting from two different isomers of methyl-1-pentene (Fig. 4b). Successful execution of our developed protocol followed by a sequential acidic and basic hydrolysis led to the corresponding aminoalcohols **56** and **58** in moderate yields.

Mechanistic investigations. After developing a suitable method for alkene oxyimination, subsequent efforts were directed towards corroborating the postulated mechanism (Fig. 5). First, control reactions highlighted the requirement for light and photosensitizer for successful product formation. UV-Vis absorption spectroscopy confirmed that thioxanthone (**5**) is the only light-absorbing species in the reaction mixture near the excitation wavelength (λ_{max} = 405 nm, Fig. 5a). The lack of absorption for **2h** in the wavelength range of photocatalyst's (**5)** phosphorescence, overrule the Förster energy transfer pathway. Besides, direct correlations between the product yields with the triplet energies of the photocatalysts indicate the Dexter type TTEnT process is likely operative (Fig. 2c).[55] This was further supported by the computed solution phase triplet energy for **2h** (46.8 kcal mol^{-1}, Supplementary Method 3.3). In contrary, the thermodynamic feasibility of a single electron transfer (SET) reduction of the oxime carbonate **2h** by **5*** was precluded by the cyclic voltammetry data (Supplementary Figure 6). Moreover, the SET events must require the presence of a photocatalyst. Alternatively, a reaction proceeding from the triplet state of the substrate should also be feasible through direct excitation, clearly distinguishing it from a SET mechanism.[56] Indeed, the formation of **4** was observed when the reaction mixture was irradiated with higher energy light sources (λ_{max} = 365 nm) in the absence of photocatalyst, albeit in low yield (Fig. 5b). With extended irradiation time and 365 nm LEDs in absence of any photocatalyst, increased product yield was observed (Fig. 5b). This also rules out any non-innocent role of the photosensitizer in stabilizing the N-centred iminyl radical apart from participating in the energy transfer process. Next, complete inhibition of the formation of **6a** in the presence of 2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO) as a radical scavenger hinted towards the radical nature of the reaction (Fig. 5c). The involvement of both alkoxycarbonyloxyl and iminyl radicals was identified from the formation of **59** through 5-*exo*-trig radical cyclization/addition (Fig. 5d, Supplementary Figures 7 and 8). Finally, observation of the crossover products in a radical crossover study employing oxime carbonates **2h** and **2n** with styrene elucidated the occurrence of radical-radical cross coupling step outside the solvent cage (Fig. 5f). This also undoubtedly proves the presence of both O- and N-centred radicals in the reaction system. Furthermore, the longer lifetime of the N-centred iminyl radical can be inferred by the observation of all probable N–N dimeric species by GC/MS (Supplementary Figures 9 and 10). Linking these data together, the proposed mechanism begins with the photo-induced TTEnT event between the excited photocatalyst **5*** and oxime carbonate **2h**.[32] Next, **2h*** readily generates an alkoxycarbonyloxyl and iminyl radical pair **60** and **61** through the homolytic cleavage of the N–O bond. The transient alkoxycarbonyloxyl radicals **60** are captured by the alkene to generate a stabilized C-centred radical **62** at a rate approaching diffusion.[57] Finally, this C-centred radical **62** and long lived N-centred iminyl radical **61** participates in a radical-radical cross coupling process to generate the desired 1,2-oxyimination product. We anticipated the rate of such a radical-radical cross coupling should be slower than that of a 5-exo-radical cyclization (5×10^6 s^{-1}) and trapping of alkyl radical by styrenes (1.3×10^5 s^{-1}, Supplementary Method 3.6).[58,59] High cross selectivity in such radical-radical couplings can be explained by the persistent radical effect (PRE).[60] However, involvement of a radical chain propagation by **62** directly attacking **2h** to provide the 1,2-oxyimination product along with the concomitant generation of **60** cannot be excluded completely. Quantum yield measurement (Φ = 0.84) could not invalidate an inefficient chain propagation (Supplementary Method 3.8). Our efforts to use various radical initiators under thermal conditions failed to initiate the reaction (Fig. 5e). Specifically, the presence of N-centred iminyl radicals does not converge with a chain propagation pathway (Fig. 5f and Supplementary Figure 9). This further supports the proposed TTEnT mediated radical-radical cross coupling pathway.

Conclusions

In summary, the metal-free, regioselective oxyimination strategy for rapid conversion of alkene feedstocks into 2-amino-1-alcohol cores provides a direct route to access these privileged motifs. With the remarkably mild reaction conditions, excellent functional group tolerance and widespread product versatility, we expect this broadly applicable oxyimination approach will enable streamlined synthesis of complex molecules containing both amine and alcohol functionalities. Lastly, building on the longer lifetime of iminyl radicals, we anticipate that the use of radical-radical cross coupling will spur the discovery of useful bond formations.

Methods

General procedure for the oxyimination of alkenes. An oven-dried 10 ml Schlenk tube equipped with a Teflon-coated magnetic stirring bar was charged with thioxanthone (3.2 mg, 0.015 mmol, 0.05 equiv.) and the appropriate oxime carbonate (0.45 mmol, 1.5 equiv.) under air. The Schlenk tube was evacuated and back-filled with argon for four times. Anhydrous ethyl acetate (0.1 M) and the appropriate alkene (0.3 mmol, 1.0 equiv.) were added under argon counter flow. The tube was sealed with a screw cap and irradiated with a 16W blue LED lamp (λ_{max} = 405 nm) for 12 hours with constant stirring. After completion, the resulting homogeneous solution was transferred to a 25 mL round bottom flask with aid of ethyl acetate (2 x 5 mL). NEt_3 (approx. 0.5 mL) and pre-basified silica gel were added to this solution and the volatiles were removed under reduced pressure, affording a powder. Purification of this powder by flash column chromatography using pre-basified silica gel afforded the desired oxyimination product.

Data availability

Details about materials and methods, experimental procedures, mechanistic studies, characterization data and NMR spectra are available in the Supplementary Information. Additional data are available from the corresponding author upon reasonable request. The atomic coordinates of the optimized models for triplet energy calculation are provided in Supplementary Data 1. CCDC-2004569 (compound **24**), -2027139 (compound **26**), -2004570 (compound **27**) and -2027138 (compound **36**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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Author contributions

T.P. and F.G. conceived this work. T.P. and M.D. performed all the experiments and analyzed the data. C.G.D. collected and analyzed the X-ray crystallographic data. T.P. and F.G. prepared the manuscript with contributions from all authors.

Competing interests

The authors declare no competing interests.

Figures

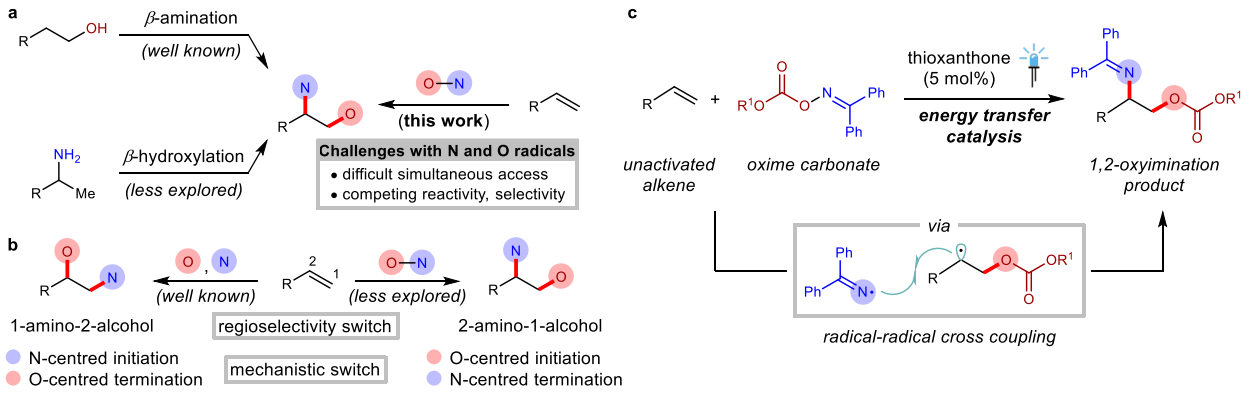
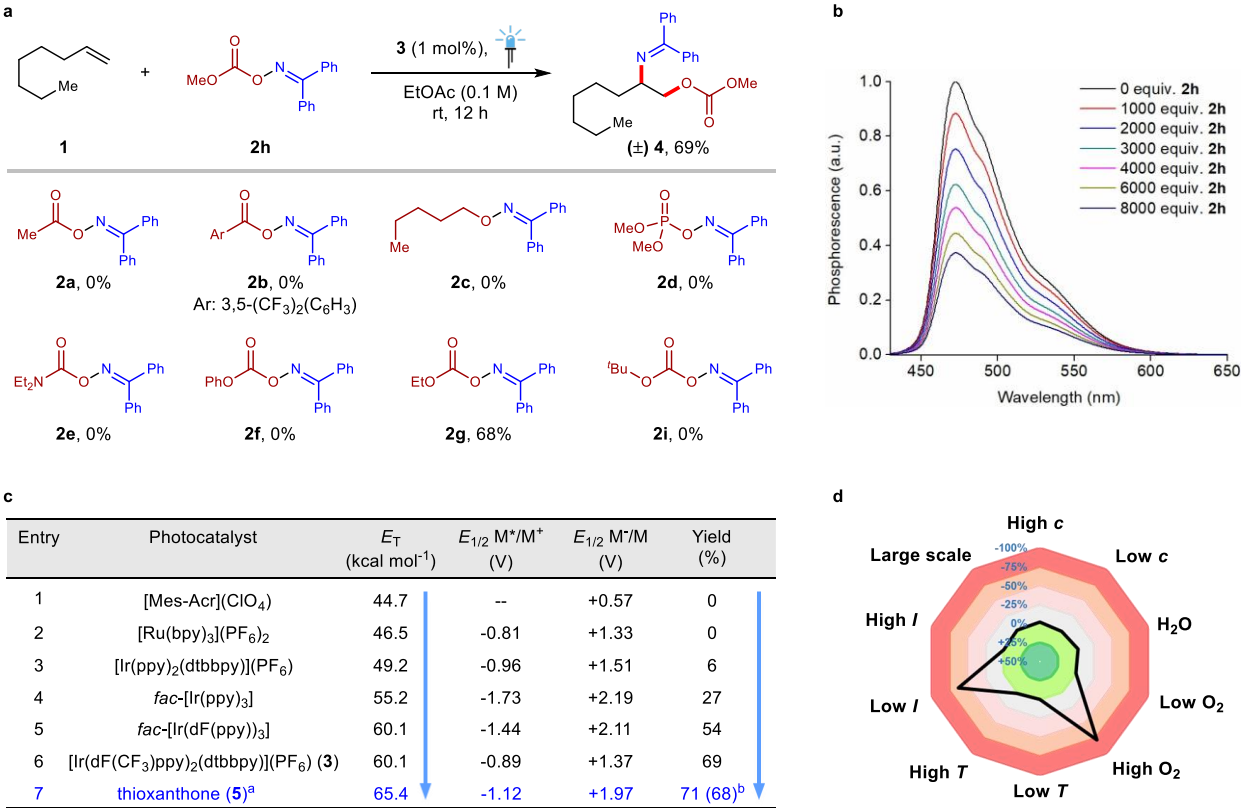


Fig. 1. Strategies for vicinal aminoalcohol synthesis. a, Introduction of one functionality versus introduction of both functionalities in one step for 2-amino-1-alcohol synthesis. **b**, Aminohydroxylation of olefin is a well-known strategy for 1-amino-2-alcohol synthesis, but a similar concept is not utilised for 2-amino-1-alcohol synthesis through O-centred initiation. **c**, Introduction of oxime carbonates as bifunctional O- and N-radical sources for vicinal oxyimination of unactivated alkenes through radical-radical cross coupling.



Entry	Photocatalyst	E_T (kcal mol^{-1})	$E_{1/2}$ M*/M$^+$ (V)	$E_{1/2}$ M$^-$/M (V)	Yield (%)
1	[Mes-Acr](ClO$_4$)	44.7	--	+0.57	0
2	[Ru(bpy)$_3$](PF$_6$)$_2$	46.5	-0.81	+1.33	0
3	[Ir(ppy)$_2$(dtbbpy)](PF$_6$)	49.2	-0.96	+1.51	6
4	*fac*-[Ir(ppy)$_3$]	55.2	-1.73	+2.19	27
5	*fac*-[Ir(dF(ppy))$_3$]	60.1	-1.44	+2.11	54
6	[Ir(dF(CF$_3$)ppy)$_2$(dtbbpy)](PF$_6$) (**3**)	60.1	-0.89	+1.37	69
7	thioxanthone (**5**)[a]	65.4	-1.12	+1.97	71 (68)[b]

Fig. 2. Development of an intermolecular radical oxyimination of alkenes. a, Identification of bifunctional reagent as suitable O- and N-radical sources. Conditions: **1** (0.1 mmol), **2** (0.15 mmol) and **3** (1 mol%) in EtOAc (1 mL), irradiating with 30 W blue LEDs (λ_{max} = 450-455 nm) under an argon atmosphere at room temperature for 12 h. Yields were determined by ^{1}H NMR of crude reaction mixture using an internal standard. **b**, Luminescence quenching studies for **3** using **2h** as the quencher. **c**, Systematic evaluation of different visible light photocatalysts with oxime carbonate **2h**. Triplet energies (E_T) and potentials ($E_{1/2}$) are literature values.[34] [a]5 mol% catalyst loading was used with 16 W blue LEDs (λ_{max} = 405 nm) irradiation. [b]Isolated yield. **d**, Reaction conditions based sensitivity assessment.

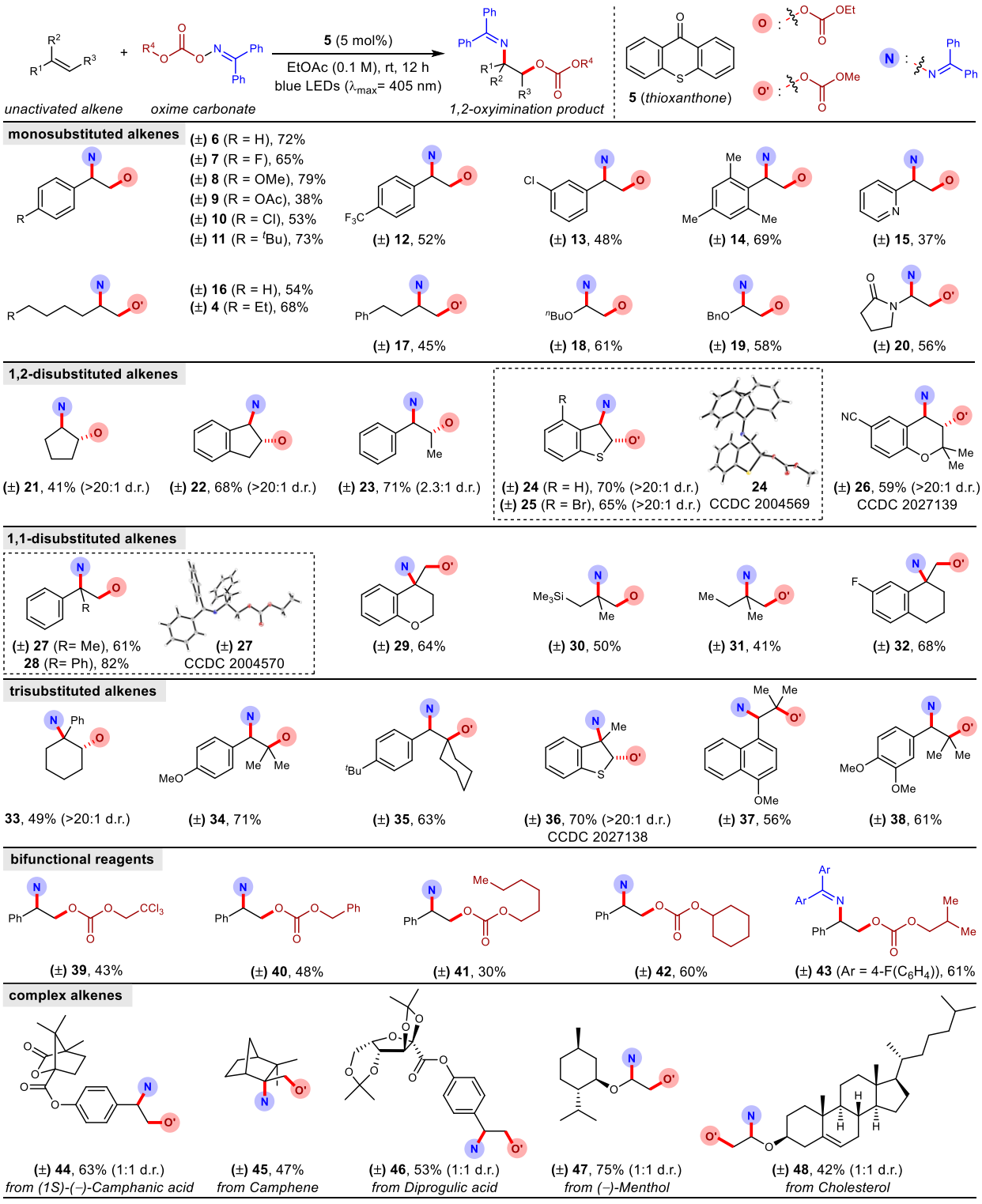


Fig. 3. Substrate scope of the intermolecular oxyimination of alkenes. Reaction conditions: alkene (0.3 mmol), oxime carbonate (0.45 mmol) and photocatalyst **5** (5 mol%) in EtOAc (0.1 M), irradiating with 16 W blue LEDs (λ_{max} = 405 nm) under an argon atmosphere at room temperature for 12 h. Isolated yields are given. Diastereomeric ratios (d.r.) were determined from the GCMS and ^{1}H NMR analysis of the crude reaction mixture.

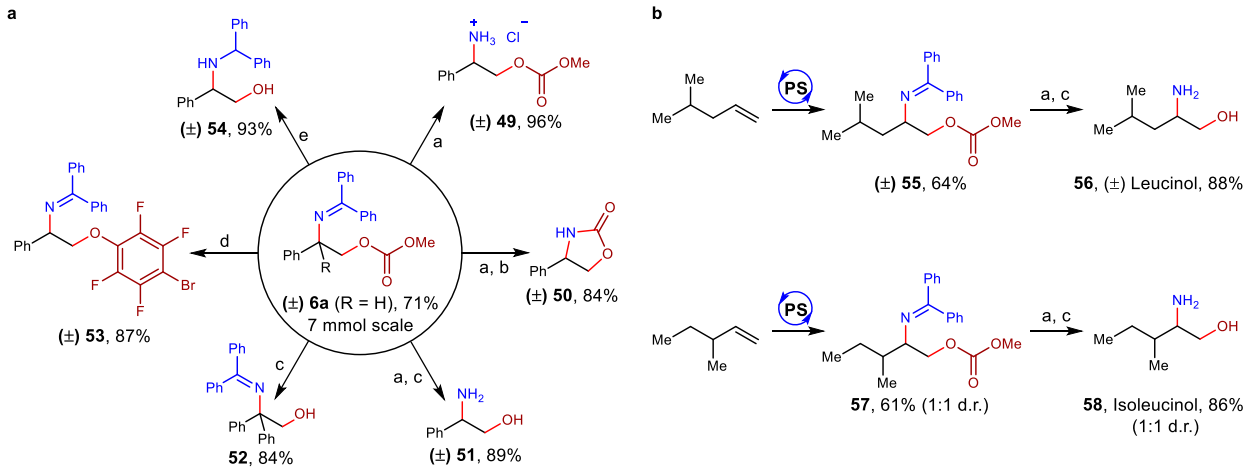


Fig. 4. Application of the metal free oxyimination of alkenes. a, Various synthetic diversifications of the oxyimination product. [a]2 M HCl (0.5 mL), Et_2O. [b]K_2CO_3 (2.0 equiv.), EtOH, 130 °C. [c]2 M KOH/MeOH (2/1), 80 °C. [d]Bromopentafluorobenzene (2.0 equiv.), [t]BuOK (1.5 equiv.), toluene. [e]$LiAlH_4$ (3.0 equiv.), THF. **b**, Synthesis of naturally occurring 2-aminoalcohols. PS, photosensitizer.

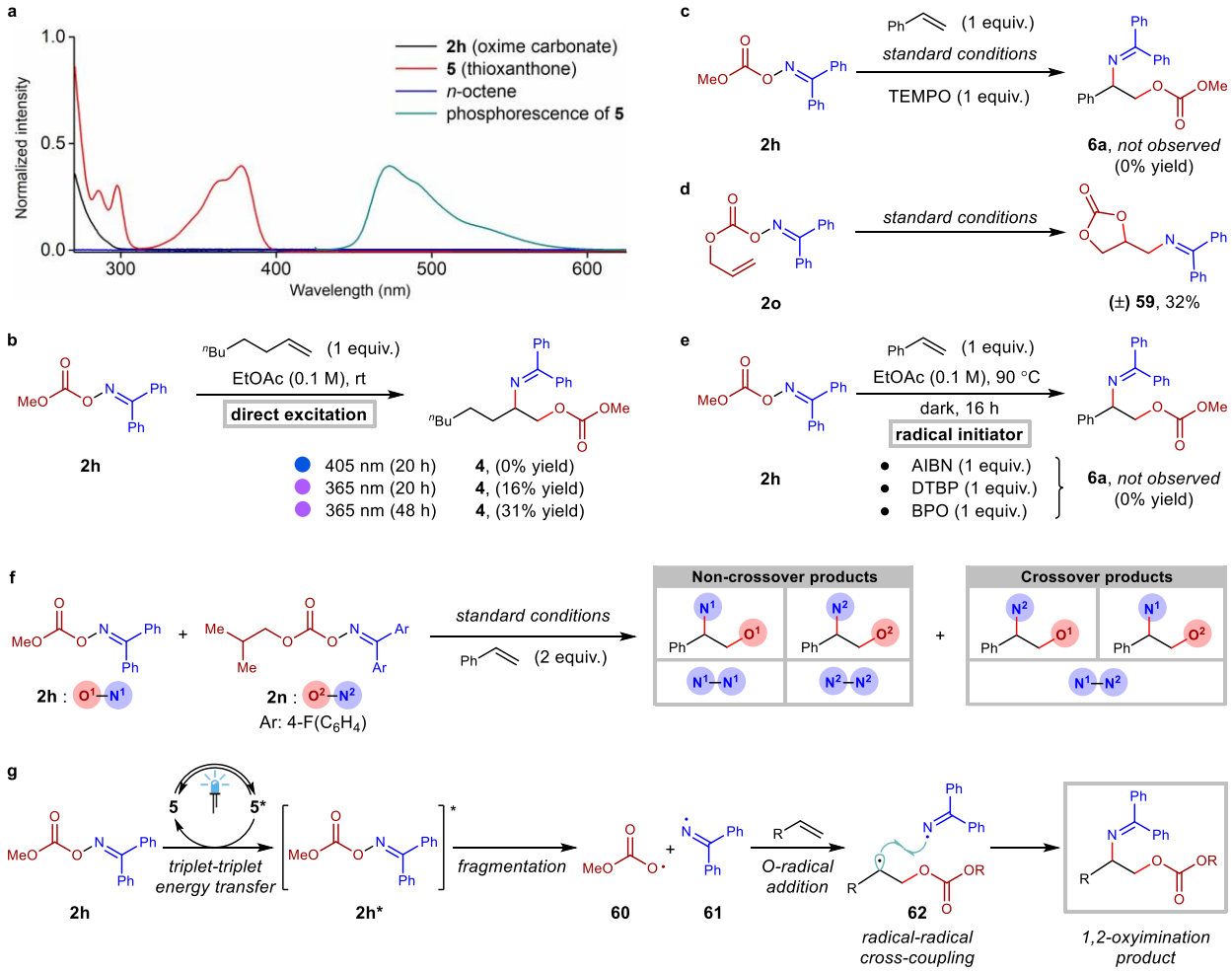


Fig. 5. Mechanistic investigations and proposed reaction mechanism. a, UV-Vis absorption spectroscopy of each reaction components and phosphorescence of **5** indicates no Förster overlap. **b**, Feasibility of direct photosensitisation disproves redox pathway. **c**, TEMPO inhibits the radical oxyimination reaction. **d**, Intramolecular radical ring closing experiment confirms the involvement of O- and N-centred radicals. **e**, Different radical initiators cannot be used to initiate the reaction. **f**, Radical crossover study confirms presence of both O- and N-centred radicals as well as radical capture outside the solvent cage. **g**, Proposed reaction mechanism as suggested by different mechanistic experiments. TEMPO, 2,2,6,6-tetramethylpiperidin-1-yl)oxyl; AIBN, azobisisobutyronitrile; DTBP, di-*tert*-butyl peroxide; BPO, benzoyl peroxide.