A general arene C–H functionalization strategy via electron donor-acceptor complex photoactivation

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The photoactivation of electron donor-acceptor (EDA) complexes has emerged as a sustainable, selective and versatile strategy for the generation of radical species. However, when it comes to aryl radical formation, this strategy remains hamstrung by the electronic properties of the aromatic radical precursors and electron-deficient aryl halide acceptors are required. This has prevented the implementation of a general synthetic platform for aryl radical formation. Our study introduces triarylsulfonium salts as acceptors in photoactive EDA-complexes, used in combination with catalytic amounts of newly-designed amine donors. The sulfonium salt label renders inconsequential the electronic features of the aryl radical precursor and, more importantly, it is installed regioselectively in native aromatic compounds by C–H sulfenylation. Using this general, site-selective aromatic C–H functionalization approach, we have developed metal-free protocols for the alkylation and cyanation of arenes, and showcased their application in both the synthesis and the late-stage modification of pharmaceuticals and agrochemicals.

Synthetic methods exploiting the visible-light activation of organic compounds – be they colored substrates[1], catalytic intermediates[2-3] or enzyme cofactors[4] – have enabled previously unknown transformations, diverted conventional reaction pathways, and fostered the invention of new catalytic modes. The potential of these approaches lies in the ability to utilize the energy of photon radiation to access highly energetic intermediates – such as radical species. However, as the majority of organic molecules are colorless and present absorption profiles within the UV-region, the presence of either expensive dyes[5] or precious transition metal-based photocatalysts[6-7] is often required in order to absorb the low energy visible-light radiation and trigger the desired radical reactivity. To overcome this intrinsic limitation, recent photochemical protocols have exploited charge transfer interactions between two colorless organic molecules – one electron-rich (donor) and the other electron-deficient (acceptor) – to form colored, visible-light absorbing aggregates: electron donor-acceptor (EDA) complexes[8] (Figure 1a). Light irradiation of EDA-complexes triggers an intracomplex single electron transfer (SET), from the donor to the acceptor, which produces discrete radical species – upon fast loss of a leaving group present in either of the partners. The photoactivation of EDA-complexes has emerged as a selective and sustainable alternative to the state-of-the-art photoredox methods for radical generation[5-7], since it facilitates single electron manifolds specifically between the partners forming the aggregate, uses simple and readily-accessible organic molecules, and thus negates the need for light-absorbing transition metal-complexes and dyes.

Early methods exploiting EDA-complex photoactivation were limited to the use of electronically-biased partners to secure productive charge transfer interactions. To broaden the generality of this strategy, the field has since evolved towards the use of substrates tailored with redox-active moieties ("redox tag" in Figure 1b), which serve as both partners in the EDA-complex and labile fragmenting groups. This approach renders the formation of the EDA-complex independent of the substrate's structure, thus enabling the development of general radical generation platforms[9-11]. While this strategy has been successful for the formation of heteroatomic-[12] and alkyl carbon-centered radicals[9-11], its translation to aromatic systems has proved elusive. Current protocols for the generation of aryl radicals through EDA-complex activation are limited to the use of electron-poor aryl halides as acceptors[13-14], where electron-withdrawing groups are required in order to induce efficient charge interactions with donors, and the pre-installation of halide functionality is needed to facilitate fragmentation upon SET reduction (Figure 1c). If a suitable redox-active label could be identified that overcame the electronic features of the aryl radical precursor and drove the formation of colored EDA-complexes, this would realize a broadly applicable process for the generation of aryl radicals.

Pursuing this goal, we identified triarylsulfonium salts as competent acceptors in EDA-complexes: These compounds are both susceptible to SET reduction[15-17] and easily obtained through site-selective C–H sulfenylation of unfunctionalized arene precursors, by means of interrupted Pummerer reactivity[18-19] with activated sulfoxides (Figure 1d). We envisaged that the sulfonium salt moiety could serve as both the electron-deficient system able to engage suitable electron-donors in charge transfer interactions[20] – regardless of the electronic features of the native aromatic substrate – and a traceless, recyclable, leaving group upon photoinduced SET reduction and aryl radical formation. Using this approach, it would be possible to predictively install a redox tag at unactivated C–H sites within simple arene feedstock chemicals, and more complex bioactive scaffolds, and generate highly reactive carbon-centered radicals at the expense of inert C(sp^2)–H bonds – simply by using readily-available organic molecules and visible light – thus streamlining an overall C–H functionalization process. Herein, we report that exposure of *in situ* generated heterocyclic triarylsulfonium salts to a set of newly-designed triarylamine donors – present in substoichiometric to catalytic amounts – promotes the formation of blue-light absorbing EDA-complexes, whose photoactivation fosters the formation of aryl radicals. In the presence of either silyl enol ethers or commercially available *tert*-butyl isocyanide, the aryl radicals are trapped and C–H alkylation and C–H cyanation products, respectively, result from expedient metal-free one pot processes. Crucially, this approach facilitates transformations – namely, the α-arylation of carbonyl compounds[21-22] and the regioselective C–H cyanation of arenes[23-24] – that are hard to achieve in the absence of transition metal catalysts and organometallic reagents.

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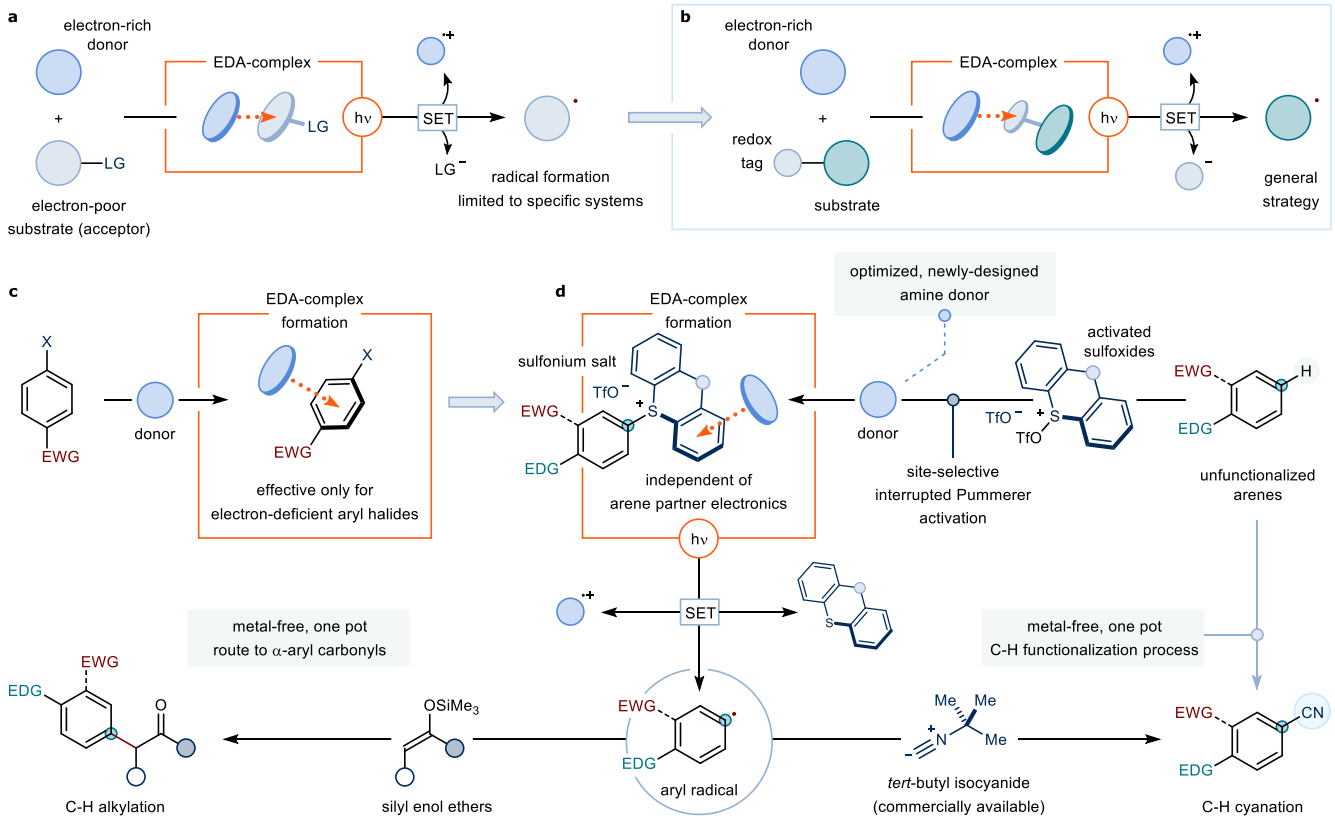


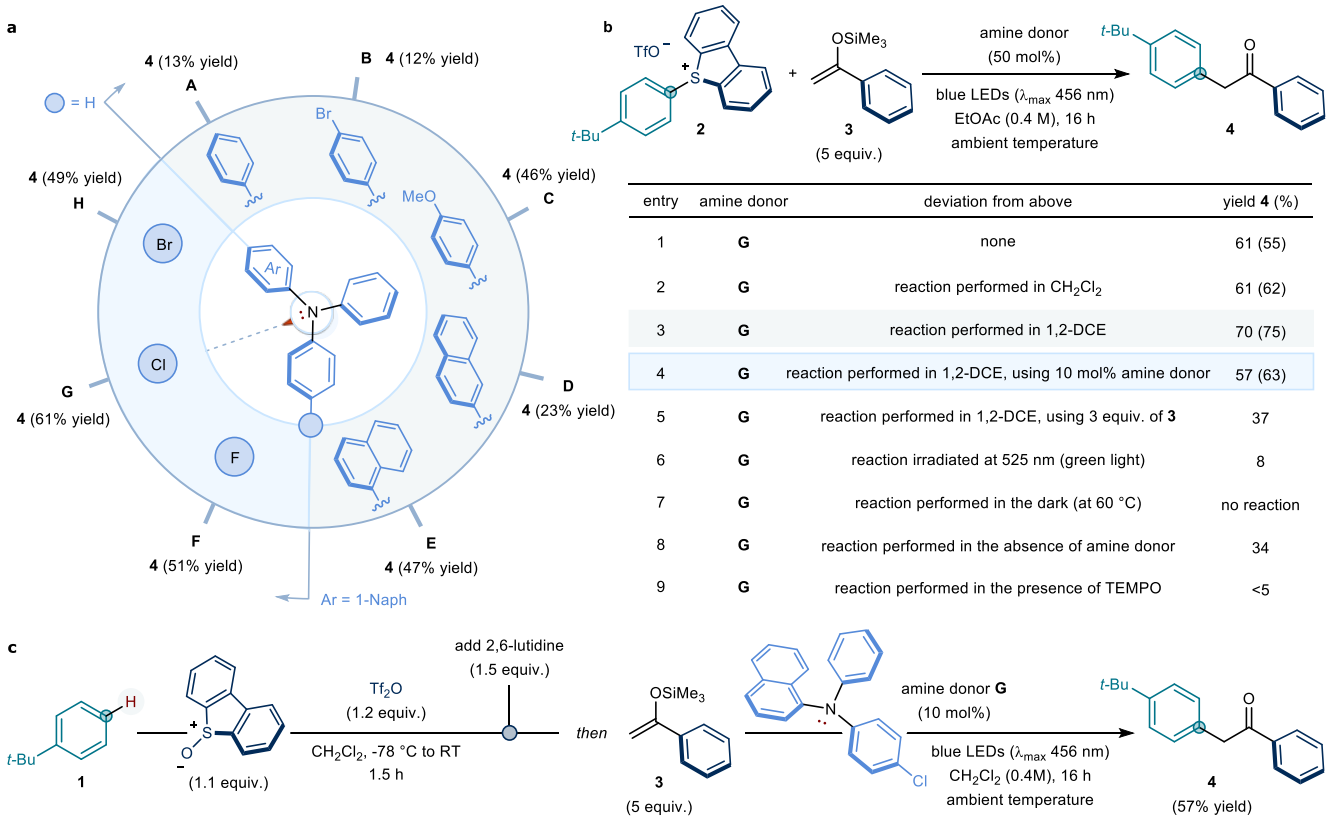
Figure 1 | Photoactivation of EDA-complexes drives the metal-free, radical C–H functionalization of arenes. **a,** Radical formation through the excitation of photoactive EDA-complexes. **b,** The incorporation of labile redox-active functionality within substrates, broadens the generality of this radical generation strategy. **c,** Electronic requirements limit the participation of aromatic substrates in EDA-complex photoactivation to electron-poor aryl halides. **d,** Site-selective C–H sulfenylation of unfunctionalized arenes installs a transient redox tag, which serves as the acceptor partner in EDA-complexes with suitable donors. Visible-light activation of these complexes provides a general platform for the generation of aryl radicals, that is independent of the substitution on the aromatic compound. This strategy has been applied to the C–H alkylation and cyanation of native aromatics, in the absence of any transition metal-catalyst. LG, leaving group; EDA complex, electron donor-acceptor complex; EWG, electron-withdrawing group; EDG, electron-donating group; SET, single-electron transfer.

Results

Design of the method. We first identified a suitable class of electron-donors capable of charge transfer interactions with triarylsulfonium salts. Triarylamines were selected for their availability, the possibility to modulate their electronic properties by structural modification of their aromatic substituents[25], the relative stability of their corresponding radical cations[26], and thus, their ability to mediate single electron reduction. The competence of an array of triarylamines – either commercially available or readily synthesized – to serve as donors was tested on the photochemical reaction between 4-*tert*-butylphenyl dibenzothiophenium (DBT^+) salt **2** – readily prepared from *tert*-butylbenzene **1** – and 1-phenyl-1-trimethylsiloxyethylene **3**, to produce α-arylated acetophenone **4** (Figure 2a). Pleasingly, when the experiment was run in the presence of 50 mol% of triphenylamine (donor **A**), blue-light irradiation (λ_{max} centered at 456 nm) of the reaction mixture delivered **4** in a promising 13% NMR-yield. The introduction of electron-donating functionalities or extended aromatic systems on one of the aromatic substituents of the donor – as in amines **C**, **D** and **E** – proved to be beneficial, enhancing the efficiency of the photochemical α-arylation protocol up to 47% NMR-yield (using donor **E**). The 1-naphthyl-diphenylamine core of **E** was selected to continue donor optimization: The presence of a chlorine atom at the C4-position of one of the two phenyl rings of donor **G** promoted the formation of **4** in 61% yield (isolated in 55% yield). Whereas, an analogous positive effect was not observed for either bromine or fluorine substituents, as exemplified by the trials performed with donors **F** and **H**.

Using the newly-designed donor **G**, further screening of the reaction conditions identified 1,2-DCE as the best solvent for the photochemical α-arylation process (**4** obtained in 75% yield, entry 3, Figure 2b). Under these conditions, the loading of the amine donor can be reduced to 10 mol%, with minimal erosion of the product yield (entry 4). When the light-driven reaction was irradiated with green LEDs (λ_{max} centered at 525 nm), traces of product **4** were detected; while performing the protocol in the dark resulted in no reactivity – even upon heating the reaction mixture at 60 °C – and the starting materials were recovered. Interestingly, the control experiment run in the absence of donor **G** delivered product **4** in 34% yield (entry 8). This result suggests that additional charge transfer interactions might be taking place (presumably between sulfonium salt **2** and silyl enol ether **3**) or, alternatively, that the generation of aryl radicals via photolysis of the C–S bond within **2** could be a competitive pathway, even at irradiation wavelengths outside of the UV region (*vide infra*, Figure 6a). Finally, the radical nature of the photochemical protocol was corroborated by the lack of product formation observed when the reaction was performed in the presence of radical scavenger TEMPO (entry 9).

With optimized conditions for the photochemical coupling between **2** and **3** in hand, we implemented a one-pot sequence for the direct C–H alkylation of *tert*-butylbenzene **1** (Figure 2c). This was accomplished by addition of **1** to a mixture of dibenzothiophene (DBT) *S*-oxide and trifluoromethanesulfonic anhydride in CH_2Cl_2, forming **2** *in situ*. The crude mixture was treated with 2,6-lutidine – to neutralize the excess triflic acid that would otherwise consume the radical trap – before charging the reaction vessel with silyl enol ether **3** and catalytic amounts of donor **G** (10 mol%). Irradiation of the resulting mixture with blue LEDs gave α-arylated product **4** in 57% yield after purification, thus replicating the efficiency of the direct coupling of **2** (*c.f.* Figure 2b – entry 2).



entry	amine donor	deviation from above	yield **4** (%)
1	**G**	none	61 (55)
2	**G**	reaction performed in CH_2Cl_2	61 (62)
3	**G**	reaction performed in 1,2-DCE	70 (75)
4	**G**	reaction performed in 1,2-DCE, using 10 mol% amine donor	57 (63)
5	**G**	reaction performed in 1,2-DCE, using 3 equiv. of **3**	37
6	**G**	reaction irradiated at 525 nm (green light)	8
7	**G**	reaction performed in the dark (at 60 °C)	no reaction
8	**G**	reaction performed in the absence of amine donor	34
9	**G**	reaction performed in the presence of TEMPO	<5

Figure 2 | Development of the photochemical C-H alkylation protocol. a and **b,** Design and optimization of efficient amine donors and reaction conditions to enable the coupling of sulfonium salt **2** with silyl enol ether **3**, under blue-light irradiation. **c,** Implementation of a one-pot C–H alkylation sequence for the provision of α-arylated acetophenone **4**, directly from unfunctionalized *tert*-butylbenzene **1**. Reactions performed on a 0.2 mmol scale. Yields were determined by ^{1}H-NMR spectroscopy using mesitylene as internal standard; isolated yields are reported in parentheses. LED, light-emitting diode; 1,2-DCE, 1,2-dichloroethane.

Scope of the C–H alkylation sequence. The one-pot procedure, set out in Figure 2c, was used to test the generality of the approach to α-aryl carbonyl compounds (Figure 3). A selection of feedstock aromatic substrates was submitted to the C–H alkylation sequence, using 4-fluorophenyl-1-trimethylsiloxyethylene as the coupling partner for the photochemical step. Benzene, as well as alkyl- and aryl-substituted aromatic hydrocarbons, all performed well under the optimized conditions, to provide products **5**-**8** in good yields. Aryl sulfonamides and esters were also competent substrates, yielding the corresponding *para*-substituted products **9**-**10**, selectively. The use of anisole derivatives as substrates showcased the compatibility of our method with a broad array of functionality (*e.g.* trifluoromethyl-, trifluoromethoxy-, methoxycarbonyl-, sulfonyl- and heterocycle benzodioxole), including transition metal-sensitive moieties, such as bromo-, methanesulfonyl- and cyano-groups (**11**-**19**). To assess the efficiency of the EDA-photoactivation step, the photochemical coupling leading to adduct **15** – obtained in 73% yield using the one pot procedure – was performed on the isolated (4-methoxy-3-(methoxycarbonyl)phenyl)-dibenzothiophenium salt to afford **15** in 85% yield. In order to facilitate the experimental set-up, the latter DBT^+-salt was employed to evaluate the scope with regard to the silyl enol ether partner (Figure 3). Both phenyl- and its *ortho*-substituted methyl-, fluoro- and naphthyl-analogues successfully provided α-arylated products **20**-**23** in high yields. *Meta*- and *para*-substitution was also well tolerated, enabling the formation of an array of acetophenones bearing strategic synthetic handles (such as alkynyl-, bromo-, iodo-, methoxycarbonyl- and nitro-functionalities in compounds **26**-**30**). The structure of products **27** and **29** was confirmed by X-ray crystallographic analysis. Pleasingly, β-alkyl-substituted silyl enol ethers successfully participated in the radical arylation process, affording α-disubstituted acetophenones **32** and **33**; while the formation of products **34** and **35** indicate that heterocyclic substituents can also be tolerated. The EDA-complex photoactivation strategy proved to be amenable also for the α-arylation of imides, esters and aliphatic ketones (compounds **36**-**39**), thus expanding the generality of our method to diverse carbonyl systems. Finally, the one-pot C–H alkylation sequence performed well on a 2 mmol scale affording product **20** (319 mg) in 56% yield. Here, upon purification of the crude mixture, the DBT-sulfide by-product was recovered in 87% yield and recycled to the corresponding sulfoxide, by oxidation.

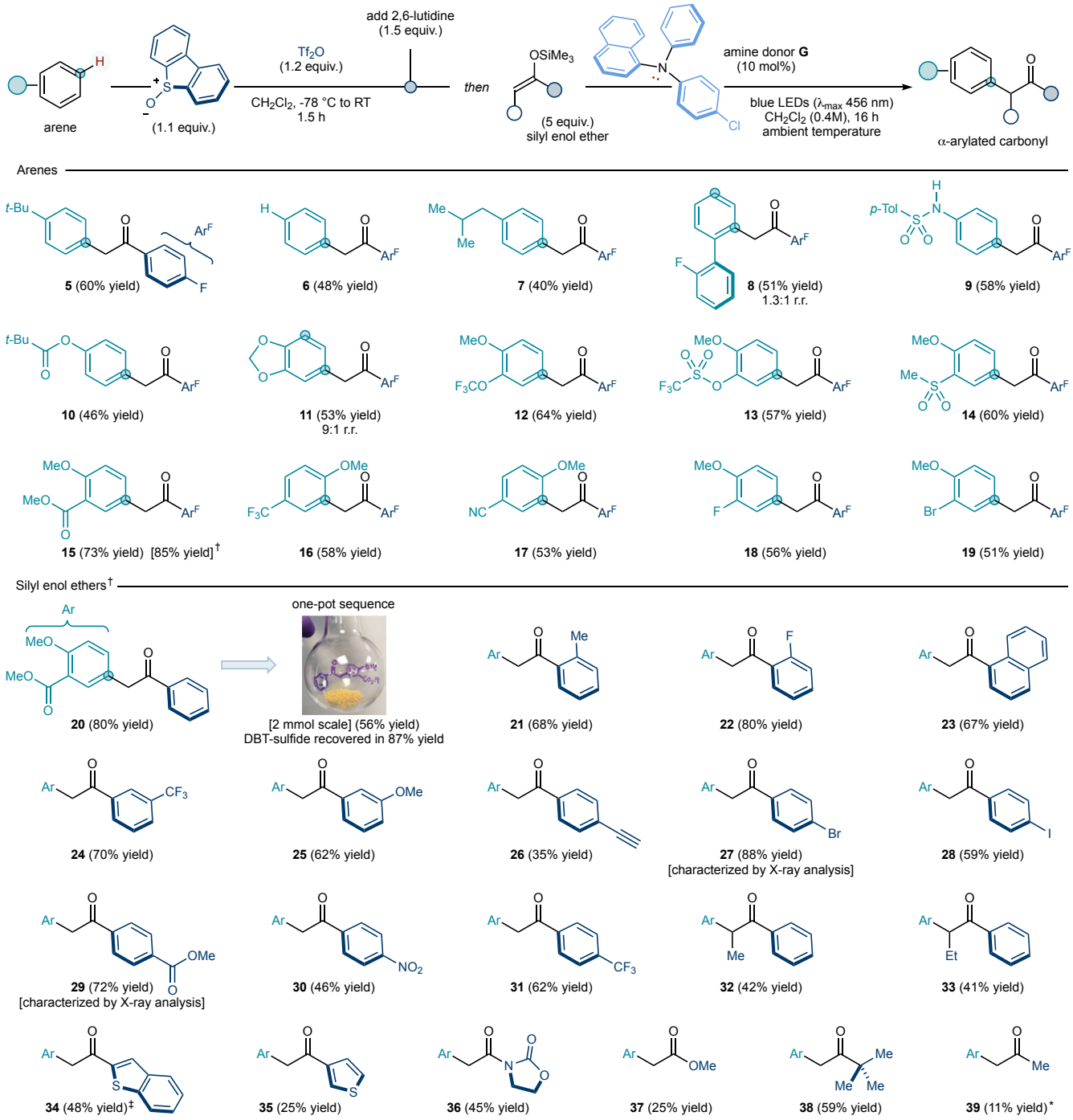
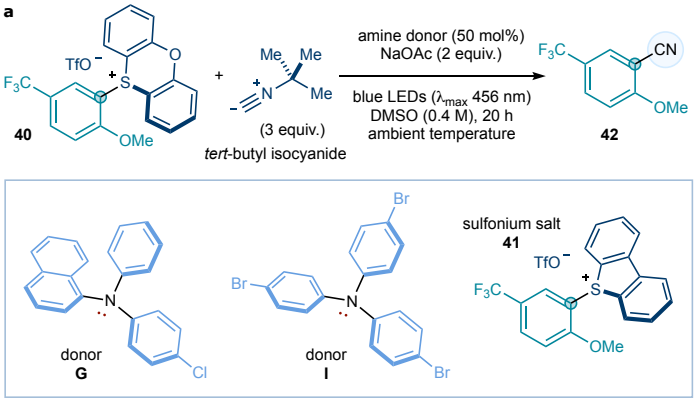


Figure 3 | Evaluation of the substrate scope for the photochemical C-H alkylation sequence. Reactions performed on a 0.2 mmol scale (unless otherwise stated); isolated yields are reported in parentheses. Reaction run; †using the corresponding pre-formed sulfonium salt as substrate; ‡in the presence of 50 mol% of amine donor **G**; *using 10 equivalents of trimethyl(prop-1-en-2-yloxy)silane trap.

Development of a C–H cyanation protocol. Having demonstrated the validity of our design plan, we next used our aryl radical generation strategy to target other C–H functionalization processes, involving alternative radical traps. To this end, we recognized in the commercially available *tert*-butyl isocyanide, a powerful organic cyanide surrogate for the formation of aryl nitriles upon aryl radical addition[27]. First adopted by Stork[28] in 1983 for the formation of C(sp^3)–CN bonds from alkyl radicals, this reagent has surprisingly found limited application in cyanation processes,[29] which mostly rely on the use transition metal-catalysts in combination with metal cyanides[30]. Thus, we foresaw the possibility to apply our EDA-complex photoactivation strategy to the development of a regioselective, metal-free arene cyanation protocol. We began our endeavors by investigating the coupling reaction between phenoxathiinium (PXT^+) salt **40** and *tert*-butyl isocyanide, mediated by substoichiometric amounts of the previously optimized donor **G** (Figure 4a). Gratifyingly, the experiment run in DMSO, in the presence of 2 equivalents of a basic additive (NaOAc), under blue-light irradiation, yielded aryl nitrile **42** in 57% yield (entry 1). Screening of different amine electron-donors indicated that commercially available tris(4-bromophenyl)amine **I** is a viable alternative to donor **G**; aryl nitrile **42** was obtained

in a slightly increased yield (entry 2). This time, both the use of DBT^{+}-salts – such as **41** – and 1,2-DCE as solvent led to a less efficient photochemical process (entries 3 and 4). Pleasingly, for this process, the reaction performed in the presence of catalytic amounts of donor **I** (25 mol%) led to an increased yield of product **42** (71% yield, entry 5). Control experiments highlighted that visible-light irradiation is required to trigger radical reactivity, and the absence of either amine donor or base additive severely impacted on the efficiency of the cyanation procedure (entries 6-8).

As before, the optimized photochemical conditions were instrumental to design a one pot arene C–H cyanation sequence (Figure 3b). In this case, a solvent switch – from CH_2Cl_2 to DMSO – prior to the addition of the isocyanide trap and the amine donor, allows the formation of the aryl nitrile products in good yields: Using 4-trifluoromethyl-anisole as substrate, the C–H cyanation protocol delivered **42** in 57% overall yield. A selection of substituted anisoles – adorned with cyano-, sulfonyl-, methoxycarbonyl-, keto- and halo-functionalities, amongst others – were submitted to the optimized sequence, affording the corresponding aryl nitriles in good yields and with complete regioselectivity (compounds **43-52**). Different aryl ethers (such as **53**), an aryl ester (**54**), amides (**55-58**), and aromatic hydrocarbons (**59-61**) also performed well in the C–H cyanation sequence. To showcase the scalability of our photochemical process, the C–H cyanation on 2-methyl-*N*-(*meta*-tolyl)benzamide was performed on a 1 mmol scale: in this case, *para*-cyano-derivative **58** was obtained in 51% yield (128 mg) and 94% of the PXT-sulfide was recovered.



entry	amine donor	deviation from benchmark conditions	yield **42** (%)
1	**G**	none	(57)
2	**I**	none	(64)
3	**I**	reaction performed on sulfonium salt **41**	(55)
4	**I**	reaction performed in 1,2-DCE	53
5	**I**	reaction performed using 25 mol% amine donor	(71)
6	**I**	reaction performed in the dark	no reaction
7	**I**	reaction performed in absence of amine donor	17
8	**I**	reaction performed in absence of base additive	6

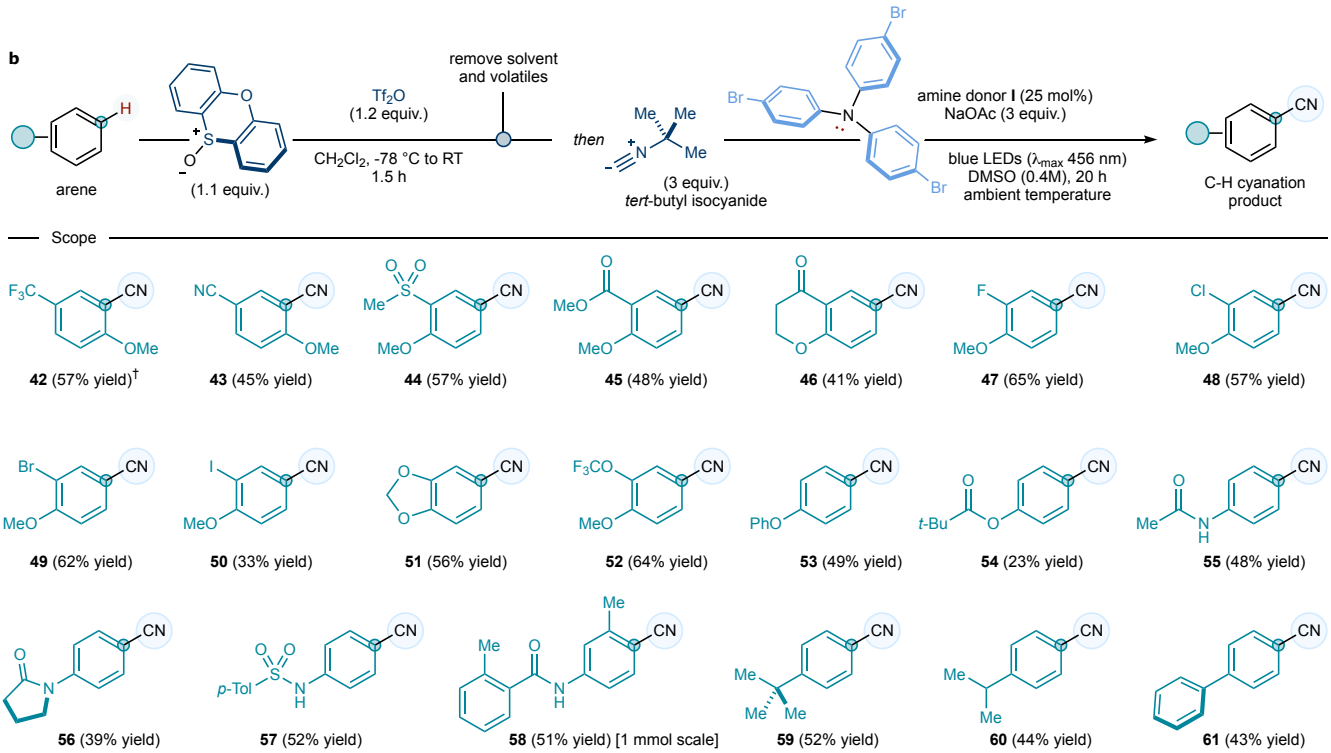


Figure 4 | Optimization and scope evaluation for the photochemical C-H cyanation protocol. **a,** Optimization of the reaction conditions for the radical cyanation of sulfonium salt **40** with *tert*-butyl isocyanide. **b,** Scope of the photochemical arene C–H cyanation sequence. All reactions performed on a 0.2 mmol scale. Yields were determined by ^{1}H-NMR spectroscopy using dibromomethane as internal standard; isolated yields are reported in parentheses. †Reaction run in the presence of 50 mol% of amine donor **I**.

Application to medicinal and agrochemistry. Both C–H functionalization protocols, enabled by the photoexcitation of EDA-complexes, are synthetically relevant to medicinal chemistry and agrochemistry. Specifically, the mild conditions and the high site-selectivity shown by our methods suggest that they can be used as precision tools to perform late stage modifications of complex biologically-relevant scaffolds[31]. As outlined in Figure 5a, aromatic rings embedded in pharmaceuticals and agrochemicals underwent regioselective C–H sulfenylation, by interrupted Pummerer activation, to deliver the corresponding sulfonium salts,

which were exposed to visible-light irradiation in the presence of donor **G** and the appropriate radical trap. Using this strategy, both homobenzoyl- and cyano-analogues of fungicide boscalid, hormone estrone, non-steroidal anti-inflammatory drug (NSAID) naproxen, hyperlipidemia medication gemfibrozil, and arrhythmias remedy mexiletine were obtained in good yield, as single regioisomers, with no further optimization of our previously identified reaction conditions. Furthermore, our arene C–H functionalization strategy can be applied to the *de novo* synthesis of pharmaceutical targets. To exemplify this, we performed two sequential C–H cyanation reactions on *iso*-butoxybenzene **72** – *para*- then *ortho*-selective cyanation – to obtain dicyano-derivative **74**, which is a synthetic precursor to gout and hyperuricemia treatment febuxostat (Uloric®, Figure 5b).[32]

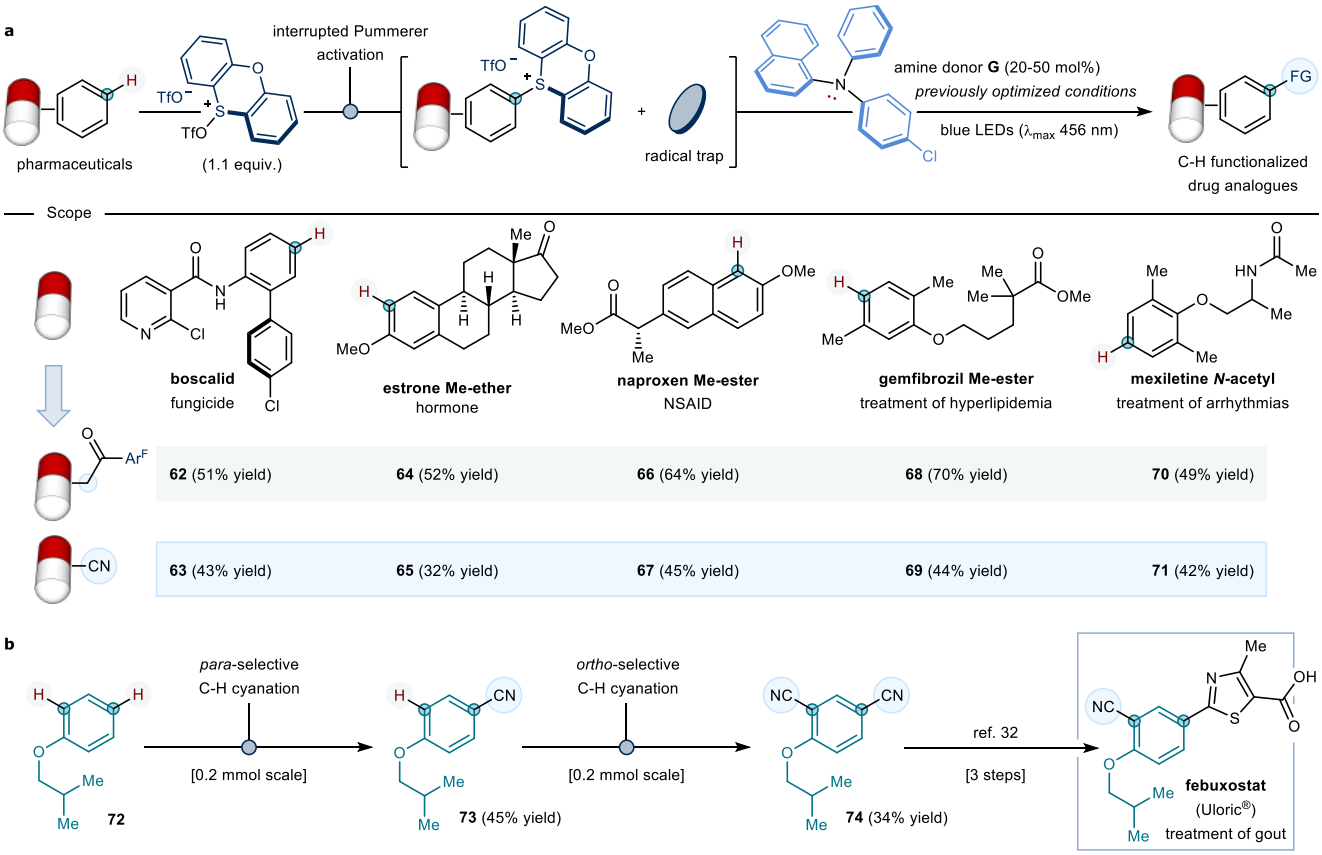


Figure 5 | Synthesis and late-stage functionalization of pharmaceuticals and agrochemicals. **a**, Participation of biologically-relevant molecules in the new radical C–H functionalization protocols involving EDA-complex photoactivation. **b**, Application of the photochemical C–H cyanation method to the synthesis of gout treatment febuxostat. Reactions performed on a 0.2 mmol scale; isolated yields are reported in parentheses. For optimized reaction conditions, refer to Figures 3&4. NSAID, non-steroidal anti-inflammatory drug. Ar^F, *para*-fluorophenyl-moiety (*c.f.* Figure 3).

Mechanistic insights. UV-vis studies were performed to corroborate the existence of charge transfer interactions between triarylsulfonium salts and the amine donors. The formation of EDA-complexes is characterized by a red-shift in the absorption spectra of the EDA-aggregate, with respect to the UV-vis profiles of the individual partners[33]. Figure 6a reports the spectroscopic characterization of the reaction components involved in the coupling between DBT^+-salt **2** and silyl enol ether **3**. Here, both sulfonium salt **2** and donor **G** present weak absorption profiles at the irradiation wavelength. Whereas, their interaction (**2**+**G**) provides the required shift towards the red region that grants a more intense – and thus productive – light-absorption at 456 nm. Interestingly, a distinct red-shift is also observed upon mixing **2** with silyl enol ether trap **3**, with the profile's absorption tail falling within the near-visible region. As previously suggested, a less efficient charge-transfer interaction between **2** and **3** is likely responsible for the low reactivity observed in the absence of donor **G** (*c.f.* Figure 2b, entry 8). An analogous study was performed on the reaction components employed in the photochemical cyanation protocol (Figure 6b). In this case, a less sizable red-shift was observed in the UV-vis spectrum of an equimolar mixture of PXT^+-salt **40** and donor **I** – compared to the absorption of donor **I** – however, a tail was seen that reaches the emission profile of the LED-light source used. Conversely, both equimolar solutions of sulfonium salt **40** and either the isocyanide trap, or the base additive (NaOAc)[34], had absorptions that did not stretch to the visible region, thus rendering unlikely the photoactivation of these aggregates under blue-light irradiation.

Having acquired experimental evidence for the formation of visible-light absorbing EDA-complexes between triarylamines and both DBT^+- and PXT^+-salts, we sought to test the participation of alternative sulfonium salt labels in charge-transfer interactions with amine donors. To this end, the photochemical arylation reaction of silyl enol ether **3**, catalyzed by donor **G**, was performed in the presence of a series of arylsulfonium salts, presenting different substitution at sulfur (Figure 6c). The photochemical coupling of DBT^+-salt **2** – which delivered **4** in 57% NMR-yield – was selected as the benchmark for this study. As expected, heterocyclic

triarylsulfonium salts, such as PXT$^+$- and thianthrenium (TT$^+$)-derivatives **75** and **76**, proved to be suitable substrates for the photochemical protocol, although their employment produced **4** in lower yields. Conversely, when aryl diphenylsulfonium salt **77** and its tetrahydrothiophenium-analogue **78** were used, only trace amounts of product **4** were detected, and the sulfonium salt starting materials were, in both cases, recovered in high yield after irradiation. The latter results indicate that the aromatic system of the sulfonium redox-active tag, as opposed to the one of the native arene precursor, is responsible for EDA-complex formation. Furthermore, this study highlights that the heteroaromatic character of the sulfonium salt label is a paramount requirement to ensure productive charge transfer interactions with the electron-donor.

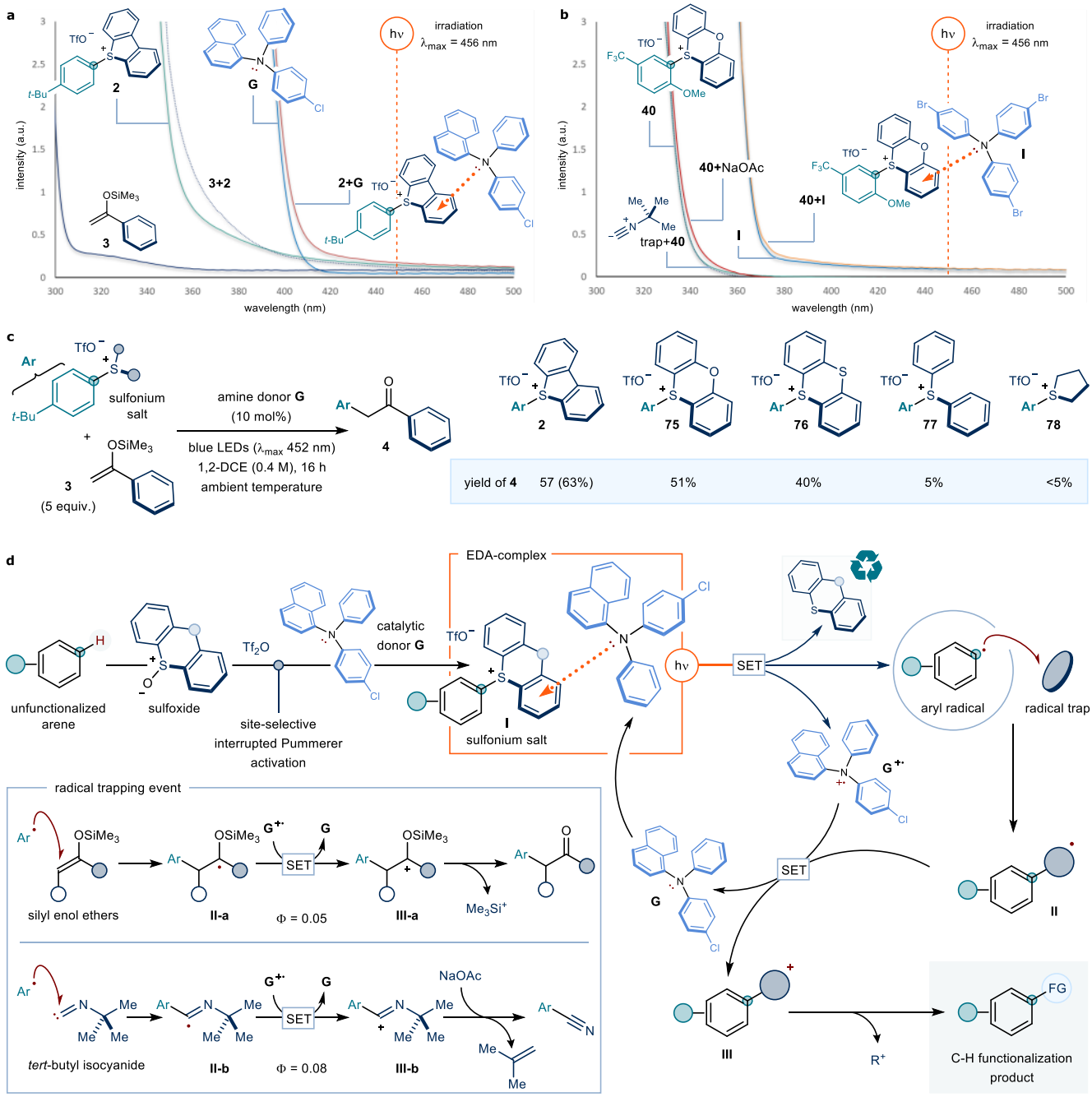


Figure 6 | Mechanistic studies and proposed reaction pathway. Spectroscopic characterization (UV-vis) of the reaction components of (**a**) the C–H alkylation and (**b**) the C–H cyanation protocols, revealed the occurrence of charge transfer interactions (red shift) between triarylsulfonium salts and amine donors. UV-vis analyses were carried out on 0.04 M solutions of analyte. **c**, Ability of different sulfonium salts to participate in EDA-complex photoactivation with amine **G**. **d**, Postulated mechanistic steps underpinning the photochemical arene C–H functionalization strategy. FG; functional group.

The low quantum yield determined for both the photochemical arylation and cyanation processes (Φ = 0.05 and 0.08, respectively – see Supporting Information for more details) suggests that a radical chain manifold, triggered by the photoactivation of the EDA-complexes, is either very unlikely or highly unproductive.[33] Based on this and our other mechanistic studies, we propose the fol-

lowing mechanistic pathway for our C–H functionalization methods (Figure 6d): Site-selective addition of activated heteroaromatic sulfoxides to unfunctionalized arenes, by means of interrupted Pummerer reactivity, generates sulfonium salts **I**. The electron-deficient heteroaromatic system of the sulfonium salt label is able to form photoactive EDA-complexes with suitable triarylamine electron-donors, such as **G**, present in substoichiometric to catalytic amounts. Blue-light irradiation of the EDA-complex triggers SET from the amine to salt **I**, which generates the radical cation of the electron-donor ($\mathbf{G}^{\bullet+}$ in Figure 6d) and drives the formation of the aryl radical, upon extrusion of the sulfide heterocycle. Interception of the aryl radical intermediate by a radical trap delivers open shell species **II**, which are oxidized by $\mathbf{G}^{\bullet+}$ to give cations **III**, thus restoring the active electron-donor catalyst. Finally, fragmentation of either trimethylsilyl cation or isobutene – from **III** (*c.f.* radical trapping event in Figure 6d) – produces the desired C–H functionalization products.

Conclusions

Heterocyclic sulfonium moieties, embedded in triarylsulfonium salts, can be exploited as redox-active labels to form visible light-absorbing EDA-complexes in combination with simple Lewis basic organic compounds – such as triarylamines – present in catalytic amounts. The photoactivation of these complexes offers a metal-free strategy for the formation of aryl radicals. This approach is the first to enable the generation of aryl radicals, by means of EDA-complex photoactivation, independent of the electronics of the aromatic substrates. Furthermore, the possibility to regioselectively install the sulfonium labels on unfunctionalized arenes, via C–H sulfenylation, allows the development of programmable C–H functionalization sequences. This strategy was used to develop site-selective, metal-free procedures for both the C–H alkylation and C–H cyanation of native arenes; thus delivering high value α-arylated carbonyl compounds and aryl nitriles, respectively, whose formation would otherwise require transition metal-catalysts. The synthetic potential of the radical C–H functionalization protocols was showcased through the facile modification and *de novo* synthesis of blockbuster drug molecules and agrochemicals. We envisage that our EDA-complex photoactivation strategy will serve as a launchpad for the invention of novel organocatalytic aromatic C–H functionalization processes.

Supplementary Information is linked to the online version of the paper at www.nature.com/nature.

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Author contributions J.A.R.A., G.E.M.C. and D.J.P. conceived the project. L.v.D. and A.D. designed and performed the experimental work, with contributions from J.A.R.A., E.G. and G.E.M.C. All authors contributed to the analysis and interpretation of data. G.E.M.C. and D.J.P. wrote the manuscript with input from all authors. L.v.D. and A.D. contributed equally to this work and, thus, they both have the right to list their name first on their *curriculum vitae*.

Data availability Materials and methods, experimental procedures, useful information, mechanistic studies, ^{1}H NMR spectra, ^{13}C NMR spectra and mass spectrometry data are available in the Supplementary Information. Crystallographic data for compounds **2**, **27**, **29**, **40**, **58** and **62** have been deposited with the Cambridge Crystallographic Data Centre, with deposition numbers CCDC 2120242, 2120244, 2120243, 2122516, 2122517, 2120245, respectively. Reprints and permissions information is available at www.nature.com/reprints. The authors declare no competing financial interests. Correspondence and requests for materials/raw data should be addressed to the corresponding author (david.j.procter@manchester.ac.uk).

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