Organophotoredox Catalyzed C–O Bond Cleavage: A Chemoselective Deprotection Strategy for Phenolic Ethers and Esters Driven by the Oxophilicity of Silicon

Tanumoy Mandal,[a] Malekul Islam,‡[a] Sanat Kumar Mahapatra,‡[b] Sanju Das,[a] Aznur Azim,[a] Lisa Roy*[b], and Suman De Sarkar*[a]

[a]Department of Chemical Sciences, Indian Institute of Science Education and Research Kolkata, Mohanpur 741246, India.

[b]Institute of Chemical Technology Mumbai, IOC Odisha Campus, Bhubaneswar 751013, India.

ABSTRACT: An organo-photocatalyzed approach for the chemoselective dealkylation and de-esterification of phenols is developed by employing trimethyl silyl chloride as the C–O bond activator and 9-Mes-10-MeAcr$^+$ClO$_4^-$ as the photoredox catalyst. This method demonstrates an exceptional selectivity towards the cleavage of phenolic ethers and esters over equivalent aliphatic scaffolds, presenting a broad range of functional group sustainability. This strategy also enables selective debenzylation of phenols in the presence of reduction-sensitive functional groups. The photocatalytic efficiency was further extrapolated in the fragmentation of lignin models and synthetic modification in manufacturing a FLAP inhibitor. Mechanistic studies, photophysical experiments and computations provide evidence for the involvement of an oxonium intermediate, generated through the photo-oxidation of the arene ring, which ultimately leads to the selective disintegration of C–O bond, facilitated by the oxophilicity of silicon.

Protection and deprotection strategies operate as an inevitable tool to perform specific synthetic steps in the presence of multiple mutually competitive functional groups in target-oriented transformations.[1] Phenolic compounds are considered as a primitive class of structural motifs to construct the core backbone of numerous complex molecular architectures amidst oxygen-based synthetic handles (Fig 1).[2]

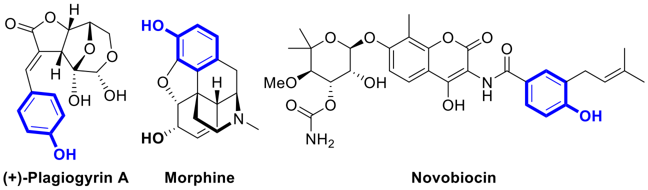
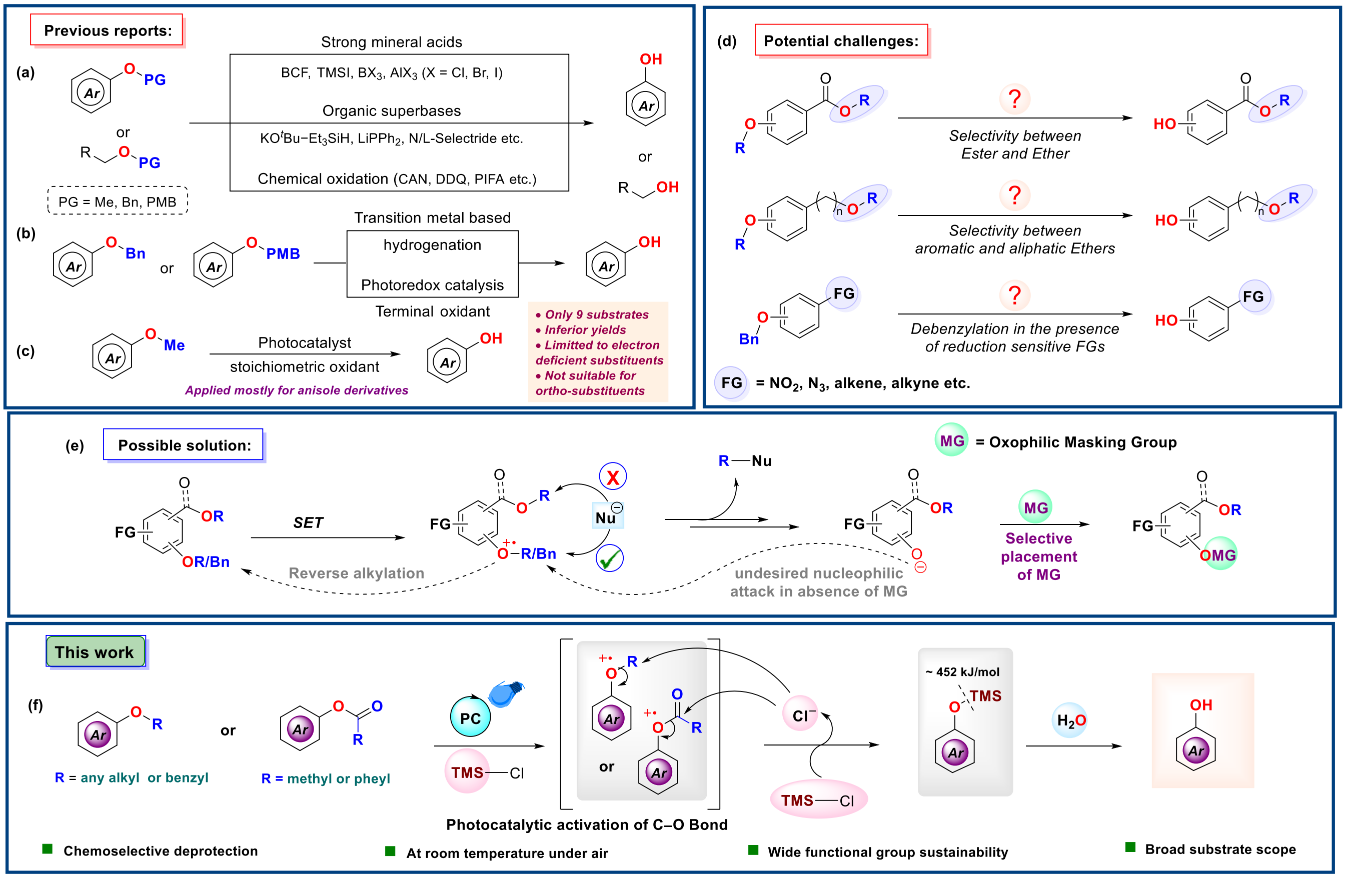


Figure 1: Phenolic-OH containing bioactive molecules.

From an obligatory synthetic perspective, masking phenolic-OH with appropriate protecting groups is necessary to prevent undesired side reactions.[3] Among the wide variety of protection strategies, anisole derivatives, aryl benzyl or other aryl alkyl ethers and acetoxy arenes are most extensively utilized in organic synthesis as the precursors of phenols owing to their easy installation procedures and inherent sustainability during the targeted conversion. Consequently, different deprotection methods of the phenol functionality have been reported in the literature depending on the protecting groups. The most steadfast approaches for the demethylation of anisole derivatives are commonly explored with the involvement of strong hydrohalic acids (e.g., HBr and HI)[4] at elevated temperature, Lewis acids (e.g., BCl_3, BBr_3, $AlCl_3$, AlI_3, TMSI etc.),[5] nucleophilic reagents (e.g., NaSEt, $NaN(SiMe_3)_2$, $LiPPh_2$, L-Selectride),[6] and organic super bases[7] generally at low temperatures (Scheme 1a). However, the employment of stoichiometric amount of highly reactive reagents, specially designed catalysts, harsh reaction conditions, cumbersome handling protocols, and unwanted byproduct formations restrict the widespread applications of these orthodox procedures. Often the above methods are incompetent to be utilized as the general dealkylation process for the phenolic ethers, consisting of alkyl groups other than methyl. In addition, many of those display uncontrollable reactivities, which might disrupt chemo- and regioselectivity issues between aliphatic and aromatic ethers and esters.[5b, 8] Alternatively, the most frequently applied process to remove benzyl or other comparable protecting analogs is the transition-metal catalyzed hydrogenation (Scheme 1b).[9] It is noteworthy to mention that the existence of reduction-sensitive functional groups like CN, NO_2, CHO, alkene, alkyne etc. are often sacrificed under this hydrogenation process at high pressure. Strong oxidant-based C(sp^3)–O cleavage of benzyl and PMB (*p*-methoxy benzyl) groups is another widely used strategy.[10] However, the overall process produces copious byproducts due to their unselective reactivity patterns and generates a significant amount of noxious inorganic wastes.[11] On the other hand, deacetylation of acetoxybenzene derivatives requires acidic or basic hydrolysis with a high concentration of inorganic acids or bases, which are found to be indiscriminating towards other carboxylic acids.[12]

Over the last two decades, visible-light-mediated photoredox catalysis has shown a new horizon and illustrates superior ways for selective bond disconnections by virtue of specific redox properties of the photocatalysts, which were elusive in traditional synthetic procedures.[13] In the recent past, several photoredox-catalyzed methods have been documented for the deprotection of PMB-protected phenols and aliphatic alcohols by Stephenson, Cheng, Pieber and others.[14] However, all these reports explored the undeniable participation of stoichiometric amounts of terminal oxidants like $BrCCl_3$, peroxides, per disulfates, DDQ etc.

https://doi.org/10.26434/chemrxiv-2024-czccz **ORCID:** https://orcid.org/0000-0002-6342-4711



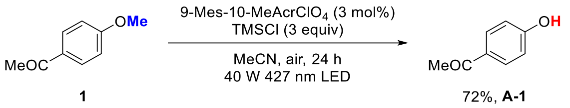
Scheme 1. Prior strategies on phenolic ether/ester cleavage, existing limitations, and planned solution.

Consequently, Xia developed an innovative route for the intrinsic removal of the benzyl group from benzyloxy phenols, which proceeds via arene radical anion species by means of the super photo-reductive ability of an especially designed organophotocatalyst.[15] Nevertheless, the current photoredox-catalyzed approaches are predominantly restricted only to the removal of benzylated ethers[16] and protocols covering a broader substrate class is extremely limited.[17] Lei employed a combination of 9-Mes-10-MeAcr$^+$ClO$_4^-$ and stoichiometric selectfluor for the successive HAT and photo-oxidation to demask corresponding phenols (Scheme 1c).[17b] This method was confined only for demethylation and displayed narrow substrate scope. In these circumstances, a general synthetic route is highly desirable, which will enable chemoselective fragmentation of phenolic esters over alkyl benzoates; between aliphatic and aromatic ethers and will facilitate selective debenzylation of phenols in the presence of reduction-sensitive functional groups (Scheme 1d).

We observed that the fundamental working principle in previously described photoredox-catalyzed dealkylation approaches is rather general.[18] Initially, the phenol-based aromatic ring undergoes single electron oxidation to produce an arene radical cationic intermediate through reductive quenching of the photocatalyst and this crucial step is identical in most cases.[19] Comprehending these redox behaviours of the photocatalyst and the substrate, we envisioned that the arene radical cationic intermediate can undergo chemoselective nucleophilic dealkylation or de-esterification giving rise to phenoxy anionic species (Scheme 1e). The appropriate selection of a masking group could efficiently bind with the oxygen atom of this phenoxy anionic intermediate to prevent the reverse alkylation process and effectively facilitate the dealkylation or deacetylation process in a chemoselective fashion. In line with our recent endeavours on sustainable redox chemistry,[20] herein, we report a versatile method for the chemoselective deprotection of phenolic ethers and esters through the fragmentation of C(sp^3)–O bond under visible-light promoted photoredox catalysis (Scheme 1f).

The prime impediment in initiating our research was the excerption of a scrupulous masking group that could irreversibly bind with the phenoxy anion generated from phenolic ether or ester and promote the chemoselective deprotection process. We presumed that a mild reagent (masking group) consisting of boron or silyl moiety might be the benefitting predilection for the postulated transformation as O–B and O–Si bond formation are thermodynamically favorable because of high bond energies (~536 KJ/mol and ~452 KJ/mol, respectively).[21] Consequently, the selection of a suitable photocatalyst is also important to oxidize the protected phenol derivatives. Considering the reports in the literature, 9-Mes-10-MeAcr$^+$ClO$_4^-$ was strategically elected as the photocatalyst because it offers a high photo-oxidation window of +2.18 V vs SCE.[22] Accordingly, we commenced our investigation with the demethylation reaction by choosing 4-methoxy acetophenone (**1a**) as the model substrate and trimethyl silyl chloride (TMSCl) as the C–O bond activator. An equimolar mixture of **1a** and TMSCl was treated with 3 mol% of 9-Mes-10-MeAcr$^+$ClO$_4^-$ (**PC**) and the mixture was irradiated under 427 nm 40 W Kessil LED in MeCN under air. Gratifyingly, this reaction resulted in the formation of 4-acetyl phenol (**A-1**) in 72% isolated yield after 24 hours (Table 1, entry 1). We examined the individual requirement of the photocatalyst, light source, and TMSCl at this stage. As per our expectation, the reaction hardly occurred without any of these (see SI for details). Other photocatalysts, like, Ir[(dF-CF$_3$ppy)$_2$dtbbpy]PF$_6$, 4-CzIPN and triphenyl pyrilium salt (TPP) were employed separately to carry out this transformation (entry 3). Unfortunately, the demethylated product was obtained in poor yield (18 to 40%). Next, we performed an experiment using B$_2$Pin$_2$ as the activating group and it was found to be less impactful on the reaction outcome (entry 4). Among other silyl chloride derivatives, Et$_3$SiCl was effective, albeit at a much inferior yield of 54% (entry 5), whereas other bulky silyl-agents (TIPSCl, TBDMSCl, TBDPSCl) hardly produced **A-1** (entry 6). Lowering the equivalent of TMSCl was inefficient (entry 7). The yield of **A-1** decreased significantly when a 1:1 mixture of MeCN and water was used as the reaction medium (entry 8). Other polar, non-polar and chlorinated solvents were also utilized as the solvent, but no improvement in productivity was noticed (entry 9). Pleasingly, increasing the catalyst loading to 5 mol% and prolonging the reaction time to 36 hours was found to be more efficient and the demethylation process was finished with 84% isolated yield (entries 10 and 11). Notably, utilization of other Fukuzumi catalyst[23] provided slightly diminished yield (entry 12).

Table 1. Optimization of the reaction conditions[a]

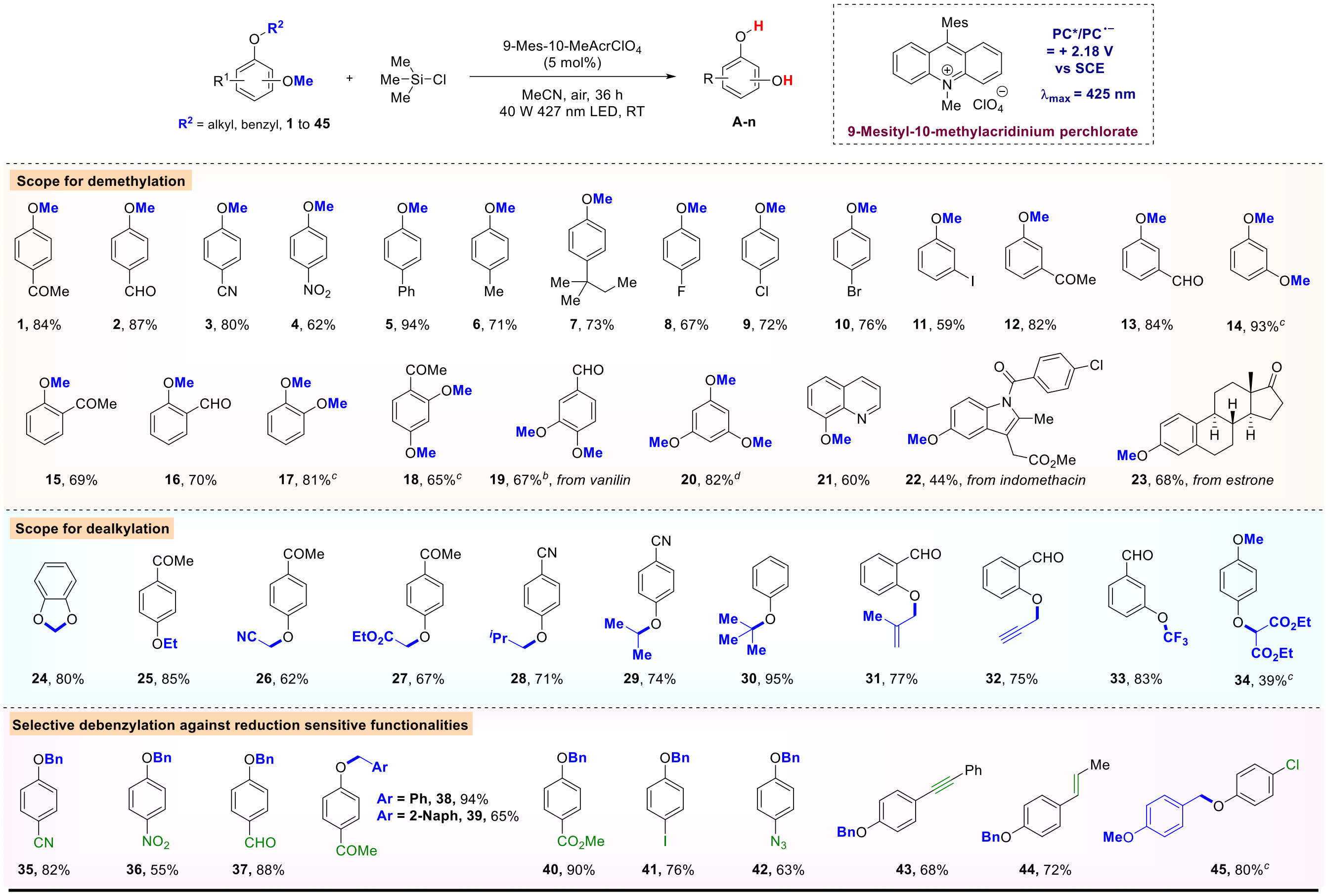


entry	deviation from standard conditionss	yield[b] (%)
1	none	72
2	no TMSCl/no PC/in dark	trace
3	[Ir]/4-CZIPN/TPP as the photocatalyst	18-40
4	B$_2$Pin$_2$ as activating agent	23
5	Et$_3$SiCl as activating agent	54
6	TIPSCl/TBDMSCl/TBDPSCl	trace
7	2 equiv of TMSCl was used	60
8	MeCN : H$_2$O (1:1) as the solvent	46
9	DCE/DMF/DMSO/toluene/1,4-dioxane was used as the solvent	15-52
10[c]	5 mol% 9-Mes-10-MeAcrClO$_4$ was used	78
11[c]	the reaction was continued for 36 h	84
12[c]	3,6-di-^{t}Bu-9-Mes-10-PhBF$_4$ was used	70

[a]Reaction conditions: **1** (0.5 mmol), TMSCl (1.5 mmol), photocatalyst (3 mol%), MeCN (3 mL), irradiation under 427 nm Kessil LED (40 W), 24 h. [b]Isolated yield. nd = Not detected. [c]5 mol% photocatalyst was used.

Once the optimum conditions were identified, we were interested in exploring the scope of demethylation to check the versatility and sustainability of this method (Table 2). Accordingly, *para*-substituted anisole derivatives containing electron withdrawing groups like COMe, CHO, CN, NO$_2$ (**1** to **4**), electron neutral groups Ph, Me, *tert*-amyl, and halogens (F, Cl, Br) were tested under the optimized reaction conditions. To our delight, all of those were successfully converted to the corresponding phenols with good to excellent yield (62% to 94%). Subsequently, the effect of *meta*- and *ortho*-substituent on this transformation was scrutinized against electronically deficient COMe and CHO groups (**12**, **13**, **15** and **16**), electron-rich OMe group (**14** and **17** to **19**) and halogen (3-iodo, **11**). The demethylation of these substrates occurred smoothly to produce the demasked phenols with moderate to excellent yields (59 to 93%). Interestingly, anisole derivatives bearing more than one methoxy group eventually underwent demethylation twice to deliver resorcinol (from **14** and **18**), catechol (from **17**) and protocatechualdehyde (from **19**). Similarly, 1,3,5-trimethoxy benzene was also smoothly transformed to phloroglucinol with 82% yield. The efficiency of this protocol remained unaltered for methoxy substituent attached to hetero aromatic (**21**) ring and the desired hydroxylated product was obtained in 60% yield. Pleasantly, the demethylation method was also found to be benevolent in producing demethylated indomethacin methyl ester (**22**) and estrone (**23**) from the corresponding methylated modification in 44% and 68% yield, respectively. Afterward, we concentrated on applying this strategy to the phenols protected with alkyl groups other than methyl. The newly developed protocol was found to be general and displayed profound efficiency in the C(sp^3)–O bond cleavage of diverse aryl alkyl ethers. In this context, catechol was obtained from 1,3-benzodioxole (**24**) with 80% of isolated yield. Next, we carried out the experiments for both the electron-deficient and electron-rich phenol analogs protected with the primary or secondary alkyl group like ethyl (**25**), cyanomethyl (**26**), acetyl (**27**), isobutyl (**28**), isopropyl (**29**) and *tert*-butyl (**30**) groups. Delightfully, all these substrates proficiently participated in the reaction to afford the corresponding phenols with moderate to high yield. Concomitantly, salicylaldehyde derivatives comprising allyl and propargyl substituents (**30** to **32**) were also compatible under the optimized reaction conditions to reconstruct the mother phenol substrate. Trifluoromethylated benzaldehyde derivative, **33**, also underwent fruitful dealkylation to afford 3-hydroxy benzaldehyde with 83% yield. Subsequently, malono-anisole **34** experienced simultaneous dealkylation of both the malonate protection and demethylation to construct *p*-quinol in 39% yield. To verify the potential ability of the photoredox-catalyzed dealkylation procedure, we decided to employ it on several benzyl-protected phenols comprising reduction-sensitive substituents like, -CN, -NO$_2$, -CHO, -COMe, -CO$_2$Me, -I, azide, alkyne, and alkene (**35** to **45**). We were pleased to experience the irrevocability of this process. Accordingly, the corresponding phenols were isolated in moderate to high yield (55 to 90%) with the preservation of the aforementioned functional groups (Table 2). In this regard, 2-naphthylmethyl (**39**) and PMB (**45**) protected phenols were also subjected to the standard reaction conditions and the consequent C(sp^3)–O bond fragmentation manufactured the 4-acetyl and 4-chloro phenol with 65% and 80% yields, respectively. Thereafter, we shifted our attention to the chemoselectivity issues which are often confronted during the dealkylation process with common strong Lewis acid, like BBr$_3$. Simultaneous dealkylation and de-esterification of alkyl alkoxy benzoates is a recurring problem.

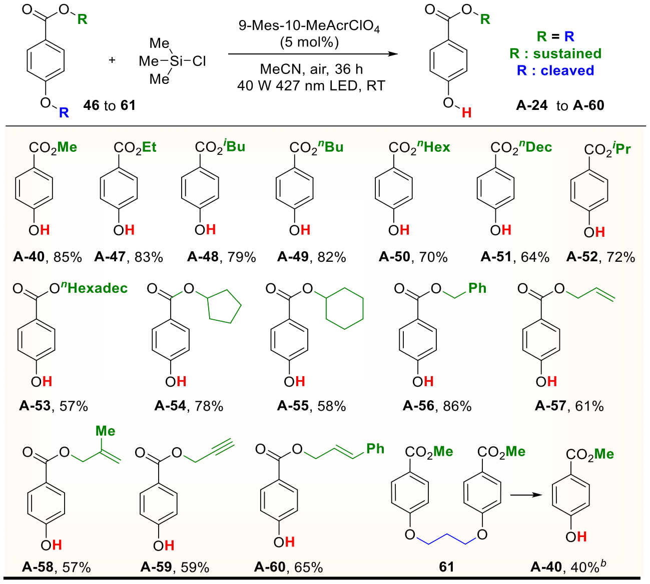
Table 2. Substrate Scope for demethylation, general dealkylation and selective debenzylation processes[a,b]



[a] Reaction conditions: Phenolic ether (0.5 mmol), TMSCl (3 equiv), 9-Mes-10-MeAcrClO4 (5 mol%), MeCN (3 mL), irradiation under 427 nm Kessil LED (40 W), 36 h. [b] Isolated yield. [c] TMSCl (6 equiv) and photocatalyst (10 mol%) were used. [d] TMSCl (9 equiv), photocatalyst (15 mol%) were used.

We anticipated that the TMSCl-mediated photocatalyzed dealkylation process could be adroit to circumvent this abiding challenge. Therefore, reactions with different alkyl-4-alkoxy benzoate derivatives, enclosed to the same alkyl groups at both carboxyl and hydroxyl ends were performed (Table 3). Accordingly, benzoate scaffolds bearing small to long-chain primary alkyl substituents like, Me (**46**), Et (**47**), propyl (**48**), *n*-butyl (**49**), *n*-hexyl (**50**), *n*-decyl (**51**), and *n*-hexadecyl (**53**) and secondary alkyl groups like, isopropyl (**52**), cyclopentyl (**54**), and cyclohexyl (**55**) were advantageously transformed to the corresponding 4-hydroxy benzoate frameworks (**A-40** to **A-60**) in 58 to 85% yield without cleaving the ester functionalities. Consequently, benzyl (**56**), allyl (**57**, **58**), propargyl (**59**) and cinnamyl (**60**) containing alkyl-4-alkoxy benzoates were engaged in the reaction under standard reaction conditions to fabricate the corresponding 4-hydroxy alkenylated esters with 57 to 86% yields. Finally, we carried out this chemoselective dealkylation with the methyl 4-hydroxybenzoate derivative, connected with a propyl chain (**61**). The desired doubly dealkylated product **A-40** was accomplished with 40% yield.

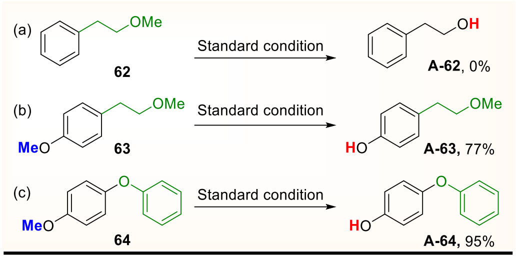
Table 3. Scope for selective dealkylation of alkyl alkoxy benzoate derivatives.[a,b]



[a] Reaction conditions: Alkyl alkoxy benzoate (0.5 mmol), TMSCl (3 equiv), 9-Mes-10-MeAcrClO4 (5 mol%), MeCN (3 mL), irradiation under 427 nm Kessil LED, 36 h. [b] Isolated yield. [c] TMSCl (6 equiv) and 9-Mes-10-MeAcrClO4 (10 mol%) were used.

As discussed earlier, the regioselectivity between aliphatic and aromatic ethers is typically sacrificed in the conventional alkyl deprotection methods. Therefore, we were interested in resolving the selectivity concerns of this dealkylation process. An unorthodox reactivity pattern was observed while **62**, **63** and **64** were treated individually under photocatalyzed dealkylation conditions (Table 4). **62**, containing only the aliphatic methoxy group, remained unreacted during the course of the reaction, while **63** underwent a regioselective demethylation only at the phenolic ether end to afford **A-63** in 77% isolated yield. Interestingly, **64** demonstrated a reactivity exclusively at the anisole end and offered **A-64** with 95% yield.

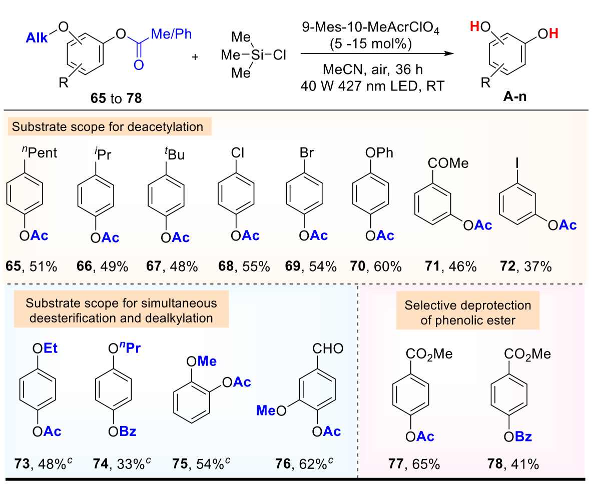
Table 4. Scope for selective dealkylation of phenolic ethers.[a,b]



[a]Reaction conditions: Ether (0.5 mmol), TMSCl (3 equiv), 9-Mes-10-MeAcrClO$_4$ (5 mol%), MeCN (3 mL), irradiation under 427 nm Kessil LED (40 W), 36 h. [b]Isolated yield.

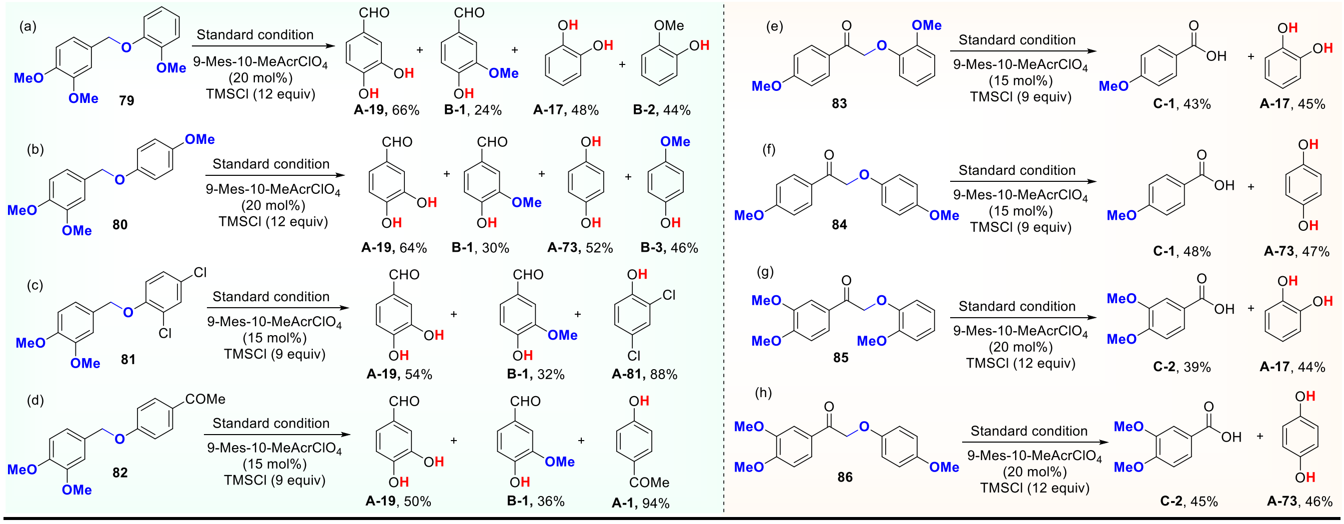
Encouraged by the fascinating proficiency of the dealkylation process, we were enthusiastic to check the credibility of this method on the de-esterification of the phenolic esters (Table 5).[24] The deacetylation of *para*-, *meta*-, and *ortho*-substituted acetoxy benzenes attached to electronically diverse functionalities such as *n*-pentyl (**65**), *iso*propyl (**66**), *tert*-butyl (**67**), chloro (**68**), bromo (**69**), iodo (**72**), and COMe (**71**) group was effectively carried out to deliver the corresponding phenols in acceptable yields (37 to 55%). A similar reactivity was noticed in the case of 4-phenoxy acetoxy benzene (**70**) with subsequent de-esterification occurred on the phenolic ester with 60% yield. Notably, simultaneous dealkylation and deacetylation occurred for **73**, **75** and **76** to access the completely unprotected quinol, catechol and vanillin, respectively, with satisfactory yields (48 to 62%). Similarly, the standard reaction conditions were competent to disrupt both the C–O bonds in **74** and lead to concurrent dealkylation and debenzoylation to produce quinol. Next, we moved our focus to investigate the chemoselectivity between phenolic esters and alkyl benzoates. In this context, two methyl benzoate derivatives comprising acetyloxy (**77**) and benzoyloxy (**78**) functionalities were treated under standard photochemical conditions. Pleasantly, the chemoselective deprotection of the phenolic esters occurred without disrupting the CO_2Me group to deliver 4-hydroxy derivatives in acceptable yields.

Table 5. Scope for selective de-esterification of phenolic esters[a,b]



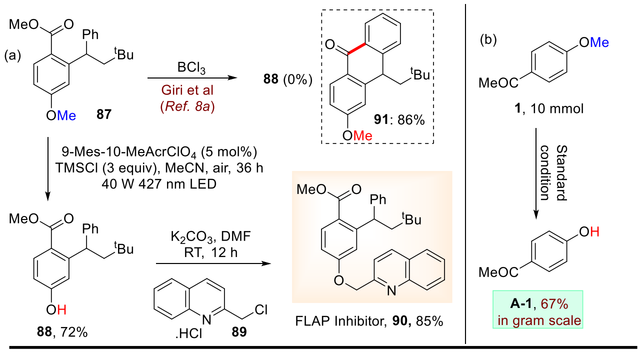
[a]Reaction conditions: Ester derivative (0.5 mmol), TMSCl (3 equiv), 9-Mes-10-MeAcrClO$_4$ (5 mol%), MeCN (3 mL), irradiation under 427 nm Kessil LED (40 W), 36 h. [b]Isolated yield. [c]TMSCl (6 equiv), 9-MesAcrClO$_4$ (10 mol%) were used.

Table 6. Cleavage of lignin models[a,b]



[a]Reaction conditions: Lignin model (0.5 mmol), TMSCl (3-12 equiv), 9-Mes-10-MeAcrClO$_4$ (5-20 mol%), MeCN (3 mL), irradiation under 427 nm Kessil LED (40 W), 36 h. [b]Isolated yield.

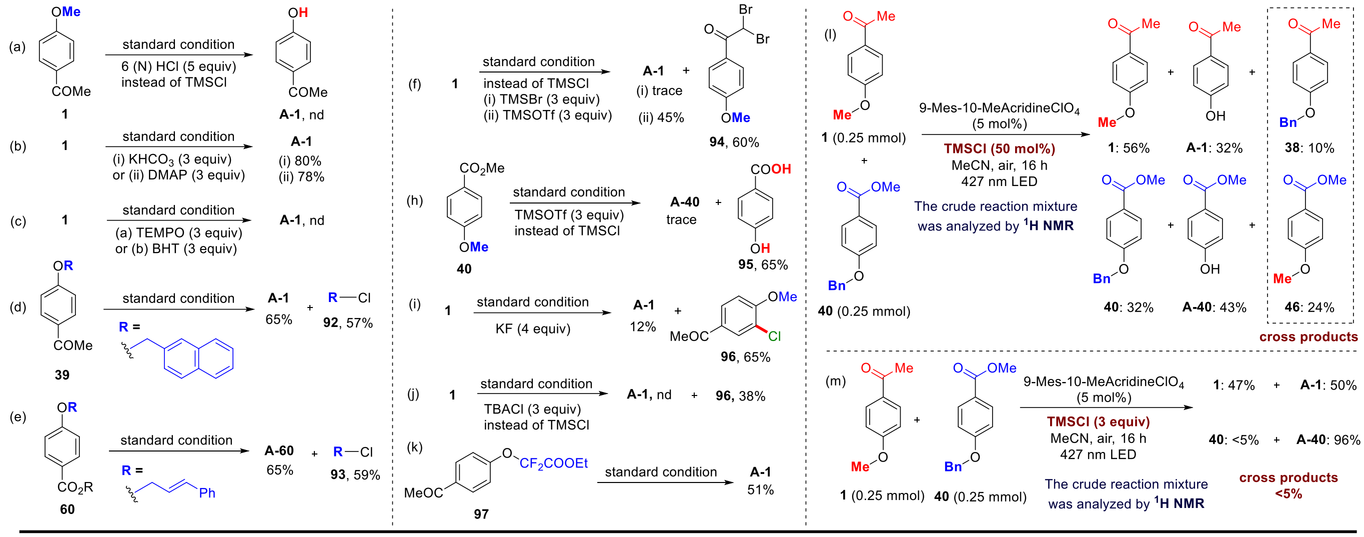
Lignin is an important source of phenol derivatives and has the potential to serve as a raw material for several valuable moieties.[25] After realizing the distinguishable reactivity trend towards the chemo- and regioselective dealkylation and de-esterification of the phenol derivatives by the cooperative effect of TMSCl and photocatalyst, this strategy was applied to the controlled fragmentation of lignin models. In this regard, the disintegration of the lignin models with α-O-4 linkage and the keto model of β-O-4 linkage (Table 6) were performed under the optimized reaction conditions.[26] The amounts of the photocatalyst and TMSCl were determined according to the number of fragmentable C(sp^3)–O bonds. A satisfactory reactivity pattern was observed for all the lignin models with α-O-4 linkage (**79** to **82**) and they were disrupted to the separable mixture of corresponding phenols (**A-17**, **A-73**, **A-81** and **A-1**), mono methoxy phenols (**B-2** and **B-3** for **79** and **80**, respectively), veratraldehyde (**A-19**) and vanillin (**B-1**). The transformation with the keto model (**83** to **86**) proceeded with the cleavage of β-O-4 linkage and subsequent oxidation produced the corresponding benzoic acid derivatives **C-1** (for **83** and **84**) and **C-2** (for **85** and **86**) along with dihydroxy benzene derivatives (**A-17** and **A-73**).



Scheme 2. Synthetic application and scale-up experiment.

Next, the developed strategy was applied in the synthesis of a FLAP inhibitor **90** (Scheme 2a, see SI for details). In this target-oriented transformation, we envisioned resolving an inescapable problem of activation of the ester over the methoxy group in the presence of strong Lewis acid BCl$_3$, which leads to the formation of an undesired product **91**.[8a] In the current approach, the chemoselective demethylation protocol was applied in the crucial step (from **87** to **88**) to access the potential 5-lipoxygenase activating protein (FLAP) inhibitor **90**. Furthermore, the practical viability of this method was demonstrated in a gram-scale demethylation of the model substrate **1** (1.5 g) to deliver 4-hydroxy acetophenone in 67% yield (Scheme 2b).

Several control experiments were conducted to authenticate the mechanistic pathway operating in this photoredox-catalyzed C–O bond cleavage (Scheme 3). To investigate the possible involvement of *in situ* generated HCl in the dealkylation and de-esterification process, an experiment was performed using 6 (N) aq. HCl as an additive instead of TMSCl, which did not deliver the demethylated phenol **A-1** (Scheme 3a). Additionally, the presence of stoichiometric inorganic or organic base additive did not restrict the productivity of this transformation and **A-1** was isolated in high yield (Scheme 3b). These sets of experiments evidently invalidate any influence of HCl during the dealkylation or de-esterification process. Thereafter, the standard model reaction was executed in the presence of radical quenchers like TEMPO and BHT, independently (Scheme 3c). Both the reactions were completely shut down, indicating the possible involvement of any radical intermediate(s). Next, the reaction outcome of the alkyl fragment was investigated in detail (Schemes 3d and 3e). Accordingly, **39** and **60** were subjected under the standard conditions separately and naphthyl chloride (**92**, 57%) and cinnamyl chloride (**93**, 59%) were isolated, respectively. This conclusively proves the important role of chloride anion during the final removal of the alkyl group in the form of alkyl chloride. We also performed the reaction in the presence of TMSBr and TMSOTf in individual cases (Scheme 3f). Surprisingly, dibromination occurred at the side chain and **94** was obtained in 60% yield along with trace amount of **A-1**. On the contrary, only 45% of **A-1** was produced in case of TMSOTf and the rest of the starting material was decomposed (Scheme 3h). In addition, when **40** was treated under standard reaction conditions using TMSOTf (instead of TMSCl), the chemoselectivity issues were sacrificed in the presence of this strong Lewis acid and both dealkylation and de-esterification delivered salicylic acid **94** in 65% yield. Notably, trapping the TMS group using a fluoride salt significantly lowers the efficacy and results in undesired chlorination (Scheme 3i). Similar chlorinated byproduct **96** was isolated using super stoichiometric chloride reagent in the absence of silyl source (Scheme 3j), proving the vital part of the oxophilic Si-atom[27] for selective deprotection. To discard the probability of HAT during the dealkylation process, the difluoroalkyl substrate **95** was smoothly transformed to phenol **A-1** in 51% yield (Scheme 3k). Furthermore, to shed light on the inevitable role of TMSCl, a cross-over experiment was performed by mixing equimolar ratio of **1** and **40** (Scheme 3l). The mixture was irradiated under standard conditions in presence of 50 mol% of TMSCl for 16 hours. Interestingly, significant amounts of cross-products **38** and **46** were detected (by ^{1}H NMR study). This experiment suggests the formation of the phenoxide intermediate which reacts with the oxidized radical cationic intermediate of the other ether and generate the cross product. In contrast, the same experiment was replicated using 3 equiv of TMSCl under standard reaction conditions and we obtained the mixture of deprotected phenols **A-1** and **A-40** along with some amount of unreacted starting materials after 16 hours of photoexcitation. Notably, no cross-over alkylated product **38** and **46** was detected in this case (Scheme 3m). These findings suggest the formation of phenoxide intermediate (**D**, *vide infra*) which immediately binds with the TMSCl due to the high oxophilicity of silicon. This oxophilicity of silicon and strong O–Si bond formation triggers the transformation to proceed in the forward direction by restricting the re-alkylation of the phenoxide. Rather, the catalytically generated chloride abstracts the alkyl counter-part from the photo-oxidized aryl alkyl ether and facilitates the reaction in the desired direction. .



Scheme 3. Control experiments.

The luminescence quenching experiment of the photocatalyst was performed against phenol derivatives (**1**, **46** and **66**) and TMSCl (Figure 2a). It was observed that quenching of emission intensity of the photocatalyst occurred more effectively with the phenol derivatives compared to TMSCl, upon the gradual increase in the concentration of the quenchers and the Stern-Volmer plot was portrayed accordingly. Furthermore, cyclic voltammograms of the different phenol derivatives[28] (Figure 2b) indicated the feasible oxidation by the excited acridinium catalyst (**PC***/**PC**$^{\bullet-}$ = +2.18 V vs SCE).[22a]

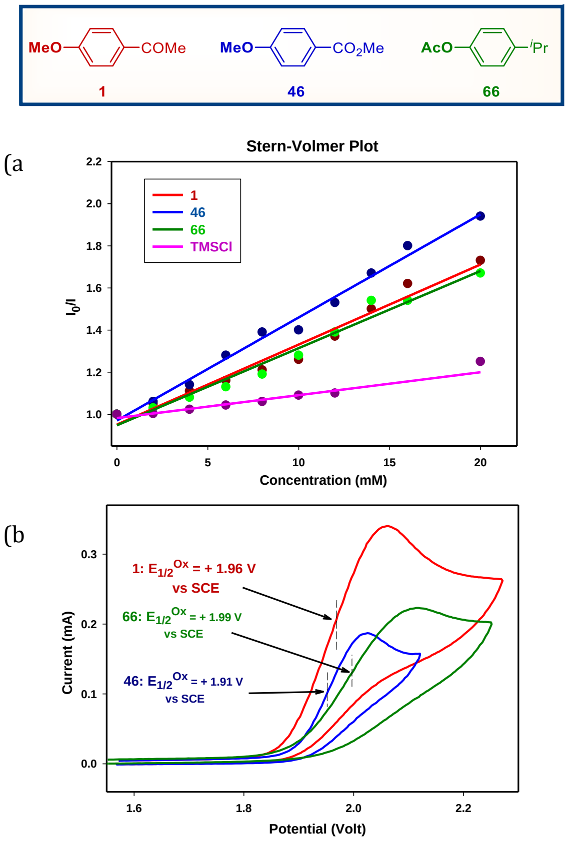
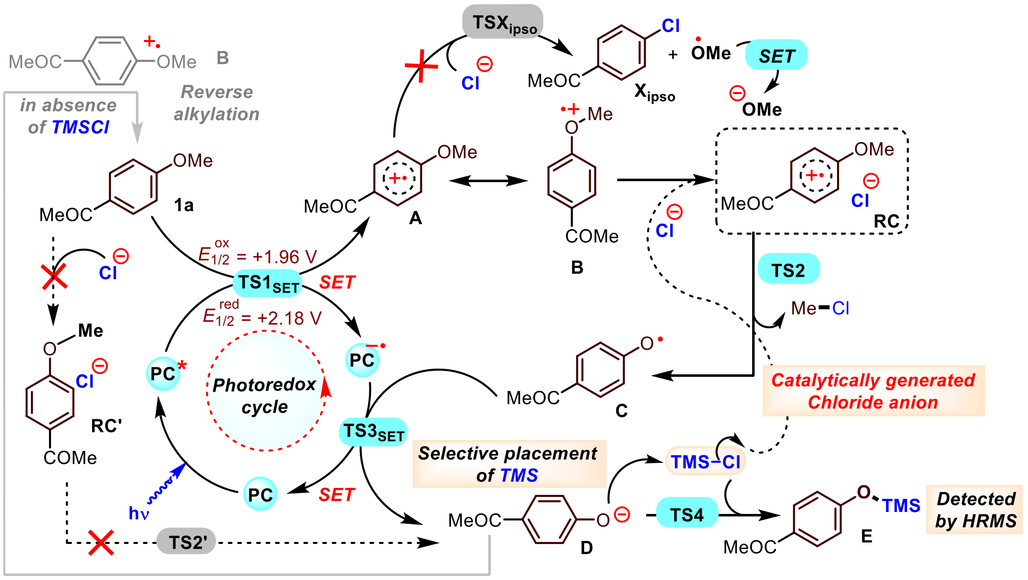


Figure 2: (a) Stern-Volmer studies and (b) Cyclic voltammograms of phenol derivatives.

Based on the previous reports,[29] control experiments, photophysical studies, and computational investigations, a plausible mechanistic route is depicted in Scheme 4. Mechanistic studies with the density functional theory (DFT) at B3LYP-D3(BJ)/SMD(Acetonitrile)/6-311+G(d,p) and computations of molecular excitation energies with time dependent density functional theory (TD-DFT) at M06L/SMD(Acetonitrile)/6-311+G(d,p) level of theory in Figure 3 and SI.[30] TDDFT calculations predict that the photocatalyst (PC, 9-Mes-10-MeAcrClO$_4$) demonstrates a maximum absorption wavelength at $\lambda_{\text{Calc.}}$ = 425 nm with a highest oscillator strength f = 0.0445, in line with experimental observations (See SI for further details).

Initially, the photocatalyst (PC) oxidizes the protected phenol **1a** to generate arene radical cation intermediate **A** $(\mathbf{E^{Ox}_{1/2(Calc.)} = 1.96\ V})$, or the resonance hybrid **B**, together with an anionic radical PC$^{\bullet-}$ at a SET barrier of 15.8 kcal/mol from the excited species PC* (see Figure S1). The SET barrier (TS1$_{\text{SET}}$) has been estimated using the Marcus theory.[31] From the spin density plots in the inset of Figure 3 it is observed that the radical is delocalized over the π-cloud of the phenyl group (see Figure S3 in SI for the total atomic spin densities and total atomic Mulliken charge distribution of the species). Subsequently, we hypothesize demethylation from the cationic radical species **A** through **^{2}TS2,** with explicit involvement of a catalytically generated chloride anion from TMS-Cl (Figure 3, black pathway), at an energetic expense of 18.5 kcal/mol with regard to the reference reactant complex, ^{2}RC. Nucleophilic attack of Cl$^-$ on the C-centered $\sigma_{\text{C-O}}$*-orbital of –OMe group releases the radical species 4-Oxo-acetophenone (**^{2}C**) and concomitantly produces the alkyl chloride, CH$_3$Cl. The photoredox cycle is predicted to complete by the reductive electron transfer to the phenoxy radical and give rise to phenoxy anionic intermediate **D**. Hence, a spontaneous single electron transfer from *in situ* generated PC$^{\bullet-}$ to **^{2}C** leads to the anionic species **D**, with the simultaneous formation of a neutral photosensitizer **PC**. The phenoxide is immediately arrested by the TMSCl due to high oxophilicity of Si and constructs strong O–Si bond to produce TMS-protected phenolic



Scheme 4: Plausible mechanism. PC = photocatalyst, 9-Mes-10-MeAcr^{+}ClO$_4^{-}$.

intermediate **E** by making the overall process thermodynamically favorable as well as kinetically feasible (energy barrier of 4.5 kcal/mol), with liberation of chloride. This oxophilicity of silicon and thereby strong and irreversible Si–O bond formation drives the reaction towards the forward direction by preventing the reverse alkylation process. Subsequent *in situ* hydrolysis of **E** delivers the unprotected phenol.

Alternatively, we have explored the ipso-attack of Cl^{-} on intermediate A. As shown by the grey lines in Figure 3, it takes a relatively higher energy pathway with an effective barrier of 41.0 kcal/mol to form an alternative 4-chloro-acetophenone ^{1}X$_{ipso}$. Moreover, with the neutral 4-methoxy acetophenone 1a, the demethylation process is comparatively difficult (^{1}TS2' with ΔG = 31.0 kcal/mol, Figure S1) with respect to its reactant complex ^{1}RC'.[31a, 32] Hence, these alternative pathways are discarded due to predominantly high energy requirements.

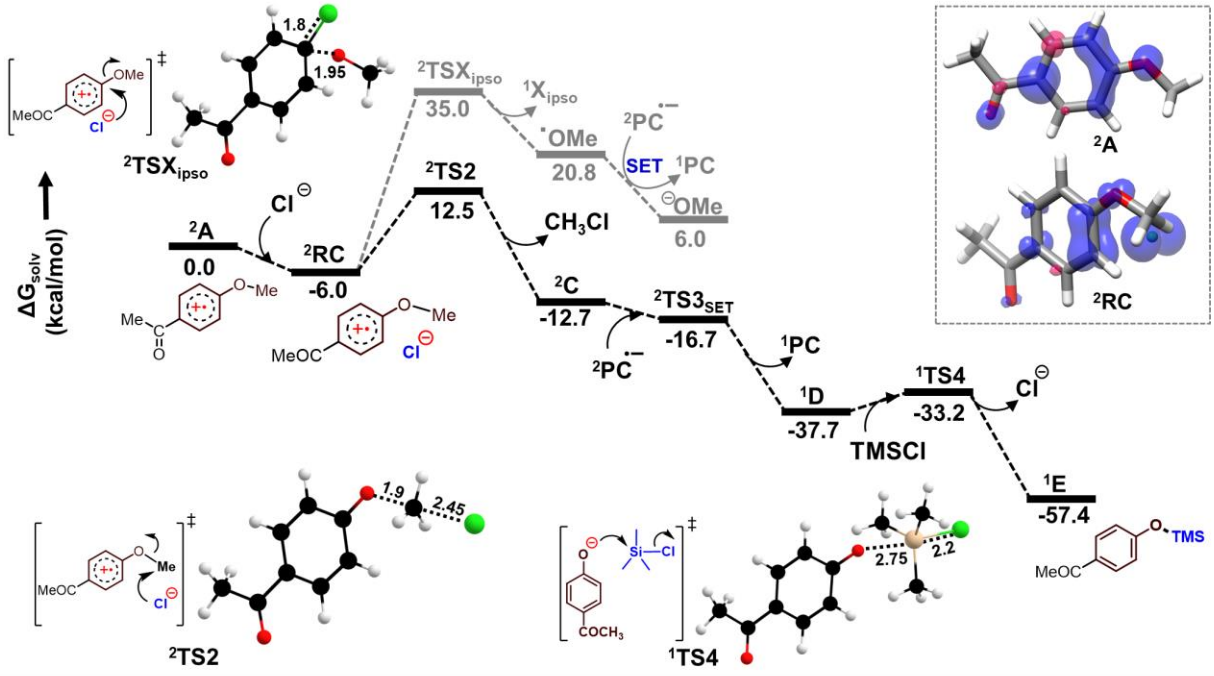


Figure 3: Relative Gibbs Free Energy Profile at B3LYP-D3(BJ)/SMD(Acetonitrile)/6-311 + G (d, p) in kcal/mol for the reaction mechanism from **A** to **E**. Color code: C(black), O(red), Cl(green), Si(golden) and H(white). Superscripts denote the spin multiplicity of the respective species. Inset: Spin density plots of ^{2}**A** and ^{2}**RC**. Interatomic distances shown are in Å.

In conclusion, a photoredox-catalyzed general deprotection strategy for phenolic ethers and esters is developed. This method is effective for the deprotection of diverse aryl-alkyl ethers through C(sp^3)–O bond cleavage and demonstrates remarkable selectivity towards phenolic ethers/esters over chemically equivalent aliphatic frameworks. This protocol also describes a superior versatility and sustainability towards diverse functional groups attached to the arene ring. Thus, the overall process unfolds a unique photocatalytic process and resolves the inevitable shortcomings of the traditional Lewis acid-promoted, oxidant-mediated and hydrogenation-based deprotection techniques. The practical utility of the developed method was demonstrated in the degradation of multiple lignin models and in the efficient production of a FLAP inhibitor. The mechanism of this chemoselective transformation is established through control studies and photophysical experiments which is further supported by computational studies.

AUTHOR INFORMATION

Corresponding Author

Suman De Sarkar – Department of Chemical Sciences, Indian Institute of Science Education and Research Kolkata, Mohanpur 741246, India; orcid.org/0000-0002-6342-4711; Email: sds@iiserkol.ac.in

Lisa Roy – Institute of Chemical Technology Mumbai, IOC Odisha Campus Bhubaneswar, Bhubaneswar 751013, India; E-mail: l.roy@iocb.ictmumbai.edu.in.

Authors

Tanumoy Mandal – Department of Chemical Sciences, Indian Institute of Science Education and Research Kolkata, Mohanpur 741246, India.

Malekul Islam – Department of Chemical Sciences, Indian Institute of Science Education and Research Kolkata, Mohanpur 741246, India.

Sanat Kumar Mahapatra – Institute of Chemical Technology Mumbai, IOC Odisha Campus Bhubaneswar, Bhubaneswar 751013, India.

Sanju Das – Department of Chemical Sciences, Indian Institute of Science Education and Research Kolkata, Mohanpur 741246, India.

Aznur Azim – Department of Chemical Sciences, Indian Institute of Science Education and Research Kolkata, Mohanpur 741246, India.

Author Contributions

The manuscript was written through contributions of all authors.

ǂ These authors contributed equally to this work.

ACKNOWLEDGMENT

Generous support by the CSIR [fellowship to TM, SD, AA and 02(0407)/21/EMR-II to SDS], SERB [SPG/2020/000754 to L. R.], ICT-IOCB (fellowship to SKM), and IISER Kolkata (fellowship to MI and infrastructure) is gratefully acknowledged.

Notes

The authors declare no competing financial interest.

REFERENCES

1. (a) Wuts, P. G. M.; Greene, T. W., *Greene's protective groups in organic synthesis*. John Wiley & Sons: Hoboken, NJ, 2006. (b) Kocieński, P. J., *Protecting Groups*. 3rd ed.; Georg Thieme Verlag KG: Stuttgart, 2005.
2. Scott, K. A.; Cox, P. B.; Njardarson, J. T., Phenols in Pharmaceuticals: Analysis of a Recurring Motif. *J. Med. Chem.* **2022,** *65*, 7044-7072.
3. Wuts, P. G. M.; Greene, T. W., Protection for Phenols and Catechols. In *Greene's Protective Groups in Organic Synthesis*: Hoboken, NJ, 2006; pp 367-430.
4. (a) Bomon, J.; Bal, M.; Achar, T. K.; Sergeyev, S.; Wu, X.; Wambacq, B.; Lemière, F.; Sels, B. F.; Maes, B. U. W., Efficient demethylation of aromatic methyl ethers with HCl in water. *Green Chem.* **2021,** *23*, 1995-2009. (b) Li, G.; Patel, D.; Hruby, V. J., An efficient procedure for the demethylation of aryl-methyl ethers in optically pure unusual amino acids. *Tetrahedron Lett.* **1993,** *34*, 5393-5396.
5. (a) Brooks, P. R.; Wirtz, M. C.; Vetelino, M. G.; Rescek, D. M.; Woodworth, G. F.; Morgan, B. P.; Coe, J. W., Boron Trichloride/Tetra-n-Butylammonium Iodide: A Mild, Selective Combination Reagent for the Cleavage of Primary Alkyl Aryl Ethers. *J. Org. Chem.* **1999,** *64*, 9719-9721. (b) Jung, M. E.; Lyster, M. A., Quantitative dealkylation of alkyl ethers via treatment with trimethylsilyl iodide. A new method for ether hydrolysis. *J. Org. Chem.* **1977,** *42*, 3761-3764.
6. (a) Hwu, J. R.; Tsay, S. C., Counterattack reagents sodium trimethylsilanethiolate and hexamethyldisilathiane in the *bis-O*-demethylation of aryl methyl ethers. *J. Org. Chem.* **1990,** *55*, 5987-5991. (b) Bernard, A. M.; Ghiani, M. R.; Piras, P. P.; Rivoldini, A., Dealkylation of Activated Alkyl Aryl Ethers Using Lithium Chloride in Dimethylformamide. *Synthesis* **1989,** *1989*, 287-289. (c) Feutrill, G. I.; Mirrington, R. N., Demethylation of aryl methyl ethers with thioethoxide ion in dimethyl formamide. *Tetrahedron Lett.* **1970,** *11*, 1327-1328.
7. (a) Shigeno, M.; Hayashi, K.; Korenaga, T.; Nozawa-Kumada, K.; Kondo, Y., Organic superbase *t*-Bu-P4-catalyzed demethylations of methoxyarenes. *Org. Chem. Front.* **2022,** *9*, 3656-3663. (b) Fedorov, A.; Toutov, A. A.; Swisher, N. A.; Grubbs, R. H., Lewis-base silane activation: from reductive cleavage of aryl ethers to selective ortho-silylation. *Chem. Sci.* **2013,** *4*, 1640. (c) Hwu, J. R.; Wong, F. F.; Huang, J.-J.; Tsay, S.-C., Sodium Bis(trimethylsilyl)amide and Lithium Diisopropylamide in Deprotection of Alkyl Aryl Ethers: α-Effect of Silicon. *J. Org. Chem.* **1997,** *62*, 4097-4104.
8. (a) Kc, S.; Dhungana, R. K.; Aryal, V.; Giri, R., Concise Synthesis of a Potential 5-Lipoxygenase Activating Protein (FLAP) Inhibitor and Its Analogs through Late-Stage Alkene Dicarbofunctionalization. *Org. Process Res. Dev.* **2019,** *23*, 1686-1694. (b) Sang, D.; Yi, C.; He, Z.; Wang, J.; Tian, J.; Yao, M.; Shi, H., Chemoselective ester/ether C–O cleavage of methyl anisates by aluminum triiodide. *Tetrahedron Lett.* **2018,** *59*, 1469-1472.
9. (a) Sergeev, A. G.; Hartwig, J. F., Selective, nickel-catalyzed hydrogenolysis of aryl ethers. *Science* **2011,** *332*, 439-43. (b) Heathcock, C. H.; Ratcliffe, R., A Stereoselective Total Synthesis of the Guaiazulenic Sesquiterpenoids *α*-Bulnesene and Bulnesol. *J. Am. Chem. Soc.* **1970,** *93*, 1746-1757. (c) Felix, A. M.; Heimer, E. P.; Lambros, T. J.; Tzougraki, C.; Meienhofer, J., Rapid removal of protecting groups from peptides by catalytic transfer hydrogenation with 1,4-cyclohexadiene. *J. Org. Chem.* **1978,** *43*, 4194-4196.
10. (a) Hamada, S.; Sugimoto, K.; Elboray, E. E.; Kawabata, T.; Furuta, T., Chemoselective Oxidation of *p*-Methoxybenzyl Ethers by an Electronically Tuned Nitroxyl Radical Catalyst. *Org. Lett.* **2020,** *22*, 5486-5490. (b) Bull, S. D.; Davies, S. G.; Fenton, G.; Mulvaney, A. W.; Prasad, R. S.; Smith, A. D., Chemoselective debenzylation of *N*-

benzyl tertiary amines with ceric ammonium nitrate. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3765-3774. (c) Oikawa, Y.; Yoshioka, T.; Yonemitsu, O., Specific removal of o-methoxybenzyl protection by DDQ oxidation. *Tetrahedron Lett.* **1982,** *23*, 885-888.

11. Hori, H.; Nishida, Y.; Ohrui, H.; Meguro, H., Regioselective de-O-benzylation with Lewis acids. *J. Org. Chem.* **1989,** *54*, 1346-1353.

12. Baddar, F. G.; Wahhab, S. A.; Awad, B. M.; Guindy, N. M.; Wahba, M.; Malek, B. A. A., Phenolic esters. Part I. Rate of hydrolysis of phenyl, *p*-tolyl, and *p*-chlorophenyl hydrogen succinate. *J. Chem. Soc. B* **1970**, 739.

13. (a) Tay, N. E. S.; Lehnherr, D.; Rovis, T., Photons or Electrons? A Critical Comparison of Electrochemistry and Photoredox Catalysis for Organic Synthesis. *Chem. Rev.* **2022,** *122*, 2487-2649. (b) Wang, C. S.; Dixneuf, P. H.; Soule, J. F., Photoredox Catalysis for Building C-C Bonds from C(sp^2)-H Bonds. *Chem. Rev.* **2018,** *118*, 7532-7585. (c) König, B., Photocatalysis in Organic Synthesis - Past, Present, and Future. *Eur. J. Org. Chem.* **2017,** *2017*, 1979-1981. (d) Prier, C. K.; Rankic, D. A.; MacMillan, D. W., Visible light photoredox catalysis with transition metal complexes: applications in organic synthesis. *Chem. Rev.* **2013,** *113*, 5322-63. (e) Klan, P.; Solomek, T.; Bochet, C. G.; Blanc, A.; Givens, R.; Rubina, M.; Popik, V.; Kostikov, A.; Wirz, J., Photoremovable protecting groups in chemistry and biology: reaction mechanisms and efficacy. *Chem. Rev.* **2013,** *113*, 119-91. (f) Narayanam, J. M.; Stephenson, C. R., Visible light photoredox catalysis: applications in organic synthesis. *Chem. Soc. Rev.* **2011,** *40*, 102-13.

14. (a) Cavedon, C.; Sletten, E. T.; Madani, A.; Niemeyer, O.; Seeberger, P. H.; Pieber, B., Visible-Light-Mediated Oxidative Debenzylation Enables the Use of Benzyl Ethers as Temporary Protecting Groups. *Org. Lett.* **2021,** *23*, 514-518. (b) Ahn, D. K.; Kang, Y. W.; Woo, S. K., Oxidative Deprotection of *p*-Methoxybenzyl Ethers via Metal-Free Photoredox Catalysis. *J. Org. Chem.* **2019,** *84*, 3612-3623. (c) Liu, Z.; Zhang, Y.; Cai, Z.; Sun, H.; Cheng, X., Photoredox Removal of *p*-Methoxybenzyl Ether Protecting Group with Hydrogen Peroxide as Terminal Oxidant. *Adv. Synth. Catal.* **2015,** *357*, 589-593. (d) Tucker, J. W.; Narayanam, J. M.; Shah, P. S.; Stephenson, C. R., Oxidative photoredox catalysis: mild and selective deprotection of PMB ethers mediated by visible light. *Chem. Commun.* **2011,** *47*, 5040-2.

15. Liang, K.; Li, X.; Wei, D.; Jin, C.; Liu, C.; Xia, C., Deprotection of benzyl-derived groups via photochemically mesolytic cleavage of C–N and C–O bonds. *Chem* **2023,** *9*, 511-522.

16. Lu, P.; Hou, T.; Gu, X.; Li, P., Visible-light-promoted conversion of alkyl benzyl ether to alkyl ester or alcohol via O-α-sp^3 C-H cleavage. *Org. Lett.* **2015,** *17*, 1954-7.

17. (a) Hu, R.-G.; Sang, Y.; Tan, F.-F.; Sun, Y.-L.; Xue, X.-S.; Li, Y., Photoredox and Vanadate Cocatalyzed Hydrolysis of Aryl Ethers at Ambient Temperature. *ACS Catal.* **2023,** *13*, 9264-9273. (b) Wang, S.; Liu, J.; Niu, L.; Yi, H.; Chiang, C.-W.; Lei, A., Oxidation induced C(sp^3)-O cleavage via visible-light photoredox catalysis. *J. Photochem. Photobiol., A: Chem.* **2018,** *355*, 120-124.

18. Reed, N. L.; Yoon, T. P., Oxidase reactions in photoredox catalysis. *Chem. Soc. Rev.* **2021,** *50*, 2954-2967.

19. (a) Chen, W.; Huang, Z.; Tay, N. E. S.; Giglio, B.; Wang, M.; Wang, H.; Wu, Z.; Nicewicz, D. A.; Li, Z., Direct arene C-H fluorination with $^{18}F^-$ via organic photoredox catalysis. *Science* **2019,** *364*, 1170-1174. (b) McManus, J. B.; Nicewicz, D. A., Direct C-H Cyanation of Arenes via Organic Photoredox Catalysis. *J. Am. Chem. Soc.* **2017,** *139*, 2880-2883. (c) Romero, N. A.; Margrey, K. A.; Tay, N. E.; Nicewicz, D. A., Site-selective arene C-H amination via photoredox catalysis. *Science* **2015,** *349*, 1326-30.

20. (a) Mandal, T.; Mallick, S.; Kumari, N.; De Sarkar, S., Visible-Light-Mediated Synthesis of Phenanthrenes through Successive Photosensitization and Photoredox by a Single Organocatalyst. *Org. Lett.* **2022,** *24*, 8452-8457. (b) Das, S.; Parida, S. K.; Mandal, T.; Hota, S. K.; Roy, L.; De Sarkar, S.; Murarka, S., An organophotoredox-catalyzed redox-neutral cascade involving *N*-(acyloxy)phthalimides and maleimides. *Org. Chem. Front.* **2021,** *8*, 2256-2262. (c) Das, S.; Mandal, T.; De Sarkar, S., Acridine Orange Hemi(Zinc Chloride) Salt as a Lewis Acid-Photoredox Hybrid Catalyst for the Generation of α-Carbonyl Radicals. *Adv. Synth. Catal.* **2021,** *364*, 755-765.

21. Sanderson, R. T., *Chemical Bonds and Bond Energy. 2nd Ed*. Academic1976.

22. (a) Romero, N. A.; Nicewicz, D. A., Organic Photoredox Catalysis. *Chem. Rev.* **2016,** *116*, 10075-166. (b) Vincent, C. A.; Chiriac, M. I.; Troian-Gautier, L.; Tambar, U. K., Photocatalytic Sulfonyl Fluorination of Alkyl Organoboron Substrates. *ACS Catal.* **2023,** *13*, 3668-3675. (c) Cao, Y. X.; Zhu, G.; Li, Y.; Le Breton, N.; Gourlaouen, C.; Choua, S.; Boixel, J.; Jacquot de Rouville, H. P.; Soule, J. F., Photoinduced Arylation of Acridinium Salts: Tunable Photoredox Catalysts for C-O Bond Cleavage. *J. Am. Chem. Soc.* **2022,** *144*, 5902-5909.

23. (a) Kotani, H.; Ohkubo, K.; Fukuzumi, S., Photocatalytic oxygenation of anthracenes and olefins with dioxygen via selective radical coupling using 9-mesityl-10-methylacridinium ion as an effective electron-transfer photocatalyst. *J. Am. Chem. Soc.* **2004,** *126*, 15999-6006. (b) Fukuzumi, S.; Kotani, H.; Ohkubo, K.; Ogo, S.; Tkachenko, N. V.; Lemmetyinen, H., Electron-transfer state of 9-mesityl-10-methylacridinium ion with a much longer lifetime and higher energy than that of the natural photosynthetic reaction center. *J. Am. Chem. Soc.* **2004,** *126*, 1600-1.

24. Speckmeier, E.; Zeitler, K., Desyl and Phenacyl as Versatile, Photocatalytically Cleavable Protecting Groups: A Classic Approach in a Different (Visible) Light. *ACS Catal.* **2017,** *7*, 6821-6826.

25. Das, A.; König, B., Transition metal- and photoredox-catalyzed valorisation of lignin subunits. *Green Chem.* **2018,** *20*, 4844-4852.

26. (a) Karkas, M. D.; Bosque, I.; Matsuura, B. S.; Stephenson, C. R., Photocatalytic Oxidation of Lignin Model Systems by Merging Visible-Light Photoredox and Palladium Catalysis. *Org. Lett.* **2016,** *18*, 5166-5169. (b) Luo, N.; Wang, M.; Li, H.; Zhang, J.; Liu, H.; Wang, F., Photocatalytic Oxidation–Hydrogenolysis of Lignin β-O-4 Models via a Dual Light Wavelength Switching Strategy. *ACS Catal.* **2016,** *6*, 7716-7721.

27. Kepp, K. P., A Quantitative Scale of Oxophilicity and Thiophilicity. *Inorg. Chem.* **2016,** *55*, 9461-70.

28. Nicewicz, D.; Roth, H.; Romero, N., Experimental and Calculated Electrochemical Potentials of Common Organic Molecules for Applications to Single-Electron Redox Chemistry. *Synlett* **2015,** *27*, 714-723.

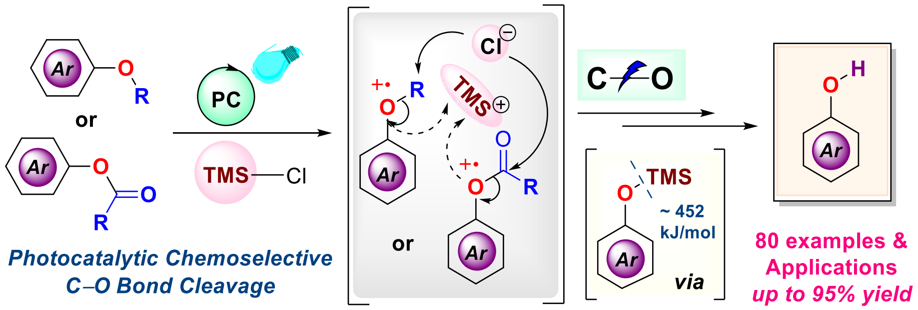
29. (a) Klare, H. F. T.; Albers, L.; Susse, L.; Keess, S.; Muller, T.; Oestreich, M., Silylium Ions: From Elusive Reactive Intermediates to Potent Catalysts. *Chem. Rev.* **2021,** *121*, 5889-5985. (b) Ghosh, S.; Lai, D.; Hajra, A., Visible-light-induced silylation: an update. *Org. Biomol. Chem.* **2021,** *19*, 2399-2415. (c) Lu, L.; Siu, J. C.; Lai, Y.; Lin, S., An Electroreductive Approach to Radical Silylation via the Activation of Strong Si-Cl Bond. *J. Am. Chem. Soc.* **2020,** *142*, 21272-21278.

30. (a) Hota, S. K.; Panda, S. P.; Das, S.; Mahapatra, S. K.; Roy, L.; De Sarkar, S.; Murarka, S., Photoinduced Electron Donor-Acceptor Complex-Mediated Radical Cascade Involving N-(Acyloxy)phthalimides: Synthesis of Tetrahydroquinolines. *J. Org. Chem.* **2023,** *88*, 2543-2549. (b) Charaf-Eddin, A.; Planchat, A.; Mennucci, B.; Adamo, C.; Jacquemin, D., Choosing a Functional for Computing Absorption and Fluorescence Band Shapes with TD-DFT. *J. Chem. Theory Comput.* **2013,** *9*, 2749-60.

31. (a) Meher, P.; Panda, S. P.; Mahapatra, S. K.; Thombare, K. R.; Roy, L.; Murarka, S., A General Electron Donor-Acceptor Photoactivation Platform of Diaryliodonium Reagents: Arylation of Heterocycles. *Org. Lett.* **2023,** *25*, 8290-8295. (b) Mallojjala, S. C.; Nyagilo, V. O.; Corio, S. A.; Adili, A.; Dagar, A.; Loyer, K. A.; Seidel, D.; Hirschi, J. S., Probing the Free Energy Landscape of Organophotoredox-Catalyzed Anti-Markovnikov Hydrofunctionalization of Alkenes. *J. Am. Chem. Soc.* **2022,** *144*, 17692-17699. (c) Fu, M. C.; Shang, R.; Zhao, B.; Wang, B.; Fu, Y., Photocatalytic decarboxylative alkylations mediated by

triphenylphosphine and sodium iodide. *Science* **2019,** *363*, 1429-1434.

32. Baidya, M.; Maiti, D.; Roy, L.; De Sarkar, S., Trifluoroethanol as a Unique Additive for the Chemoselective Electrooxidation of Enamines to Access Unsymmetrically Substituted NH-Pyrroles. *Angew. Chem. Int. Ed.* **2022,** *61*, e202111679.


Ar
O
R
or
Ar
O
O
R
PC
TMS
Cl
Photocatalytic Chemoselective
C–O Bond Cleavage
Cl
+•
O
R
TMS
Ar
O
+•
O
R
or
Ar
C
O
O
TMS
~ 452
kJ/mol
Ar
via
O
H
Ar
80 examples &
Applications
up to 95% yield