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Visible-Light-Catalyzed Benzylic C-H Bond Chlorination by a Combination of Organic Dye (Acr^+-Mes) and *N*-Chlorosuccinimide

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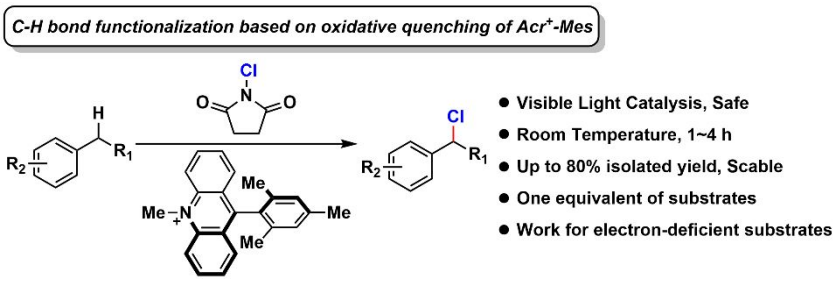


ABSTRACT: Combining "*N*-chlorosuccinimide (NCS)" as the safe chlorine source with "Acr^+-Mes" as the photocatalyst, we successfully achieved benzylic C-H bond chlorination under visible-light irradiation. Furthermore, benzylic chlorides could be converted to benzylic ethers smoothly in a one-pot manner by adding sodium methoxide. This mild and scalable chlorination method worked effectively for diverse toluene derivatives, especially for electron-deficient substrates. Careful mechanistic

studies supported that NCS provided hydrogen abstractor "*N*-centered succinimidyl radical", which was responsible for the cleavage of benzylic C-H bond, relying on the reducing ability of Acr^+-Mes.

INTRODUCTION

Direct benzylic C-H bond chlorination is one of the most essential and important transformations[1] due to its wide applications in the pharmaceutical synthesis[2], and such transformation provides the useful feedstock for fine chemical industry[3]. Up to now, numerous methods have been developed for the conversion of toluene derivatives to benzylic chlorides. Traditionally, benzylic chlorination reactions involved the use of explosive, corrosive or toxic chlorine sources, such as: Cl_2, $SOCl_2$ or CCl_4, under heating or irradiation conditions (Figure 1a).[3b,4] These methods produced the uncontrollable amount of chlorine radical, in which substrates needed to be acted as the solvent to avoid polychlorination, thus restricting the promotion of reaction yields. To provide the controlled chlorine radical, great efforts have been made by combining the stoichiometric amount of oxidants, like peroxides, NaOCl, and chloride anion. Although previous chlorinated processes have been optimized during the last few decades (Figure 1b),[5] the drawback of such tactics was the formation of oxygenated byproduct. Recently, many chlorinating reagents,[6] such as *N*-chlorophthalimide (NCP), *N*-chlorosuccinimide (NCS) or trichloroisocyanuric acid (TCCA), as safe, environmentally friendly and alternative chlorine sources were increasingly used in different chlorination reactions (Figure 1c).[7] With the help of metal complex

additives[7c], sunlight irradiation[7d] or heating with oxidant[7e], N-centered radical[8] could be obtained from these reagents, which is responsible for the activation of the benzylic C-H bond via a hydrogen atom transfer (HAT) process, then the generated benzylic radical can abstract a chlorine atom from the N-Cl moiety to afford benzylic chloride. Clearly, the development of simpler and milder benzylic chlorination methods is of considerable need for chlorinated processes.

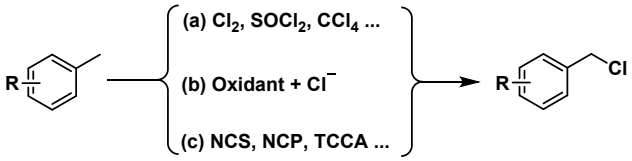


Figure 1. Classic chlorination methods for benzylic C-H bond.

In recent years, visible light catalysis has emerged as a powerful synthesis tool relying on the strong redox ability of excited photocatalysts.[9] Specifically, photocatalyst should cooperate with appropriate oxidant or reductant to realize single electron transfer (SET) process. The famous Fukuzumi dye "Acr^+-Mes" is generally recognized as a strong oxidant to realize the activation of electron-rich arenes and alkenes under the visible light.[10] Significantly, it also possesses the reducing ability for activating hypervalent iodine reagents and halogenated reagents.[11] As a consequence, we proposed that it could be a practicable plan to accomplish the benzylic chlorination via the combination of Acr^+-Mes and appropriate chlorinating reagent (Figure 2).[12]

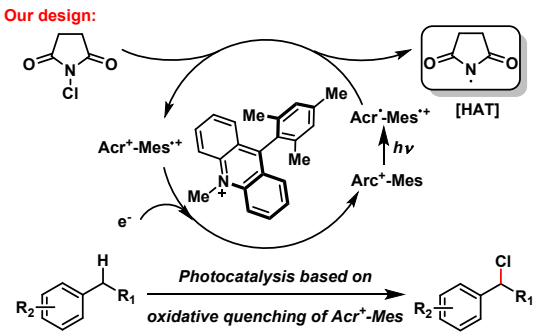


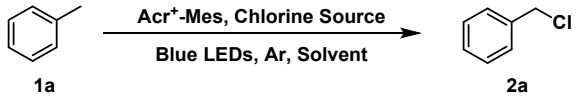
Figure 2. Our design for benzylic chlorination based on oxidative quenching of Acr^+-Mes.

RESULTS AND DICUSSION

Initially to realize the benzylic C-H chlorination reaction, we selected *N*-chlorophthalimide (NCP) as the chlorine source. As shown in Table 1, the desired chlorinated product **2a** was obtained in 68% yield with 100% conversion of methylbenzene **1a** when using acetonitrile as the solvent under ambient argon atmosphere with 1 hour blue LEDs ($\lambda = 450 \pm 10$ nm) irradiation (entry 1). Among chlorine sources screened, including *N*-chlorosuccinimide (NCS), *N*-chloro-*N*-methyl-4-toluenesulfonamide (Ts-NClMe) and 4-toluenesulfonyl chloride (Ts-Cl), NCS provided the optimal efficiency (entry 2-4). Subsequently, examination of different solvents suggested that CH_2Cl_2 could give a slightly higher yield (entries 5-7). Considering that substrate **1a** was not completely consumed after 1 hour irradiation in CH_2Cl_2, we prolonged the reaction time. Further optimization of reaction time revealed that all of **1a** was converted with the optimal yield 78% when **1a** (0.3 mmol), Acr^+-Mes ClO_4^- (5 mol %), and NCS (2.0 equiv) were combined in CH_2Cl_2 (3 mL) irradiated by blue LEDs for 4 hours (entries 8-9). Lastly, control experiments confirmed the nature of this

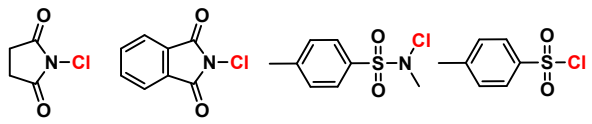
photocatalytic reaction that no desired product was observed without the photocatalyst or light (entry 10).

Table 1. Optimization of the reaction condition[a]



1a 2a

Entry	Chlorine Source	Solvent	Time (h)	Yield (%)[b]
1	NCP	CH_3CN	1	68
2	NCS	CH_3CN	1	73
3	Ts-NClMe	CH_3CN	1	21
4	Ts-Cl	CH_3CN	1	0
5	NCS	DCM	1	76
6	NCS	$CHCl_3$	1	71
7	NCS	DCE	1	43
8	NCS	DCM	4	78
9	NCS	DCM	8	75
10[c]	NCS	DCM	4	0



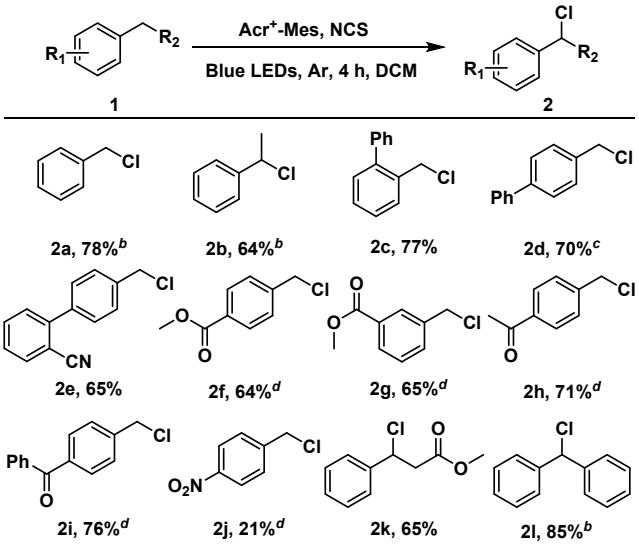
NCS NCP Ts-NClMe Ts-Cl

[a]Standard conditions: **1a** (0.3 mmol), Acr$^+$-Mes (5 mol %) and Chlorine source (2.0 equiv) in the solvent (3 mL) were irradiated by blue LEDs under an argon atmosphere. [b]Determined by GC using *n*-tetradecane as an internal standard. [c]General conditions, but with no Acr$^+$-Mes or light.

Under the optimized conditions, some representative alkylbenzene derivatives were examined to explore the generality of this new chloration method. As summarized in Scheme 1, both benzylic methyl and methylene groups could be chlorinated (**2a-2b**, 64%-78%), though the reaction yield of ethylbenzene was lower than that of toluene. To our delight, substrates containing different functional groups on the aromatic ring were smoothly converted to the

corresponding chlorides in moderate to good yields (**2c**-**2i**, **2k**-**2l**, 64%-85%). Electron-deficient groups such as cyan, ester carbonyl and ketone carbonyl were tolerated well for this transformation while nitro group was also suitable for this system albeit with low reactivity (**2j**, 21%). Especially, meta-electron-withdrawing substituted toluene derivative methyl 3-methylbenzoate **1g**, which has a significant electronic property on benzylic C-H bond, showed good reactivity with 65% yield. On the other hand, it should be pointed out that the amount of NCS needed to be decreased to improve reaction yields of electron-rich substrates (**1d**) because too much NCS would lead to the chlorination of aromatic ring. As for more electron-rich benzene derivative like 1,3,5-trimethoxybenzene, it worked with NCS to generate 2-chloro-1,3,5-trimethoxybenzene in 95% yield. Moreover, substrate **1k** involving a carboxylic ester group on the alkyl chain was also competent for this reaction (**2k**, 65%). Notably, our reaction system would not result in benzylic oxidation for all substrates examined above.

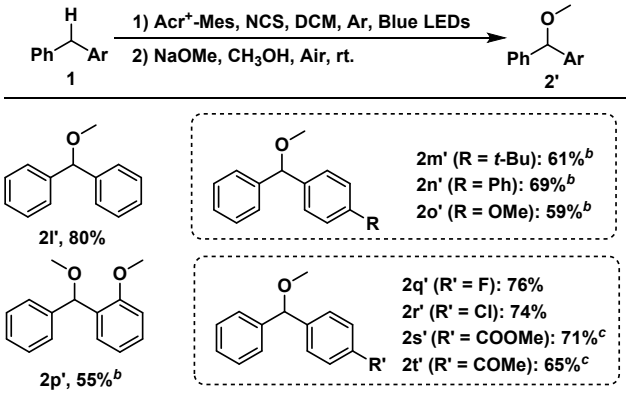
Scheme 1. Scope of alkylbenzene derivatives for benzylic C-H chlorination[a]



[a]Reaction conditions: **1** (0.3 mmol), Acr^+-Mes (5 mol %) and NCS (2.0 equiv) in DCM (3 mL) were irradiated by blue LEDs for 4 hours under an argon atmosphere. Isolated yields are shown. [b]Determined by GC using *n*-tetradecane as an internal standard (Figure S1-S3). [c]1.1 equiv of NCS. [d]2.2 equiv of NCS.

With respect to the more reactive substrate "diphenylmethane **1l**", corresponding benzylic chloride could be obtained in 85% yield (**2l**, determined by GC). However, the product was not able to be obtained as a pure compound due to the hydrolysis issue. We therefore transformed the benzylic chloride to the benzylic ether by using NaOMe as the nucleophile (Scheme 2, **2l'**, 80%). Moreover, diphenylmethanes bearing different electron-donating group (*t*-Bu, Ph or OMe) or various electron-withdrawing group (F, Cl, COOMe or COMe) were successfully suitable to accomplish this two-step transformation (Scheme, **2m'-2t'**, 55%-76%), which provided a feasible protocol for benzylic C-O bond construction.

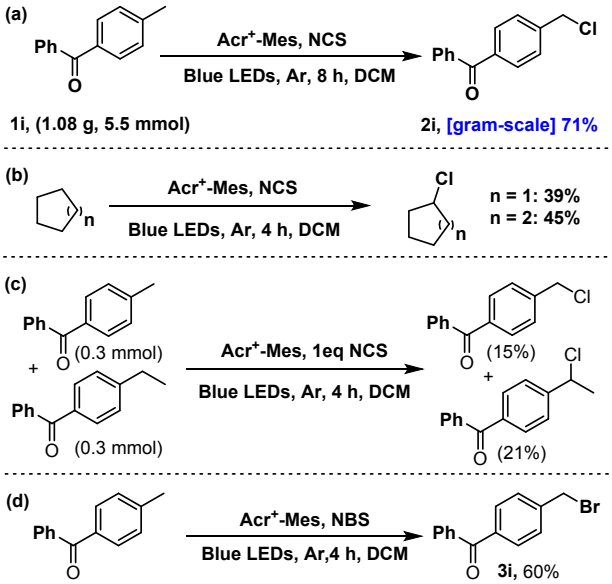
Scheme 2. Scope of diphenylmethane derivatives for one-pot benzylic C-O bond construction[a]



[a]Reaction conditions: **1** (0.3 mmol), Acr^+-Mes (5 mol %) and NCS (2.0 equiv) in DCM (3 mL) were irradiated by blue LEDs for 1 hour under an argon atmosphere. Then CH_3OH (3 mL) and NaOMe (1 mmol) were added into the mixture, which was stirred for 3 hours at room temperature. Isolated yields are shown. [b]1.1 equiv of NCS. [c]2.2 equiv of NCS and irradiation for 3 hours; after adding NaOMe, the mixture was heated to reflux for 12 hours.

Considering that light penetration affected photocatalytic reaction efficiency significantly, special reaction equipment, like the continuous flow setup, was needed for the large-scale reaction.[13] However, a scale-up reaction for **1i** (5.5 mmol, 1.08 g) gave **2i** in 71% yield, which was comparable with that of a small-scale reaction for **1i** (0.3 mmol, 76% yield), without an aid of a flow technology (Scheme 3a). In addition, cyclic aliphatic hydrocarbons could be chlorinated[14] albeit with relatively low yields (39-45%), which further expanded the substrate scope of this new chlorination method (Scheme 3b). Because the excited Acr^+-Mes could not oxidize substrate alkane to cation radical, we speculated that the direct oxidation/deprotonation pathway could be excluded in our photoredox reaction. Furthermore, the competition experiment with diphenylketone derivatives were operated in our reaction condition to provide the corresponding product in 15% and 21% yields respectively (Scheme 3c), which indicated there was no obvious regioselectivity between primary and secondary C-H bonds. Finally, when *N*-bromosuccinimide (NBS) was used as the bromine resource, **1i** could directly provide the bromide product **3i** with 60% yield, which highlights the versatility of this strategy (Scheme 3d).

Scheme 3. (a) Gram-Scale benzylic C-H chlorination of **1i**; (b) Alphatic C-H chlorination; (c) The competition experiment; (d) Benzylic C-H bromination of **1i**.



To shed light on the reaction mechanism, several control experiments were carried out. 1) No chlorination product was afforded in the absence of NCS under standard condition, ruling out the effect of CH_2Cl_2 in chlorination (Figure S4a). 2) when 2 equiv 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) or 2,6-di-tert-butyl-4-methylphenol (BHT) as radical inhibitors was added into the model condition, the yield of desired product was suppressed to trace and almost all of substrate **1l** was remained (Figure S4b). 3) We observed benzylic bromide under our chlorination conditions with diethyl bromomalonate (DEBM), and DEBM did not give benzylic bromide when combining with photocatalyst Acr^+-Mes (Figure S4c), which indicated that benzylic radical was involved in our system. 4) In the absence of substrate toluene, NCS was also reduced to succinimide relying on photocatalyst Acr^+-Mes (Figure S5). Thus, the excited Acr^+-Mes could reduce NCS, and solvent CH_2Cl_2 provided hydrogen source for the reduction product succinimide. 5) When replacing oxidant NCS with O_2, no

benzaldehyde or benzoic acid could be detected and nearly all substrate **1a** and **1l** were remained after 4 hours of irradiation (Figure S6), which meant that the excited Acr^+-Mes could not directly oxidize them in CH_2Cl_2. Although we could not exclude the possibility that the reaction proceeded via direct oxidation of substrates by excited photocatalyst, especially for electron-rich ones, it was not the main reaction process in our reaction system. 6) We conducted time-resolved transient absorption spectrum to confirm the SET from the charge-separated state $Acr^{\cdot}$-$Mes^{\cdot+}$ to NCS.[15] As shown in Figure 3, the lifetime of $Acr^{\cdot}$-$Mes^{\cdot+}$ was decreased with increasing concentration of NCS, and the quenching rate constant was obtained from the slope of the liner plot of k_{decay} *versus* [NCS] to be 1.1×10^7 $M^{-1}s^{-1}$.[10b] Meanwhile, the rate constant of electron transfer from toluene to $Acr^{\cdot}$-$Mes^{\cdot+}$ was 2.0×10^6 $M^{-1}s^{-1}$ according to Fukuzumi's report.[16] These observations collectively supported that this photoredox reaction was initiated through the oxidative quenching of Acr^+-Mes, namely the SET oxidation of the excited Acr^+-Mes by NCS. 7) Although benzylic radical would react with NCS directly to afford benzylic chloride resulting in radical chain propagation process, the time profile of benzylic chlorination using diphenylmethane **1l** as substrate revealed that continuous visible-light irradiation was necessary to this photocatalytic transformation and the propagating chain reaction was short-lived (Figure S7). We therefore speculated that Acr^+-$Mes^{\cdot+}$, coming from oxidation of $Acr^{\cdot}$-$Mes^{\cdot+}$, would oxidize benzylic radical regenerating Acr^+-Mes, which restarted the short chain propagation under illumination.

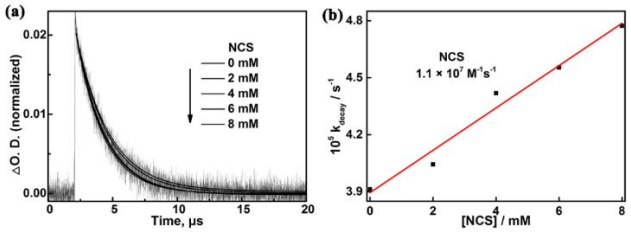


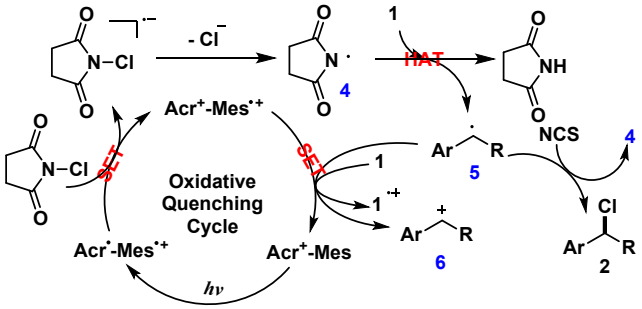
Figure 3. Quenching experiments (a) Decay of transient absorbance of Acr$^{\cdot}$-Mes$^{\cdot+}$ at 500 nm in the absence and presence of NCS (0-8 mM) in deaerated MeCN containing Acr^{+}-Mes (0.05 mM) after nanosecond laser flash photolysis (λ_{ex} = 430 nm). (b) Plot of k_{decay} *versus* [NCS] for the reaction of Acr$^{\cdot}$-Mes$^{\cdot+}$ with NCS.

Not only that, related electrochemical potential and binding dissociation energy data also match with our experiment results. The reduction potential (E_{red}) of NCS is -0.27 V vs SCE, which is higher than the oxidation potential of Acr^{+}-Mes$^{\cdot+}$ (E_{ox}^{*} = -0.57 V vs SCE),[17] so the electron transfer from the excited Acr^{+}-Mes to NCS is thermodynamically feasible. The reduced NCS would then leave a chlorine anion to generate the succinimidyl radical. Furthermore, the bond dissociation energy of benzylic C-H bond (89.7 kcal mol^{-1}) is lower than that of N-H bond strength in succinimide (118 kcal mol^{-1}),[18] so it is reasonable that the succinimidyl radical can abstract a hydrogen atom from benzylic C-H bond to give benzylic radical.

On the basis of above discussion, a likely mechanism of this chlorination reaction is outlined in Scheme 4. Initially, Acr^{+}-Mes is excited by visible light, forming the charge-separated state Acr$^{\cdot}$-Mes$^{\cdot+}$ via the intramolecular electron transfer. NCS would oxidize Acr$^{\cdot}$-Mes$^{\cdot+}$, and further release Cl^{-} with the generation of N-centered succinimidyl radical **4** and Acr^{+}-Mes$^{\cdot+}$. Subsequently, **4** abstracts a hydrogen atom from substrate **1** to give benzylic radical **5**. Next, **5**

accepts a chlorine atom from NCS affording benzylic chloride **2** and hydrogen abstractor **4**, which results in chain propagation reaction. Finally, Acr^{+}-$Mes^{\cdot+}$ may oxidizes **5** or some electron-rich substrates to accomplish photocatalytic cycle.

Scheme 4. Proposed mechanism



In summary, we have developed a novel method for benzylic C-H bond chlorination using NCS as the cheap and safe chlorine source. Hydrogen abstractor "N-centered succinimidyl radical" was obtained through oxidative quenching of Acr^{+}-Mes, which was employed for hydrogen-atom-transfer process of benzylic C-H bond. This mild and effective chlorinated reaction only needs one equivalent of substrate, and works for a broad scope of alkylbenzenes. Remarkably, it could achieve the gram-scale transformation in a satisfactory yield, and avoid oxidation of benzylic C-H bond. Additional investigation in developing inert C-H bond functionalization based on this photocatalytic protocol is underway in our group.

EXPERIMENTAL SECTION

General information

^{1}H NMR and ^{13}C NMR spectra were recorded using a Bruker Avance DPX 400 MHz and 100 MHz instrument and referenced to the internal solvent signals. Mass spectra were obtained using a Q-Exactive instrument. GC quantitative analysis was

performed using a SHIMADZU 2010plus instrument (Helium as the carrier gas, n-tetradecane as an internal standard, SH-Rtx-5 capillary column, FID detector). In the transient absorption spectral measurements, the samples were purged with argon for 15 min. Excitation was provided by using an Nd:YAG laser (third harmonic, 10 ns) at 532 nm. The detector was a xenon lamp on the Edingburge LP920 apparatus from Analytical Instruments. The values of lifetime were calculated by exponential function fitting with luminescence spectrometer software L900. Commercially available reagents and solvents were used without further purification. All photoreactions were performed using common dry, inert atmosphere techniques. Irradiation with blue light was performed using High Power UV 1W®TaoYuan LED ($\lambda = 450 \pm 10$ nm, 300 mA). For the irradiation, the material of the reaction vessel is common glass; the distance from the light source is about 0.5 cm. No filters were used in the general procedures. Reactions were monitored by TLC, and column chromatography purification processes were carried out using silica gel GF254.

General Procedure for the Synthesis of Diphenylmethane Derivatives.

Prepared (**1m**, **1o**, **1p**, **1s**, **1t**) according to literature methods.[19] A mixture of phenyl boronic acid (4 mmol), potassium carbonate (1382 mg, 10 mmol), benzyl bromide (475 ul, 4 mmol) in acetone-water (3:1, 40 mL) was stirred at room temperature until the reaction mixture became homogeneous. Then, the mixture was cooled in an ice bath and $PdCl_2$ (12 mg, 0.068 mmol) was added at 0 °C under an argon atmosphere. Stirring was continued at room temperature for 15 hours. The acetone was removed under reduced pressure and the product was extracted with diethyl ether (10 mL × 3).

The combined organic phases were dried over $MgSO_4$ and evaporated under reduced pressure. Purification by column chromatography (eluting with pure hexane to hexane/ethyl acetate 10:1) to afforded the product. While **1m**, **1o**, **1p** and **1s** were afforded as colorless oils, only, **1t** was obtained as a white solid. Data for 1-benzyl-4-(tert-butyl)benzene (**1m**): Yield: 770.6 mg, 86%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 - 7.16 (m, 7H), 7.11 (d, J = 8.1 Hz, 2H,), 3.95 (s, 2H), 1.30 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 149.0, 141.4, 138.2, 129.1, 128.7, 128.6, 126.1, 125.5, 41.6, 34.5, 31.6. Data for 1-benzyl-4-methoxybenzene (**1o**): Yield: 649.4 mg, 82%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 - 7.24 (m, 2H), 7.18 (t, J = 7.6 Hz, 3H), 7.10 (d, J = 8.0 Hz, 2H), 6.83 (d, J = 7.7 Hz, 2H), 3.92 (s, 2H), 3.78 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 158.1, 141.7, 133.4, 130.0, 129.0, 128.6, 126.1, 114.0, 55.4, 41.2. Data for 1-benzyl-2-methoxybenzene (**1p**): Yield: 633.6 mg, 80%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 - 7.16 (m, 6H), 7.09 (d, J = 7.5 Hz, 1H), 6.91 (t, J = 7.2 Hz, 2H), 4.01 (s, 2H), 3.85 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 157.5, 141.2, 130.5, 129.8, 129.1, 128.4, 127.5, 125.9, 120.6, 110.6, 55.5, 36.0. Data for methyl 4-benzylbenzoate (**1s**): Yield: 777.4 mg, 86%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 8.0 Hz, 2H), 7.36 - 7.11 (m, 7H), 4.03 (s, 2H), 3.89 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.2, 146.7, 140.3, 130.0, 129.1, 128.8, 128.3, 126.5, 52.1, 42.1. Data for 1-(4-benzylphenyl)ethan-1-one (**1t**): Yield: 714.0 mg, 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 7.4 Hz, 2H), 7.38 - 7.12 (m, 7H), 4.03 (s, 2H), 2.57 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 197.9, 146.9, 140.2, 135.4, 129.2, 129.1, 128.8, 126.6, 42.1, 26.7. Other information of them could be found literature

methods.[19]

General procedure for the benzylic chlorination reaction.

A 10 mL reaction tube equipped with magnetic stirring bar was charged with Acr^+-Mes ClO_4^- (6.2 mg, 0.015 mmol, 5 mol %), NCS (80.1 mg, 0.6 mmol, 2 equiv), 3 mL CH_2Cl_2, alkylbenzene derivate (0.3 mmol, 1 equiv). The reaction tube was sealed and the reaction mixture was degassed by bubbling with argon for 15 minutes. The mixture was stirred and irradiated with blue LEDs (λ = 450 ± 10 nm) for 4 hours at room temperature. After that, the mixture was concentrated in vacuo, and then purified by column chromatography on silica gel (eluting with pure hexane to hexane/ethyl acetate 10:1) to afford the desired benzylic chloride. **Note:** The identity of volatile products (**2a, 2b**, **2l**) were confirmed by GC analysis using *n*-tetradecane as an internal standard because the products **2a**, **2b** are volatile, and **2l** couldn't be obtained as a pure compound due to the hydrolysis issue.

General procedure for one-pot benzylic C-O bond construction.

Initially, a 10 mL reaction tube equipped with magnetic stirring bar was charged with Acr^+-Mes ClO_4^- (6.2 mg, 0.015 mmol, 5 mol %), NCS (80.1 mg, 0.6 mmol, 2 equiv), 3 mL CH_2Cl_2, diphenylmethane derivate (0.3 mmol, 1 equiv). The reaction tube was sealed and the reaction mixture was degassed by bubbling with argon for 15 minutes. The mixture was stirred and irradiated with blue LEDs (λ = 450 ± 10 nm) for 1 h at room temperature. Then CH_3OH (3 mL) and NaOMe (54.0 mg, 1 mmol) were added into the mixture, which was stired for 3 hours at room temperature. After that, the solution was diluted with H_2O (10 mL), and extracted with CH_2Cl_2 (10 mL × 3). The

combined organic phase was dried (Na_2SO_4) and concentrated in vacuo. The mixture was purified by column chromatography on silica gel (eluting with pure hexane to hexane/ethyl acetate 10:1) to afford the desired benyzlic ether.

Experiment Procedure for gram-scale synthesis.

To a 100 mL Pyrex tube (inner diameter: 3.5 cm, length: 14 cm) equipped with a magnetic stir bar was charged with 4-methylbenzophenone **1i** (1079.1 mg, 5.5 mmol, 1 equiv), Acr^+-Mes ClO_4^- (113.2 mg, 0.275 mmol, 5 mol %), NCS (1615.4 mg, 12.1 mmol, 2.2 equiv), 55 mL CH_2Cl_2. The mixture was strictly deaerated and irradiated by blue LEDs (λ = 450 ± 10 nm) for 8 hours at room temperature. After that, the mixture was concentrated in vacuo, and then purified by column chromatography on silica gel (eluting with pure hexane to hexane/ethyl acetate 10:1) to afford the desired benzylic chloride **2i** in 71% yield (1.08 g).

Experiment procedure for the competition reaction.

A 10 mL reaction tube equipped with magnetic stirring bar was charged with Acr^+-Mes ClO_4^- (6.2 mg, 0.015 mmol, 5 mol %), NCS (40.0 mg, 0.3 mmol, 1 equiv), 3 mL CH_2Cl_2, 4-methylbenzophenone **1i** (0.3 mmol, 58.9 mg, 1 equiv) and 4-ethylbenzophenone (0.3 mmol, 63.1 mg, 1 equiv). The reaction tube was sealed and the reaction mixture was degassed by bubbling with argon for 15 minutes. The mixture was stirred and irradiated with blue LEDs (λ = 450 ± 10 nm) for 4 hours at room temperature. After that, the mixture was analyzed by ^1H NMR directly using 1,3,5-trimethoxybenzene as an internal standard. The competition reaction provided the corresponding product with 15% and 21% yields for primary and secondary C-H

bonds respectively.

Experiment procedure for benzylic bromination reaction.

A 10 mL reaction tube equipped with magnetic stirring bar was charged with Acr^+-Mes ClO_4^- (6.2 mg, 0.015 mmol, 5 mol %), NBS (117.5 mg, 0.66 mmol, 2.2 equiv), 3 mL CH_2Cl_2, 4-methylbenzophenone **1i** (0.3 mmol, 58.9 mg, 1 equiv). The reaction tube was sealed and the reaction mixture was degassed by bubbling with argon for 15 minutes. The mixture was stirred and irradiated with blue LEDs (λ = 450 ± 10 nm) for 4 hours at room temperature. After that, the mixture was concentrated in vacuo, and then purified by column chromatography on silica gel (eluting with pure hexane to hexane/ethyl acetate 10:1) to afford the desired benzylic bromide **3i**.

Experiment procedures for the control experiments (Figure S4).

Figure S4a: A 10 mL reaction tube equipped with magnetic stirring bar was charged with Acr^+-Mes ClO_4^- (6.2 mg, 0.015 mmol, 5 mol %), toluene **1a** (31.7 μL, 0.3 mmol, 1 equiv), 3 mL CD_2Cl_2. The reaction tube was sealed and the reaction mixture was degassed by bubbling with argon for 15 minutes. Then, the mixture was stirred and irradiated with blue LEDs (λ = 450 ± 10 nm) for 4 hours at room temperature. After that, the mixture was analyzed by ^1H NMR directly using 2,2-diphenylacetonitrile as an internal standard. The yield of chlorination product was 0% and almost all of substrate **1l** was remained.

Figure S4b: A 10 mL reaction tube equipped with magnetic stirring bar was charged with Acr^+-Mes ClO_4^- (6.2 mg, 0.015 mmol, 5 mol %), NCS (80.1 mg, 0.6 mmol, 2 equiv), BHT (132.2 mg, 0.6 mmol) or TEMPO (93.7 mg, 0.6 mmol), 3 mL CH_2Cl_2,

diphenylmethane **1l** (50.5 mg, 0.3 mmol, 1 equiv). The reaction tube was sealed and the reaction mixture was degassed by bubbling with argon for 15 minutes. Then, the mixture was stirred and irradiated with blue LEDs (λ = 450 ± 10 nm) for 1 hour at room temperature. After that, the mixture was analyzed by GC using *n*-tetradecane as an internal standard. The yield of desired product was trace and almost all of substrate **1l** was remained.

Figure S4c: A 10 mL reaction tube equipped with magnetic stirring bar was charged with Acr^+-Mes ClO_4^- (6.2 mg, 0.015 mmol, 5 mol %), NCS (80.1 mg, 0.6 mmol, 2 equiv), diethyl bromomalonate (DEBM, 256 ul, 1.5 mmol), 3 mL CH_2Cl_2, diphenylmethane **1l** (50.5 mg, 0.3 mmol, 1 equiv). The reaction tube was sealed and the reaction mixture was degassed by bubbling with argon for 15 minutes. Then, the mixture was stirred and irradiated with blue LEDs (λ = 450 ± 10 nm) for 1 hour at room temperature. After that, the mixture was analyzed by GC using *n*-tetradecane as an internal standard. The desired product (bromomethylene)dibenzene and (chloromethylene)dibenzene could be afforded with 13% and 61% yields respectively. However, it couldn't produce the benzylic bromide product under the same condition just without the NCS.

Model benzylic chlorination reaction in the absence of substrate toluene (Figure S5).

A 10 mL reaction tube equipped with magnetic stirring bar was charged with Acr^+-Mes ClO_4^- (6.2 mg, 0.015 mmol, 5 mol %), NCS (80.1 mg, 0.6 mmol, 2 equiv), 3 mL CH_2Cl_2. We first concentrated the mixture in vacuo and detected ^1H NMR

spectrum of them in $CDCl_3$ before irradiation. Subsequently, the mixture of Acr^+-Mes and NCS in an argon-saturated DCM (3 mL) was irradiated by blue LEDs for 10 min, 30 min and 4 hours, and corresponding ^1H NMR spectra were detected. It was very clear that NCS (δ 2.93) was gradually converted into succinimide (δ 2.76) as the reaction progress.

Model benzylic chlorination reaction replacing oxidant NCS with O_2 (Figure S6).

A 10 mL reaction tube equipped with magnetic stirring bar was charged with Acr^+-Mes ClO_4^- (6.2 mg, 0.015 mmol, 5 mol %), NCS (80.1 mg, 0.6 mmol, 2 equiv), **1a** or **1l** (0.3 mmol, 1 equiv.), 3 mL CH_2Cl_2 under the air. Subsequently, the mixture of was irradiated by blue LEDs for 1 hour, 2 hours, 3 hours and 4 hours, and the residue of substrate substrate was detected by GC using *n*-tetradecane as an internal standard. The result indicated after 4 hours of irradiation, nearly all substrate toluene was remained (**1a**, 93%; **1l**, 97%).

Experiment procedure for the light-dark cycle experiment (Figure S7).

Six 10 mL reaction tubes were equipped with magnetic stirring bars, and each tube was charged with Acr^+-Mes ClO_4^- (6.2 mg, 0.015 mmol, 5 mol %), NCS (80.1 mg, 0.6 mmol, 2 equiv), 3 mL CH_2Cl_2, diphenylmethane **1l** (50.5 mg, 0.3 mmol, 1 equiv). The reaction tubes were sealed and the reaction mixtures were degassed by bubbling with argon for 15 minutes. Then, each mixture was stirred and irradiated with blue LEDs ($\lambda = 450 \pm 10$ nm) at room temperature. The first one: stir with light for 5 mins; The second one: stir with light for 5 mins, then without light for 5 mins; The third one: stir with light for 5 mins, then without light for 5 mins, then with light for 5

mins; The fourth one: stir with light for 5 mins, then without light for 5 mins, then with light for 5 mins, then without light for 5 mins; The fifth one: stir with light for 5 mins, then without light for 5 mins, then with light for 5 mins, then without light for 5 mins, then with light for 5 mins; The sixth one: stir with light for 5 mins, then without light for 5 mins; then with light for 5 mins, then without light for 5 mins, then with light for 5 mins, then without light for 5 mins. After that, 2,6-di-tert-butyl-4-methylphenol BHT (132.2mg, 0.6 mmol) was added to terminate the reaction. At last, the yield was determined by acquiring GC using *n*-tetradecane as an internal standard.

2-(chloromethyl)-1,1'-biphenyl (2c). Yield: 46.8 mg, 77%. Colorless oil. Purified by column chromatography on silica gel (eluting with pure hexane to hexane/ethyl acetate 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 - 7.54 (m, 1H), 7.53 - 7.36 (m, 7H), 7.34 - 7.29 (m, 1H), 4.56 (s, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 142.3, 140.4, 135.2, 130.6, 130.5, 129.3, 128.6, 128.5, 128.1, 127.6, 44.6; HRMS (EI): m/z calcd for $C_{13}H_{11}Cl$ $[M]^+$ 202.0544, found 202.0557.

4-(chloromethyl)-1,1'-biphenyl (2d). Yield: 42.6 mg, 70%. White solid. Purified by column chromatography on silica gel (eluting with pure hexane to hexane/ethyl acetate 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 - 7.58 (m, 4H), 7.55 - 7.44 (m, 4H), 7.43 - 7.36 (m, 1H), 4.67 (s, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 141.5, 140.6, 136.6, 129.2, 129.0, 127.7, 127.6, 127.3, 46.2; HRMS (EI): m/z calcd for $C_{13}H_{11}Cl$ $[M]^+$ 202.0544, found 202.0553.

4'-(chloromethyl)-[1,1'-biphenyl]-2-carbonitrile (2e). Yield: 44.4 mg, 65%. White solid. Purified by column chromatography on silica gel (eluting with pure hexane to

hexane/ethyl acetate 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.7 Hz, 1H), 7.65 (t, *J* = 7.7 Hz, 1H), 7.61 - 7.49 (m, 5H), 7.46 (t, *J* = 7.6 Hz, 1H), 4.65 (s, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 145.5, 138.9, 138.7, 134.5, 133.6, 130.7, 129.8, 129.6, 128.5, 119.2, 112.1, 46.4; HRMS (EI): m/z calcd for $C_{14}H_{10}ClN$ $[M]^+$ 227.0497, found 227.0506.

methyl 4-(chloromethyl)benzoate ***(2f)***. Yield: 35.4 mg, 64%. Colorless solid. Purified by column chromatography on silica gel (eluting with pure hexane to hexane/ethyl acetate 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.2 Hz, 2H), 7.46 (d, *J* = 8.2 Hz, 2H), 4.61 (s, 2H), 3.92 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.7, 142.4, 130.4, 130.2, 128.6, 52.3, 45.5; HRMS (EI): m/z calcd for $C_9H_9ClO_2$ $[M]^+$ 184.0286, found 184.0296.

methyl 3-(chloromethyl)benzoate ***(2g)***. Yield: 35.9 mg, 65%. Colorless oil. Purified by column chromatography on silica gel (eluting with pure hexane to hexane/ethyl acetate 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 - 7.95 (m, 2H), 7.59 (d, *J* = 7.3 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 1H), 4.62 (s, 2H), 3.93 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.7, 138.0, 133.1, 130.8, 129.8, 129.7, 129.0, 52.4, 45.6; HRMS (ESI): m/z calcd for $C_9H_9ClO_2$ $[M]^+$ 184.0286, found 184.0281.

1-(4-(chloromethyl)phenyl)ethan-1-one ***(2h)***. Yield: 35.9 mg, 71%. White solid. Purified by column chromatography on silica gel (eluting with pure hexane to hexane/ethyl acetate 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.2 Hz, 2H), 7.48 (d, *J* = 8.2 Hz, 2H), 4.61 (s, 2H), 2.60 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 197.5, 142.6, 137.3, 128.9, 128.8, 45.4, 26.7; HRMS (EI): m/z calcd for C_9H_9ClO $[M]^+$ 168.0337, found 168.0344.

(4-(chloromethyl)phenyl)(phenyl)methanone ***(2i)***. Yield: 52.6 mg, 76%. Colorless solid. Purified by column chromatography on silica gel (eluting with pure hexane to

hexane/ethyl acetate 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.1 Hz, 4H), 7.61 - 7.53 (m, 1H), 7.53 - 7.41 (m, 4H), 4.62 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 195.9, 141.7, 137.5, 137.4, 132.6, 130.4, 130.0, 128.4, 128.3, 45.4; HRMS (EI): m/z calcd for $C_{14}H_{11}ClO$ $[M]^+$ 230.0493, found 230.0500.

1-(chloromethyl)-4-nitrobenzene (2j). Yield: 11.0 mg, 21%. White solid. Purified by column chromatography on silica gel (eluting with pure hexane to hexane/ethyl acetate 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 7.1 Hz, 4H), 7.58 (d, *J* = 7.1 Hz, 4H), 4.66 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) 148.0, 144.4, 129.5, 124.1, 44.6; HRMS (ESI): m/z calcd for $C_7H_6ClNO_2$ $[M]^+$ 171.0082, found 171.0078.

methyl 3-chloro-3-phenylpropanoate (2k). Yield: 38.7 mg, 65%. Colorless oil. Purified by column chromatography on silica gel (eluting with pure hexane to hexane/ethyl acetate 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 7.3 Hz, 2H), 7.40 - 7.31 (m, 3H), 5.36 (dd, *J* = 9.1, 5.7 Hz, 1H), 3.71 (s, 3H), 3.19 (dd, *J* = 16.0, 9.1 Hz, 1H), 3.04 (dd, *J* = 16.0, 5.7 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 170.1, 140.5, 128.9, 128.9, 127.0, 58.2, 52.1, 44.9; HRMS (EI): m/z calcd for $C_{10}H_{11}ClO_2$ $[M]^+$ 198.0443, found 198.0448.

(methoxymethylene)dibenzene (2l'). Yield: 47.6 mg, 80%. Colorless oil. Purified by column chromatography on silica gel (eluting with pure hexane to hexane/ethyl acetate 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 - 7.28 (m, 8H), 7.24 (dd, *J* = 7.8, 5.8 Hz, 2H), 5.24 (s, 1H), 3.38 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 142.3, 128.5, 127.6, 127.1, 85.7, 57.1; HRMS (EI): m/z calcd for $C_{14}H_{14}O$ $[M]^+$ 198.1040, found 198.1048.

1-(tert-butyl)-4-(methoxy(phenyl)methyl)benzene (2m'). Yield: 46.5 mg, 61%. Colorless oil. Purified by column chromatography on silica gel (eluting with pure hexane to hexane/ethyl acetate 10:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.37 - 7.29

(m, 6H), 7.29 - 7.19 (m, 3H), 5.28 (s, 1H), 3.25 (s, 3H), 1.24 (s, 9H); $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ 149.5, 142.5, 139.4, 128.2, 127.1, 126.4, 126.1, 125.0, 84.0, 56.3, 34.1, 31.1; HRMS (EI): m/z calcd for $C_{18}H_{22}O$ $[M]^+$ 254.1666, found 254.1683.

4-(methoxy(phenyl)methyl)-1,1'-biphenyl ***(2n')***. Yield: 56.8 mg, 69%. White solid. Purified by column chromatography on silica gel (eluting with pure hexane to hexane/ethyl acetate 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (dd, J = 7.5, 5.4 Hz, 4H), 7.44 - 7.36 (m, 6H), 7.33 (q, J = 7.4 Hz, 3H), 7.27 - 7.22 (m, 1H), 5.28 (s, 1H), 3.41 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 142.2, 141.3, 141.0, 140.5, 128.9, 128.6, 127.7, 127.5, 127.4, 127.3, 127.2, 127.1, 85.4, 57.2; HRMS (EI): m/z calcd for $C_{20}H_{18}O$ $[M]^+$ 274.1353, found 274.1363.

1-methoxy-4-(methoxy(phenyl)methyl)benzene ***(2o')***. Yield: 40.4 mg, 59%. Colorless oil. Purified by column chromatography on silica gel (eluting with pure hexane to hexane/ethyl acetate 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 - 7.28 (m, 4H), 7.25 (d, J = 8.6 Hz, 3H), 6.85 (d, J = 8.6 Hz, 2H), 5.20 (s, 1H), 3.77 (s, 3H), 3.36 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 159.3, 142.6, 134.6, 128.5, 128.4, 127.5, 127.0, 114.0, 85.2, 57.0, 55.4; HRMS (EI): m/z calcd for $C_{15}H_{16}O_2$ $[M]^+$ 228.1145, found 228.1161.

1-methoxy-2-(methoxy(phenyl)methyl)benzene ***(2p')***. Yield: 37.7 mg, 55%. Colorless oil. Purified by column chromatography on silica gel (eluting with pure hexane to hexane/ethyl acetate 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 7.6 Hz, 1H), 7.38 (d, J = 7.6 Hz, 2H), 7.28 (t, J = 7.5 Hz, 2H), 7.25 - 7.19 (m, 2H), 6.96 (t, J = 7.5 Hz, 1H), 6.84 (d, J = 8.2 Hz, 1H), 5.68 (s, 1H), 3.79 (s, 3H), 3.38 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 156.8, 142.2, 130.7, 128.5, 128.3, 127.2, 127.1, 127.0, 120.9, 110.7, 78.9, 57.2, 55.6; HRMS (EI): m/z calcd for $C_{15}H_{16}O_2$ $[M]^+$ 228.1145, found 2281161.

1-fluoro-4-(methoxy(phenyl)methyl)benzene ***(2q')***. Yield: 49.3 mg, 76%. Colorless oil. Purified by column chromatography on silica gel (eluting with pure hexane to hexane/ethyl acetate 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 - 7.22 (m, 7H), 7.06 - 6.92 (m, 2H), 5.21 (s, 1H), 3.36 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 162.3 (d, J = 245.6 Hz), 142.0, 138.1 (d, J = 3.1 Hz), 128.7 (d, J =8.1 Hz), 128.6, 127.7, 127.0, 115.4 (d, J = 21.4 Hz), 84.8, 57.1; ^{19}F NMR (375 MHz, $CDCl_3$) δ -115.22; HRMS (EI): m/z calcd for $C_{14}H_{13}FO$ $[M]^+$ 216.0945, found 216.0957.

1-chloro-4-(methoxy(phenyl)methyl)benzene ***(2r')***. Yield: 51.6 mg, 74%. Colorless oil. Purified by column chromatography on silica gel (eluting with pure hexane to hexane/ethyl acetate 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 - 7.29 (m, 4H), 7.28 (s, 4H), 7.25 (dd, J = 5.7, 2.8 Hz, 1H), 5.20 (s, 1H), 3.36 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 141.7, 140.9, 133.3, 128.7, 128.7, 128.4, 127.9, 127.0, 84.9, 57.1; HRMS (EI): m/z calcd for $C_{14}H_{13}ClO$ $[M]^+$ 232.0650, found 232.0659.

methyl 4-(methoxy(phenyl)methyl)benzoate ***(2s')***. Yield: 54.6 mg, 71%. Colorless oil. Purified by column chromatography on silica gel (eluting with pure hexane to hexane/ethyl acetate 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, J = 8.2 Hz, 2H), 7.43 (d, J = 8.2 Hz, 2H), 7.33 (d, J = 4.3 Hz, 4H), 7.29 - 7.25 (m, 1H), 5.28 (s, 1H), 3.89 (s, 3H), 3.38 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 167.1, 147.5, 141.5, 129.9, 129.4, 128.7, 128.0, 127.2, 126.8, 85.2, 57.2, 52.2; HRMS (EI): m/z calcd for $C_{16}H_{16}O_3$ $[M]^+$ 256.1094, found 256.1098.

1-(4-(methoxy(phenyl)methyl)phenyl)ethan-1-one ***(2t')***. Yield: 46.8 mg, 65%. Colorless oil. Purified by column chromatography on silica gel (eluting with pure hexane to hexane/ethyl acetate 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 - 7.91 (m, 1H), 7.91 - 7.89 (m, 1H), 7.45 (d, J = 8.2 Hz, 2H), 7.33 (d, J = 4.4 Hz, 4H), 7.28 - 7.25 (m, 1H), 5.28 (s, 1H), 3.39 (s, 3H), 2.57 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 197.9, 147.7, 141.4, 136.5, 128.7, 128.7, 128.0, 127.1, 127.0, 85.1, 57.2,

26.7; HRMS (EI): m/z calcd for $C_{16}H_{16}O_2$ $[M]^+$ 240.1145, found 240.1157.

(4-(bromomethyl)phenyl)(phenyl)methanone ***(3i)***. Yield: 49.5 mg, 60%. White solid. Purified by column chromatography on silica gel (eluting with pure hexane to hexane/ethyl acetate 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 - 7.75 (m, 4H), 7.64 - 7.57 (m, 1H), 7.55 - 7.41 (m, 4H), 4.54 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.1, 142.2, 137.6, 137.5, 132.7, 130.7, 130.1, 129.1, 128.5, 32.4; HRMS (ESI): m/z calcd for $C_{14}H_{11}BrO$ $[M+H]^+$ 275.0067, found 275.0058.

SUPPORTING INFORMATION

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Notes

The authors declare no competing financial interest.

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