# Visible-Light-Promoted Metal-Free Ammoxidation of C(sp^3)-H bonds

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ABSTRACT: The metal-free activation of C(sp^3)-H bonds to value-added products is of paramount importance in organic synthesis. Herein, we report the use of the commercially available organic dye 2,4,6-triphenylpyrylium tetrafluoroborate (TPP) for the conversion of methylarenes to the corresponding aryl nitriles via a photo process. Applying this methodology, a variety of cyanobenzenes have been synthesized in good to excellent yield under metal- and cyanide-free conditions. We demonstrate the scope of the method with over 50 examples including late-stage functionalization of drug molecules (celecoxib) and complex structures such as L-menthol, amino acids and cholesterol derivatives. Further, the presented synthetic protocol is applicable for gram-scale reactions. In addition to methylarenes, selected examples for the cyanation of aldehydes, alcohols and oximes are demonstrated as well. Detailed mechanistic investigations have been carried out using time-resolved luminescence quenching studies, control experiments and NMR- spectroscopic as well as kinetic studies, all supporting the proposed catalytic cycle.
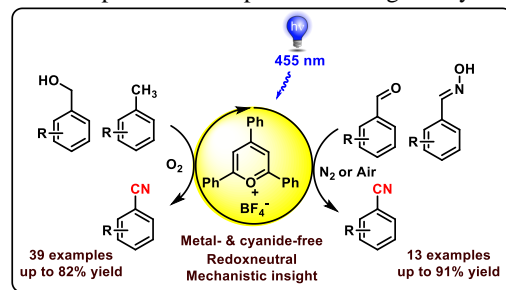
INTRODUCTION

Transition-metal based catalysts have an indispensable role in several chemical reactions,[1] industrial production,[1a-e, 1h] fine and bulk chemical synthesis.[1t] However, due to their high price,[2] less abundance[3] and toxicity,[4] the interest in using alternative metal-free catalysts is growing within the scientific community, especially for the late-stage functionalization of inert C(sp^3)-H bonds.[5] During the last two decades, several transition-metal based catalysts[1q, 6] have been developed for the activation of C-H bonds in sp^3 centres via thermal and photochemical pathways.[1q, 6] One of the most important transformations is the conversion of petroleum by-products into fine chemicals,[1a, 1b] e.g. the synthesis of benzonitrile from toluene.[1b, 1c] Industrially, benzonitrile is produced by ammoxidation of toluene using a transition-metal catalyst (vanadium) and applying a high NH_3 and O_2 pressure at 300-500 °C.[1b, 1c] Although the industrial ammoxidation process is an atom economic and sustainable route for the synthesis of nitriles starting from the unfunctionalized CH_3 group, but several functional groups are not tolerated due to the high reaction temperature and pressure.[1b, 1c] The nitrile moiety is an essential functional group in various drugs and bioactive compounds,[7] as well as an important building block for the preparation of fine and bulk chemicals, such as amines, carboxylic acids, amides and esters.[8] In conventional approaches, nitriles have been synthesized using the Sandmeyer reaction,[9] Rosenmund-von Braun reaction[10] and halide/CN exchange.[11] Further, transition-metal and photoredox catalyzed ammoxidations of aldehydes have been reported.[12] A few examples for the synthesis of nitriles from sp^2 C-H bonds via photocatalysis were reported by Nicewicz[13] and others.[14] However, the above-mentioned methods often suffer from several drawbacks, such as the use of transition metals leading to metal residue waste, high temperature, low selectivity or the generation of toxic cyanide. [11]

The direct conversion of methylarenes to nitriles in a one-step procedure is highly desired, but one-pot protocols to prepare nitriles from toluene are underdeveloped.[15] Wang et al. reported[15a] a Palladium-catalyzed cyanation of methylarenes in 2013, using an over stoichiometric amount of tBuONO and NHPI at 70 °C.

Scheme 1. Industrial ammoxidation process
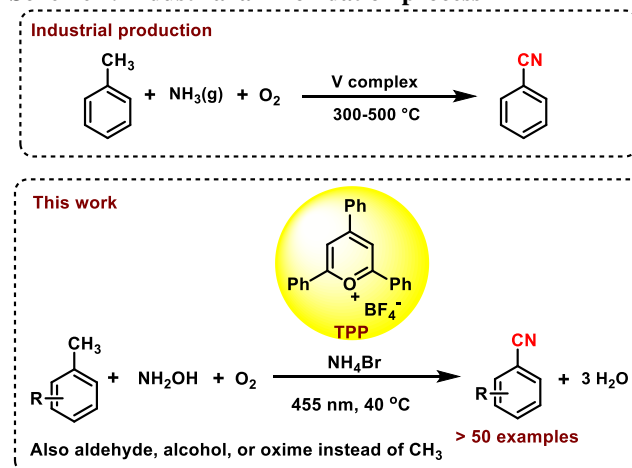
Recently, Kang and co-workers[15b] reported a similar strategy to Wang, where $AlCl_3$ was used as Lewis acid for the conversion of the oxime intermediates to nitriles at 80 °C. Major drawbacks of the reported methods are the harsh reaction conditions together with the use of hazardous reagents and transition metals.

In principle, a greener way to produce nitriles is by an oxidation process using molecular oxygen or simply air. Interestingly, a few examples to synthesize nitriles from alcohols[16] or amines[17] employing oxygen as oxidant are known to date.

However, the reported methods mainly rely on transition metal catalysts and applying harsh reaction conditions (> 100 °C).

We envisioned that an alternative metal- and cyanide-free methylarene to nitrile protocol could be developed by using a visible-light-assisted ammoxidation approach. Several challenges need to be addressed for this aim, such as the desired, yet difficult oxidation of the methylarene substrate (e.g. $E_{1/2}$ = +2.36 V vs SCE for toluene),[18] especially in case of electron deficient substituents, opposed to a more facile oxidation of ammonia ($E_{1/2}$ = + 0.63 V vs SCE),[19] and the prevention of an over oxidation of the methylarenes to the carboxylic acid. Herein we describe the use of the commercially available organic dye 2,4,6-triphenylpyrylium tetrafluoroborate (TPP)[20] for the synthesis of nitriles from methylarenes. In addition to this, a detailed mechanistic investigations was carried out to support our mechanistic hypothesis. All experimental results and spectroscopic analyses support the proposed catalytic cycle. To the best of our knowledge, this is the first example for a photocatalytic ammoxidation of methylarenes using abundant feedstock materials, ammonium salts and molecular oxygen without the use of metals and toxic reagents.

RESULTS AND DISCUSSION

At the start of our investigation, we tested different commercially available organic dyes for the desired transformation (Table 1).

Table 1. Organic dye photocatalysts in the ammoxidation of methyl 4-methylbenzoate to methyl 4-cyanobenzoate.
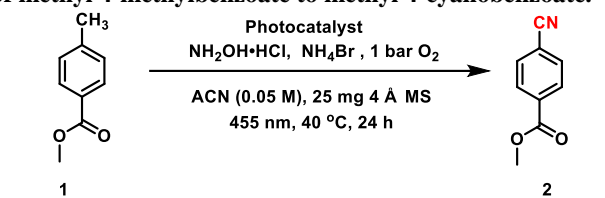
Entry	Photocatalyst (PC)	Ammonia source	Yield of 2 (%)
1[a]	PC-1	NH₂OH•HCl	26
2[a]	PC-2	NH₂OH•HCl	15
3[a]	PC-3	NH₂OH•HCl	35
4[a]	**PC-4**	**NH₂OH•HCl**	**76**
5[a]	PC-5	NH₂OH•HCl	12
6[a]	PC-6	NH₂OH•HCl	14
7[a]	PC-4	NH₄(OAc)₂	NR
8[a]	PC-4	Aq. NH₃	NR
9[a]	PC-4	HCOONH₄	NR
10[a]	PC-4	7N NH₃ in MeOH	NR

PC-1   PC-2   PC-3
PC-4 (TPP)   PC-5   PC-6
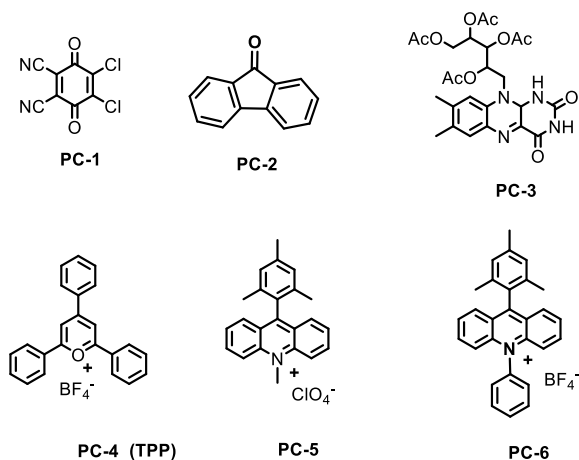
Reaction conditions: [a]0.1 mmol substrate, 20 mol% PC, 3 eq. ammonia source, 2.5 eq. NH₄Br, 25 mg 4 Å MS, 1 bar O₂, 2 mL acetonitrile (0.05 M), 455 nm, 40 °C, 24 h, yields were determined by GC using n-decane as standard.

The initial screening revealed DDQ and 9-fluorenone as ineffective catalysts for this reaction giving a yield of 26% and 15%, respectively (Table 1, entries 1-2). Interestingly, the use of RFTA led to a moderate yield of 35% (Table 1, entry 3), while the more sensitive photocatalyst TPP (PC-4) ($E_{1/2}$ = + 2.3 V),[21] yielded 76% of methyl 4-cyanobenzoate (Table 1, entry 4). Surprisingly, employing acridinium photocatalysts ($E_{1/2}$ = + 2.28 V)[1u] resulted in poor yields of 12% and 14%, respectively (Table 1, entries 5-6). Further, different ammonium salts were screened for the cyanation of methylarenes. Notably, merely hydroxylamine hydrochloride gave the desired product 2, while all other tested ammonium sources, such as ammonium acetate, aqueous ammonia, ammonium formate and methanolic ammonia failed to render the desired product (Table 1, entries 7-10). Possible reasons for this observations are that the oxidation of simple ammonia ($E_{1/2}$ = + 0.63 V vs SCE) might be faster than the required oxidation of the substrate and the potential degradation of PC-4 in the presence of a base or nucleophiles.

Kinetic investigations. After having identified a potential photocatalyst (PC-4, TPP), kinetic investigations on this system were performed, examining the effect of (a) reaction time, (b) concentration of the catalyst, (c) temperature, (d) hydroxylamine to substrate ratio, (e) ammonium bromide concentration, and (f) wavelength (Fig. 1). Regarding the reaction time (Fig. 1a), 30% of the starting material was converted after 2 h, with the major product being the oxime intermediate 3 (16%) and only small amounts of product (2). After 8 h, the starting material was almost completely converted. At this time, the oxime (3) concentration is beginning to decrease slowly, while the yield of the desired product 2 is steadily increasing.

Varying the catalyst loading (Fig. 1b), the starting material was predominant with 2 mol%. For 5 mol% catalyst, product 2, 3 and starting material 1 were almost at an equal level (28-38%) and the maximum product yield of 76% was obtained when the photocatalyst loading was raised to 20 mol%. The reaction temperature had a significant effect on the product yield, as shown in Fig. 1(c). At 0 °C, product 2 together with 3 were observed in 42% and 38%, respectively. The oxime to

nitrile conversion was increased by elevating the reaction temperature, revealing 40 °C as the optimum. The absence or low concentration of hydroxylamine hydrochloride led to an increased amount of by-product **4** (Fig. 1d), whereas a loading of 3 eq. gave the product in a good yield. A catalytic amount of ammonium bromide was sufficient for the complete conversion of starting material. However, to reach the maximum yield an excess of ammonium bromide is required (Fig. 1e). When investigating the effect of different wavelength, we found that 365 nm and 455 nm LEDs are efficient light sources for this transformation (Fig. 1f).

In addition to this, the role of different solvents and additives were examined (Supporting Information, Table S1 and S2). Acetonitrile was identified as the ideal solvent, together with NH$_4$Br as the optimal additive (Supporting Information, Table S1 and S2). Crucially, control experiments revealed the necessity of light, photocatalyst, O$_2$ and NH$_2$OH.HCl for the formation of the desired product (Supporting Information, Table S3, entries 2-4 and 7). However, in the absence of an additive or molecular sieves the desired product was observed as well, albeit in a low yield of 25
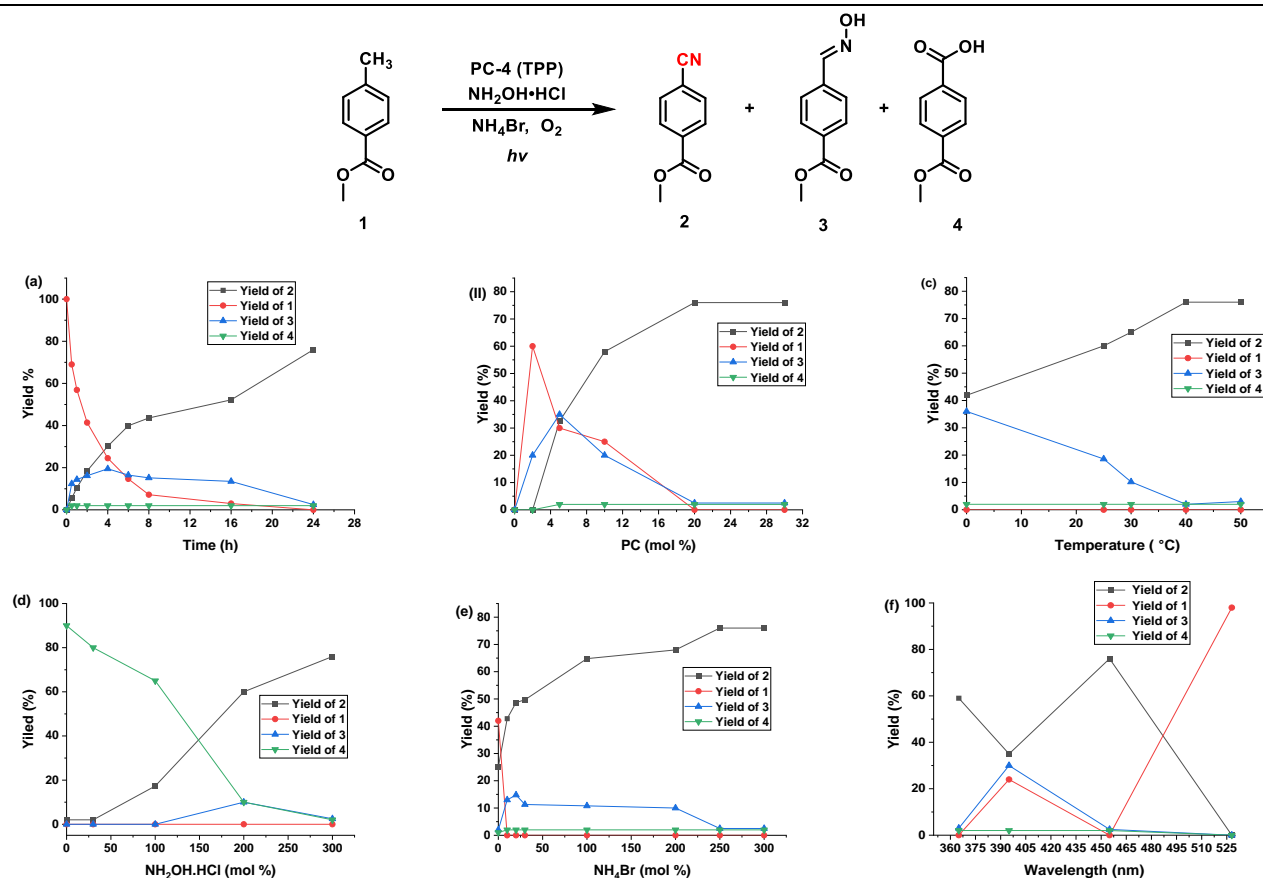

Fig. 1: Kinetic investigation on the photocatalytic ammoxidation. (a) Yield vs time, (b) yield vs concentration of TPP, (c) yield vs temperature, (d) yield vs mol% of NH$_2$OH•HCl, (e) yield vs mol% of NH$_4$Br, (f) yield vs wavelength. Reaction conditions: For Fig. 1(a): 0.1 mmol substrate, 20 mol% PC, 3 eq. NH$_2$OH•HCl, 2.5 eq. NH$_4$Br, 25 mg 4 Å MS, 1 bar O$_2$, 2 mL acetonitrile (0.05 M), 455 nm, 40 °C, 0-24 h. Fig. 1(b): 0.1 mmol substrate, 2-20 mol% PC, 3 eq. NH$_2$OH•HCl, 2.5 eq. NH$_4$Br, 25 mg 4 Å MS, 1 bar O$_2$, 2 mL acetonitrile (0.05 M), 455 nm, 40 °C, 24 h. Fig. 1(c): 0.1 mmol substrate, 20 mol% PC, 3 eq. NH$_2$OH•HCl, 2.5 eq. NH$_4$Br, 25 mg 4 Å MS, 1 bar O$_2$, 2 mL acetonitrile (0.05 M), 455 nm, 0-40 °C, 24 h. Fig. 1(d): 0.1 mmol substrate, 20 mol% PC, 0.3-3 eq. NH$_2$OH•HCl, 2.5 eq. NH$_4$Br, 25 mg 4 Å MS, 1 bar O$_2$, 2 mL acetonitrile (0.05 M), 455 nm, 40 °C, 24 h. Fig. 1(d): 0.1 mmol substrate, 20 mol% PC, 3 eq. NH$_2$OH•HCl, 0.1-2.5 eq. NH$_4$Br, 25 mg 4 Å MS, 1 bar O$_2$, 2 mL acetonitrile (0.05 M), 455 nm, 40 °C, 24 h. Fig. 1(e): 0.1 mmol substrate, 20 mol% PC, 3 eq. NH$_2$OH•HCl, 2.5 eq. NH$_4$Br, 25 mg 4 Å MS, 1 bar O$_2$, 2 mL acetonitrile (0.05 M), 365-528 nm, 40 °C, 24 h. Yields were determined by GC using n-decane as standard.

and 51%, respectively (Supporting Information, entries 5-6).

Mechanistic hypothesis. The initial kinetic studies suggest that the oxime is one of the key intermediates, as its depletion is accompanied by the formation of the product. Further, the control experiment yielding no product in the absence of O$_2$ indicates that the oxime might be formed from the corresponding aldehyde. Based on this we envisioned following catalytic

cycle (Cycle A): the substrate (E$_{1/2}$ (1/1$^{•+}$) = + 2.45 V vs SCE, supporting information) is oxidised by the excited photocatalyst (E$_{1/2}$ (PC-4^{+*}/ PC-4$^{•}$) = + 2.3 V Vs SCE) via electron transfer, generating radical cation **II** and the reduced photocatalyst species (PC-4$^{•}$). The photocatalytic cycle is closed by the oxidation of the reduced photocatalyst with O$_2$, giving a superoxide anion (O$_2$ $^{•-}$). Intermediate **II** loses a proton to form the more stable benzylic radical (**III**), which combines with

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the superoxide anion to peroxide derivative **V** after protonation. Elimination of water from **V** leads to the corresponding aldehyde intermediate (**VI**). Intermediate **VI** can yield oxime **VII** upon condensation with NH$_2$OH•HCl, which can be converted into the desired nitrile in a second cycle (Fig. 2, Cycle A'). In this cycle, the oxime (**VII**) is oxidised to **VIII** via reductive quenching of PC-4* followed by elimination of water to give intermediate **IX**. The reduced PC undergoes SET with **IX** to render the desired product **X**, closing the photocatalytic cycle and completing a redox-neutral process.

The presence of NH$_4$Br is crucial to obtain a satisfactory yield. Thus, another catalytic cycle may be operative, yielding the

same reaction product (Fig. 2, Cycle B). Bromide anions are known hydrogen atom transfer (HAT) catalysts.[23] In presence of visible-light, the excited PC can oxidise Br$^-$ to generate the Br$^•$ radical, which is capable to abstract the H-atom from the methylarene to yield a benzyl radical (**III**) and HBr. The combination of superoxide anion and **III** yields intermediate **IV**, which deprotonates HBr to regenerate the Br$^-$ while generating intermediate **V**. After its formation, **V** follows the same mechanistic pathway as described above (Cycle A and A').
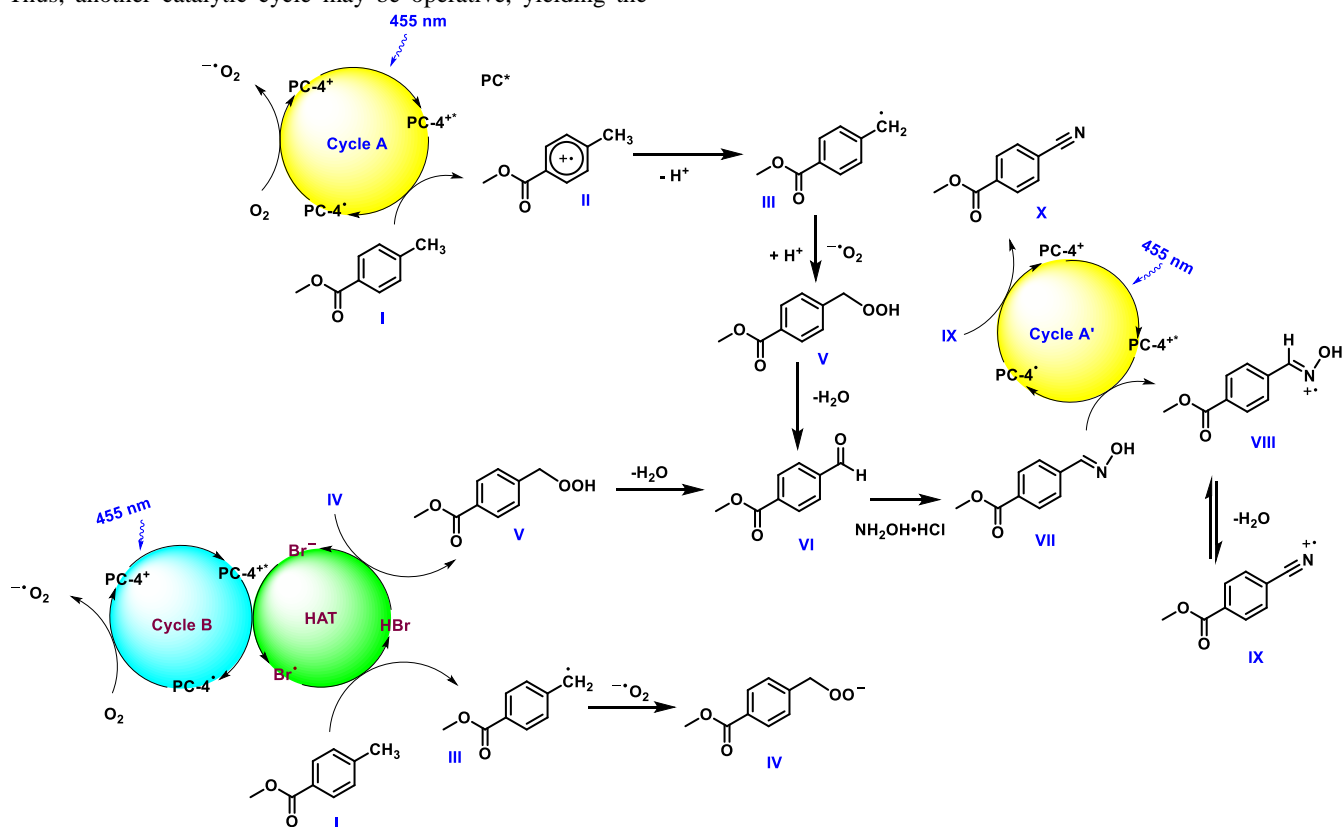

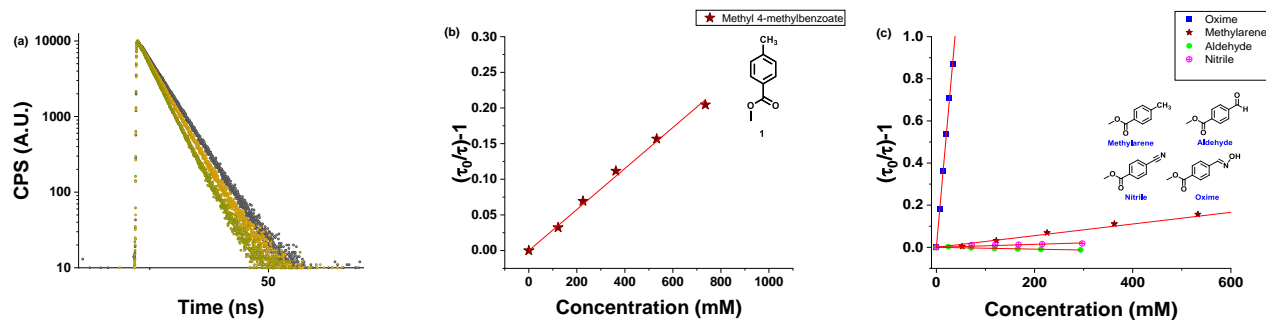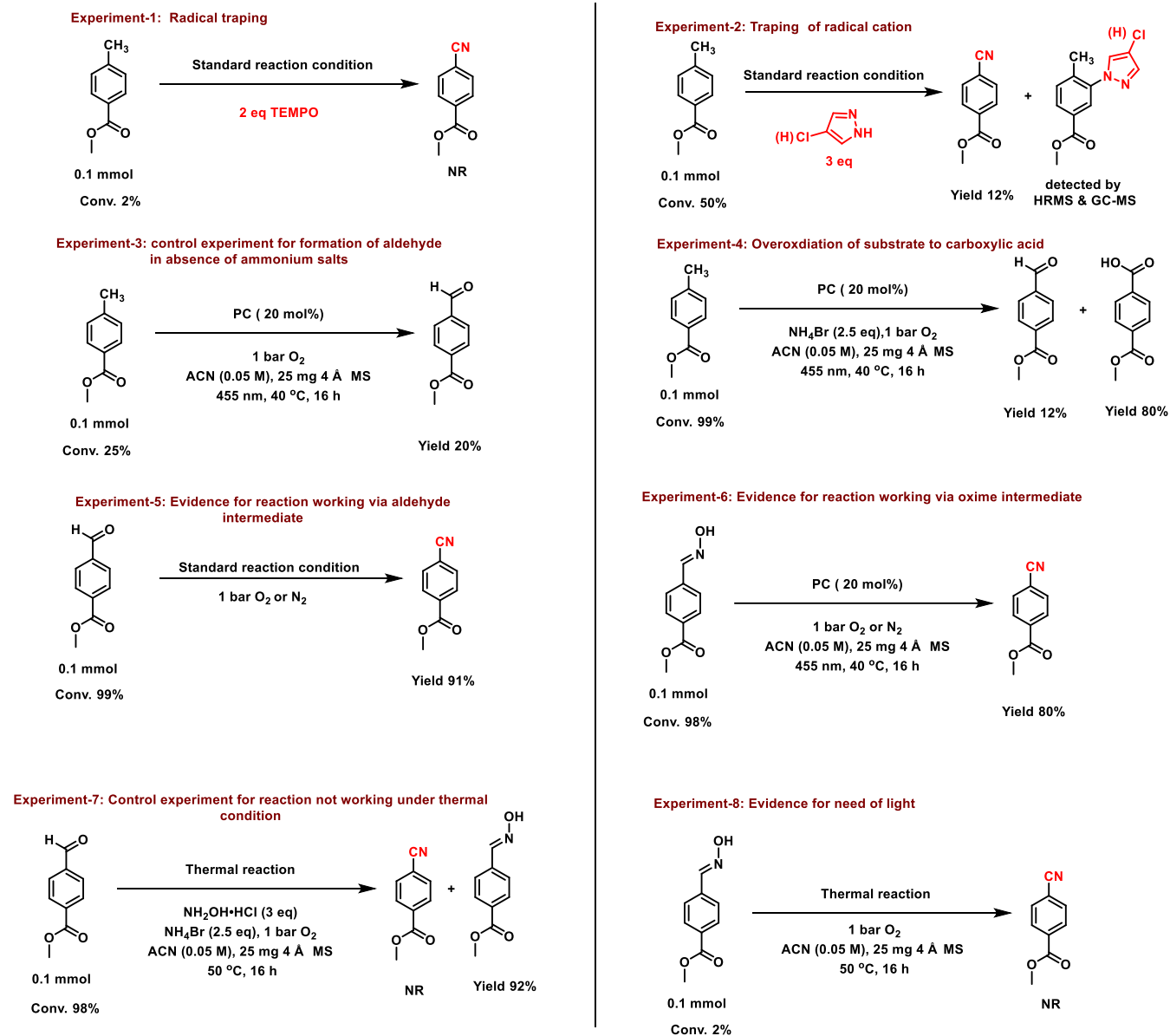**Fig. 2:** Proposed catalytic cycles for the ammoxidation of methylarenes.

Fig. 3: Quenching studies. Fig. 3(a) Time-resolved luminescence quenching decay of methyl 4-methylbenzoate with TPP; Fig. 3(b) Stern-Volmer plot for the TPP with methyl 4-methylbenzoate; Fig. 3(c) Stern-Volmer plot for the comparison of different substances with TPP.

To support this proposed hypothesis, we performed several mechanistic experiments, starting with spectroscopic investigations. Time-resolved luminescence quenching experiments indicated that methyl 4-methylbenzoate (**1**) can be oxidized by

the excited TPP (PC-4) (Fig. 3), as a slight decrease of the luminescence lifetime with increasing concentration of **1** was observed (Fig. 3a). The corresponding Stern-Volmer plot

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showed a linear correlation between the quencher concentra- tion and the luminescence lifetime (Fig. 3b)

Scheme 2. Mechanistic experiments to support the proposed catalytic hypothesis

Experiment-1: Radical traping

Experiment-2: Traping of radical cation

Experiment-3: control experiment for formation of aldehyde in absence of ammonium salts

Experiment-4: Overoxdiation of substrate to carboxylic acid

Experiment-5: Evidence for reaction working via aldehyde intermediate

Experiment-6: Evidence for reaction working via oxime intermediate

Experiment-7: Control experiment for reaction not working under thermal condition

Experiment-8: Evidence for need of light

Yields were determined by GC using n-decane as standard

Further, the quenching of the starting material (**1**) was compared to the product (**2**) and the two crucial proposed intermediates methyl 4-formylbenzoate and methyl 4-((hydroxyimino)methyl)benzoate (**3**) under the same conditions. The starting material (**1**) was identified as a more efficient quencher than the corresponding aldehyde intermediate and nitrile product. On the other hand, the oxime intermediate (**3**) showed a superior quenching to methyl 4-methylbenzoate (**1**) (Fig. 3c), illustrating the possible interaction of the excited photocatalyst with the oxime intermediate under the applied reaction condition (Cycle A'). The quenching efficiencies of NH₂OH•HCl and NH₄Br were investigated as well, with the

former exhibiting a poorer quenching than the later one (Supporting Information, Fig. S3), which reveals that Cycle B can be active as well. Comparing the luminescence lifetime quenching of NH₄Br and the methyl 4-methylbenzoate starting material (**1**), NH₄Br seems to decrease the lifetime more effectively (Supporting Information, Fig. S4). However, an electron-rich (4-methyl anisole) instead of an electron-deficient (**1**) substrate proved to be a more potent quencher as well (Supporting Information, Fig. S6), showing similar quenching ability as NH₄Br. Thus, based on the time-resolved luminescence quenching experiments, both proposed catalytic cycles A and B can be operative, with their respective importance

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likely being dependent on the electronic nature of the starting material.

Next, several mechanistic control experiments were performed to directly or indirectly detect reaction intermediates vital for the mechanistic process. Further, selected stable intermediates were used as starting materials for the formation of the final product under specific reaction conditions to establish the mechanistic pathways more clearly (Scheme 2). The model reaction was performed under standard reaction condition in presence of TEMPO, yielding no product, which indicates a radical pathways (Scheme 2, Experiment-1). Further, the radical cation intermediate (Fig. 2, **II**) could be trapped in the presence of pyrazole or 4-cholorpyrazole as nucleophiles under standard reaction condition, in a similar reaction as reported by Nicewicz,[22] supporting its formation (Scheme 2, Experiment-2). Looking at the more stable intermediates, the methylarene is proposed to be oxidized to the corresponding aldehyde first (Fig. 2, **VI**). This was confirmed by performing the model reaction in absence of both ammonium salts (to avoid the formation of the oxime), providing the corresponding aldehyde as product in 20% GC yield (Scheme 2, experiment-3), with an incomplete starting material conversion of 25%. In contrast, a full conversion was observed when NH_4Br was added (Experiment 4, Scheme 2), showcasing its crucial role, likely due to the thus opened alternative Br^- HAT-pathway[6h, 23] (Cycle B, Fig. 2). The main product in this case was the corresponding carboxylic acid (80%) resulting from an over-oxidation of the aldehyde (12%). With no observable nitrile formation, the experiment further suggests, that $NH_2OH \cdot HCl$ is the main nitrogen source. It is proposed to rapidly form the oxime from the aldehyde, avoiding its oxidation to the carboxylate.

The generation of an aldehyde and oxime intermediate was further supported by using those as starting materials for the synthesis of the final nitrile product (Scheme 2, Experiment 5 and 6). In both cases, the product was formed with a yield of 91% and 80%, respectively. Additionally, the conversion of the aldehyde or oxime to the nitrile did not proceed under solely thermal condition in the absence of light (Scheme 2, Experiment 7 and 8), supporting the proposed catalytic cycle A'. To further indicate the necessity of more than one photon for the formation of one product molecule, the product yield dependent on the irradiation intensity was observed as well (Supporting Information, Fig. S12).[24]

In order to follow the mechanistic pathway in more detail, NMR studies were performed analysing the reaction mixture after defined time intervals (Fig. 4). The signal corresponding to the methyl ester (-$COOCH_3$) of the starting material (**1**) shows a singlet resonance at δ 3.84 ppm in the ^{1}H-NMR spectrum, while the oxime (**3**) gives a singlet at δ 3.87, and nitrile (**2**) a singlet at δ 3.91, allowing for a facile distinction between the species of interest. At the beginning, the depletion of the starting material is accompanied by the increase of the oxime intermediate as well as nitrile product, with all three compounds being clearly observable at the same time after 4 h of irradiation. Further increasing the reaction time leads to the
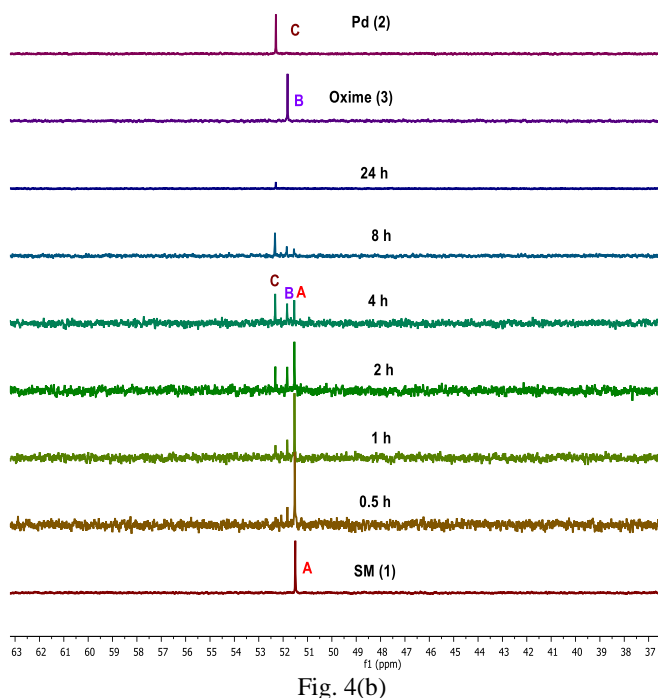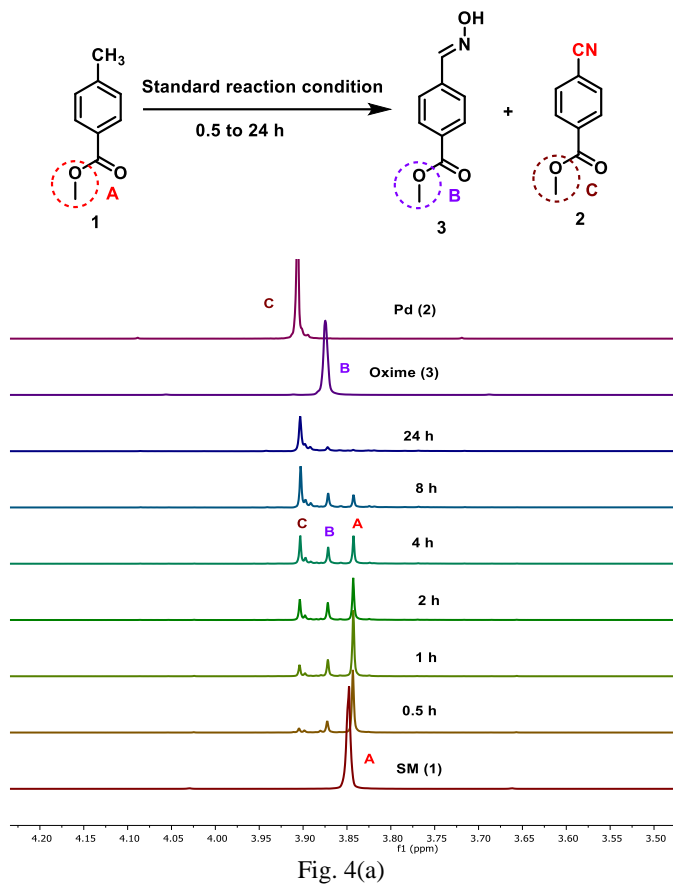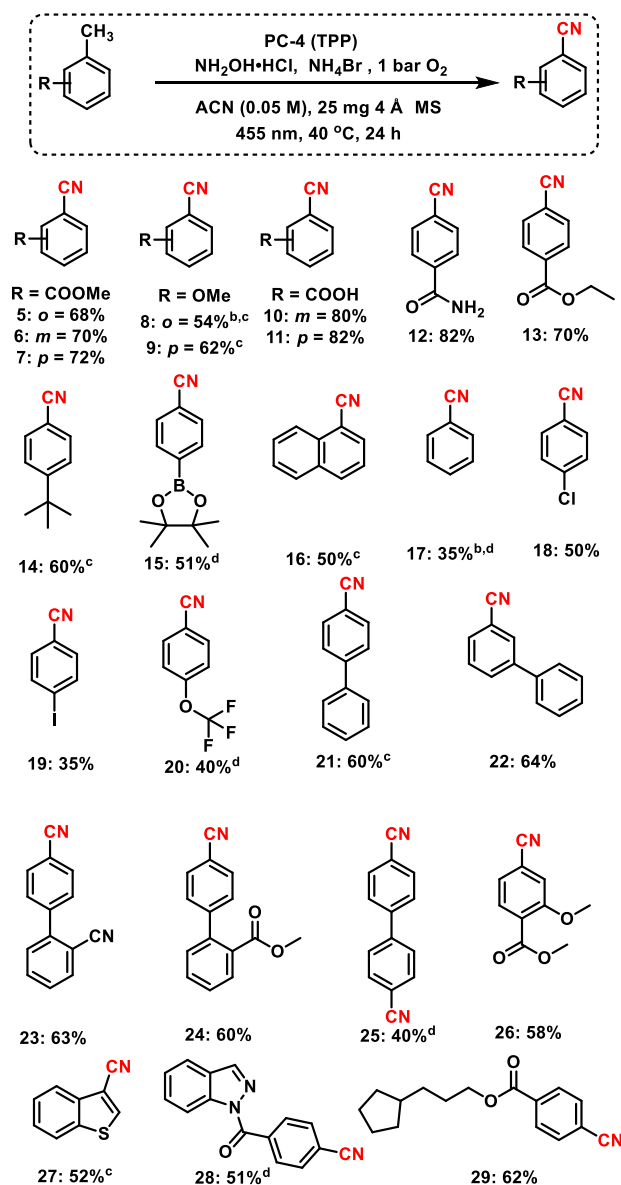

Fig. 4(a)

Fig. 4(b)

Fig. 4: NMR investigation. Fig. 4(a) ^{1}H NMR and Fig. 4(b) ^{13}C NMR.

(almost) full conversion of the starting material and the oxime with the dominant signal being the product peak.

Scheme 3. Substrate scope for synthesis of functionalized cycanobenzenes

R = COOMe
5: *o* = 68%
6: *m* = 70%
7: *p* = 72%

R = OMe
8: *o* = 54%[b,c]
9: *p* = 62%[c]

R = COOH
10: *m* = 80%
11: *p* = 82%

12: 82%

13: 70%

14: 60%[c]   15: 51%[d]   16: 50%[c]   17: 35%[b,d]   18: 50%

19: 35%   20: 40%[d]   21: 60%[c]   22: 64%

23: 63%   24: 60%   25: 40%[d]   26: 58%
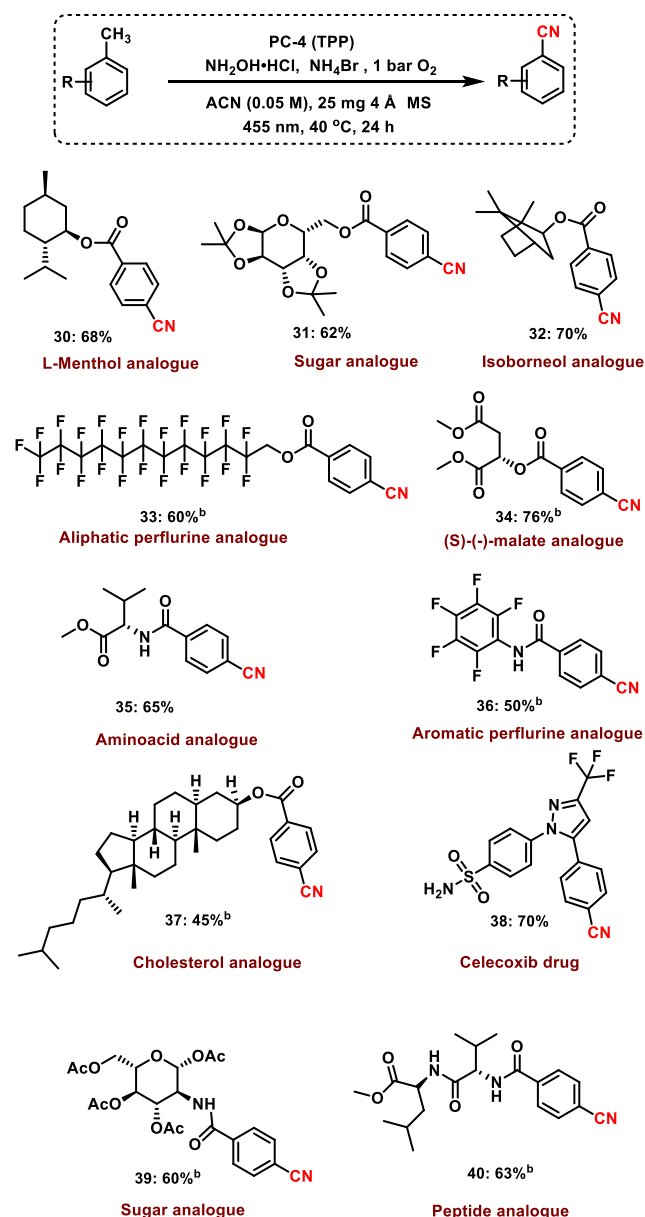
27: 52%[c]   28: 51%[d]   29: 62%

Reaction conditions: [a]0.1 mmol substrate, 20 mol% PC, 3 eq. NH₂OH•HCl, 2.5 eq. NH₄Br, 25 mg 4 Å MS, 1 bar O₂, 2 mL acetonitrile (0.05 M), 455 nm, 40 °C, 24 h, isolated yields. [b]GC yields using n-decane as standard. [c]same as 'a' using 1 eq. of PTSCl. [d]same as 'a ' 48 h instead of 24 h.

A similar tendency was observed in the ¹³C-NMR for the corresponding methyl ester carbon (Fig. 4b), all together further supporting the formation of the oxime as crucial intermediate to render the nitrile.

Collectively, the spectroscopy investigation, control experiments and kinetic investigation all support the proposed photocatalytic cycles. In addition, the catalyst deactivation pathway also studied under the standard reaction conditions, suggesting 2,4,6-triphenylpyridine as the degradation product, which could further be observed in the scale-up batch as minor by-product supported by HRMS (Supporting Information, Scheme-S1).

Scheme 4. Late-stage functionalization of challenging and drug-like molecules

30: 68%
L-Menthol analogue

31: 62%
Sugar analogue

32: 70%
Isoborneol analogue

33: 60%[b]
Aliphatic perflurine analogue

34: 76%[b]
(S)-(-)-malate analogue

35: 65%
Aminoacid analogue

36: 50%[b]
Aromatic perflurine analogue

37: 45%[b]
Cholesterol analogue

38: 70%
Celecoxib drug

39: 60%[b]
Sugar analogue

40: 63%[b]
Peptide analogue

Reaction conditions: [a]0.1 mmol substrate, 20 mol% PC, 3 eq. NH₂OH•HCl, 2.5 eq. NH₄Br, 25 mg 4 Å MS, 1 bar O₂, 2 mL acetonitrile (0.05 M), 455 nm, 40 °C, 24 h, isolated yields. [b]same as 'a ' 48 h instead of 24 h.

With the successful conditions in hand, we explored the C(sp^3)-H functionalization of different methylarenes (Scheme 3 and 4). Substrates bearing electron-donating and -withdrawing groups, as well as heterocycles, gave the respective products in good to excellent yields (Scheme 3, **5-29**). Functional groups such as carboxylic acid, ester, amide, halogens, cyanide and boronic ester were untouched during the reaction (Scheme 3, **5-13**, **15**, **18-20** and **23-24**). Applying this methodology, a dinitrile could also be synthesized in a one-pot procedure with a moderate yield (Scheme 3, **25**).
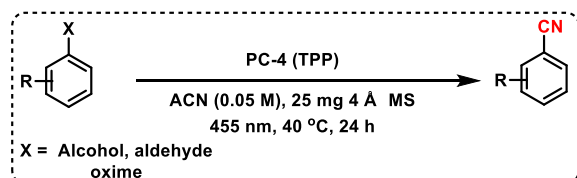
Scheme 5. Gram-scale synthesis

2: 65%
(1 g scale)

38: 60%
(1 g scale)
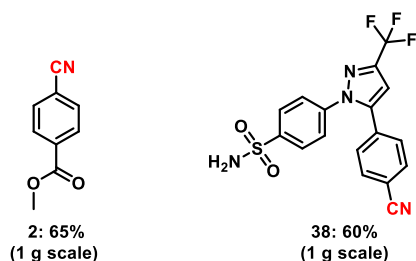
Reaction conditions: [a]1 g substrate, 20 mol% PC, 3 eq. NH$_2$OH•HCl, 2.5 eq. NH$_4$Br, 25 mg 4 Å MS for 0.1 mmol, 1 bar O$_2$, acetonitrile (0.05 M), 455 nm, 40 °C, 36 h, isolated yields.
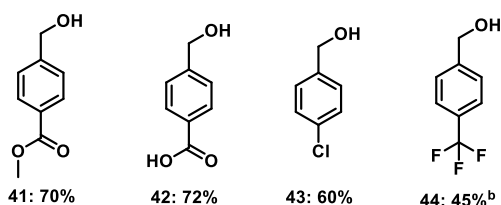
Structurally complex, bioactive- and drug- molecules could be employed for a selective cyanation as well, rendering the desired product in good to excellent yields up to 76% (Scheme 4). Delightfully, substrates bearing multiple oxygen atoms, which are usually not stable under photochemical conditions in the presence of oxygen, are viable, too.[25] Using the developed protocol, sugar derivatives **31** and **39** were obtained in 62% and 60% yield, respectively. Further, more challenging substrates such as cholesterol, isoborneol, amino acid and peptide derivatives gave the corresponding products in 45-70% yield. Interestingly, anti-inflammatory drug (Celecoxib) gave the desired product in 70% yield. For the example of a bulk-scale preparation, compound **2** and Celecoxib were cyanated in a 1 g scale to give the desired product in 65 and 60% yield respectively (Scheme 5).

After the screening of methylarenes, we were interested to apply this methodology using alcohols, aldehydes and oximes as starting materials for the synthesis of aromatic nitriles as well (Scheme 6). Similar to methylarenes, alcohols, aldehydes and oximes gave good to excellent yields up to 91%. Notably, isophthalaldehyde (**49**) was cyanided twice to isophthalonitrile in 78% yield. Sterically crowded 2,6-dichlorobenzaldehyde (**52**) was a viable substrate, too, giving 2,6-dichlorobenzonitrile (DCBN) in 82% yield, which is used as herbicide and regarded as a potential intermediate for pesticides and agrochemicals.
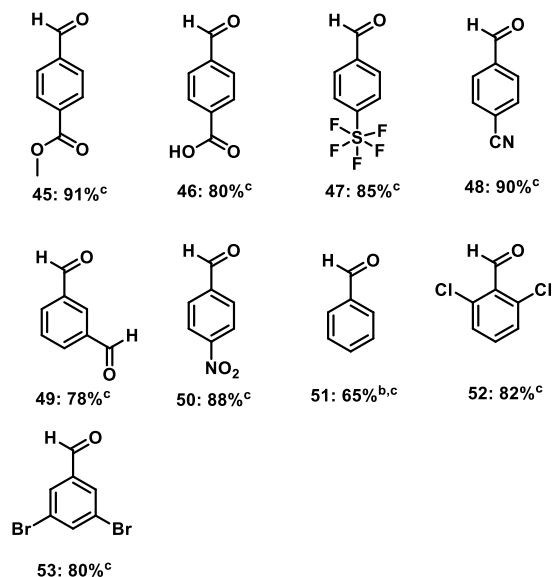
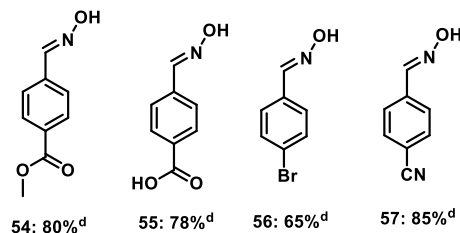**Scheme 6. Synthesis of nitriles from alcohols, aldehydes, and oximes**

From alcohols

41: 70% **42: 72%** **43: 60%** **44: 45%**[b]

From aldehydes

45: 91%[c] **46: 80%**[c] **47: 85%**[c] **48: 90%**[c]

49: 78%[c] **50: 88%**[c] **51: 65%**[b,c] **52: 82%**[c]

53: 80%[c]

From oximes

54: 80%[d] **55: 78%**[d] **56: 65%**[d] **57: 85%**[d]

Reaction conditions: [a]0.1 mmol substrate, 20 mol% PC, 3 eq. NH$_2$OH•HCl, 2.5 eq. NH$_4$Br, 25 mg 4 Å MS, 1 bar O$_2$, 2 mL acetonitrile (0.05 M), 455 nm, 40 °C, 24 h, isolated yields of nitriles. [b]GC yields of nitriles using n-decane as standard. [c]0.1 mmol substrate, 20 mol% PC, 3 eq. NH$_2$OH•HCl, 25 mg 4 Å MS, N$_2$, 2 mL acetonitrile (0.05 M), 455 nm, 40 °C, 24 h, isolated yields of nitriles. [d]0.1 mmol substrate, 20 mol% PC, 25 mg 4 Å MS, N$_2$, 2 mL acetonitrile (0.05 M), 455 nm, 40 °C, 24 h, isolated yields of nitriles.

CONCLUSION

In conclusion, we present the first metal- and cyanide-free visible-light-induced photocatalytic ammoxidation of C(sp^3)-H bonds using an abundant ammonia source and molecular oxygen. A detailed mechanistic investigation was carried out to support the proposed mechanistic hypothesis including various spectroscopy experiments. Applying this methodology, more than 50 aromatic and heteroaromatic substrates, as well as steroids and existing drug molecules containing methyl groups

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could be converted to the nitrile in good to excellent yields. In addition to this, the method could be executed on gram scale and alcohols, aldehydes and oximes could be used as starting materials for their conversion to nitriles in up to 91% yield in the same manner.

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Visible-Light-Promoted Metal-Free Ammoxidation of C(sp^3)-H bonds

Kathiravan Murugesan, Karsten Donabauer, and Burkhard König *

455 nm

O$_2$

N$_2$ or Air

CN

CN

Ph

Ph   Ph

O
+
BF$_4^-$

HO

CH$_3$

R

R

R

**39 examples
up to 82% yield**

**13 examples
up to 91% yield**

OH

O

N

R

R

R

 # Metal- & cyanide-free   **# Mechanistic insight**   **# Redox-neutral**

 # Abundant chemical feedstocks   **# Greener methodology**

 # Late-stage functionalizations