ABSTRACT: Seven FDA-certified food dyes have been investigated as organocatalysts. As a result, Fast Green FCF and Brilliant Blue FCF have been discovered as catalysts for the chlorination of a wide range of arenes and heteroarenes in moderate to excellent yields and high regioselectivity. Mechanistic investigations of the separate systems indicate that different modes of activation are in operation, with Fast Green FCF being a light-promoted photo-redox catalyst that is facilitating a one-electron oxidation of N-chlorosuccinimide (NCS) and Brilliant Blue FCF serving as a chlorine-transfer catalyst in its sulfonphthalein form with 1,3-dichloro-5,5-dimethylhydantoin (DCDMH) as stoichiometric chlorine source. Dearomatization of naphthol and indole substrates was observed in some examples using the Brilliant Blue/DCDMH system.

INTRODUCTION

In the realm of drug discovery and medicinal chemistry, organocatalysis offers distinct advantages to organometallic and enzymatic catalysis. For example, organocatalysts are usually robust, inexpensive, non-toxic, and more inert toward conditions containing moisture and oxygen. The avoidance of hazardous metallic traces in final products make organocatalytic methods especially attractive for the synthesis of materials that interact in biological systems such as pharmaceuticals, agrochemicals, food preservatives/additives, biocompatible materials, and drug delivery agents. The use of organocatalysts for important reactions in medicinal chemistry has received attention in the past 20 years, largely in the realm of asymmetric catalysis, but many of the most frequently performed reactions in the construction of bioactive molecules are still heavily mediated by metals.

The halogenation of an arene or heteroarene scaffold is one of the top 20 most frequently employed reactions in medicinal chemistry. The installation of a halogen, such as chlorine, can provide products (i.e., Zoloft, Plavix, Lorazepam, etc.) with altered electronic and physical properties or intermediates for further functionalization via nucleophilic aromatic substitution ($S_{N}Ar$) reactions and other various methods of derivatization. Halogenation approaches that employ transition metals (i.e., Ni, Rh, Pd, Au, Ag, etc.) for aromatic chlorination can be highly predictable regarding regioselectivity; however, the catalysts are relatively expensive. Direct C(sp$^2$)--H electrophilic aromatic substitution ($S_{E}Ar$) mechanistic pathways are attractive with regard to selectivity and economy, and many chlorinating agents operate through the presence of an electrophilic chlorine. Recent development of chlorinating agents such as Palau’s chlor, N-chloro-N-fluorobenzenesulfonylamine (CFBSA), 1-chloro-1,2-benzodioxol-3-one, and others have expanded the toolkit for chlorination of arenes and heteroarenes; however, there is still a strong reliance on using commercially available, stable chlorinating agents such as N-chlorosuccinimide (NCS), 1,3-dichloro-5,5-dimethylhydantoin (DCDMH), and trichloroisocyanuric acid (TCCA). These air- and temperature-stable chlorinating agents require activation, frequently by a harsh acid or metal. The necessity for acidic activation is not conducive for chlorination of many of the heteroarenes and other privileged scaffolds found in medicinal chemistry that contain basic sites or acid-sensitive features. Thus, further exploration toward the discovery of environmentally and biologically benign, inexpensive, mild, and selective organocatalysts that operate under non-acidic conditions for the chlorination of arenes and heteroarenes remains a valuable pursuit.
As shown in Scheme 1, reports of organocatalytic methods for chlorination of arenes and/or heteroarenes with an N-chloro reagent can be broadly categorized into systems that operate through either transfer of the chlorine atom to a catalyst (Method A) or amplification of the electrophilicity of the N-chloro reagent (Methods B and C). Organocatalysts reported as chlorine transfer agents include Ph₃P=S,¹² trimethylsilyl chloride (TMSCl),¹³ 2,4,6-trimethylaniline,¹⁴ secondary ammonium salts,¹⁵ and imidazolium salts.¹⁶ Electrophilic amplification is the most common approach and is dominated by traditional acidic activation (Scheme 1, Path B).

As an alternative approach, an organic dye visible-light photoredox catalyst (VLPC) is used to initiate a single electron oxidation of the chlorinating agent, effectively amplifying the electrophilicity of the chlorine atom by increasing the polarization of the N−Cl bond (Scheme 1, Path C).¹⁷ Due to our previous success employing the food dye erythrosine B as a VLPC for activation of N-bromosuccinimide (NBS) in the bromination of arenes and heteroarenes,¹⁸ we turned our attention toward exploring additional food dyes in light-promoted activation of chlorinating agents.

In the United States, there are seven water-soluble synthetic food colorants (Figure 1) approved for general use. In contrast to colors extracted from natural sources, these synthetic dyes are subject to batch certification by the U. S. Food and Drug Administration (FDA) and are widely used due to their high stability, consistency, safety, and strict regulation. To date, investigations regarding these compounds have focused upon the development of analytical methods for their detection,¹⁹ their biological or environmental evaluation,²⁰ or the development of methods for their degradation.²¹ Despite the widespread availability, low cost, and benign environmental impact of the dyes, reports of their use as organocatalysts in the development of new synthetic methodology are extremely limited. Herein, we report the use of FDA-certified food dyes as light-promoted organocatalysts in the chlorination of aromatic and heteroaromatic substrates using N-chloro reagents.

**RESULTS AND DISCUSSION**

**Initial Screening.** To begin our investigation, seven FDA-certified food dyes (Figure 1) were screened for activity as catalysts in the chlorination of a representative aromatic, naphthalene, using NCS and DCDMH as stoichiometric chlorinating agents (Table 1). Initial conditions were chosen to screen for a highly practical reaction (i.e., open to air, room temperature).

| Table 1. Screening of Food Dyes for Chlorination of Naphthalene |
| --- |
| entry | food dye | excited-state energy (eV) | E°red (V) | % yield¹ |
| --- | --- | --- | --- | --- |
| 1 | none | 3 (2) | 2 (0) |
| 2 | Allura Red AC | 2.24 | +1.81 | 5 (0) |
| 3 | Brilliant Blue FCF | 1.94 | +1.35 | 11 (0) |
| 4 | Erythrosine B | 2.28 | +1.57 | 23 (0) |
| 5 | Fast Green FCF | 1.98 | +1.31 | 59 (10) |
| 6 | Indigo Carmine | 1.98 | +1.46 | 6 (12) |
| 7 | Sunset Yellow FCF | 2.39 | +2.02 | 0 (0) |
| 8 | Tartrazine | 2.62 | +2.14 | 0 (0) |

¹Gas chromatography (GC) yields calculated using adamantane as internal standard. Reactions were run in duplicate, and the product yields were averaged. All values vs SCE. Yields in parentheses correspond to reactions performed in the dark.

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temperature, and white LED). Anticipating a potential role of the dyes as photoredox catalysts, the excited-state reduction ($E^*_{red}$) potential of each dye was determined (see the Supporting Information) and is reported in Table 1. As a result of screening with NCS, Fast Green FCF produced a 59% yield of 1-chloronaphthalene 1 and was selected as the best performing catalyst. Screening the catalysts with DCDMH as a chlorinating agent, however, resulted in Brilliant Blue FCF emerging as the most efficient catalyst as 1 was produced in 84% yield. Interestingly, a 77% yield was obtained in the absence of light, indicating that the catalyst is operating through a different reactive mechanism than the light-activated VLPC mode shown in Scheme 1, Path C.

Fast Green FCF and Brilliant Blue FCF both belong to the triphenylmethane dye structural classification, which is conspicuously underutilized in the realm of VLPCs. Fast Green FCF has been reported as a photosensitizer, and Brilliant Blue FCF has been used to modify electrodes in materials as a humidity indicator and in photogalvanic cells, but to our knowledge, this is the first report to utilize either Fast Green FCF or Brilliant Blue FCF in an organocatalytic role. Due to the initial indication of different modes of chlorinating agent activation from the comparison of yields in the presence and absence of light, the Fast Green FCF and Brilliant Blue FCF catalytic systems were investigated separately.

**Investigation of Fast Green FCF and NCS.** Using naphthalene with NCS and catalytic Fast Green FCF, an optimization of stoichiometry and reaction conditions was performed (Table 2), which resulted in the following conditions: 1 equiv of naphthalene, 1.1 equiv of NCS, 0.02 equiv of Fast Green FCF in acetonitrile (0.1 M relative to naphthalene) open to air in a white LED photochamber for 24 h at ambient temperature. Though slightly higher yields were obtained using either 3 equiv of NCS (Table 2, entry 3) or from a longer reaction time (entry 4), the conditions shown in entry 2 were chosen for economy and convenience. Increased catalyst loading, adjustments to solvent and concentration, and addition of external oxidants all resulted in decreased yield of 1.

With optimized reaction conditions, the scope of arene and heteroarene substrates was explored using the NCS/Fast Green chlorinating system (Figure 2). The use of mono-substituted benzene derivatives such as anisole and acetanilide resulted in chlorination at the para position in yields substantially above non-catalyzed NCS chlorination (products 2 and 3). Disubstituted benzene derivatives were also tested, and examples that contain at least one deactivating (electron-withdrawing) group resulted in moderate to good yields of chlorinated products (4−7). In examples where a mixture of mono- and dichlorinated products was observed, 2.2 equiv of NCS was used to exclusively form dichlorinated product (6 and 17). Electron-rich aromatics and naphthalene derivatives resulted in good to excellent yields of monochlorinated products (8−12). Lidocaine, a local anesthetic, was chlorinated in modest yield to produce 13. Nitrogen-containing heteroarenes are of particular significance to drug discovery and medicinal chemistry as privileged scaffolds, therefore, we tested a range of representative heteroarene substrates using the optimized conditions (Figure 2, 14−19). Pyrrole, indole, and substituted benzene derivatives such as anisole and acetanilide resulted in chlorination at the para position in yields substantially above non-catalyzed NCS chlorination (products 2 and 3). Disubstituted benzene derivatives were also tested, and examples that contain at least one deactivating (electron-withdrawing) group resulted in moderate to good yields of chlorinated products (4−7). In examples where a mixture of mono- and dichlorinated products was observed, 2.2 equiv of NCS was used to exclusively form dichlorinated product (6 and 17). Electron-rich aromatics and naphthalene derivatives resulted in good to excellent yields of monochlorinated products (8−12). Lidocaine, a local anesthetic, was chlorinated in modest yield to produce 13. Nitrogen-containing heteroarenes are of particular significance to drug discovery and medicinal chemistry as privileged scaffolds, therefore, we tested a range of representative heteroarene substrates using the optimized conditions (Figure 2, 14−19). Pyrrole, indole,

| entry | NCS (equiv) | solvent (0.1 M) | catalyst (mol %) | time (h) | additive (equiv) | yield 1 (%) |
|-------|-------------|-----------------|------------------|---------|-----------------|-------------|
| 1     | 1           | MeCN            | 2                 | 24      |                 | 59          |
| 2     | 1.1         | MeCN            | 2                 | 24      |                 | 68          |
| 3     | 3           | MeCN            | 2                 | 24      |                 | 72          |
| 4     | 1.1         | MeCN            | 2                 | 48      |                 | 74          |
| 5     | 1.1         | MeCN            | 1                 | 24      |                 | 34          |
| 6     | 1.1         | MeCN            | 5                 | 24      |                 | 59          |
| 7     | 1.1         | MeCN            | 10                | 24      |                 | 56          |
| 8     | 1.1         | MeCN            | 2                 | 24      |                 | 42          |
| 9     | 1.1         | DCM             | 2                 | 24      |                 | 0           |
| 10    | 1.1         | 4:1 MeCN/H₂O    | 2                 | 24      |                 | 3           |
| 11    | 1.1         | MeCN (0.2 M)    | 2                 | 24      |                 | 64          |
| 12    | 1.1         | MeCN (0.05 M)   | 2                 | 24      |                 | 52          |
| 13    | 1.1         | MeCN            | 2                 | 24      | (NH₄)₂S₂O₈ (1)  | 41          |
| 14    | 1.1         | MeCN            | 2                 | 24      | (NH₄)₂S₂O₈ (0.1) | 45          |
| 15    | 1.1         | MeCN            | 2                 | 24      | oxone (1)       | 20          |

*Gas chromatography (GC) yields calculated using adamantane as internal standard.
indazole, and pyridine heteroaromatics all performed well with significant improvement over uncatalyzed reactions. Finally, known pharmaceuticals antipyrine (phenazone) and caffeine were chlorinated cleanly without evidence of byproduct formation (products 20 and 21). Throughout the substrate scope investigation, regioselectivity of chlorination was consistent with a $S_{N}Ar$ mechanism. The substrate scope of the mild, non-acidic reaction demonstrates the tolerance of a wide range of functionalities including aryl halide, ether, phenol, aniline and 3° amine, nitrile, ketone, amide, aldehyde, ester, and benzylidene and α to carbonyl C(sp³)−H's.

Initial indications from the screening (Table 1) led us to believe that light plays a crucial role as observed by the enhancement under visible-light conditions, suggesting that Fast Green FCF may be serving as a light-promoted photoredox catalyst. In order to ascertain the mode of action of the Fast Green FCF catalyst, an additional series of control experiments were performed (Table 3). Known radical experimental results that include the following observations: (i) increasing catalyst loading did not increase the product yield (Table 2), (ii) small background reaction obtained in dark (Table 3), (iii) inhibition by radical inhibitor (Table 3); (iv) faint positive result from iodide test, (v) regioselectivity consistent with $S_{N}Ar$ (Figure 2), and (vi) indication of a lack of significant light-initiated radical chain propagation$^{27}$ (Table 3, entry 5). The conclusion drawn from these results is that Fast Green FCF most likely serves as a light-promoted, photoredox initiator for the oxidation of NCS to promote $S_{N}Ar$ chlorination of arenes. In the proposed mechanism shown in Scheme 2, excited-state Fast Green FCF activates NCS to produce oxidized species B, which can then undergo aromatic chlorination. Species C, which results from the loss of chlorine, most likely servers to return the reduced Fast Green to its ground state in a closed catalytic cycle, as opposed to a chain propagation step. Fast Green FCF may also serve in a minor capacity as a chlorine transfer agent as evidenced by the formation of a chlorinated product in the absence of light.

**Investigation of Brilliant Blue FCF and DCDMH.** A separate optimization of stoichiometry and reaction conditions using naphthalene, DCDMH, and Brilliant Blue FCF (Supporting Information, Table S1) resulted in the following set of optimized conditions: 1 equiv of naphthalene, 1.1 equiv of NCS, 0.04 equiv of Brilliant Blue FCF in acetonitrile (0.1 M relative to naphthalene) open to air for 24 h at ambient temperature.

With optimized reaction conditions, we turned our attention toward exploring the substrate scope. In a number of examples, the DCDMH/Brilliant Blue FCF system behaved similarly to the NCS/Fast Green FCF system, resulting in comparable yields of chlorinated products (Figure 3; compounds 22, 23, 28) and as major product (26), indicating that the method of chlorination is more active than the NCS/Fast Green FCF system. Improved yields of products 13 (lidocaine) and 24 were obtained using the DCDMH/Brilliant Blue FCF system. Of particular interest, the chlorination of acetanilide using the light-activated NCS/Fast Green system resulted in the exclusive production of the para-chlorinated isomer in 47% yield (Figure 2, product 3), whereas chlorination using the DCDMH/Brilliant Blue system (Figure 3, product 24)
resulted in the ortho-chlorinated isomer being the major product formed (90% yield total, 2:7 p/o). A handful of additional substrates that contain at least one electron-withdrawing substituent (25−27) or a heteroaromatic core (29) were chlorinated in moderate to good yield. Similar to the NCS/Fast Green system, the regioselectivity of chlorination using the DCDMH/Brilliant Blue method was consistent with a SEAr mechanism. A wide range of functionalities are tolerated by the chlorination reaction, including aryl ether, phenol, 3° amine, nitrile, nitro, ketone, amide, aldehyde, ester, and benzylic and α to carbonyl C(sp3)−H’s.

During the substrate scope investigation using DCDMH/Brilliant Blue, we observed the dearomatization of 2-naphthol and indole (Scheme 3), which was not detected using the milder NCS/Fast Green system. A great deal of attention has been recently devoted to dearomatization of polycyclic aromatic cores as a valuable synthetic approach to produce stereogenic centers.28 Dearomatization of naphthol derivatives to produce monochlorinated products has previously been reported using DCDMH.28a However, using catalytic Brilliant Blue, an 88% of dichlorinated product 30 was isolated. A plausible mechanism for the production of 30 is provided in the Supporting Information (Scheme S1). Additionally, difunctionalization across the 2,3-positions of indole derivatives has garnered attention recently from the synthetic community.28d,29 The attempted chlorination of indole using Brilliant Blue/DCDMH resulted in a 38% yield of dichlorinated product 31 (Scheme 3), with di- and monochlorinated indanone derivatives resulting as minor components (32 and 33).

With clear differences in the reactivity of the DCDMH/Brilliant Blue system compared to the NCS/Fast Green method, we set out to determine the mechanism of the Brilliant Blue organocatalyzed chlorination of aromatics. During the screening of catalysts, a gradual color change of the reaction mixture over a 24 h period was observed. The UV−Vis spectra of Brilliant Blue FCF in MeCN and Brilliant Blue with DCDMH over a 24 h mixing time are shown in Figure 4. The bathochromic shift observed (dark blue to a pale yellow) upon mixing with DCDMH indicates that Brilliant Blue is likely adopting the sulfonphthalein form,30 which would result in disruption of the π-conjugation of the dye and lead to a yellow appearance.31

To compare the reactivity of the dark blue mixture of Brilliant Blue/DCDMH at time zero (BB, DCDMH, and substrate are all added at the same time to begin the reaction) with the pre-formed yellow mixture of Brilliant Blue/DCDMH (BB and DCDMH are stirred for 18 h, then the aromatic substrate is added to begin the reaction), an experiment was conducted to monitor the rate of chlorination of 2-methyl naphthalene using each of the versions of Brilliant Blue (Figure 5). It was observed that the yellow mixture produces 12 significantly faster, indicating that this species that

Figure 3. Substrate scope of DCDMH/Brilliant Blue FCF chlorination of arenes and heteroarenes.

Scheme 3. Dearomatization of Arenes and Heteroarenes Using the DCDMH/Brilliant Blue FCF Chlorination System

Figure 4. UV−Vis absorbance of Brilliant Blue FCF (shown in blue), Brilliant Blue stirred with 1 equiv of DCDMH for 24 h (shown in red), and DCDMH (shown in green).

Figure 5. Monitoring of the chlorination of 2-methyl naphthalene by DCDMH with pre-formed (18 h) Brilliant Blue/DCDMH mixture (red curve) versus Brilliant Blue/DCDMH performed under standard conditions (no pre-mixing; blue curve).
forms over a 24 h period in a standard reaction is most likely the actual chlorinating species in the reaction. A plausible mechanism for DCDMH/Brilliant Blue chlorination is shown in Scheme 4, which is based upon experimental results that include the following observations: (i) increasing catalyst loading did not decrease product yield (Supporting Information, Table S1); (ii) comparable yield obtained in the absence of light (Table 3); (iii) evidence of a chlorinated dye species, which, when pre-formed, reacts more efficiently than Brilliant Blue (Figures 4 and S); and (iv) regioselectivity consistent with $S_{E}Ar$ (Figure 2). The conclusion drawn from these results is that Brilliant Blue FCF most likely serves as an organocatalytic chlorine-transfer agent (such as Scheme 1, A) in the presence of stoichiometric DCDMH to promote $S_{E}Ar$ chlorination of arenes. In the proposed mechanism shown in Scheme 4, Brilliant Blue is initially chlorinated by DCDMH to produce species A. Formation of the dichlorinated, neutral sulfonphthalein species B results in a loss of $\pi$-conjugation and the observed yellow color.30,31 Dichlorinated species B then serves as the source of electrophilic chlorine for (hetero)arene chlorination reactions. Upon electrophilic aromatic chlorination, monochlorinated sulfonphthalein species C is produced, which can convert back to the active catalytic chlorinating species B by obtaining another chlorine atom from stoichiometric DCDMH.

### CONCLUSIONS

In conclusion, we have described two new systems that employ FDA-certified food dyes for mild, organocatalyzed chlorination of arenes and heteroarenes. Mechanistic investigations of the separate systems indicate that different modes of activation are in operation, with Fast Green FCF being a light-promoted photoredox catalyst that is facilitating a one-electron oxidation of NCS and Brilliant Blue FCF serving as a chlorine-transfer catalyst with DCDMH in its sulfonphthalein form. The organocatalytic systems are highlighted by their inexpensive and readily available materials, operational simplicity, generation of chlorinated arenes and heteroarenes in moderate to excellent yields, and tolerance of a wide variety of functionalities that might be present during the synthesis of complex molecules. Differences in reactivity of the two systems toward (hetero)aromatic substrates were also observed. For example, the NCS/Fast Green FCF proved to be a milder method with monochlorination substrates were also observed. For example, the NCS/Fast Green FCF proved to be a milder method with monochlorination substrates being preferred, whereas the Brilliant Blue FCF system is capable of forming dichlorinated products from substrates containing deactivating (electron-withdrawing) groups and generating dearomatized naphthol and indole products. In addition to providing new catalysts for chlorination and insight into the photoelectronic properties of FDA-certified food dyes, this work may also lead to new investigations regarding the degradation of food dyes and/or organic pollutants under visible-light (solar) conditions.

### EXPERIMENTAL SECTION

**Materials and Instrumentation.** All reagents and solvents were purchased from commercial sources and used without further purification. Fast Green FCF (CAS #2353-45-9; FW = 808.86), Brilliant Blue FCF (CAS #3844-45-9; FW = 792.84), and Indigo Carmine (CAS #860-22-0; FW = 466.36) were purchased from Alfa Aesar. Erythrosine B (CAS #16423-68-0; FW = 879.86) and Tartrazine (CAS #1934-21-0; FW = 534.36) were purchased from Spectrum. Allura Red AC (CAS #25956-17-6; FW = 496.42) and Sunset Yellow FCF (CAS #2783-94-0; FW = 452.36) were purchased from TCI America. $^1$H and $^{13}$C NMR spectra were recorded on a Varian 400/100 (400 MHz) spectrometer in deuterated chloroform (CDCl$_3$), dimethyl sulfoxide (DMSO), or methanol (CD$_3$OD) with the solvent residual peak as internal reference unless otherwise stated (CDCl$_3$: $^1$H = 7.26 ppm, $^{13}$C = 77.02 ppm; DMSO: $^1$H = 2.50 ppm, $^{13}$C = 39.52 ppm; CD$_3$OD: $^1$H = 3.31 ppm, $^{13}$C = 49.00 ppm). Data are reported in the following order: Chemical shifts ($\delta$) are reported in ppm, and spin–spin coupling constants ($J$) are reported in Hz, while multiplicities are abbreviated by $s$ (singlet), bs (broad singlet), d (doublet), dd (doublet of doublets), t (triplet), dt (double of triplets), td (triplet of doublets), m (multiplet), and q (quartet). Infrared
spectra were recorded on a Nicolet iS50 FT-IR spectrometer, and peaks are reported in reciprocal centimeters (cm⁻¹). Melting points (m.p.) were recorded on a Mel-Temp II (Laboratory Devices, USA) and were uncorrected. Nominal MS (EI) were obtained using a Shimadzu GC-2010 Plus with GCMS-QP2010. Relative intensity (in percentage) is shown in parentheses following the fragment peak where appropriate.

**Determination of Photoexcited Energy via Fluorescence Emission.** Excitation energy ($E_{0,0}$) was determined by calculating the energy of the wavelength (in nm) where the substrate’s UV–Vis absorption and fluorescence emission spectra overlap. The wavelength (nM) was converted to eV using an energy converter described in the Supporting Information.

**Procedure.** UV–Vis spectroscopy was performed using a Shimadzu UV-1800 spectrometer using a 3D-printed vial adaptor for convenience, while fluorescence measurements were performed using a Tecan Safire spectrometer with a clear-bottom 96-well plate. Solutions were prepared by saturating a pure ACN solution or a 7:1 ACN:water solution with the dye of interest, centrifuging the sample at 1500 rpm for 2 min, then analyzing the supernatant. In most cases, the solution was diluted for UV–Vis measurements to keep the absorbance value below 1.5. For fluorescence measurements, excitation was performed at 15 nm below the peak absorption value to determine overlap with the absorbance spectra. The wavelength of this emission and absorbance spectra was used in combination with the reduction potential determined in the electrochemical analysis to determine the excited-state reduction potential as has been previously reported in the literature.

**Determination of Ground-State Dye Reduction Potential.** Electrochemical experiments were performed using a Biologic SP300 Potentiostat with a glassy carbon working electrode (3 mm diameter), a platinum counter electrode (2 mm diameter), and an Ag/AgCl reference electrode. All voltage data was adjusted to SCE by adding 0.045 V to the experimental data. The electrolyte consisted of a 7:1 ACN:water solution, 1 mM tetrabutylammonium hexafluorophosphate, and saturated with the dye of interest. Cyclic voltammetry was performed at a scan rate of 100 mV/s, starting at the open-circuit potential and scanning across the voltage range displayed (see the Supporting Information for individual cyclic voltammograms).

**General Procedure A for Light-Promoted (Fast Green/NCS) Chlorination of Aromatics/Heteroaromatics.** To an oven-dried flask was added a magnetic stir bar, Fast Green FCF (8.1 mg, 0.02 equiv, 0.01 mmol), arene/heteroarene (1 equiv, 0.5 mmol), acetonitrile (2.5 mL), and then DCDMH (108.4 mg, 1.1 equiv, 0.55 mmol). The reaction mixture was stirred open to air at room temperature (20 °C) for 24 h. Upon completion of the reaction, the crude mixture was evaporated under pressure, and the chlorinated product was isolated via column chromatography on silica gel.

**Product Characterization.** All chloroarenes were isolated according to general procedure unless otherwise noted and display the characterization data shown below (spectra available in the Supporting Information).

1-Chloronaphthalene (1). The title compound was prepared according to general procedure A or B and quantified using gas chromatography with adamantane as an internal standard. A standard curve of 1-chloronaphthalene was prepared in six separate reaction vessels by adding varying amounts of 1-chloronaphthalene (between 0 and 0.25 mmol) to 3 mL of acetonitrile. To each of the 3 mL acetonitrile solutions was added 8 mL of hexanes and 0.156 mmol (20 mg) of adamantane. The acetonitrile solution was extracted with the hexanes, and 1 mL of the hexanes portion was reserved for gas chromatography injection. Gas chromatography was performed using a Shimadzu GC-2010 Plus with GCMS-QP2010 with a Restek Rtx-5MS capillary column (30 m; 0.25 mm ID; 0.25 μm df; Crossbond – 5% diphenyl/95% dimethyl polysiloxane). The GC method was as follows: 40 °C for 5 min, then increase at 10 °C/min for 16 min (up to 200 °C). A 200 °C temperature is maintained for 10 additional min. The title compound 1-chloronaphthalene is observed at 16.8 min and confirmed by MS (EI) m/z 164 (M+2, 30), 162 (M+, 100), 127(48), 74(36), 63(56).

4-Chloroanisole and 2-Chloroanisole (2). The title compounds were prepared according to general procedure A or B, and characterization spectra were consistent with literature values. A mixture (according to 1H NMR integration) of para/ortho isomers was isolated, and data regarding the para (major) isomer is reported below. Clear oil (Procedure A: 44.9 mg, 63% yield total, 8:1 para/ortho; Procedure B: 46.3 mg, 65% yield total, 20:1 para/ortho). Purification (6 mL of 4 M NaOH was added to the crude reaction mixture and extraction using EtOAc (3 × 10 mL) was performed followed by drying with sodium sulfate). 1H NMR (400 MHz, CDCl₃) from product of Procedure A – peaks reported correspond to major (para) isomer: δ = 7.23 (d, J = 6.9 Hz, 2H), 6.83 (d, J = 6.9 Hz, 2H), 3.78 (s, 3H) ppm. 13C NMR (100 MHz, CDCl₃) from product of Procedure A – peaks reported correspond to major (para) isomer: δ = 158.2, 129.3, 125.5, 115.2, 55.5. MS (EI): m/z 144 (M+2, 30), 142 (M+, 84), 127(60), 99(100), 75(40), 73(40), 63(52).

4-Chloroacetanilide (3). The title compound was prepared according to general procedure A, and characterization spectra were consistent with literature values. White solid (39.8 mg, 47% yield). m.p. 178–181 °C. Purification (6 mL of 4 M NaOH was added to the crude reaction mixture and extraction using EtOAc (3 × 10 mL) was performed followed by drying with sodium sulfate). Column chromatography using a 4:1 hexanes:EtOAc eluent resulted in pure compound. Rₖ = 0.13. 1H NMR (400 MHz, CDCl₃): δ = 7.45 (d, J = 8.6 Hz, 2H), 7.27 (d, J = 8.6 Hz, 2H), 7.21 (bs, 1H), 2.17 (s, 3H) ppm. 13C NMR (100 MHz, CDCl₃): δ = 168.3, 136.4, 129.3, 129.0, 24.6. MS (EI): m/z 171 (M+2, 3), 169 (M+, 11), 129(23), 127(75), 65(10), 63(11), 43(100), 39(12).
4-Bromo-3-chloroanisole (4).\(^{1,2b}\) The title compound was prepared according to general procedure A, and characterization spectra were consistent with literature values. Clear oil (60.0 mg, 54% yield). Purification (6 mL of 4 M NaOH was added to the crude reaction mixture and extraction using EtOAc (3 x 10 mL) was performed followed by drying with sodium sulfate. Column chromatography using a 95:5 hexanes:EtOAc eluent resulted in pure compound). \(R_f = 0.44. \) \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.50 \) (d, \(J = 2.4 \) Hz, 1H), 7.33 (dd, \(J_1 = 8.8 \) Hz, \(J_2 = 2.4 \) Hz, 1H), 6.80 (d, \(J = 8.8 \) Hz, 1H), 3.88 (s, 3H) ppm. \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 154.3, 132.7, 130.5, 123.6, 113.3, 112.5, 56.3. \) MS (EI): \(m/z\) 224 (M+4, 16), 222 (M+2, 56), 220 (M+, 53), 207(51), 205(42), 179(45), 177(37), 75(36), 63(100), 62(40), 50(36).

3-Chloro-4-methoxyacetophenone (5).\(^{10c}\) The title compound was prepared according to general procedure A, and characterization spectra were consistent with literature values. White solid (32.2 mg, 34% yield). m.p. 73–76 °C. Purification (Hexanes:DCM = 30:70). \(R_f = 0.40. \) \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.98 \) (d, \(J = 2.0 \) Hz, 1H), 7.86 (dd, \(J_1 = 8.6 \) Hz, \(J_2 = 2.0 \) Hz, 1H), 6.96 (d, \(J = 8.6 \) Hz, 1H), 3.96 (s, 3H), 2.55 (s, 3H) ppm. \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 195.7, 158.7, 130.7, 128.6, 122.8, 111.2, 56.4, 26.3. \) MS (EI): \(m/z\) 186 (M+2, 11), 184 (M+, 31), 171(20), 169(100), 141(15), 77(40), 75(15), 63(42), 62(12), 43(76).

4-Bromo-2,6-dichloroaniline (6).\(^{17b}\) The title compound was prepared according to general procedure A with 2.2 equiv of NCS, and characterization spectra were consistent with literature values. Red solid (85.3 mg, 70% yield). m.p. 77–80 °C. Purification (Hexanes:EtOAc = 95:5). \(R_f = 0.31. \) \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.31 \) (s, 2H), 4.45 (bs, 2H) ppm. \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 139.4, 130.2, 120.0, 107.9. \) MS (EI): \(m/z\) 243 (M+4, 41), 242 (M+3, 40), 241 (M+2, 100), 239(M+5, 55), 162(17), 160(127), 63(50), 62(62), 61(35), 52(32).

3-Chloro-4-hydroxyphenol (7).\(^{17c}\) The title compound was prepared according to general procedure A, and characterization spectra were consistent with literature values. White solid (162.2 mg, 21% yield). m.p. 158–160 °C. Purification (Hexanes:DCM = 1:3). \(R_f = 0.10. \) \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.66 \) (d, \(J = 2.0 \) Hz, 1H), 7.50 (dd, \(J_1 = 8.2 \) Hz, \(J_2 = 2.0 \) Hz, 1H), 7.10 (d, \(J = 8.2 \) Hz, 1H), 6.23 (bs, 1H) ppm. \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 155.4, 133.1, 132.8, 120.8, 117.7, 117.2, 104.9. \) MS (EI): \(m/z\) 178 (M+5, 155 (M+2, 32), 153 (M+, 100), 89(53), 63(52), 62(68), 38(73), 37(54).

2-Chlororesorcinol (8).\(^{15}\) The title compound was prepared according to general procedure A or B, and characterization spectra were consistent with literature values. Clear oil (Procedure A: 79.4 mg, 90% yield; Procedure B: 73.2 mg, 84%). Purification (Hexanes). \(R_f = 0.55. \) \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 8.33 \) (d, \(J = 8.2 \) Hz, 1H), 7.83 (d, \(J = 8.2 \) Hz, 1H), 7.69 (d, \(J = 8.2 \) Hz, 1H), 7.60 (ddd, \(J_1 = 8.2 \) Hz, \(J_2 = 7.0 \) Hz, \(J_3 = 1.2 \) Hz, 1H), 7.50 (ddd, \(J_1 = 8.2 \) Hz, \(J_2 = 7.0 \) Hz, \(J_3 = 1.2 \) Hz, 1H), 7.36 (d, \(J = 8.2 \) Hz, 1H), 2.62 (s, 3H) ppm. \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 133.4, 133.0, 131.1, 130.6, 128.7, 128.0, 127.0, 126.4, 125.6, 124.1, 20.8. \) MS (EI): \(m/z\) 178 (M+2, 17), 176 (M+, 52), 141(100), 139(28), 115(24), 70(72).

N-(4-Chloro-2,6-dimethylphenyl)-2-(diethy lamino)-acetamide (13).\(^{13}\) The title compound was prepared according to general procedure A or B, and characterization spectra were consistent with literature values. White solid (Procedure A: 28.9 mg, 22% yield; Procedure B: 68.5 mg, 51% yield). m.p. 33–36 °C. Purification (Hexanes:EtOAc = 1:1) with 2% NEt\(_3\). \(R_f = 0.25. \) \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 8.92 \) (bs, 1H), 7.09 (s, 2H), 3.22 (s, 2H), 2.69 (s, 2H), 1.14 (t, \(J = 7.0 \) Hz, 6H) ppm. \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 170.3, 135.1, 134.0, 128.2, 127.1, 57.5, 49.0, 18.6, 12.7. \) MS (EI): \(m/z\) 234(1), 134(1), 132(1), 120(1), 86(100), 58(14), 42(9).

4-Chloro-1-phenylpyrazole (14).\(^{9}\) The title compound was prepared according to general procedure A, and characterization spectra were consistent with literature values. White solid (80.1 mg, 90% yield). m.p. 58–60 °C. Purification (Hexanes:EtOAc 85:15). \(R_f = 0.50. \) \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.90 \) (d, \(J = 0.6 \) Hz, 1H), 7.65–7.61 (m, 3H), 7.45 (m, 2H), 7.34–7.31 (t, \(J_1 = 7.4 \) Hz, \(J_2 = 1.2 \) Hz, 1H) ppm. \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 139.7, 139.4, 129.5, 127.0, 124.8, 118.9, 112.4. \) MS (EI): \(m/z\) 180 (M+2, 21), 178 (M+, 73), 152(18), 143(17), 116(21), 89(29), 77(71), 51(100).
3-Chloro-1H-indole-5-carboxaldehyde (15).^{17b} The title compound was prepared according to general procedure A on a 0.25 mmol scale (5-formylindo1), and characterization spectra were consistent with literature values. Pale yellow solid (33.7 mg, 74% yield). m.p. 133−137 °C. Purification (Hexanes:EtOAc 60:40). \( R_f = 0.40. \) \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta = 10.08 \) (s, 1H), 8.66 (bs, 1H), 8.18 (s, 1H), 7.83 (m, 1H), 7.57 (m, 1H), 7.40 (m, 1H), 7.31 (m, 1H), 7.24 (m, 1H), 7.18 (m, 1H). \(^13\)C NMR (100 MHz, CDCl\(_3\)): \( \delta = 194.2, 140.2, 130.9, 126.4, 124.9, 124.4, 123.2, 113.6, 108.0. \) MS (EI): \( m/z \) 181 (M+2, 10), 179 (M+, 100), 159(60), 119(56), 103(100).

3-Chloro-1H-indazole (16).^{12c} The title compound was prepared according to general procedure A, and characterization spectra were consistent with literature values. White solid (52.8 mg, 68% yield). m.p. 140−144 °C. Purification (Hexanes:EtOAc 80:20). \( R_f = 0.22. \) \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta = 11.01 \) (bs, 1H), 7.73 (m, 2H), 7.70 (m, 1H), 7.66 (m, 1H), 7.37 (m, 1H). \(^13\)C NMR (100 MHz, CDCl\(_3\)): \( \delta = 141.4, 135.1, 128.1, 121.7, 120.5, 119.6, 110.4. \) MS (EI): \( m/z \) 154 (M+2, 26), 152 (M+, 100), 117(54), 90(71), 64(32), 63(53), 62(33), 39(65), 38(46), 37(31).

2-Chloroacetonilide and 4-Chloroacetanilide (24).^{17c} The title compounds were prepared according to general procedure A, and characterization spectra were consistent with literature values. White solid (60.1 mg, 80% yield). m.p. 92−95 °C. Purification (Hexanes:EtOAc 70:30). \( R_f = 0.46. \) \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta = 7.92 \) (bs, 1H), 7.59 (m, 1H), 7.27 (m, 1H), 7.22 (d, J = 7.8 Hz, 1H), 7.20 (m, 1H). \(^13\)C NMR (100 MHz, CDCl\(_3\)): \( \delta = 134.9, 125.3, 123.1, 120.8, 120.4, 118.2, 111.5, 106.4. \) MS (EI): \( m/z \) 153 (M+2, 29), 151 (M+, 100), 116(21), 89(64), 63(25), 62(19), 57(18), 75(22).

Ethyl 3-Chloroindole-2-carboxylate (19).^{17b} The title compound was prepared according to general procedure A or B, and characterization spectra were consistent with literature values. White solid (Procedure A: 25.6 mg, 23% yield; Procedure B: 31.3 mg, 28%). m.p. 148−150 °C. Purification (Hexanes:EtOAc 90:10). \( R_f = 0.44. \) \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta = 8.85 \) (bs, 1H), 7.72 (m, 1H), 7.39 (m, 2H), 7.23 (m, 1H). \(^13\)C NMR (100 MHz, CDCl\(_3\)): \( \delta = 160.9, 134.6, 126.6, 126.2, 122.4, 121.3, 120.3, 112.5, 112.0, 61.4, 14.4. \) MS (EI): \( m/z \) 225 (M+2, 8), 223 (M+, 24), 179(30), 178(18), 177(100), 149(29), 123(21), 114(29).

4-Chloro-1,2-dihydro-1,5-dimethyl-2-phenyl-3H-pyrazol-3-one (20).^{17b} The title compound was prepared according to general procedure A or B, and characterization spectra were consistent with literature values. Light green solid (Procedure A: 102.3 mg, 92% yield; Procedure B: 87.8 mg, 79% yield). m.p. 117−121 °C. Purification (Hexanes:EtOAc 80:20). \( R_f = 0.20. \) \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta = 7.69 \) (m, 2H), 7.42 (m, 2H), 7.24 (m, 1H), 2.86 (s, 3H). \(^13\)C NMR (100 MHz, CDCl\(_3\)): \( \delta = 161.7, 136.1, 129.2, 126.3, 120.7, 91.7, 86.0, 37.6, 20.2. \) MS (EI): \( m/z \) 191(61), 190(49), 189(95), 77(84), 43(82), 36(77), 51(56), 42(40), 38(39), 39(36).

8-Chlorocaffeine (21).^{17b} The title compound was prepared according to general procedure A, and characterization spectra were consistent with literature values. White solid (103.1 mg, 90% yield). m.p. 102−105 °C. Purification (Hexanes:EtOAc 1:1). \( R_f = 0.30. \) \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta = 3.92 \) (bs, 3H), 3.50 (s, 3H). \(^13\)C NMR (100 MHz, CDCl\(_3\)): \( \delta = 154.5, 151.2, 147.0, 138.9, 108.1, 32.6, 29.7, 27.9. \) MS (EI): \( m/z \) 230 (M+2, 21), 228 (M+, 63), 143(50), 82(33), 67(94), 55(100).

2,4-Dichloroanisole (22).^{17b} The title compound was prepared according to general procedure B, and characterization spectra were consistent with literature values. Yellow oil (40.0 mg, 35% yield). Purification: 3 mL of 4 M NaOH was added to the crude reaction mixture, and extraction using EtOAc (3 × 10 mL) was performed followed by drying with sodium sulfate and chromatography (100% benzene). \( R_f = 0.90. \) \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta = 7.36 \) (d, J = 2.4 Hz, 1H), 7.19 (d, J = 8.8 Hz, J = 2.4 Hz, 1H), 6.84 (d, J = 8.8 Hz, 1H). \(^13\)C NMR (100 MHz, CDCl\(_3\)): \( \delta = 153.9, 130.0, 127.6, 125.6, 123.3, 112.8, 56.4. \) MS (EI): \( m/z \) 178 (M+2, 50), 176 (M+, 78), 163(62), 161(100), 135(40), 133(65), 75(26), 73(26).

2,4-Dichloro-1,3,5-trimethylbenzene (23).^{39,40} The title compound was prepared according to general procedure B. White solid (27.4 mg, 29% yield). m.p. 56−59 °C. Purification (Hexanes:EtOAc 9:1). \( R_f = 0.90. \) \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta = 6.97 \) (s, 1H), 2.49 (s, 3H), 2.32 (s, 6H). \(^13\)C NMR (100 MHz, CDCl\(_3\)): \( \delta = 134.2, 134.0, 132.7, 129.8, 20.6, 18.4. \) MS (EI): \( m/z \) 190 (M+2, 25), 188 (M+, 32), 155(30), 153(100), 115(32), 57(43), 51(28).
3-Chloro-4-methoxybenzaldehyde (27). The title compound was prepared according to general procedure B, and characterizational spectra were consistent with literature values. Red solid (16.9 mg, 18% yield). m.p. 137 °C. Purification (Hexanes:EtOAc 80:20). Rf = 0.50. 1H NMR (400 MHz, DMSO): δ = 9.85 (s, 1H), 7.90 (d, J = 2.0 Hz, 1H), 7.77 (d, J = 8.6 Hz, J2 = 2.0 Hz, 1H), 7.04 (d, J = 8.6 Hz, 1H), 3.99 (s, 3H) ppm. 13C NMR (100 MHz, DMSO): δ = 135.2, 130.6, 130.3, 123.7, 111.7, 56.5.

3-Chloro-4-methoxybenzaldehyde (28). The title compound was prepared according to general procedure B, and characterizational spectra were consistent with literature values. White solid (15.1 mg, 18% yield). m.p. 156–158 °C. Purification (Hexanes:EtOAc 80:20). Rf = 0.30. 1H NMR (400 MHz, DMSO): δ = 9.87 (s, 1H), 7.82 (s, 2H), 3.99 (s, 3H) ppm. 13C NMR (100 MHz, DMSO) δ 188.7, 157.3, 133.1, 130.6, 130.3, 123.7, 111.7, 65.6.

3-Chloro-2-oxindole (33). The title compound was prepared according to general procedure B, and characterizational spectra were consistent with literature values. Brown oily solid (27.5 mg, 31% yield). Purification (Hexanes:EtOAc 80:20). Rf = 0.40. 1H NMR (400 MHz, DMSO): δ = 9.01 (dd, J1 = 4.3 Hz, J2 = 1.6 Hz, 1H), 8.10 (dd, J1 = 8.2 Hz, J2 = 1.6 Hz, 1H), 7.61 (d, J = 8.2 Hz, 1H), 7.39 (m, 2H), 2.61 (s, 3H) ppm. 13C NMR (100 MHz, DMSO) δ 150.8, 144.6, 137.7, 136.2, 132.1, 129.4, 127.7, 125.7, 120.9, 21.0. MS (EI) m/z 179(15), 177(54), 142(100), 141(25), 89(29), 75(23), 71(25), 57(26), 39(24).

1,1-Dichloronaphthalene-2(1H)-one (30). The title compound was prepared according to general procedure B, and characterizational spectra were consistent with literature values. Yellow oily solid (27.5 mg, 31% yield). Purification (Hexanes:EtOAc 80:20). Rf = 0.58. 1H NMR (400 MHz, DMSO): δ = 8.07 (dd, J1 = 7.8 Hz, J2 = 1.0 Hz, 1H), 7.53 (td, J1 = 7.8 Hz, J2 = 1.0 Hz, 1H), 7.47 (td, J1 = 7.6 Hz, J2 = 1.2 Hz, 1H), 7.45 (d, J = 10.0 Hz, 1H), 7.33 (dd, J1 = 7.6 Hz, J2 = 1.2 Hz, 1H), 6.34 (d, J = 10.0 Hz, 1H), 13C NMR (100 MHz, DMSO) δ 185.9, 144.9, 140.7, 131.2, 130.6, 129.54, 129.52, 126.9, 122.6, 80.4.

3,5-Dichloro-1H-indole (31). The title compound was prepared according to general procedure B, and characterizational spectra were consistent with literature values. Red-brown solid (35.2 mg, 38% yield). m.p. 102–104 °C. Purification (Hexanes:EtOAc 80:20). Rf = 0.80. 1H NMR (400 MHz, DMSO): δ = 8.03 (bs, 1H), 7.54 (d, J = 7.8 Hz, 1H), 7.26–7.16 (m, 3H) ppm. 13C NMR (100 MHz, DMSO) δ = 133.2, 125.5, 123.4, 121.1, 120.0, 117.8, 110.8, 103.8. MS (EI): m/z 187 (M +2, 64), 185 (M+, 100), 152(28), 150(81), 123(32), 114(29), 92(28), 74(27), 61(25).

3,3-Dichloro-2-oxindole (32). The title compound was prepared according to general procedure B, and characterizational spectra were consistent with literature values. Brown solid (9.8 mg, 10% yield). m.p. 163–166 °C. Purification (Hexanes:EtOAc 80:20). Rf = 0.47. 1H NMR (400 MHz, DMSO): δ = 9.15 (bs, 1H), 7.62 (d, J = 7.6 Hz, 1H), 7.37 (t, J = 7.6 Hz, 1H), 7.18 (t, J = 7.6 Hz, 1H), 7.00 (d, J = 7.6 Hz, 1H) ppm. 13C NMR (100 MHz, DMSO) δ = 171.1, 137.8, 132.0, 129.7, 125.1, 124.4, 111.3, 74.6 ppm. FT-IR (neat, cm−1): ν = 3146, 2940, 1730, 1681, 1621, 1486, 1469, 1396, 1206, 1188. MS (EI): m/z 169 (M+2, 7), 167 (M+, 26), 133(23), 132(100), 104(45), 77(39), 52(50), 51(81), 50(41), 38(24).

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.0c00631.

Experimental details, additional optimization tables, mechanistic schemes, compound characterization, 1H and 13C NMR, fluorescence emission, and cyclic voltammograms of catalysts (PDF)

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