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# Cu-Catalyzed Site-Selective Benzylic Chlorination Enabling Net C—H Coupling with Oxidatively Sensitive Nucleophiles

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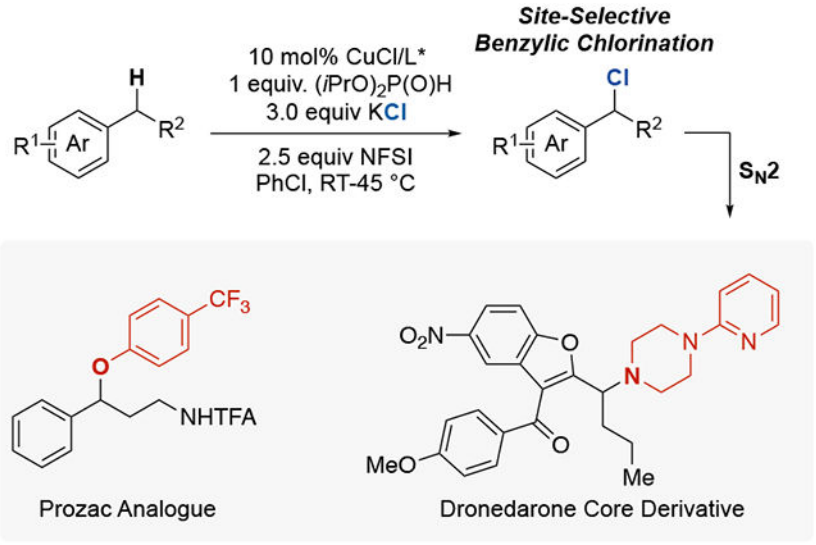
## Abstract

Site-selective chlorination of benzylic C—H bonds is achieved using a $Cu^{I}Cl$/bis(oxazoline) catalyst with *N*-fluorobenzenesulfonimide as the oxidant and KCl as a chloride source. This method exhibits higher benzylic selectivity relative to established chlorination protocols and is compatible with diverse alkyl arenes. Sequential benzylic C—H chlorination/nucleophilic substitution affords C—O, C—S, and C—N coupling products with oxidatively sensitive coupling partners.

## Graphical Abstract

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Supporting Information
Experimental procedures, characterization data, NMR spectra. (PDF)

The authors declare no competing financial interest.

Benzylic chlorides are versatile synthetic intermediates that react readily with heteroatom- and carbon-based nucleophiles in conventional substitution[1] and catalytic cross-coupling reactions.[2-6] These compounds may be accessed via radical-chain chlorination,[7,8] leveraging the comparatively low bond dissociation energy and higher reactivity of benzylic C—H bonds (Figure 1A). Radical-chain chlorination methods that involve chlorine radical (Cl•) as the hydrogen-atom transfer (HAT) reagent, however, often exhibit poor C—H site selectivity. Consequently, benzylic chlorides are commonly prepared by the reaction of benzylic alcohols with $SOCl_2$ or via other functional-group interconversion methods.[2,3,6,9,10] C—H chlorination methods that employ species other than Cl• for the HAT step can show improved selectivity.[11-22] In this context, Cu catalysts in combination with *N*-fluorobenzenesulfonimide as the oxidant (Cu/NFSI) promote diverse C—H functionalization and oxidative cross-coupling reactions (e.g., Figure 1B)[23-35] that exhibit high benzylic site selectivity. These methods involve a radical-relay mechanism, in which HAT generates a diffusible benzylic radical that undergoes subsequent functionalization by $Cu^{II}$ and a nucleophilic coupling partner. Here, we report the development of a Cu/NFSI method for benzylic chlorination that uses KCl as the source of chloride (Figure 1C). A comparison with other chlorination reactions highlights the unique benzylic selectivity of Cu/NFSI reactivity. The method uses the C—H substrate as the limiting reagent, and it may be paired with a subsequent nucleophilic substitution step to achieve net C—H coupling with nucleophiles that are not compatible with direct oxidative C—H functionalization.

Several mechanistic considerations contributed to initial efforts in this study. A possible C—H chlorination mechanism, shown in Figure 2, reflects insights from other Cu/NFSI C—H functionalization reactions.[30,32] Copper(I) reacts with NFSI to generate a bis(sulfonyl)imidyl radical (•NSI) that can promote HAT. The resulting benzylic radical could undergo $Cu^{II}$-mediated functionalization via one of several possible mechanisms (inner-sphere[24,26,29] or outer-sphere[30,31] coupling with a coordinated ligand, or radical-polar crossover involving a benzylic cation intermediate[30,31,34,35]). Cu/NFSI C—H functionalization reactions often require a sacrificial reductant or "redox buffer," such as a dialkylphosphite[30,34,35]) to support catalytic turnover. The reductant provides a means to regenerate $Cu^{I}$ if all of the $Cu^{I}$ catalyst is oxidized to $Cu^{II}$ via undesired reaction of •NSI (see red/blue pathways in Figure 2).

Initial screening studies were initiated with isobutyl benzene (**1a**) as the substrate and reaction conditions incorporating a Cu salt, ancillary ligand, NFSI, and a chloride source (Table 1). Trimethylsilyl (TMS)-substituted nucleophiles have been used in previous Cu/NFSI reactions, including those with TMSCN,[24] $TMSN_3$,[31] TMSNCO.[34] These reagents are expected to transfer anionic ligands to $Cu^{II}$, promoted by Si—F bond formation; however, TMSCl proved rather ineffective. No reactivity was observed in the absence of a phosphite additive (Table 1, entry 1), and only 22% yield of the benzylic chloride was observed in the presence of phosphite (entry 2). Chlorination of the phosphite additive was observed under these conditions (see Figure S3 in the Supporting Information). Use of alkali metal chlorides improved the reaction outcome (entries 3-7), with use of KCl contributing to the best yield (entry 7). Soluble chloride sources, such as $NBu_4Cl$, inhibit the reaction (see Table S8 in the Supporting Information). The identity of the ancillary ligand influenced

the reaction outcome (entries 7-10; see Table S3 in the Supporting Information for other ligands). The best yields were obtained with bathophenantroline **L1** and the bis(oxazoline) (BisOx) ligand **L4** (entries 7 and 10); however, the latter generally led to higher yields for different substrates (see Figure S2 in Supporting Information).[36] Thus, **L4** was selected for subsequent studies, even though no enantioselectivity was observed from the reactions. The latter observation is rationalized by a radical-polar crossover mechanism in which the intermediate benzylic radical is oxidized by $Cu^{II}$ to a benzylic cation, which then reacts with the chloride nucleophile. The latter mechanism is consistent with the seminal early studies of Kochi,[37] which showed that $Cu^{II}$ salts promote oxidation of organic radicals to the corresponding cations. This mechanism resembles other recently reported Cu/NFSI C—H functionalization reactions.[30,31,34,35]

Once optimal reaction conditions were identified, the Cu/NFSI-promoted chlorination reaction was then compared with other established C—H chlorination methods (Figure 3). Specifically, isobutyl and isopentyl benzene (**1a** and **2a**) were used to compare the reaction yield and selectivity for 2° benzylic versus 3° aliphatic C—H chlorination. The different methods included the following: (a) Cu/NFSI (see Table 1), (b) Ag(phen)/$^t$BuOCl (phen = 1,10-phenanthroline),[15] in which $^t$BuO• or a $Ag^{II}O^tBu$ species is proposed to initiate HAT, (c) *N*-chlorosuccinimide (NCS)/dibenzoylperoxide (DBPO),[38] with radical-chain chlorination propagated by HAT from a succinimidyl radical, (d) $Cu(OAc)_2$/*N*-hydroxyphthalimide (NHPI)/trichloroisocynanuric acid (TCA),[13] proposed to involve HAT by oxygen- and nitrogen-centered radicals, (e) light-promoted benzophenone ($Ph_2CO$)/NCS,[12] with HAT promoted by the excited state ketone, (f and g) radical-chain chlorination $SO_2Cl_2$/DBPO,[8] propagated by Cl•-mediated HAT, and (h) Mn(tetraphenylporphyrin)Cl (Mn(TPP)Cl)/NaOCl,[11] which involves HAT by a $Mn^v$=O species.

Bond dissociation energies for the benzylic and tertiary C—H sites (~89 and ~93 kcal/mol, respectively[39]) suggest that reactivity should be strongly favored at the benzylic position. The data in Figure 3, however, reveal a wide range of outcomes from the different chlorination methods. Cu/NFSI conditions support benzylic chlorination in good yield and selectivity, with benzylic:tertiary (B:T) ratios of 10:1 and 20:1 for **1a** and **2a**. Ag(phen)/$^t$BuOCl affords the highest yields and selectivities among the other seven conditions, with benzylic chlorination yields of 37% and 53% for **1a** and **2a**, respectively, and B:T ratios of ~2:1, relative to Cu/NFSI. Conventional radical-chain chlorination conditions (methods c, f, and g) afford lower yields and B:T selectivities, and even slightly favoring tertiary over benzylic chlorination in some cases (see methods f with **1a** and method g with **1a** and **2a**). All reaction conditions generate side products corresponding to dichlorination and/or oxygenation of the substrate (in gray).

The results in Figure 3 highlight the unique benzylic selectivity of •NSI-mediated HAT and provide a starting point for testing of Cu/NSFI C—H chlorination with a series of other substrates (Figure 4). *Para*-substituted alkyl benzenes and 2-ethyl naphthalene, **3**-**5**, **9**, **10**, undergo chlorination in good-to-excellent yields (69-97%), with the exception of the 4-ethyl anisole **5** (24%), which generates the benzylic bis(sulfonyl)imide as a significant byproduct (~50%). Propyl arenes with various substituents at the terminal position lead to benzylic chlorination products in good yield (75-84%, **6**-**8**), providing versatile

bifunctional electrophilic building blocks. 3-Phenylpropanoic acid methyl ester and alkyl trifluoroacetamides are chlorinated solely at the benzylic position in good yields (**11**-**14**, 70-74%).[40] The lack of functionalization next to the carbonyl or trifluoroacetamide groups is consistent with electronic deactivation of these sites toward reaction with the electrophilic •NSI species. A bromo-substituted fluorene derivative reacts effectively (**15**, 79%). Common pharmacophores 6-bromochroman **16** and alpha-tetralone **17** afford chlorination products in good yield (75% and 60%, respectively), while pyridine-containing substrates exhibit lower yields (**20**, 34%; **21**, 38%). Benzylic chlorination of more complexes structures also proved effective (cf. **18**, **19**, **22**-**26**), including successful reaction of Celestolide (**18**, >99%), Ibuprofen methyl ester (**19**, 52%), the tetrahydroquinoline precursor to a GnRH antagonist (**22**, 40%), the xanthine oxidase inhibitor, benzbromarone (**23**, 68%), and a dronedarone derivative (**24**, 89%). The data in Figure 4 reflect isolated yields, with product volatility accounting for $^{1}$H NMR yields in a few cases (**1**, **3**-**5**). In addition, separation challenges resulted in several products being isolated as a mixture with unreacted C—H substrate (**2**, **6**, **7**, **12**, **13**, **20**, **21**). This issue is not considered problematic because the substrate will be inert in the subsequent reactions of the benzylic chloride and is readily separated at that stage (see below).

The data in Figure 4 complement previously reported Cu/NFSI methods for C—H functionalization (cf. Figure 1B), but they also introduce new synthetic opportunities. Cu/NFSI oxidative coupling methods are not compatible with oxidatively sensitive nucleophiles, such as phenols, thiophenols, and alkylamines, due to undesirable side reactivity between these nucleophiles and NFSI. The reactivity here provides a means to bypass this limitation via sequential C—H chlorination/diversification in which the benzylic chlorides are used in subsequent coupling reactions. This concept is illustrated in Figure 5, using benzylic chlorides derived from the trifluoroacetyl-protected aminopropylbenzene (**12**) and the dronedarone derivative (**26**). Coupling of **12** with a series of phenols and thiophenols affords analogues of the antidepressant drug, fluoxetine (i.e., Prozac) (**27**-**30**). The observed C—O coupling products **27** and **28** are noteworthy because a recently reported[33] C—H fluorination/substitution sequence leads to C—C coupling (i.e., Friedel-Crafts alkylation) in reactions with phenol nucleophiles. The different outcome reflects the different reaction conditions employed to support phenol displacement of the halide leaving group: basic conditions (chloride) versus acidic (fluoride). A complementary set of nucleophilic substitution reactions were carried out with **26**, using thiophenol and cyclic secondary amines coupling partners.

Overall, the reactions presented herein establish a new Cu/NFSI-based method for benzylic C—H chlorination, with KCl as the source of chloride. The •NSI HAT species contributes to very high benzylic site selectivity, relative to a broad cross section of other C—H chlorination methods. The ability to pair C—H chlorination in sequence with nucleophilic substitution or cross-coupling steps provide a strategy to achieve rapid diversification of core structures bearing benzylic C—H bonds.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## ACKNOWLEDGMENT

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## REFERENCES

(1). Schaumann E Science of Synthesis: Houben-Weyl Methods of Molecular Transformations Vol. 35: Chlorine, Bromine, and Iodine; Georg Thieme Verlag, 2014.

(2). Wang Z; Bachman S; Dudnik AS; Fu GC Nickel-Catalyzed Enantioconvergent Borylation of Racemic Secondary Benzylic Electrophiles. Angew. Chem., Int. Ed 2018, 57, 14529–14532.

(3). Iwamoto H; Endo K; Ozawa Y; Watanabe Y; Kubota K; Imamoto T; Ito H Copper(I)-Catalyzed Enantioconvergent Borylation of Racemic Benzyl Chlorides Enabled by Quadrant-by-Quadrant Structure Modification of Chiral Bisphosphine Ligands. Angew. Chem., Int. Ed 2019, 55, 11112–11117.

(4). Cybularczyk-Cecotka M; Szczepanik J; Giedyk M Photocatalytic Strategies for the Activation of Organic Chlorides. Nat Catal 2020, 3, 872–886.

(5). Poremba KE; Dibrell SE; Reisman SE Nickel-Catalyzed Enantioselective Reductive Cross-Coupling Reactions. ACS Catal. 2020, 10, 8237–8246. [PubMed: 32905517]

(6). Li Z; Cheng X-Y; Yang N-Y; Chen J-J; Tang W-Y; Bian J-Q; Cheng Y-F; Li Z-L; Gu Q-S; Liu X-Y A Cobalt-Catalyzed Enantioconvergent Radical Negishi $C(sp^3)$—$C(sp^2)$ Cross-Coupling with Chiral Multidentate *N, N, P*-Ligand. Organometallics 2021, 40, 2215–2219.

(7). Walling C; Jacknow BB Positive Halogen Compounds. I. The Radical Chain Halogenation of Hydrocarbons by *t*-Butyl Hypochlorite. J. Am. Chem. Soc 1960, 82, 5–9

(8). Kharasch MS; Brown HC Chlorinations with Sulfuryl Chloride. I. The Peroxide-Catalyzed Chlorination of Hydrocarbons. J. Am. Chem. Soc 1939, 61, 2142–2150.

(9). Mohite AR; Phatake RS; Dubey P; Agbaria M; Shames AI; Lemcoff NG; Reany O Thiourea-Mediated Halogenation of Alcohols. J. Org. Chem 2020, 85, 12901–12911. [PubMed: 32938176]

(10). Stach T; Dräger J; Huy PH Nucleophilic Substitutions of Alcohols in High Levels of Catalytic Efficiency. Org. Lett 2018, 20, 2980–2983. [PubMed: 29745673]

(11). Liu W; Groves JT Manganese Porphyrins Catalyze Selective C—H Bond Halogenations. J. Am. Chem. Soc 2010, 132, 12847–12849. [PubMed: 20806921]

(12). Han L; Xia J-B; You L; Chen C Ketone-Catalyzed Photochemical $C(sp^3)$—H Chlorination. Tetrahedron 2017, 73, 3696–3701. [PubMed: 28717256]

(13). Combe SH; Hosseini A; Parra A; Schreiner PR Mild Aliphatic and Benzylic Hydrocarbon C—H Bond Chlorination Using Trichloroisocyanuric Acid. J. Org. Chem 2017, 82, 2407–2413. [PubMed: 28106993]

(14). Quinn RK; Könst ZA; Michalak SE; Schmidt Y; Szklarski AR; Flores AR; Nam S; Horne DA; Vanderwal CD; Alexanian EJ Site-Selective Aliphatic C—H Chlorination Using *N*-Chloroamides Enables a Synthesis of Chlorolissoclimide. J. Am. Chem. Soc 2016, 138, 696–702. [PubMed: 26694767]

(15). Ozawa J; Kanai M Silver-Catalyzed $C(sp^3)$—H Chlorination. Org. Lett 2017, 19, 1430–1433. [PubMed: 28256138]

(16). Sasmal S; Rana S; Lahiri GK; Maiti D Manganese-Salen Catalyzed Oxidative Benzylic Chlorination. J. Chem. Sci 2018, 130, 88.

(17). Li G; Dilger AK; Cheng PT; Ewing WR; Groves JT Selective C—H Halogenation with a Highly Fluorinated Manganese Porphyrin. Angew. Chem., Int. Ed 2018, 57, 1251–1255.

(18). Li Z-H; Fiser B; Jiang B-L; Li J-W; Xu B-H; Zhang S-J *N*-Hydroxyphthalimide/Benzoquinone-Catalyzed Chlorination of Hydrocarbon C—H Bond Using *N*-Chlorosuccinimide. Org. Biomol. Chem 2019, 17, 3403–3408. [PubMed: 30869109]

(19). Xiang M; Zhou C; Yang X-L; Chen B; Tung C-H; Wu L-Z Visible Light-Catalyzed Benzylic C—H Bond Chlorination by a Combination of Organic Dye ($Acr^+$-Mes) and *N*-Chlorosuccinimide. J. Org. Chem 2020, 85, 9080–9087. [PubMed: 32434320]

(20). Jin J; Zhao Y; Kyne SH; Farshadfar K; Ariafard A; Chan PWH Copper(I)-Catalysed Site-Selective C($sp^3$)—H Bond Chlorination of Ketones, (*E*)-Enones and Alkylbenzenes by Dichloramine-T. Nat. Commun 2021, 12, 4065 [PubMed: 34210971]

(21). McMillan AJ; Sieńkowska M; Lorenzo PD; Gransbury GK; Chilton NF; Salamone M; Ruffoni A; Bietti M; Leonori D Practical and Selective $sp^3$ C—H Bond Chlorination via Aminium Radicals. Angew. Chem., Int. Ed 2021, 60, 7132–7139.

(22). Fawcett A; Keller MJ; Herrera Z; Hartwig JF Site Selective Chlorination of C($sp^3$)—H Bonds Suitable for Late-Stage Functionalization. Angew. Chem., Int. Ed 2021, 60, 8276–8283.

(23). Ni Z; Zhang Q; Xiong T; Zheng Y; Li Y; Zhang H; Zhang J; Liu Q Highly Regioselective Copper-Catalyzed Benzylic C—H Amination by N-Fluorobenzenesulfonimide. Angew. Chem., Int. Ed 2012, 51, 1244–1247.

(24). Zhang W; Wang F; McCann SD; Wang D; Chen P; Stahl SS; Liu G Enantioselective Cyanation of Benzylic C—H Bonds via Copper-Catalyzed Radical Relay. Science 2016, 353, 1014–1018. [PubMed: 27701109]

(25). Zhang W; Chen P; Liu G Copper-Catalyzed Arylation of Benzylic C—H Bonds with Alkylarenes as the Limiting Reagents. J. Am. Chem. Soc 2017, 139, 7709–7712. [PubMed: 28562032]

(26). Zhang W; Wu L; Chen P; Liu G Enantioselective Arylation of Benzylic C—H Bonds by Copper-Catalyzed Radical Relay. Angew. Chem., Int. Ed 2019, 58, 6425–6429.

(27). Xiao H; Liu Z; Shen H; Zhang B; Zhu L; Li C Copper-Catalyzed Late-Stage Benzylic C($sp^3$)—H Trifluoromethylation. Chem 2019, 5, 940–949.

(28). Liu S; Achou R; Boulanger C; Pawar G; Kumar N; Lusseau J; Robert F; Landais Y Copper-Catalyzed Oxidative Benzylic C($sp^3$)—H Amination: Direct Synthesis of Benzylic Carbamates. Chem. Commun 2020, 56, 13013–13016.

(29). Fu L; Zhang Z; Chen P; Lin Z; Liu G Enantioselective Copper-Catalyzed Alkynylation of Benzylic C—H Bonds via Radical Relay. J. Am. Chem. Soc 2020, 142, 12493–12500. [PubMed: 32539406]

(30). Hu H; Chen S-J; Mandal M; Pratik SM; Buss JA; Krska SW; Cramer CJ; Stahl SS Copper-Catalysed Benzylic C—H Coupling with Alcohols via Radical Relay Enabled by Redox Buffering. Nat. Catal 2020, 3, 358–367. [PubMed: 32368720]

(31). Suh S-E; Chen S-J; Mandal M; Guzei IA; Cramer CJ; Stahl SS Site-Selective Copper-Catalyzed Azidation of Benzylic C—H Bonds. J. Am. Chem. Soc 2020, 142, 11388–11393. [PubMed: 32539355]

(32). Buss JA; Vasilopoulos A; Golden DL; Stahl SS Copper-Catalyzed Functionalization of Benzylic C—H Bonds with *N*- Fluorobenzenesulfonimide: Switch from C—N to C—F Bond Formation Promoted by a Redox Buffer and Brønsted Base. Org. Lett 2020, 22, 5749–5752. [PubMed: 32790419]

(33). Vasilopoulos A; Golden DL; Buss JA; Stahl SS Copper-Catalyzed C—H Fluorination/ Functionalization Sequence Enabling Benzylic C—H Cross Coupling with Diverse Nucleophiles. Org. Lett 2020, 22, 5753–5757. [PubMed: 32790420]

(34). Suh S-E; Nkulu LE; Lin S; Krska SW; Stahl SS Benzylic C—H Isocyanation/Amine Coupling Sequence Enabling High-Throughput Synthesis of Pharmaceutically Relevant Ureas. Chem. Sci 2021, 12, 10380–10387. [PubMed: 34377424]

(35). Chen S-J; Golden DL; Krska SW; Stahl SS Copper-Catalyzed Cross-Coupling of Benzylic C—H Bonds and Azoles with Controlled *N*-Site Selectivity. J. Am. Chem. Soc 2021, 143, 14438–14444. [PubMed: 34464528]

(36). **L4** is readily prepared on multigram scale in two steps from inexpensive starting materials: Hofstra JL; DeLano TJ; Reisman SE Synthesis of Chiral Bisoxazoline Ligands: (3a*R*,3a'*R*,8a*S*,8a'*S*)-2,2'-(cyclopropane-1,1-diyl)bis(3a,8a-dihydro-8*H*-indeno[1,2-d]oxazole). Org. Synth 2020, 97, 172–188. [PubMed: 34295006]

(37). Kochi JK Electron-Transfer Mechanisms for Organometallic Intermediates in Catalytic Reactions. Acc. Chem. Res 1974, 7, 351–360.

(38). Pathi SL; Kankan RN; Puppala R A Process of Preparing Imatinib. 2008MU02726, 2008.

(39). Luo Y-R Handbook of Bond Dissociation Energies in Organic Compounds; CRC Press, 2003.

(40). The effect of *N*-protecting groups, evaluated with a series of tetrahydroquinoline derivatives (cf. **22**), show that groups with increased electron-withdrawing character (e.g., electron-deficient sulfonamides) are more effective than carbamates, such as Boc and Cbz groups (see Figure S4 in the Supporting Information).

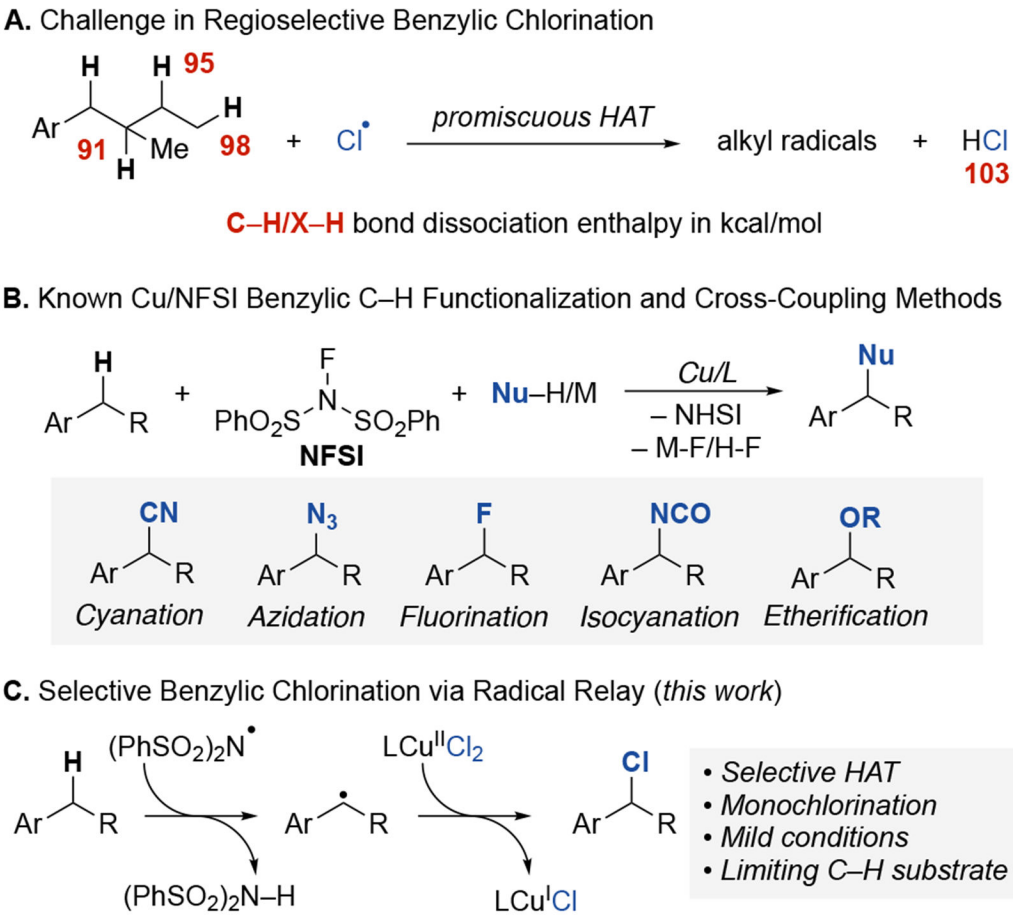



**Figure 1.**

Chlorine radical as an unselective HAT agent (A), representative Cu/NFSI benzylic functionalization methods (B), and reaction sequence illustrating Cu/NFSI benzylic chlorination (C).

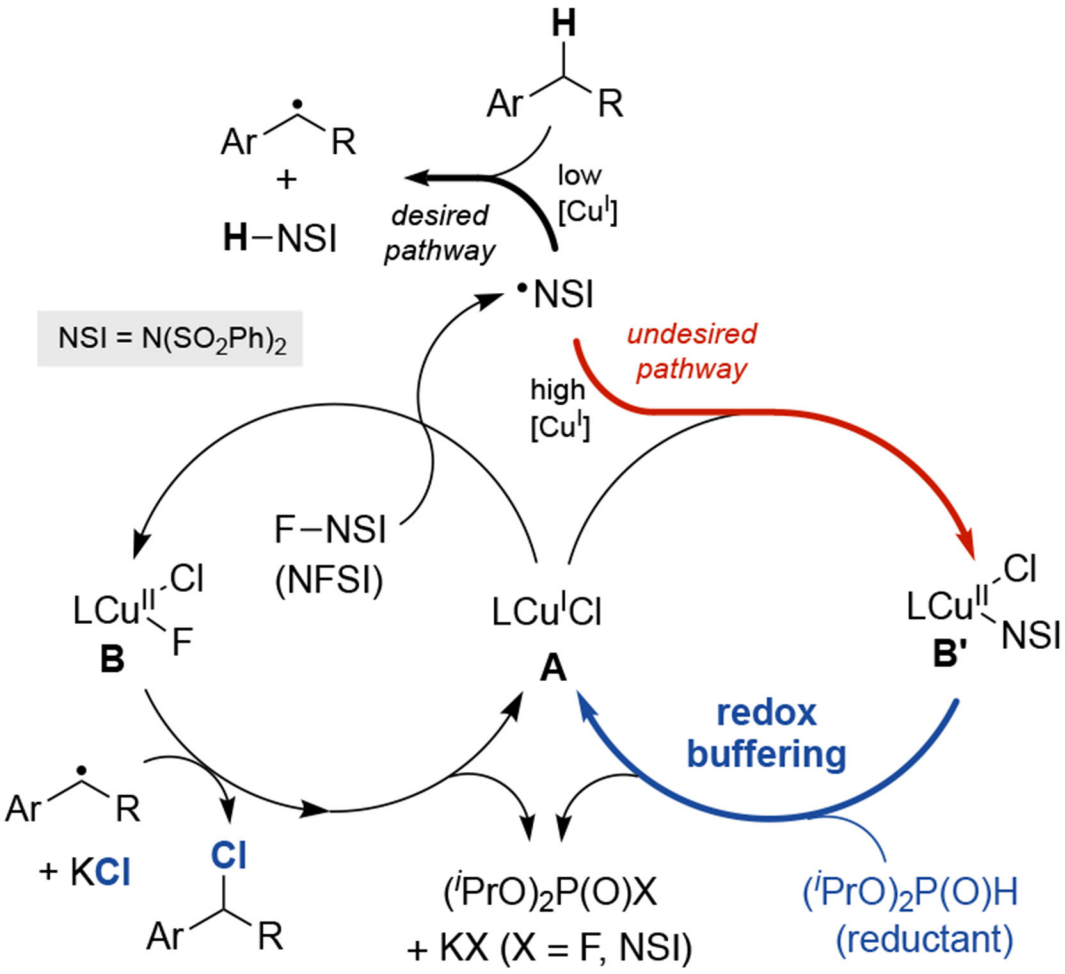



**Figure 2.**
Proposed mechanistic cycle for benzylic chlorination leveraging redox-buffering

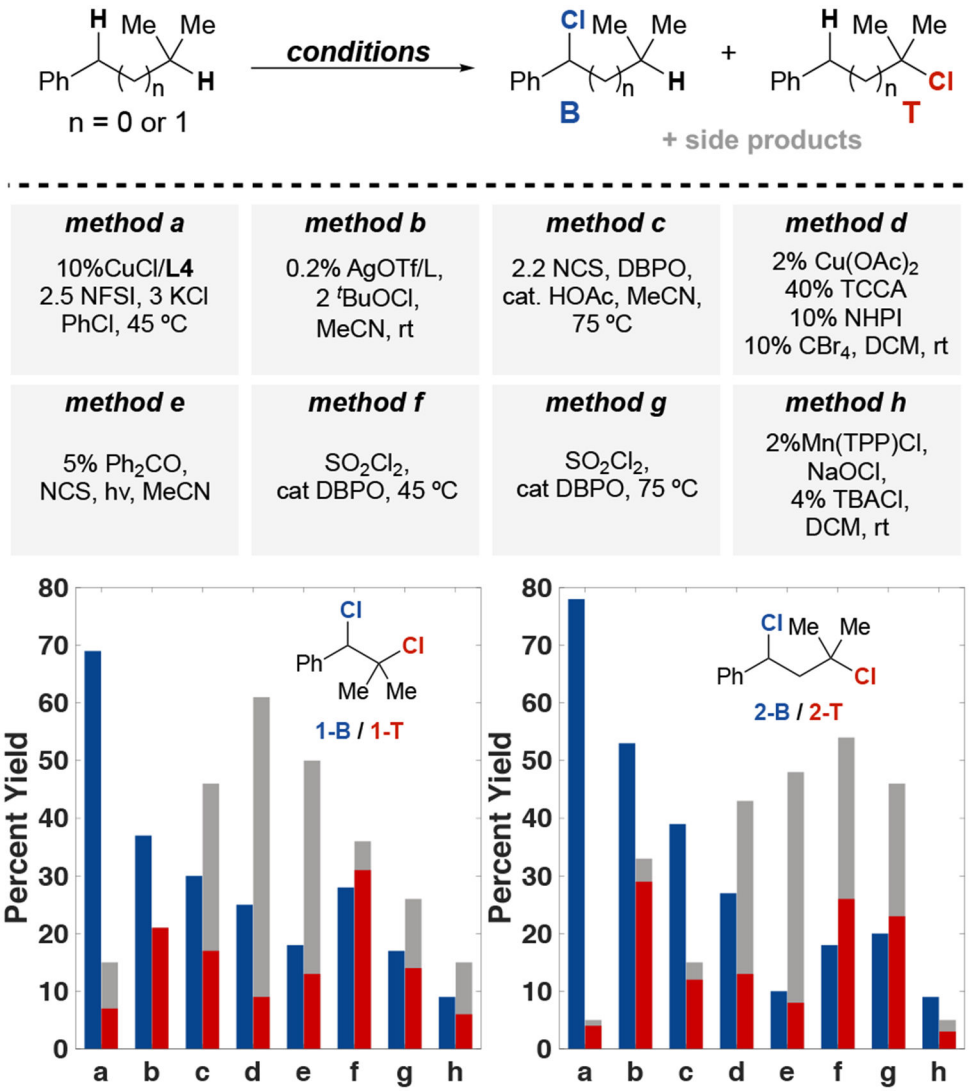



**Figure 3.**

Applications of varied C—H chlorination methods on isobutylbenzene and isopentylbenzene. Yields determined by $^{1}$H NMR spectroscopy (external std. = mesitylene).

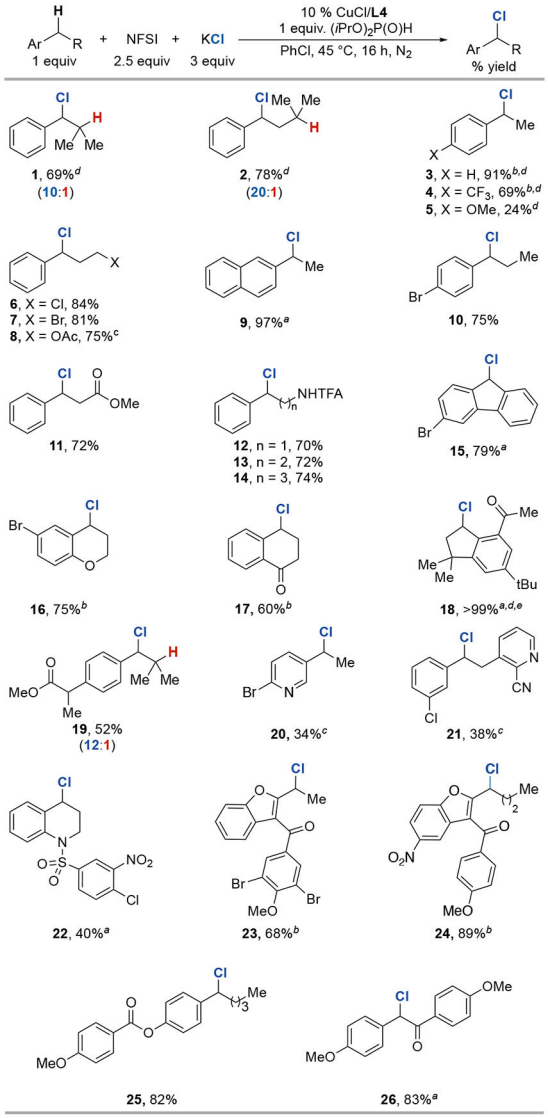



**Figure 4.**

Scope of alkylarene benzylic chlorination. Reactions were run on a 0.2, 0.5, or 1.2 mmol scale. [a]Reaction run at 35 °C. [b]Reaction run at RT. [c]Reaction run at 70 °C. [c]10 mol% TMSCl added. [d]Yields determined by $^1$H NMR spectroscopy (ext. std. = mesitylene). [e]Isolated as the alcohol.

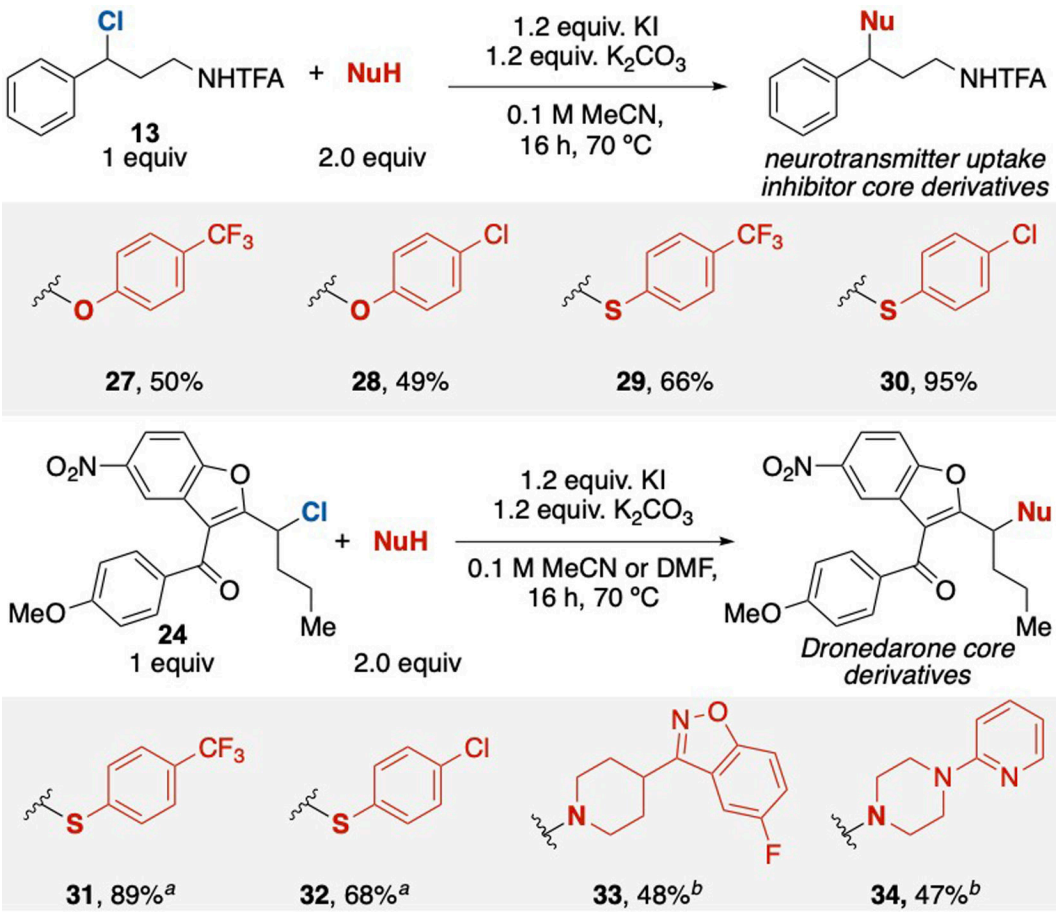
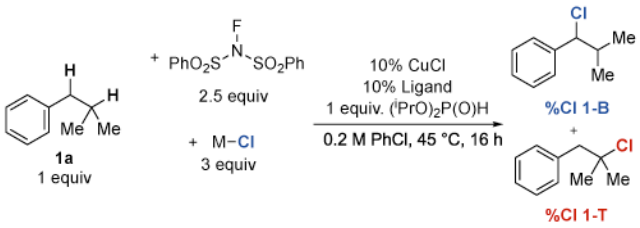



**Figure 5.**

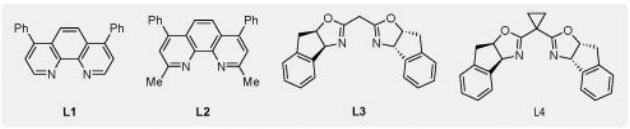
Benzylic chloride displacement. Reactions were run on a 0.2 mmol scale. [a]Reaction run with DMF. [b]Reaction run with MeCN.

**Table 1.**

Cu/NFSI Benzylic Chlorination Reaction Optimization.




| entry | ligand (mol%) | M—Cl | Conv. (%) | yield 1-B:1-T (%)[b] |
|---|---|---|---|---|
| 1 | L1 | TMSCl | 0 | 0:0[c] |
| 2 | L1 | TMSCl | 22 | 17:1 |
| 3 | L1 | LiCl | 29 | 14:2 |
| 4 | L1 | NaCl | 39 | 28:2 |
| 5 | L1 | RbCl | 53 | 39:4 |
| 6 | L1 | CsCl | 72 | 57:5 |
| 7 | L1 | KCl | 75 | 59:7 |
| 8 | L2 | KCl | 68 | 56:4 |
| 9 | L3 | KCl | 65 | 58:6 |
| 10 | L4 | KCl | 80 | 66:5 |




[a] 0.2 mmol scale.

[b] $^1$H NMR yields, ext. std. = mesitylene.

[c] Reaction conducted without phosphite reductant