OL | Organic Letters

pubs.acs.org/OrgLett Letter

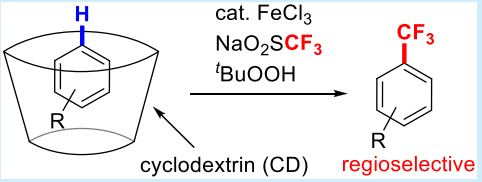
Regioselective C−H Trifluoromethylation of Aromatic Compounds by Inclusion in Cyclodextrins

Xu Lu, Ryohei Kawazu, Jizhou Song, Yusuke Yoshigoe, Takeru Torigoe, and Yoichiro Kuninobu*

Cite This: *Org. Lett.* 2021, 23, 4327−4331 Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

ABSTRACT: A regioselective radical C−H trifluoromethylation of aromatic compounds was developed using cyclodextrins (CDs) as additives. The C−H trifluoromethylation proceeded with high regioselectivity to afford the product in good yield, even on the gram scale. In the presence of CDs, some substrates underwent a single trifluoromethylation selectively, whereas mixtures of single- and double-trifluoromethylated products were formed in the absence of the CD. ^{1}H NMR experiments indicated that the regioselectivity was controlled by the inclusion of a substrate inside the CD cavity.



Fluorinated functional groups, including the trifluoromethyl (CF_3) group, are among the most important functional groups in drugs, agrochemicals, and organic functional materials. The introduction of the CF_3 group(s) results in a dramatic improvement in the molecular properties of the compound, such as lipophilicity, metabolic stability, and bioavailability.[1] The ideal method for introducing the CF_3 group is direct C−H trifluoromethylation. Radical C−H trifluoromethylation of five-membered heteroaromatic compounds proceeds regioselectively to afford only single products.[2] On the other hand, radical C−H trifluoromethylation of six-membered heteroaromatic compounds proceeds at almost all possible reaction sites, and mixtures of regioisomers are formed.[2c,d] We succeeded in the regioselective C−H trifluoromethylation and related reactions of six-membered heteroaromatic compounds using CF_3 and related anion sources.[3,4] However, regioselective C−H trifluoromethylation of aromatic compounds is more difficult than that of heteroaromatic substrates.

The CF_3 radical has generally been used in the C−H trifluoromethylation of aromatic compounds. Trifluoromethylation proceeds at various reaction sites to give mixtures of regioisomers (Figure 1a).[2a,n,5] Although there have been several reports on *ortho*-selective C−H trifluoromethylation of aromatic substrates using a directing group to control the regioselectivity, there are some drawbacks: (1) the reaction site is limited to the *ortho*-position of the substrates, and (2) it is difficult to remove the directing groups from the products after the reaction (Figure 1b).[6]

We hypothesized that regioselective C−H trifluoromethylation of aromatic compounds could be realized by protecting several reaction sites using a cyclic molecule as an additive (Figure 1c). In this reaction system, aromatic molecules are included inside the cavity of the cyclic molecule, which protects some potential reaction sites.[7] Herein, we report the regioselective C−H trifluoromethylation of multisubstituted

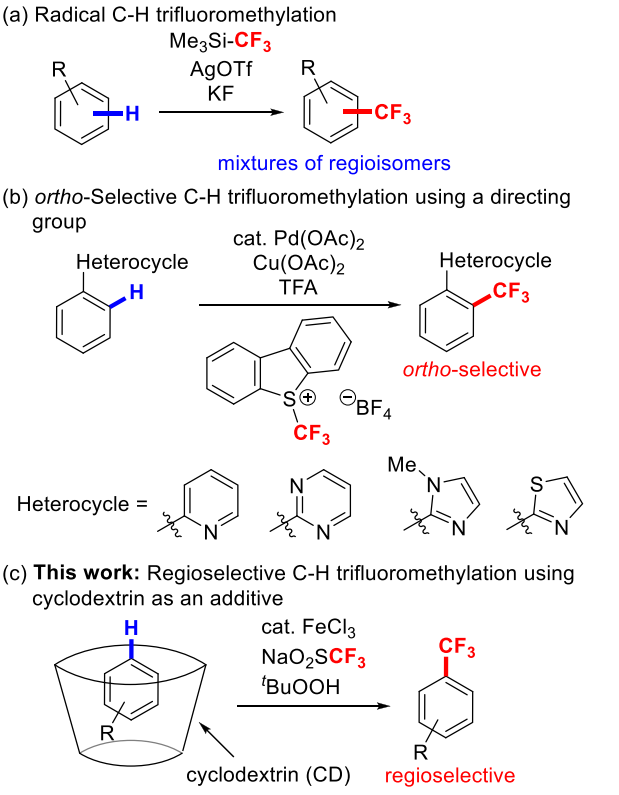
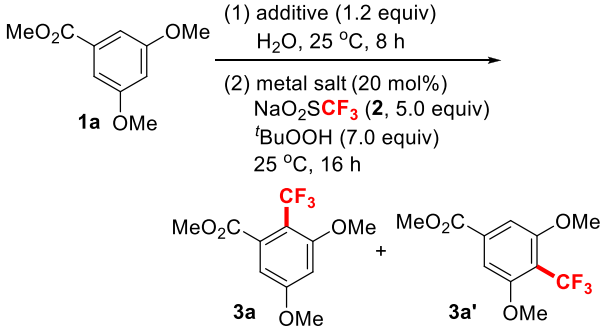


Figure 1. Several examples of C−H trifluoromethylation of aromatic compounds.

Received: April 13, 2021
Published: May 14, 2021

https://doi.org/10.1021/acs.orglett.1c01259
Org. Lett. 2021, 23, 4327−4331

Table 1. Investigation of Cyclodextrins and Several Transition Metal Salts[a]



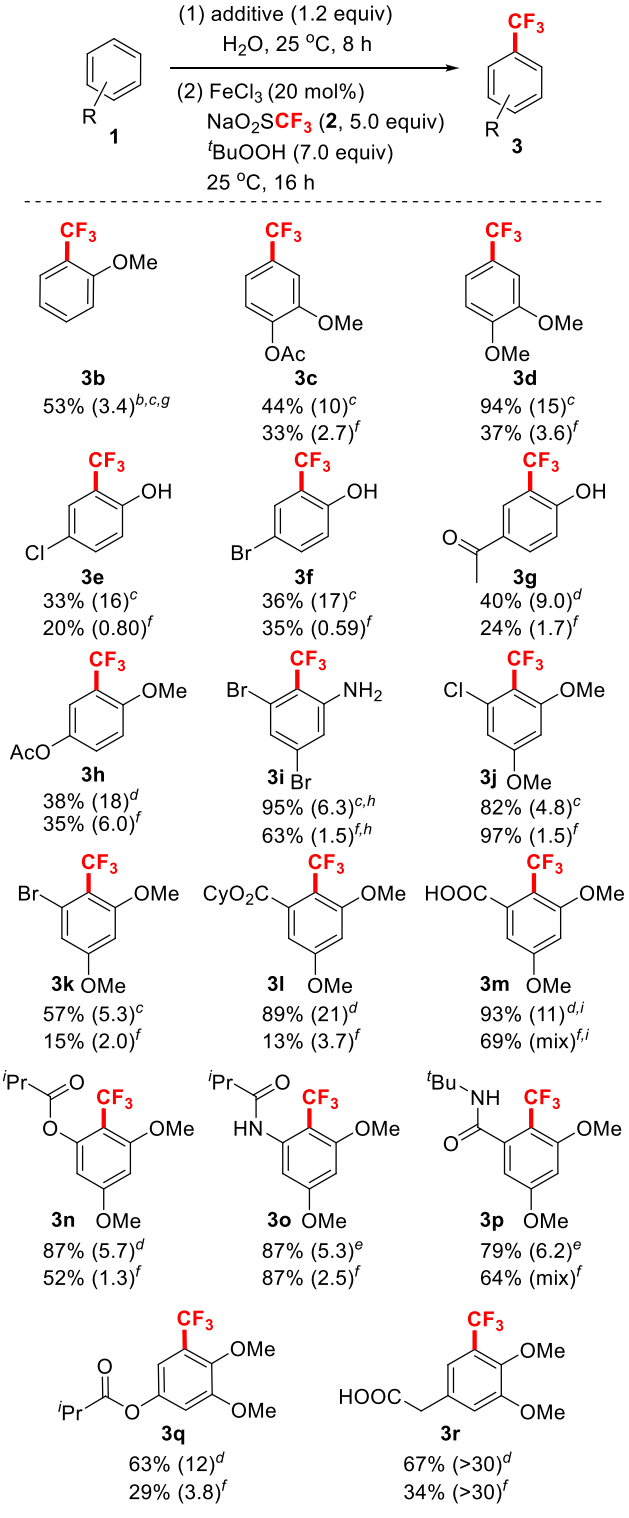
entry	additive	metal salt	yield/% (3a/3a′)
1	none	none	56 (2.2)
2	α-CD	none	55 (1.6)
3	β-CD	none	61 (5.1)
4	γ-CD	none	48 (4.4)
5	β-CD	$MnCl_2$	38 (6.0)
6	β-CD	$FeCl_3$	99 (19)
7	β-CD	$Fe(NO_3)_3$	91 (10)
8	β-CD	$CoCl_2$	46 (4.8)
9	β-CD	$NiCl_2{\cdot}6H_2O$	77 (4.2)
10	β-CD	$CuCl_2$	92 (8.1)
11	β-CD	$Cu(OTf)_2$	93 (6.7)

[a]Yield was determined by ^{19}F NMR using 2,2,2-trifluoroethanol as an internal standard. The ratio between trifluoromethylated product **3a** and its regioisomer **3a′** (**3a**/**3a′**) is described in parentheses.

aromatic compounds using cyclodextrins (CDs) as the cyclic molecules, even on the gram scale. Single trifluoromethylation of the substrates proceeded selectively in the presence of the CD, whereas both single and double trifluoromethylation occurred in the absence of the CD. ^1H NMR experiments suggested the inclusion of aromatic substrates inside the CD cavity.

The difficulty in promoting regioselective radical C−H trifluoromethylation of aromatic compounds stems from the high reactivity of the CF_3 radical and the occurrence of the reaction at various sites. Treatment of aromatic substrate **1a** with NaO_2SCF_3 (**2**) and ^{t}BuOOH in the presence of $Cu(OTf)_2$ as a catalyst in H_2O afforded a mixture of trifluoromethylated product **3a** and its regioisomer **3a′** in 56% combined yield (**3a**/**3a′** = 2.2) (Table 1, entry 1).[8] We considered the use of cyclic compounds as additives to protect some potential reaction sites of **1a** sterically and thus promote regioselective C−H trifluoromethylation. Although several cyclic compounds such as calixarenes and pillararenes could be considered as candidates, C−H trifluoromethylation may also occur at the aromatic rings of these compounds. Therefore, we selected CDs because they are inexpensive and highly water-soluble and do not contain any aromatic rings. We screened α-, β-, and γ-CDs (Table 1, entries 2−4) and achieved the best results with β-CD; that is, the ratio of trifluoromethylated product (**3a**/**3a′**) was improved to 5.1 (Table 1, entry 3). These results clearly showed that the size of the cyclic compound is important for controlling the regioselectivity. Next, several first-row transition metal salts were screened (Table 1, entries 5−11). In several entries, the yield of (**3a** + **3a′**) and the ratio (**3a**/**3a′**) were improved, and the best result was obtained when using a catalytic amount of

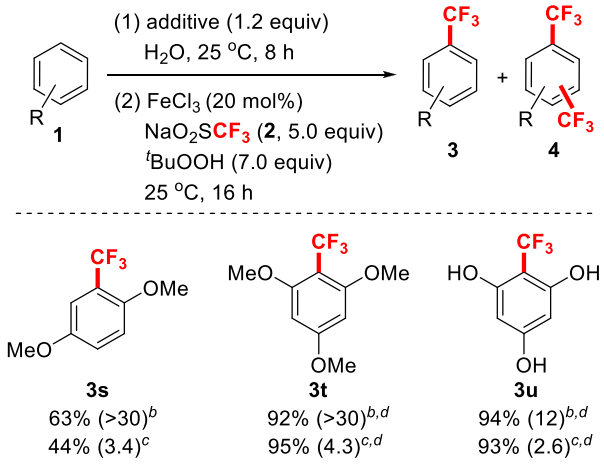
Scheme 1. Substrate Scope: Control of Regioselectivity[a]



[a]Yield was determined by ^{19}F NMR using 2,2,2-trifluoroethanol as an internal standard. The ratio between trifluoromethylated product **3a** and its regioisomer(s) **3a′** (**3a**/**3a′**) is described in parentheses. mix = complex mixture. [b]Solvent: H_2O:MeCN (5/1). [c]With α-cyclodextrin. [d]With β-cyclodextrin. [e]With γ-cyclodextrin. [f]Without cyclodextrin. [g]Catalyst: $Cu(OTf)_2$ instead of $FeCl_3$. Solvent: aqueous urea (0.10 M).[10] [h]Catalyst: $Cu(OTf)_2$ instead of $FeCl_3$. [i]Catalyst: $Cu(OTf)_2$ instead of $FeCl_3$. Solvent: H_2O:MeCN (5/1).

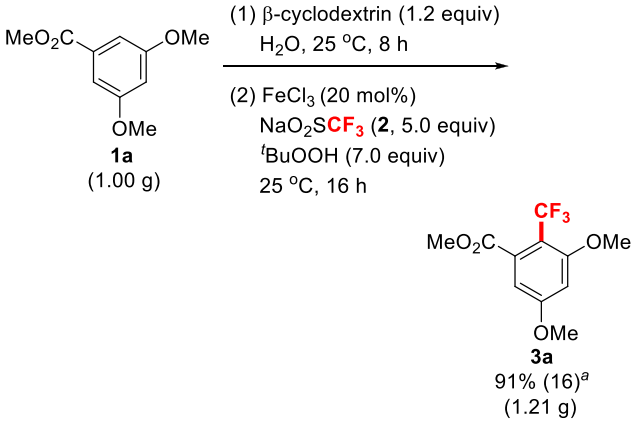
https://doi.org/10.1021/acs.orglett.1c01259
Org. Lett. 2021, 23, 4327−4331

Scheme 2. Substrate Scope: Single Trifluoromethylation[a]



[a]Yield was determined by ^{19}F NMR using 2,2,2-trifluoroethanol as an internal standard. The ratio between single trifluoromethylated product **3** and double trifluoromethylated product(s) **4** (**3**/**4**) is described in parentheses. [b]With β-cyclodextrin. [c]Without β-cyclodextrin. [d]Catalyst: $Cu(OTf)_2$ instead of $FeCl_3$. Solvent: H_2O:MeCN (5/1).

Scheme 3. Gram-Scale Synthesis of 3a



[a]The ratio between trifluoromethylated product **3a** and its regioisomer **3a′** (**3a**/**3a′**) is described in parentheses.

$FeCl_3$ (Table 1, entry 6). Therefore, we performed the subsequent experiments using $FeCl_3$ as the catalyst.

We then investigated the substrate scope of the aromatic compounds (Scheme 1). The suitable size of cyclodextrins existed depending on the size of substrates. The general trend was as follows: monosubstituted substrates, α-CD; disubstituted substrates, α- or β-CD; and trisubstituted substrates, β- or γ-CD. In all cases, the selectivity of the major products was improved dramatically when using CDs, and regioselective trifluoromethylation proceeded with good functional group tolerance. The yields of the trifluoromethylated products increased in several cases, probably owing to the improved solubility of the substrates.

The regioselectivity of trifluoromethylated anisole **3b** was improved by the addition of α-CD, and *ortho*-trifluoromethylated product **3b** was obtained as the major product.[9] In the case of 1,2- and 1,4-disubstituted aromatic compounds, C−H trifluoromethylation proceeded regioselectively when using α- or β-CD, and the corresponding trifluoromethylated aromatic

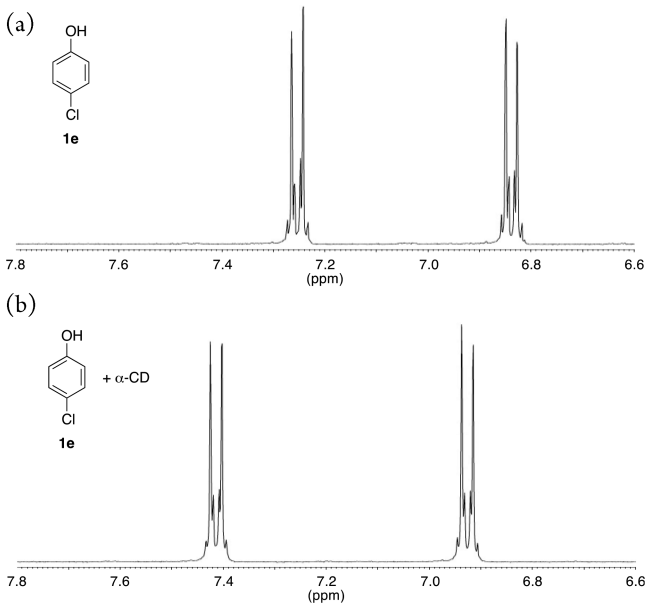


Figure 2. Partial ^1H NMR spectrum of (a) 4-chlorophenol (0.010 mmol/mL in D_2O) and (b) 4-chlorophenol and α-CD (0.010 mmol/mL in D_2O).

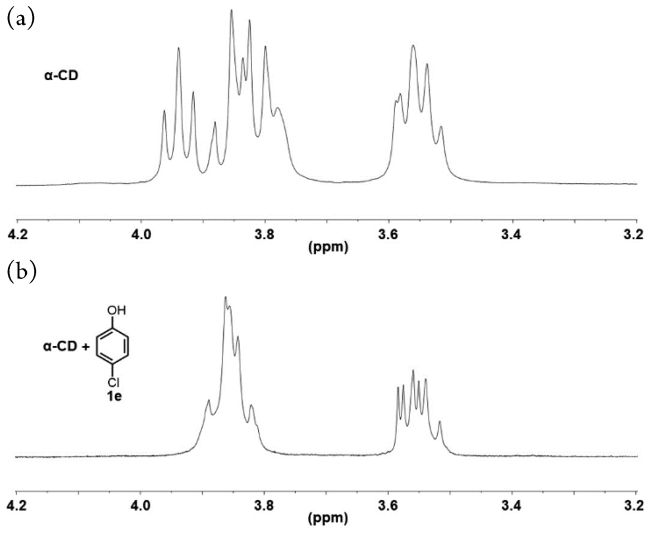


Figure 3. Partial ^1H NMR spectrum of (a) α-CD (0.010 mmol/mL in D_2O) and (b) α-CD and 4-chlorophenol (0.010 mmol/mL in D_2O).

compounds **3c**−**3h** were obtained in moderate to excellent yields with high regioselectivity. C−H trifluoromethylation of 1,3,5- and 1,2,4-trisubstituted aromatic compounds also proceeded regioselectively in the presence of β- or γ-CD, and trifluoromethylated compounds **3i**−**3r** were obtained in moderate to excellent yields. The regioselectivity was not improved under the reaction conditions using pyridin-3-yl isobutyrate, 2-acetylfuran, and 2-formylpyrrole as substrates.

Several substrates afforded a mixture of mono- and ditrifluoromethylated products **3** and **4** in the absence of CDs (Scheme 2). On the other hand, the ratio of monotrifluoromethylated products **3s**−**3u** increased dramatically when β-CD was used, and good product yields (63%−94%) and high monoselectivity were achieved. These results indicated that the CD protected the second reaction site by inclusion of the substrates.

https://doi.org/10.1021/acs.orglett.1c01259
Org. Lett. 2021, 23, 4327−4331

Trifluoromethylation proceeded in excellent yield with high regioselectivity, even on the gram scale (Scheme 3). Treatment of a mixture of 1.00 g of **1a** and β-CD in H_2O with **2**, ^{t}BuOOH, and a catalytic amount of $FeCl_3$ at 25 °C gave 1.21 g of trifluoromethylated product **3a** in 90% yield (**3a**/**3a**′ = 16).

To confirm the inclusion of aromatic substrates inside the cavity of the CD in water, ^{1}H NMR experiments were conducted in D_2O at the same concentration as the reaction mixture (Figures 2 and 3). Proton signals of the aromatic region of 4-chlorophenol (**1e**) were downfield-shifted by the addition of α-CD (Figure 2).[11] In addition, a change in the chemical shifts of the proton signals of α-CD was observed upon the addition of **1e** (Figure 3).[11] These results clearly suggested that **1e** was included inside the cavity of α-CD in water.

In summary, we have successfully developed a regioselective C−H trifluoromethylation of aromatic compounds using CDs as additives. The selectivity of the major products was improved dramatically in the presence of the CDs, and regioselective trifluoromethylation proceeded with good functional group tolerance, even on the gram scale. The general trend for the suitability of the CDs was as follows: monosubstituted substrates, α-CD; disubstituted substrates, α- or β-CD; and trisubstituted substrates, β- or γ-CD. Monotrifluoromethylated products were obtained selectively in the presence of the CD, whereas several aromatic substrates gave mixtures of mono- and ditrifluoromethylated products. The results of the ^{1}H NMR experiments indicated that the aromatic substrate was present inside the cavity of the CD in water. The investigation of more detailed mechanistic studies is underway in our group. The use of cyclic compounds such as CDs is expected to be a useful and efficient strategy to control the regioselectivity in C−H transformations.[12]

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.1c01259.

General experimental procedure and characterization data for products (PDF)

■ AUTHOR INFORMATION

Corresponding Author

Yoichiro Kuninobu − *Institute for Materials Chemistry and Engineering and Department of Molecular and Material Sciences, Interdisciplinary Graduate School of Engineering Sciences, Kyushu University, Kasuga-shi, Fukuoka 816-8580, Japan*; orcid.org/0000-0002-8679-9487; Email: kuninobu@cm.kyushu-u.ac.jp

Authors

Xu Lu − *Department of Molecular and Material Sciences, Interdisciplinary Graduate School of Engineering Sciences, Kyushu University, Kasuga-shi, Fukuoka 816-8580, Japan*

Ryohei Kawazu − *Department of Molecular and Material Sciences, Interdisciplinary Graduate School of Engineering Sciences, Kyushu University, Kasuga-shi, Fukuoka 816-8580, Japan*

Jizhou Song − *Department of Molecular and Material Sciences, Interdisciplinary Graduate School of Engineering Sciences, Kyushu University, Kasuga-shi, Fukuoka 816-8580, Japan*

Yusuke Yoshigoe − *Institute for Materials Chemistry and Engineering, Kyushu University, Kasuga-shi, Fukuoka 816-8580, Japan*

Takeru Torigoe − *Institute for Materials Chemistry and Engineering and Department of Molecular and Material Sciences, Interdisciplinary Graduate School of Engineering Sciences, Kyushu University, Kasuga-shi, Fukuoka 816-8580, Japan*; orcid.org/0000-0002-4902-1596

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.orglett.1c01259

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported in part by JSPS KAKENHI Grant Numbers JP 17H03016, 18H04656, and 20H04824, Takeda Science Foundation, The Mitsubishi Foundation, and Yamada Science Foundation.

■ REFERENCES

(1) Purser, S.; Moore, P. R.; Swallow, S.; Gouverneur, V. Fluorine in Medicinal Chemistry. *Chem. Soc. Rev.* **2008**, *37*, 320−330.

(2) (a) Nagib, D. A.; MacMillan, D. W. C. Trifluoromethylation of Arenes and Heteroarenes by Means of Photoredox Catalysis. *Nature* **2011**, *480*, 224−228. (b) Ye, Y.; Lee, S. H.; Sanford, M. S. Silver-Mediated Trifluoromethylation of Arenes Using $TMSCF_3$. *Org. Lett.* **2011**, *13*, 5464−5467. (c) Ji, Y.; Brueckl, T.; Baxter, R. D.; Fujiwara, Y.; Seiple, I. B.; Su, S.; Blackmond, D. G.; Baran, P. S. Innate C−H Trifluoromethylation of Heterocycles. *Proc. Natl. Acad. Sci. U. S. A.* **2011**, *108*, 14411−14415. (d) Fujiwara, Y.; Dixon, J. A.; O'Hara, F.; Funder, E. D.; Dixon, D. D.; Rodriguez, R. A.; Baxter, R. D.; Herlé, B.; Sach, N.; Collins, M. R.; Ishihara, Y.; Baran, P. S. Practical and Innate Carbon−Hydrogen Functionalization of Heterocycles. *Nature* **2012**, *492*, 95−99. (e) Chu, L.; Qing, F.-L. Copper-Catalyzed Direct C−H Oxidative Trifluoromethylation of Heteroarenes. *J. Am. Chem. Soc.* **2012**, *134*, 1298−1304. (f) Iqbal, N.; Choi, S.; Ko, E.; Cho, E. J. Trifluoromethylation of Heterocycles via Visible Light Photoredox Catalysis. *Tetrahedron Lett.* **2012**, *53*, 2005−2008. (g) Seo, S.; Taylor, J. B.; Greaney, M. F. Silver-Catalysed Trifluoromethylation of Arenes at Room Temperature. *Chem. Commun.* **2013**, *49*, 6385−6387. (h) Pitre, S. P.; McTiernan, C. D.; Ismaili, H.; Scaiano, J. C. Metal-Free Photocatalytic Radical Trifluoromethylation Utilizing Methylene Blue and Visible Light Irradiation. *ACS Catal.* **2014**, *4*, 2530−2535. (i) Choi, W. J.; Choi, S.; Ohkubo, K.; Fukuzumi, S.; Cho, E. J.; You, Y. Mechanisms and Applications of Cyclometalated Pt(II) Complexes in Photoredox Catalytic Trifluoromethylation. *Chem. Sci.* **2015**, *6*, 1454−1464. (j) Beatty, J. W.; Douglas, J. J.; Miller, R.; McAtee, R. C.; Cole, K. P.; Stephenson, C. R. J. Photochemical Perfluoroalkylation with Pyridine *N*-Oxides: Mechanistic Insights and Performance on a Kilogram Scale. *Chem.* **2016**, *1*, 456−472. (k) Natte, K.; Jagadeesh, R. V.; He, L.; Rabeah, J.; Chen, J.; Taeschler, C.; Ellinger, S.; Zaragoza, F.; Neumann, H.; Brîckner, A.; Beller, M. Palladium-Catalyzed Trifluoromethylation of (Hetero)Arenes with CF_3Br. *Angew. Chem., Int. Ed.* **2016**, *55*, 2782−2786. (l) Wu, Y.; Zhang, H.-R.; Jin, R.-X.; Lan, Q.; Wang, X.-S. Nickel-Catalyzed C−H Trifluoromethylation of Electron-Rich Heteroarenes. *Adv. Synth. Catal.* **2016**, *358*, 3528−3533. (m) Du, Y.; Pearson, R. M.; Lim, C.-H.; Sartor, S. M.; Ryan, M. D.; Yang, H.; Damrauer, N. H.; Miyake, G. M. Strongly Reducing, Visible-Light Organic Photoredox Catalysts as Sustainable Alternatives to Precious Metals. *Chem. - Eur. J.* **2017**, *23*, 10962−10968. (n) Liu, P.; Liu, W.; Li, C.-J. Catalyst-Free and Redox-Neutral Innate Trifluoromethylation and Alkylation of Aromatics Enabled by Light. *J. Am. Chem. Soc.* **2017**, *139*, 14315−14321. (o) Harris, C. F.; Kuehner, C. S.; Bacsa, J.; Soper, J. D. Photoinduced Cobalt(III)-Trifluoromethyl Bond Activation Enables Arene C−H Trifluoromethylation.

Angew. Chem., Int. Ed. **2018**, *57*, 1311−1315. (p) Meucci, E. A.; Nguyen, S. N.; Camasso, N. M.; Chong, E.; Ariafard, A.; Canty, A. J.; Sanford, M. S. Nickel(IV)-Catalyzed C−H Trifluoromethylation of (Hetero)arenes. *J. Am. Chem. Soc.* **2019**, *141*, 12872−12879.

(3) (a) Nishida, T.; Ida, H.; Kuninobu, Y.; Kanai, M. Regioselective Trifluoromethylation of *N*-Heteroaromatic Compounds Using Trifluoromethyldifluoroborane Activator. *Nat. Commun.* **2014**, *5*, 3387. (b) Kuninobu, Y.; Nagase, M.; Kanai, M. Benzylic C(sp^3)−H Perfluoroalkylation of Six-Membered Heteroaromatic Compounds. *Angew. Chem., Int. Ed.* **2015**, *54*, 10263−10266. (c) Nagase, M.; Kuninobu, Y.; Kanai, M. 4-Position-Selective C−H Perfluoroalkylation and Perfluoroarylation of Six-Membered Heteroaromatic Compounds. *J. Am. Chem. Soc.* **2016**, *138*, 6103−6106. (d) Shirai, T.; Kanai, M.; Kuninobu, Y. 2-Position-Selective C−H Perfluoroalkylation of Quinoline Derivatives. *Org. Lett.* **2018**, *20*, 1593−1596.

(4) For a 2-position-selective C−H trifluoromethylthiolation of six-membered heteroaromatic compounds, see: Muta, R.; Torigoe, T.; Kuninobu, Y. 2-Position-Selective Trifluoromethylthiolation of Six-Membered Heteroaromatic Compounds. *Org. Lett.* **2019**, *21*, 4289−4292.

(5) (a) Ye, Y.; Lee, S. H.; Sanford, M. S. Silver-Mediated Trifluoromethylation of Arenes Using $TMSCF_3$. *Org. Lett.* **2011**, *13*, 5464−5467. (b) Mejia, E.; Togni, A. Rhenium-Catalyzed Trifluoromethylation of Arenes and Heteroarenes by Hypervalent Iodine Reagents. *ACS Catal.* **2012**, *2*, 521−527. (c) Wu, X.; Chu, L.; Qing, F.-L. $PhI(OAc)_2$-mediated oxidative trifluoromethylation of arenes with CF_3SiMe_3 under metal-free conditions. *Tetrahedron Lett.* **2013**, *54*, 249−251. (d) Cui, L.; Matusaki, Y.; Tada, N.; Miura, T.; Uno, B.; Itoh, A. Metal-Free Direct C−H Perfluoroalkylation of Arenes and Heteroarenes Using a Photoredox Organocatalyst. *Adv. Synth. Catal.* **2013**, *355*, 2203−2207. (e) Natte, K.; Jagadeesh, R. V.; He, L.; Rabeah, J.; Chen, J.; Taeschler, C.; Ellinger, S.; Zaragoza, F.; Neumann, H.; Brückner, A.; Beller, M. Palladium-Catalyzed Trifluoromethylation of (Hetero)Arenes with CH_3Br. *Angew. Chem., Int. Ed.* **2016**, *55*, 2782−2786. (f) Li, L.; Mu, X.; Liu, W.; Wang, Y.; Mi, Z.; Li, C.-J. Simple and Clean Photoinduced Aromatic Trifluoromethylation Reaction. *J. Am. Chem. Soc.* **2016**, *138*, 5809−5812. (g) Chang, B.; Shao, H.; Yan, P.; Qiu, W.; Weng, Z.; Yuan, R. Quinone-Mediated Trifluoromethylation of Arenes and Heteroarenes with Visible Light. *ACS Sustainable Chem. Eng.* **2017**, *5*, 334−341. (h) Du, Y.; Pearson, R. M.; Lim, C.-H.; Sartor, S. M.; Ryan, M. D.; Yang, H.; Damrauer, N. H.; Miyake, G. M. Strongly Reducing, Visible-Light Organic Photoredox Catalysts as Sustainable Alternatives to Precious Metals. *Chem. - Eur. J.* **2017**, *23*, 10962−10968. (i) Yang, B.; Yu, D.; Xu, X.-H.; Qing, F. L. Visible-Light Photoredox Decarboxylation of Perfluoroarene Iodine(III) Trifluoroacetates for C−H Trifluoromethylation of (Hetero)arenes. *ACS Catal.* **2018**, *8*, 2839−2843. For a review, see: (j) Studer, A. A "Renaissance" in Radical Trifluoromethylation. *Angew. Chem., Int. Ed.* **2012**, *51*, 8950−8958. (k) Egami, H.; Ito, Y.; Ide, T.; Masuda, S.; Hamashima, Y. Simple Photo-Induced Trifluoromethylation of Aromatic Rings. *Synthesis* **2018**, *50*, 2948−2953.

(6) Wang, X.; Truesdale, L.; Yu, J.-Q. Pd(II)-Catalyzed *ortho*-Trifluoromethylation of Arenes Using TFA as a Promoter. *J. Am. Chem. Soc.* **2010**, *132*, 3648−3649.

(7) For pioneering examples of regioselective reactions using cyclic compounds as additives, see: (a) Breslow, R.; Campbell, P. Selective Aromatic Substitution within a Cyclodextrin Mixed Complex. *J. Am. Chem. Soc.* **1969**, *91*, 3085−3085. (b) Komiyama, M.; Hirai, H. Selective Syntheses Using Cyclodextrins as Catalysts. 2. Para-Oriented Carboxylation of Phenols. *J. Am. Chem. Soc.* **1984**, *106*, 174−178.

(8) Langlois, B. R.; Laurent, E.; Roidot, N. Trifluoromethylation of Aromatic Compounds with Sodium Trifluoromethanesulfinate under oxidative conditions. *Tetrahedron Lett.* **1991**, *32*, 7525−7528.

(9) **3b** was formed as a single product in water solvent, whereas the yield of **3b** was low (18%).

(10) The solubility of β-CD in H_2O is improved by the addition of urea. See: Pharr, D. Y.; Fu, Z. S.; Smith, T. K.; Hinze, W. L. Solubilization of Cyclodextrins for Analytical Application. *Anal. Chem.* **1989**, *61*, 275−279.

(11) The similar change in the chemical shifts was reported in the case of inclusion of vanillin inside the cavity of β-CD. See: Pîrnău, A.; Bogdan, N.; Floare, C. G. NMR spectroscopic characterization of β-cyclodextrin inclusion complex with vanillin. *J. Phys. Conf. Ser.* **2009**, *182*, 012013.

(12) A previous version of this manuscript has been deposited on a preprint server: DOI: 10.26434/chemrxiv.14173655.v1.

https://doi.org/10.1021/acs.orglett.1c01259
Org. Lett. 2021, 23, 4327−4331