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Solvent-Dependent Cyclization of 2-Alkynylanilines and $ClCF_2COONa$ for the Divergent Assembly of *N*-(Quinolin-2-yl)amides and Quinolin-2(1*H*)-ones

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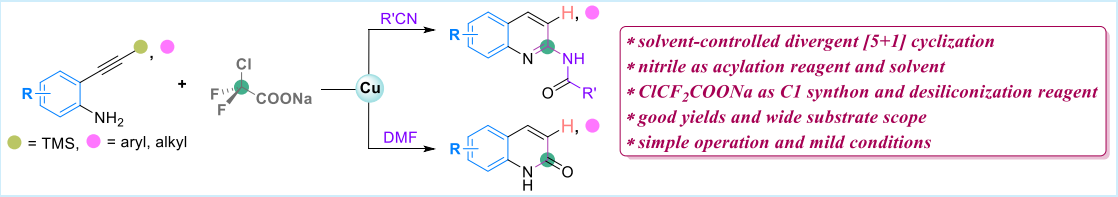

ABSTRACT: Herein, we present an expedient Cu-catalyzed [5 + 1] cyclization of 2-alkynylanilines and $ClCF_2COONa$ to divergent construction of *N*-(quinolin-2-yl)amides and quinolin-2(1*H*)-ones by regulating the reaction solvents. Notably, nitrile acts as a solvent and performs the Ritter reactions. $ClCF_2COONa$ is used as a C1 synthon in this transformation, which also represents the first example for utilization of $ClCF_2COONa$ as an efficient desiliconization reagent. The current protocol involves *in situ* generation of isocyanide, copper-activated alkyne, Ritter reaction and protonation.

Halofluorinated compounds have been witnessed as versatile building blocks in organic synthesis over the past years.[1,2] Various deconstructive modes of XCF_2R have been devoted by our group[1] and others.[2] Among the halofluorinated compounds, the elaboration of sodium chlorodifluoroacetate ($ClCF_2COONa$) has been flourishing.[3] The well-informed applications of $ClCF_2COONa$ served as the difluorocarbene precursors.[3a,b] Apart from the double cleavage of $ClCF_2COONa$, during the past few years, there is a sequence of intriguing transformations of $ClCF_2COONa$ to be harnessed as C1 synthon via quadruple cleavage of $ClCF_2COONa$.[3c,d] Despite this vigoroso advancement of $ClCF_2COONa$, the [5 + 1] cyclization of $ClCF_2COONa$ to forge quinolines has yet to be addressed. Therefore, we hypothesize that this [5 + 1] cycloaddition reaction of $ClCF_2COONa$ can be realized by introducing some possible reaction sites at the *ortho* position of the amino group. In addition, the discarded F anion in the foregone quadruple cleavage of $ClCF_2COONa$ is a waste. In fact, the F anion has proven to be a good desiliconization reagent in organic synthesis.[4] In this regard, $ClCF_2COONa$ might be a potential desiliconization reagent via cleavage of C−F bonds. However, the utilization of $ClCF_2COONa$ as an efficient desiliconization reagent has never been documented thus far.

The cyano group can be handily decorated to render diverse valuable products via reduction,[5] hydrolysis,[6] cycloaddition,[7] etc., which endows the multiple reactivities of nitriles. Apart from the electrophilic property of the C≡N triple bond,[8] nitriles also display weak nucleophilicity, owing to the lone-pair electrons of the N atom.[9] Herein, we envisage that nitrile as a nucleophilic acylation reagent and solvent could acylate the product to streamline construction of *N*-(quinolin-2-yl)amides. At the same time, quinolin-2(1*H*)-ones could be gained in decent yields by regulating the reaction solvent to dimethylformamide (DMF). The current method made use of $ClCF_2COONa$ as a promising C1 synthon for producing the isocyanide *in situ*, which was attacked by nucleophilic solvents followed by intramolecular cyclization. When 2-((trimethylsilyl)ethynyl)anilines were submitted to this reaction, C3-unsubstituted *N*-(quinolin-2-yl)acetamides and quinolin-2(1*H*)-ones were achieved in decent yields, in which $ClCF_2COONa$ was first used as a novel desiliconization reagent. Quinolines are one of the most important structural motifs, which are extensively found in therapeutic agents and natural products and pharmacologically active substances.[10] Although a plethora of tactics have been developed for the assembly of quinolines,[11] there are scarce reports for direct construction of *N*-(quinolin-2-yl)amides among the synthesis of known quinolines (Scheme 1A). The current protocol provides a facile and straightforward route for divergent construction of *N*-(quinolin-2-yl)amides and quinolin-2(1*H*)-

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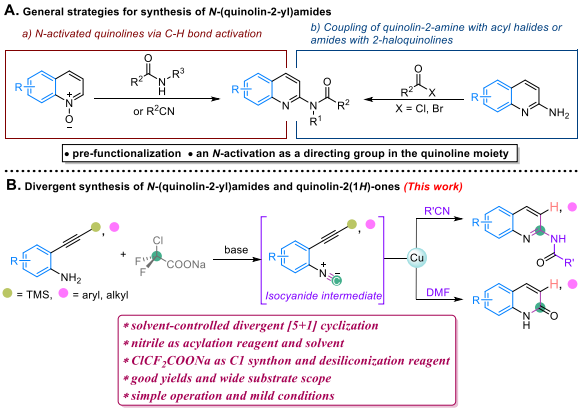
Scheme 1. Synthesis of *N*-(Quinolin-2-yl)amides

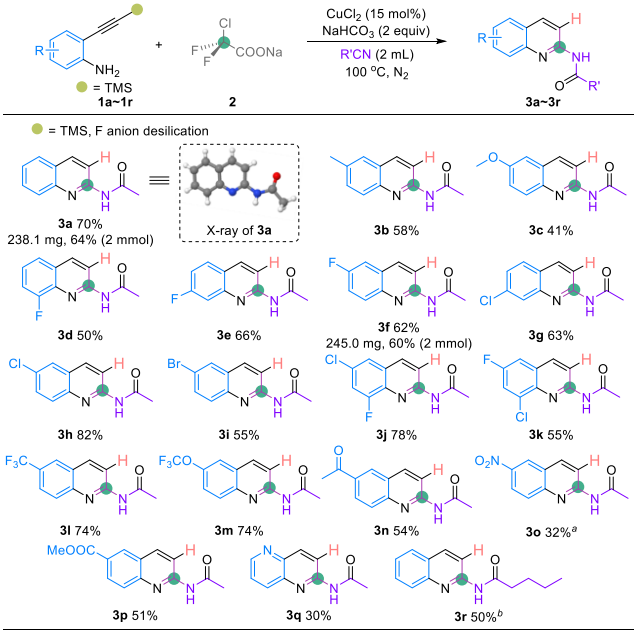


ones via [5 + 1] cyclization of 2-alkynylanilines and $ClCF_2COONa$ (Scheme 1B).

To validate our hypothesis, we commenced our proof-of-concept study with 2-((trimethylsilyl)ethynyl)aniline (**1a**) and $ClCF_2COONa$ (**2**) in CH_3CN. To our delight, when the reaction was carried out in the presence of CuI with K_3PO_4 as the base, desired *N*-(quinolin-2-yl)acetamide (**3a**) was obtained in 40% yield (see the Supporting Information for details). In this reaction, $ClCF_2COONa$ underwent the quadruple cleavage to release the F ion, which is a good desilylative reagent; thus, C3-unsubstituted *N*-(quinolin-2-yl)acetamide (**3a**) was procured. Inspired by this result, we evaluated a series of metal catalysts (see Table S1 of the Supporting Information). However, frequently used transition metal catalysts for activating alkynes, such as Ag_2O, Ag_2CO_3, and $Pd(OAc)_2$, were proven to be invalid in this transformation.[12] Subsequently, a range of bases and halodifluoroalkylating reagents were screened to examine the effect on this reaction, and it turned out that $NaHCO_3$ and $ClCF_2COONa$ were the best choice to deliver the desired product **3a** in 70% yield (see Tables S2 and S3 of the Supporting Information). Of note, ligand screening indicated that it was unserviceable for increasing the yield of compound **3a** (see entries 9 and 10 in Table S2 of the Supporting Information). Nevertheless, increasing the amount of base and lowering the temperature are unfavorable for the reaction (see entries 11−14 in Table S2 of the Supporting Information). Control experiments indicated that Cu salt and base were all indispensable for this transformation (see entries 15 and 16 in Table S2 of the Supporting Information).

With the optimized conditions in hand, we next investigated the substrate generality of this transformation (Scheme 2). When the current protocol was scaled up to 10 times, compound **3a** could be readily obtained in 64%. Then, a wide range of easily accessible 2-((trimethylsilyl)ethynyl)anilines (**1a**−**1q**) could react smoothly with $ClCF_2COONa$ (**2**) to provide the desired products *N*-(quinolin-2-yl)amides (**3a**−**3q**) in good yields using CH_3CN as the solvent and perform the Ritter reactions. The structure of compound **3a** was unambiguously confirmed by X-ray single-crystal analysis. As shown in Scheme 2, anilines bearing electron-donating groups were amenable to this cyclization reaction, enabling the formation of compounds **3b** and **3c** in modest yields. Moreover, a variety of halo-substituted anilines were also proven to be good candidates in this transformation, affording the desired products **3d**−**3i** in 50−82% yields. The steric

Scheme 2. Scope for the Synthesis of *N*-(Quinolin-2-yl)amides with Desiliconization[c]



[a]Reaction conditions: 120 °C and CH_3CN (2 mL). [b]Reaction conditions: $CH_3(CH_2)_3CN$ (2 mL). [c]Reaction conditions: **1a**−**1r** (0.2 mmol), **2** (0.3 mmol), $CuCl_2$ (15 mol %), $NaHCO_3$ (2 equiv), CH_3CN (2 mL), 100 °C, N_2, and 16 h.

hindrance of anilines had no dramatic effect on this cyclization reaction, because *ortho*-, *meta*-, and *para*-substituted anilines (**1d**−**1f**) were well-compatible in this reaction. When the current protocol was scaled up to 10 times, compound **3f** could be readily obtained in 60%. The submission of disubstituted 2-((trimethylsilyl)ethynyl)anilines to this reaction was also successful, in which expected compounds **3j** and **3k** were achieved in 78 and 55% yields, respectively. In this reaction, a series of 2-((trimethylsilyl)ethynyl)anilines containing electron-withdrawing groups were also detected, and the target products **3l**−**3p** were obtained in moderate to good yields. Gladly, heterocyclic 2-((trimethylsilyl)ethynyl)aniline (**1q**) was also engaged in the generation of quinolines via this cyclization reaction, leading to the formation of the expected product **3q** in 30% yield. Of note, in comparison to CH_3CN, valeronitrile also performs the Ritter reactions, giving rise to the production of compound **3r** in 50% yield.

Encouraged by the success for the assembly of *N*-(quinolin-2-yl)amides without substituents on the C3 position via this cyclization of $ClCF_2COONa$ with 2-((trimethylsilyl)ethynyl)-anilines, we were inquisitive whether the trimethylsilyl (TMS) substituent on ethynyl could be replaced by an aryl or alkyl group for this reaction. If so, the *N*-(quinolin-2-yl)amides with various substituents on the C3 position would be achieved in a single-vessel synthesis. To verify our hypothesis, the treatment of 2-(phenylethynyl)aniline (**1s**) and $ClCF_2COONa$ (**2**) was carried out under the identified conditions. To our delight, the corresponding product *N*-(3-phenylquinolin-2-yl)acetamide (**3s**) was obtained in 65% yield when we investigated a range of bases and Cu salts (see Table S4 of the Supporting Information). When the current protocol was scaled up to 10 times, compound **3s** could be readily obtained in 56% yield.

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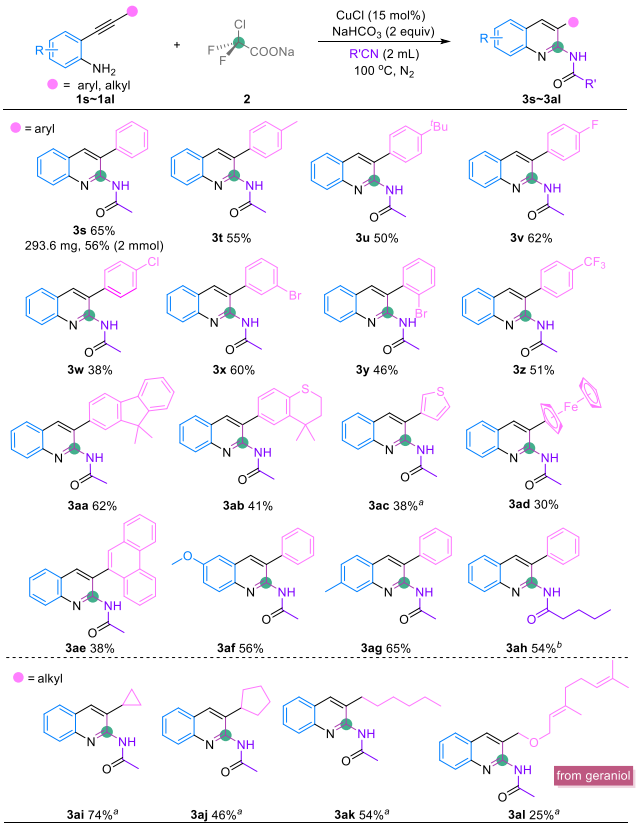
Having optimized the reaction conditions, the generality of this cyclization reaction to forge 3-substituted *N*-(quinolin-2-yl)amides was then evaluated, which was summarized in Scheme 3. Electron-donating and electron-withdrawing group

Scheme 3. Scope for the Synthesis of *N*-(Quinolin-2-yl)amides with Substituents on C3[c]



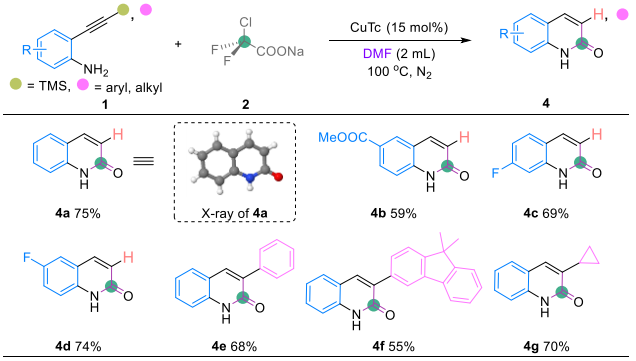
[a]Reaction conditions: $CuCl_2$ (15 mol %), Na_2CO_3 (2 equiv), and CH_3CN (2 mL). [b]Reaction conditions: $CH_3(CH_2)_3CN$ (2 mL). [c]Reaction conditions: **1s−1al** (0.2 mmol), **2** (0.3 mmol), CuCl (15 mol %), $NaHCO_3$ (2 equiv), CH_3CN (2 mL), 100 °C, N_2, and 16 h.

substitutive aromatic rings were all amenable to this cyclization reaction, providing compounds **3s−3z** in modest yields. Heterocycle and fused ring-containing 2-alkynylanilines could work smoothly in this transformation as well, delivering the expected compounds **3aa−3ae** in 30−62% yields. Trisubstituted anilines **1af** and **1ag** were also good candidates in this reaction, in which the targeted products **3af** and **3ag** were achieved in 56 and 65% yields, respectively. When the current protocol can be extended to valeronitrile, compound **3ah** could be acquired in 54% yield.

After that, we attempt to prepare 3-alkyl *N*-(quinolin-2-yl)amides to further enlarge the substrate scope of this cyclization reaction. Delightfully, a battery of functionalizated 3-alkyl *N*-(quinolin-2-yl)amides was achieved in 25−74% yields with CH_3CN as the solvent and performs the Ritter reactions, which was summarized in the bottom of Scheme 3. Of note, the current method could be applied for late-stage functionalization of geraniol, albeit with a low yield of compound **3al**.

When we use mixed solvent (CH_3CN/DMF = 1:3), quinolin-2(1*H*)-one (**4a**) was obtained in 45% yield (see Table S6 of the Supporting Information). Gratifyingly, when we increased the amount of $ClCF_2COONa$ to 2 equiv and replaced CuCl with CuTc in the absence of base, compound **4a** could be isolated in 75% yield. Then, a series of difluorocarbene reagents **2a−2h** were also inspected (see Table S7 of the Supporting Information). Among these, $ClCF_2COONa$ demonstrated not only optimal efficiency but was also the only one that facilitated the reaction work smoothly without the necessity for an additional base. Next, we tested various 2-((trimethylsilyl/aryl/alkyl)ethynyl)anilines (**1**) in this cyclization reaction, finishing the targeted products **4a−4g** in moderate to good yields (Scheme 4). The structure of compound **4a** was undoubtedly confirmed by X-ray single-crystal analysis.[13]

Scheme 4. Scope for the Synthesis of Quinolin-2(1*H*)-ones[a]



[a]Reaction conditions: **1** (0.2 mmol), **2** (0.4 mmol), CuTc (15 mol %), CH_3CN (2 mL), 100 °C, N_2, and 16 h.

As the follow-up investigation, the scalability of this cyclization reaction to access *N*-(quinolin-2-yl)amides was also inspected (see Table S9 of the Supporting Information). Further transformations of 2-((trimethylsilyl)ethynyl)aniline (**1a**) were executed as well (see Table S9 of the Supporting Information). The hydrolysis of compounds **3a** and **3f** with $NH_2NH_2{\cdot}H_2O$ could expediently afford compounds **5** and **6** in excellent yield via diacylation (see Table S9 of the Supporting Information).[14] In addition, compound **7** was readily obtained via C−H/N−H oxidative cross-coupling/cyclization of compound **5** and ethynylbenzene.[15] Compound **5** could readily react with isothiocyanate to finish compound **8** in 75% yield.[16] The synthetic utility of this approach was also showcased by the assembly of compounds **9** and **10** via metal-free annulation of 2-aminoquinoline (**5**) and *p*-xylene.[17]

We then turned our attention to shed light on the mechanism of this cyclization reaction. Radical trapping experiments were investigated firstly (see Table S10 of the Supporting Information). When 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO), 2,6-di-*tert*-butyl-4-methylphenol (BHT) and ethene-1,1-diyldibenzene served as radical scavengers under the standard conditions, the target compound **3a** is still obtained with a good yield (see Table S10a of the Supporting Information), indicating that a radical-type process might not be involved in this cyclization of $ClCF_2COONa$. Subsequently, a suite of isotope-labeling experiments was executed to gain insight into the H source in this reaction. When compound **1a** and $ClCF_2COONa$ (**2**) were exposed to CD_3CN, product **11** was obtained in 73% yield (see Table S10b of the Supporting Information), which proved that acetonitrile did not provide the H source. Next, we used

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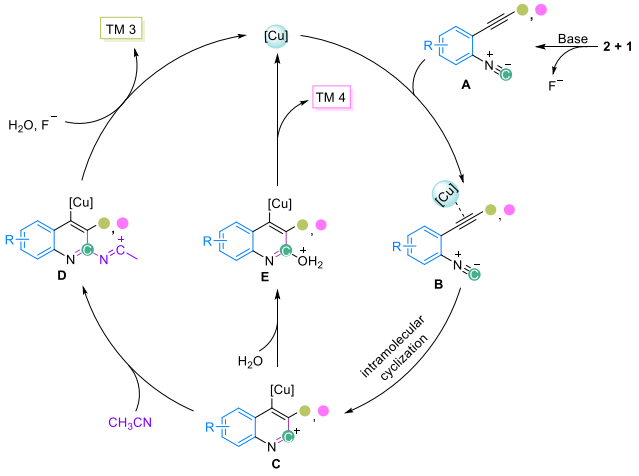
CD_3CN as the solvent and added 10 equiv of D_2O to obtain *N*-(quinolin-2-yl)acetamide compound **12** with deuterium incorporated on C3 and C4 positions (see Table S10c of the Supporting Information). This result indicates that H_2O in the solvent may be the H source of this cycloaddition reaction. When isocyanide **13** was submitted to the reaction, the desired product **3a** was obtained in 20% yield (see Table S10d of the Supporting Information), which might require desiliconization with $ClCF_2COONa$. Subsequently, we conducted a control experiment, which proved that $ClCF_2COONa$ could desiliconize because it underwent quadruple cleavage to release the F ion (see parts e and f of Table S10 of the Supporting Information). Next, on the basis of Table S10d of the Supporting Information, with the addition of $ClCF_2COONa$, compound **3a** can be obtained with a yield of 75% (see Table S10g of the Supporting Information), which manifested that isocyanide might be the key intermediate for this cyclization reaction. To clarify the origination of the carbonyl oxygen atom of the desired product **4a**, an isotope-labeling experiment was carried out. When the reaction was conducted with 40 equiv of $H_2{}^{18}O$ underlying the identified conditions, 45% of ^{18}O-labeled product **4a** was detected by gas chromatography−mass spectrometry (GC−MS) (see Table S10f of the Supporting Information), which indicated that oxygen of the carbonyl group should come from the water.

On the basis of the above experimental results and previous literature,[12c,18] a possible reaction mechanism for the cyclization reaction of 2-alkynylanilines and $ClCF_2COONa$ is depicted in Scheme 5. First, difluorocarbene is formed via dechlorination and decarboxylation of $ClCF_2COONa$. *In situ* generated difluorocarbene is immediately captured by 2-alkynylanilines (**1**) with the assistance of a base to afford isocyanide **A**. Simultaneously, isocyanide **A** reacts with Cu(II) species to give the formation of Cu species **B**, which further goes through intramolecular cyclization to render Cu complex **C**. Next, Cu complex **C** was attacked by nucleophiles (such as CH_3CN and H_2O) to obtain intermediates **D** and **E**, respectively, which subsequently undergo protonation to furnish the desired product **3** or **4**, regenerating the Cu species for the next catalytic cycle (Scheme 5).

Scheme 5. Proposed Reaction Mechanism for This Cyclization Reaction



In conclusion, we have disclosed a novel solvent-dependent divergent cyclization of 2-alkynylanilines and $ClCF_2COONa$ to streamline assembly of *N*-(quinolin-2-yl)amides and quinolin-2(1*H*)-ones. When DMF was employed as the reaction medium, a sequence of quinolin-2(1*H*)-ones was achieved in decent yields. When the reaction proceeded in nitriles, a vast array of *N*-(quinolin-2-yl)amides was gained with good functional group compatibility using nitrile as the solvent and performs the Ritter reactions in this reaction. The current protocol took advantage of $ClCF_2COONa$ as a promising C1 synthon, which also represents the first example for utilization of $ClCF_2COONa$ as a novel desiliconization reagent. In analogy of the reaction, the current protocol proceeded via transformation of *in situ* generated isocyanide, which was attacked by nucleophilic solvents, followed by intramolecular cyclization. Further applications of this unique tandem reaction are underway in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.1c01484.

General experimental procedures and spectroscopic data for the corresponding products (PDF)

Accession Codes

CCDC 1962438 and 2035896 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Ma, X.; Song, Q. Recent progress on selective deconstructive modes of halodifluoromethyl and trifluoromethyl-containing reagents. *Chem. Soc. Rev.* **2020**, *49*, 9197−9219. (b) Su, J.; Ma, X.; Ou, Z.; Song, Q. Deconstructive Functionalizations of Unstrained Carbon-Nitrogen Cleavage Enabled by Difluorocarbene. *ACS Cent. Sci.* **2020**, *6*, 1819−1826. (c) Yu, C.; Ma, X.; Song, Q. Palladium-catalyzed cyanation of aryl halides with in situ generated CN- from $ClCF_2H$ and $NaNH_2$. *Org. Chem. Front.* **2020**, *7*, 2950−2954. (d) Ma, X.; Mai, S.; Zhou, Y.; Cheng, G.-J.; Song, Q. Dual role of ethyl bromodifluoroacetate in the formation of fluorine-containing heteroaromatic compounds. *Chem. Commun.* **2018**, *54*, 8960−8963. (e) Kuang, Z.; Chen, H.; Qiu, J.; Ou, Z.; Lan, Y.; Song, Q. Cu-Catalyzed Regio- and Stereodivergent Chemoselective sp^2/sp^3 1,3- and 1,4-Diborylations of CF_3-Containing 1,3-Enynes. *Chem.* **2020**, *6*, 2347−2363. (f) Zhang, G.; Shi, Q.; Hou, M.; Yang, K.; Wang, S.; Wang, S.; Li, W.; Li, C.; Qiu, J.; Xu, H.; Zhou, L.; Wang, C.; Li, S.-J.; Lan, Y.; Song, Q. Atom Recombination of Difluorocarbene Enables 3-Fluorinated Oxindoles from 2-Aminoarylketones. *CCS Chem.* **2021**, *3*, 1613−1621. (g) Ma, X.; Huang, H.; Su, J.; Song, Z.; Nakano, T.; Song, Q. Synthesis of CF_2H-containing Oxime Ethers Derivatives from $ClCF_2H$, tert-Butyl Nitrile and Indoles. *Chin. J. Chem.* **2020**, *38*, 63−68. (h) Xu, J.; Kuang, Z.; Song, Q. Expedient Chemoselective and Catalyst-free Synthesis of 3,3-Difluorochroman-4-ones from *o*-hydroxyarylenaminones and Selectfluor. *Chin. Chem. Lett.* **2018**, *29*, 963−966. (i) Xu, J.; Song, Q. Radical Promoted Difunctionalization of Unsaturated Carbon-Carbon Bonds in the Presence of Dioxygen. *Youji Huaxue* **2016**, *36*, 1151−1162.

(2) (a) Gao, X.; Cheng, R.; Xiao, Y.-L.; Wan, X.-L.; Zhang, X. Copper-Catalyzed Highly Enantioselective Difluoroalkylation of Secondary Propargyl Sulfonates with Difluoroenoxysilanes. *Chem.* **2019**, *5*, 2987−2999. (b) Fu, X.-P.; Xue, X.-S.; Zhang, X.-Y.; Xiao, Y.-L.; Zhang, S.; Guo, Y.-L.; Leng, X.; Houk, K. N.; Zhang, X. Controllable catalytic difluorocarbene transfer enables access to diversified fluoroalkylated arenes. *Nat. Chem.* **2019**, *11*, 948−956. (c) Zhou, M.; Zhao, H.-Y.; Zhang, S.; Zhang, Y.; Zhang, X. Nickel-Catalyzed Four-Component Carbocarbonylation of Alkenes under 1 atm of CO. *J. Am. Chem. Soc.* **2020**, *142*, 18191−18199. (d) Wang, Q.; Ni, C.; Hu, M.; Xie, Q.; Liu, Q.; Pan, S.; Hu, J. From C_1 to C_3: Copper-Catalyzed gem-Bis(trifluoromethyl)olefination of α-Diazo Esters with $TMSCF_3$. *Angew. Chem., Int. Ed.* **2020**, *59*, 8507−8511. (e) Liang, H.; Liu, R.; Zhou, M.; Fu, Y.; Ni, C.; Hu, J. Difluorocarbene-Triggered Cyclization: Synthesis of (Hetero)arene-Fused 2,2-Difluoro-2,3-dihydrothiophenes. *Org. Lett.* **2020**, *22*, 7047−7051. (f) Luo, H.; Zhao, Y.; Wang, D.; Wang, M.; Shi, Z. Stereoselective fluoroarylation of 1,1-difluoroallenes enabled by palladium catalysis. *Green Synth. Catal.* **2020**, *1*, 134−142.

(3) (a) Zhang, P.; Chen, W.; Liu, M.; Wu, H. Synthesis of 3-HCF_2S-Chromones through Tandem Oxa-Michael Addition and Oxidative Difluoromethylthiolation. *Org. Lett.* **2019**, *21*, 9326−9329. (b) Wang, Y.; Zhou, Y.; Song, Q. [3 + 1+1] type cyclization of $ClCF_2COONa$ for the assembly of imidazoles and tetrazoles via in situ generated isocyanides. *Chem. Commun.* **2020**, *56*, 6106−6109. (c) Ma, X.; Zhou, Y.; Song, Q. Synthesis of β-Aminoenones via Cross-Coupling of *In-Situ*-Generated Isocyanides with 1,3-Dicarbonyl Compounds. *Org. Lett.* **2018**, *20*, 4777−4781. (d) Feng, W.; Zhang, X.-G. Organophosphine-free copper-catalyzed isothiocyanation of amines with sodium bromodifluoroacetate and sulfur. *Chem. Commun.* **2019**, *55*, 1144−1147.

(4) (a) Bosiak, M. J. A Convenient Synthesis of 2-Arylbenzo[b]-furans from Aryl Halides and 2-Halophenols by Catalytic One-Pot Cascade Method. *ACS Catal.* **2016**, *6*, 2429−2434. (b) Sun, S.; Zhu, C.; Song, D.; Li, F.; Hu, A. Preparation of conjugated polyphenylenes from maleimide-based enediynes through thermal-triggered Bergman cyclization polymerization. *Polym. Chem.* **2014**, *5*, 1241−1247. (c) Keller, J. M.; Schanze, K. S. Synthesis of Monodisperse Platinum Acetylide Oligomers End-Capped with Naphthalene Diimide Units. *Organometallics* **2009**, *28*, 4210−4216.

(5) (a) Tomioka, T.; Takahashi, Y.; Maejima, T. One-pot synthesis of 2-aminoquinoline-based alkaloids from acetonitrile. *Org. Biomol. Chem.* **2012**, *10*, 5113−5118. (b) Xiong, M.; Hu, H.; Hu, X.; Liu, Y. Copper-Catalyzed Borylative Cyclization of *o*-(Cyano)phenyl Propargyl Carbonates: Synthesis of Functionalized 1-Naphthylamines. *Org. Lett.* **2018**, *20*, 3661−3665. (c) Tong, S.; Li, K.; Ouyang, X.; Song, R.; Li, J. Recent advances in the radical-mediated decyanative alkylation of cyano(hetero)arene. *Green Synth. Catal.* **2021**, *2*, 145−155. (d) Wang, K.; Jiang, H.; Tong, M.; Xiao, Y.; Li, H.; Zhang, F. Primary amine-functionalized mesoporous phenolic resin as an effective and stable solid base catalyst for Knoevenagel reactions in water. *Green Synth. Catal.* **2020**, *1*, 79−82.

(6) (a) Fuchs, A. V.; Thurecht, K. J. Stability of Trithiocarbonate RAFT Agents Containing Both a Cyano and a Carboxylic Acid Functional Group. *ACS Macro Lett.* **2017**, *6*, 287−291. (b) Bolm, C.; Mocci, R.; Schumacher, C.; Turberg, M.; Puccetti, F.; Hernández, J. G. Mechanochemical Activation of Iron Cyano Complexes: A Prebiotic Impact Scenario for the Synthesis of α-Amino Acid Derivatives. *Angew. Chem., Int. Ed.* **2018**, *57*, 2423−2426.

(7) (a) Chen, J.; Song, Q.; Wang, C.; Xi, Z. Novel cycloaddition of nitriles with monolithio- and dilithiobutadienes. *J. Am. Chem. Soc.* **2002**, *124*, 6238−6239. (b) Concellón, J. M.; Riego, E.; Suárez, J. R.; García-Granda, S.; Díaz, M. R. Synthesis of Enantiopure Imidazolines through a Ritter Reaction of 2-(1-Aminoalkyl)aziridines with Nitriles. *Org. Lett.* **2004**, *6*, 4499−4501.

(8) Niedermann, K.; Früh, N.; Vinogradova, E.; Wiehn, M. S.; Moreno, A.; Togni, A. A Ritter-Type Reaction: Direct Electrophilic Trifluoromethylation at Nitrogen Atoms Using Hypervalent Iodine Reagents. *Angew. Chem., Int. Ed.* **2011**, *50*, 1059−1063.

(9) Hari, D. P.; Hering, T.; König, B. The Photoredox-Catalyzed Meerwein Addition Reaction: Intermolecular Amino-Arylation of Alkenes. *Angew. Chem., Int. Ed.* **2014**, *53*, 725−728.

(10) (a) Biddle, M. M.; Lin, M.; Scheidt, K. A. Catalytic Enantioselective Synthesis of Flavanones and Chromanones. *J. Am. Chem. Soc.* **2007**, *129*, 3830−3831. (b) Bowroju, S. K.; Mainali, N.; Ayyadevara, S.; Penthala, N. R.; Krishnamachari, S.; Kakraba, S.; Reis, R. J. S.; Crooks, P. A. Synthesis of Novel Hybrid 8-Hydroxy Quinoline-Indole Derivatives as Inhibitors of Aβ Self-Aggregation and Metal Chelation-Induced Aβ Aggregation. *Molecules* **2020**, *25*, 3610−3628. (c) Dhiman, S.; Saini, H. K.; Nandwana, N. K.; Kumar, D.; Kumar, A. Copper-catalyzed synthesis of quinoline derivatives via tandem Knoevenagel condensation, amination and cyclization. *RSC Adv.* **2016**, *6*, 23987−23994. (d) Wang, K.; Herdtweck, E.; Dömling, A. Cyanoacetamides (IV): Versatile One-Pot Route to 2-Quinoline-3-carboxamides. *ACS Comb. Sci.* **2012**, *14*, 316−322.

(11) (a) Nicolas, L.; Angibaud, P.; Stansfield, I.; Meerpoel, L.; Reymond, S.; Cossy, J. Copper-catalysed amidation of 2-chloropyridines. *RSC Adv.* **2013**, *3*, 18787−18790. (b) Li, J.-S.; Chen, F.-X.; Shikiya, R.; Marky, L. A.; Gold, B. Molecular Recognition via Triplex Formation of Mixed Purine/Pyrimidine DNA Sequences Using OligoTRIPs. *J. Am. Chem. Soc.* **2005**, *127*, 12657−12665. (c) Park, Y.; Fei, X.; Yuan, Y.; Lee, S.; Hur, J.; Park, S. J.; Jung, J.-K.; Seo, S.-Y. Chemoselective acylation of 2-amino-8-quinolinol in the generation of C2-amides or C8-esters. *RSC Adv.* **2017**, *7*, 41955−41961. (d) Fantasia, S.; Windisch, J.; Scalone, M. Ligandless Copper-Catalyzed Coupling of Heteroaryl Bromides with Gaseous Ammonia. *Adv. Synth. Catal.* **2013**, *355*, 627−631.

https://doi.org/10.1021/acs.orglett.1c01484
Org. Lett. 2021, 23, 5599−5604

(12) (a) Fang, G.; Bi, X. Silver-catalysed reactions of alkynes: Recent advances. *Chem. Soc. Rev.* **2015**, *44*, 8124−8173. (b) Cao, S.; Ji, Q.; Li, H.; Pang, M.; Yuan, H.; Zhang, J.; Bi, X. AgN_3-Catalyzed Hydroazidation of Terminal Alkynes and Mechanistic Studies. *J. Am. Chem. Soc.* **2020**, *142*, 7083−7091. (c) Su, L.; Ren, T.; Dong, J.; Liu, L.; Xie, S.; Yuan, L.; Zhou, Y.; Yin, S.-F. Cu(I)-Catalyzed 6-*endo*-dig Cyclization of Terminal Alkynes, 2-Bromoaryl Ketones, and Amides toward 1-Naphthylamines: Applications and Photophysical Properties. *J. Am. Chem. Soc.* **2019**, *141*, 2535−2544.

(13) Ribar, B.; Janic, I.; Kalman, A.; Argay, G. 2-Hydroxyquinoline, C_9H_7NO. *Cryst. Struct. Commun.* **1977**, *6*, 677−680.

(14) Jackson, S. A.; Sahni, S.; Lee, L.; Luo, Y.; Nieduzak, T. R.; Liang, G.; Chiang, Y.; Collar, N.; Fink, D.; He, W.; Laoui, A.; Merrill, J.; Boffey, R.; Crackett, P.; Rees, B.; Wong, M.; Guilloteau, J.-P.; Mathieu, M.; Rebello, S. S. Design, synthesis and characterization of a novel class of coumarin-based inhibitors of inducible nitric oxide synthase. *Bioorg. Med. Chem.* **2005**, *13*, 2723−2739.

(15) He, C.; Hao, J.; Xu, H.; Mo, Y.; Liu, H.; Han, J.; Lei, A. Heteroaromatic imidazo[1,2-*a*]pyridines synthesis from C−H/N−H oxidative cross-coupling/cyclization. *Chem. Commun.* **2012**, *48*, 11073−11075.

(16) Li, J.-S.; Xie, X.-Y.; Yang, P.-P.; Jiang, S.; Tao, L.; Li, Z.-W.; Lu, C.-H.; Liu, W.-D. Electrochemical Synthesis of 1,2,4-Thiadiazoles through Intermolecular Dehydrogenative S-N Coupling. *Adv. Synth. Catal.* **2020**, *362*, 771−775.

(17) Manna, S.; Matcha, K.; Antonchick, A. P. Metal-Free Annulation of Arenes with 2-Aminopyridine Derivatives: The Methyl Group as a Traceless Non-Chelating Directing Group. *Angew. Chem., Int. Ed.* **2014**, *53*, 8163−8166.

(18) Ling, F.; Song, D.; Chen, L.; Liu, T.; Yu, M.; Ma, Y.; Xiao, L.; Xu, M.; Zhong, W. Syntheses of N-Alkyl 2-Arylindoles from Saturated Ketones and 2-Arylethynylanilines via Cu-Catalyzed Sequential Dehydrogenation/Aza-Michael Addition/Annulation Cascade. *J. Org. Chem.* **2020**, *85*, 3224−3233.

https://doi.org/10.1021/acs.orglett.1c01484
Org. Lett. 2021, 23, 5599−5604