# Copper-Catalyzed N-F Bond Activation for Uniform Intramolecular C-H Amination to Pyrrolidines and Piperidines

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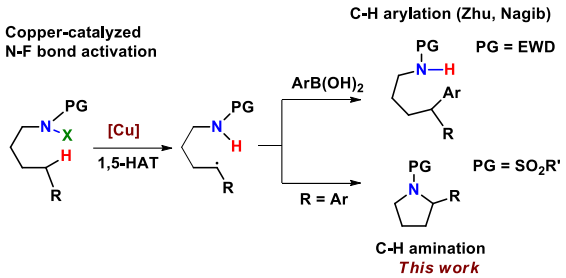
Dedication ((optional))

**Abstract:** The dual function of the N-F bond as an effective oxidant and subsequent nitrogen source in intramolecular aliphatic C-H functionalization reactions is explored. Copper catalysis is demonstrated to exercise full regio- and chemoselectivity control, which opens new synthetic venues to nitrogenated heterocycles with predictable ring size. For the first time, a uniform catalysis manifold has been identified for the construction of both pyrrolidine and piperidine cores. The individual steps of this new copper oxidation catalysis are elucidated by control experiments and computational studies, clarifying the singularity of the N-F function and characterizing the catalytic cycle to be based on a copper(I/II) manifold.

The chemistry of *N*-halogenated amines is a particularly attractive tool[1] for streamlining the oxidative halofunctionalization of hydrocarbons. In the context of an intramolecular reaction, the subsequent cyclization may be pursued,[2] which under conditions of catalysis results in a sustainable one-pot formation of aminated aliphatic heterocycles.[3,4,5] In these reactions, *N*-halogenated amides give rise to the corresponding amidyl radicals,[6] which initiate the hydrocarbon functionalization within 1,n hydrogen atom transfer (HAT) reactions. Contrarily to its heavier halogen counterparts, the related fluorine-containing substrates have N-F bonds with profoundly lower tendency toward homolytic bond cleavage. Copper catalysts have shown useful synthetic propensity in activating N-F bonds.[7] However, while Cu(I) catalysis tends to promote single electron transfers,[8] fluorinated bonds are usually activated via concerted pathways.[9] Recently, powerful copper-based redox catalysis has been explored for the activation and synthetic utility of the N-F bond by Zhu[10a] and Nagib,[10b] who explored the use of preformed N-F bonds to initiate position-selective C-H functionalization reactions from amidyl radical intermediates (Scheme 1). Notably, the alternative formation of heterocycles through pathways involving N-F and subsequent C-H bond activation, has not been explored thus far. We have previously developed copper-based catalytic systems toward C-halide (Cl, Br) bond activation via radical pathways, in the so-called atom transfer radical (ATR) reactions,[11] including the successful cyclization to cycloalkanes. We herein report on a well-defined copper catalyst enabling uniquely uniform conditions for both pyrrolidine and piperidine formation and provide experimental and computational studies that support an unprecedented copper(I/II) redox cycle.




**Scheme 1.** C-H functionalization by copper-catalyzed *N*-F bond activation.

N-alkyl-N-fluorosulfonamide **1a** (Table 1) was prepared using N-fluorobis(benzenesulfonyl)imide (NFSI) as the most convenient F-transfer reagent and was employed as the initial substrate.[12] The structure of **1a** was unambiguously assigned by X-ray analysis.[13] The N-F bond length of 1.434(9) Å compares well with that found in other common electrophilic fluorinating agents[14] and indicates that it should exercise efficient oxidative behavior. Exploratory results from Table 1 confirm this hypothesis for several copper catalysts varying from simple salts to more elaborated complexes of formula $Tp^xCu(NCMe)$ ($Tp^x$ = hydrotrispyrazolylborate ligand).[15] A blank experiment established that essentially none of the cyclization product is generated in the absence of the copper complex (entry 1). Pyrrolidine **2a** was obtained with several cationic or neutral, in situ generated or previously isolated copper catalysts, in the +1 or +2 oxidation state (entries 2-6). The best results were obtained with the Cu(I) complexes Tp*Cu(NCMe) and $Tp^{iPr2}Cu(NCMe)$ (Tp* = hydrotris(3,5-dimethyl-1-pyrazolyl)borate; $Tp^{iPr2}$ = hydrotris(3,5-diisopropyl-1-pyrazolyl)borate), that yielded quantitative conversions into the targeted product (entries 7-8). It is possible to lower the catalyst loading even to 0.1 mol%

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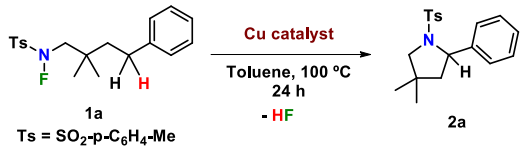
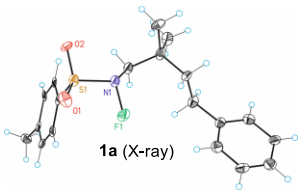
without an important loss of performance (entry 9, no further reaction after 24 h). The reaction proceeds less efficiently at 25 °C (entry 10), and within shorter reaction time (8 h, entry 11). The use of other metal-based catalysts containing Ag, Au, Ni, Fe or Ru centers were unsuccessful.[16]

The successful identification of suitable reaction conditions for formation of pyrrolidine **2a** represents a notable new entry into heterocycle formation comprising cyclization of *N*-fluorinated amine precursors **1a-q** (Scheme 2). After the above screening, $Tp^{iPr2}Cu(NCMe)$ was chosen as the catalyst for exploration of the substrate scope, since this complex is more stable than the Tp* analog toward oxidation with adventitious air. A total of 17 pyrrolidines were obtained. The scope includes alternative substitution pattern at nitrogen (**2b**,**c**) and different electronic substitution at the arene core (**2d-i**), which even tolerates potential steric impediment through 2-substitution as demonstrated with **2h** (99%). Backbone modification has been studied (**2j**,**l**, 47-87%), and even for a non-substituted alkyl chain

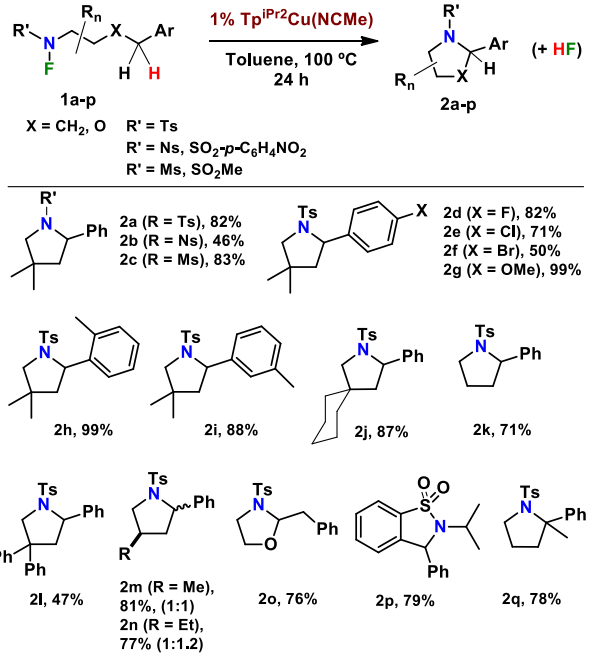
**Table 1.** Copper-Catalyzed Intramolecular N-F activation and C-H Amination: Catalyst Screening and Optimization.[a]




| Entry | Catalyst | % Yield **2a** [b] |
|---|---|---|
| 1 | --- | 0 |
| 2 | $CuCl_2$/TPMA[c] | 83 |
| 3 | CuI/TPMA[c] | 90 |
| 4 | $Tp^{Br3}Cu(NCMe)$ | 60 |
| 5 | $Tp^{*,Br}Cu(NCMe)$ | 74 |
| 6 | $Tp^{iPr2}CuCl$ | 85 |
| 7 | $Tp^{*}Cu(NCMe)$ | 99 |
| 8 | $Tp^{iPr2}Cu(NCMe)$ | 99 |
| 9[d] | $Tp^{iPr2}Cu(NCMe)$ | 93 |
| 10[e] | $Tp^{iPr2}Cu(NCMe)$ | traces |
| 11[f] | $Tp^{iPr2}Cu(NCMe)$ | 62 |
| 12[g] | $Tp^{iPr2}Cu(NCMe)$ | 99 |

[a]See SI for full details. 0.1 mmol of **1a** employed, 1% catalyst loading. [b] Yields were determined by $^1$H NMR analysis versus diphenylmethane as internal standard. [c] TPMA = tris(2-pyridylmethyl)amine. [d]0.1 mol% of catalyst employed. [e]Temperature = 25 °C. [f]8 h of reaction time. [g]Acetonitrile as solvent at 80 °C




**Scheme 2.** Scope of the Cu-catalyzed pyrrolidine synthesis. Yields of purified product (average of two experiments).

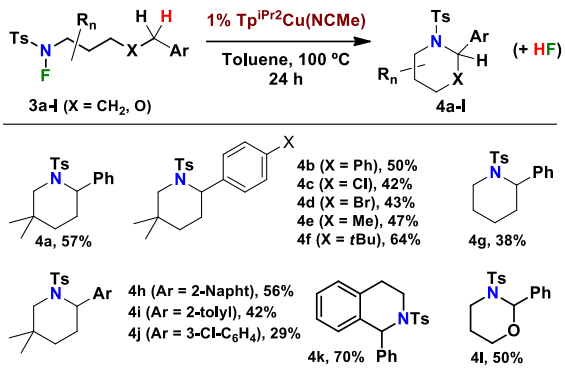
in the **1k** precursor, formation of **2k** is straightforward (71%). As expected for a radical reaction, acyclic diasterocontrol is not possible leading to diastereomeric products **2m** (d.r. = 1:1) and **2n** (d.r. = 1:1.2). The reaction can be extended to the α-amination of an ether to provide heterocycle **2o**. In addition, dioxoisothiazole derivative **2p** is also compatible with the present cyclization conditions. Substitution at the carbon next to the aryl ring is also tolerated providing *tert*-alkyl amine **2q** in good yield. It is worth mentioning that the robustness of the protocol is underlined by a 1 gram-reaction (2.95 mmol) of the parent **1a** substrate, which provides **2a** in 79% isolated yield. Related substrates other than benzylic positions are unreactive under the present conditions.[16]

As to another relevant aspect of our system, the more challenging piperidine formation within six-membered cyclization was also possible under the general conditions (Scheme 3). The exciting synthetic possibilities include the successful examples **4a-j** with and without backbone substitution and in a comparable scope to pyrrolidines and also the important tetrahydrosioquinoline core **4k** and the 1,3-oxazinane **4l**. This transformation has been a long-standing quest in radical-mediated C-H amination. It is well established that 1,5-HAT outperforms the required 1,6-HAT[17] and that, therefore, piperidines are notoriously difficult to generate under amidyl-radical promoted conditions. For example, related iodinated precursors only generate pyrrolidines due to a dominance of the 1,5-HAT.[4a] Although uniform reaction conditions to be applicable to both pyrrolidine and piperidine formation are in high demand, there has been no general solution to this problem, except recent exploration of electrochemistry.[18]

We have also investigated the intramolecular competition between five- and six-membered ring formation (Scheme 4). For substrate **1r** with two different benzylic reaction sites, only

pyrrolidine formation to **2s** was observed. Even for substrate **1s** with a statistically increased possibility for piperidine formation, again only the five-membered ring product **2r** was obtained.

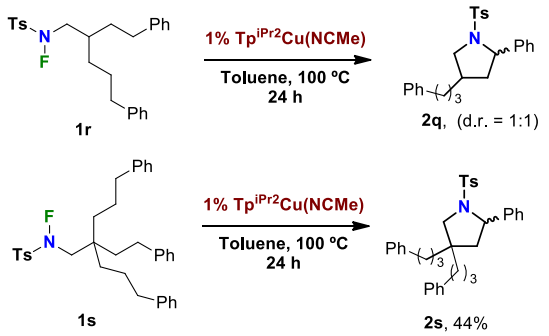
A number of experiments have been carried out with the aim of collecting mechanistic information. Experimentation under the conditions from Table 1 reveals that the presence of water or air




**Scheme 3.** Scope of the Cu-catalyzed piperidine synthesis. Yields of purified product (average of two experiments).

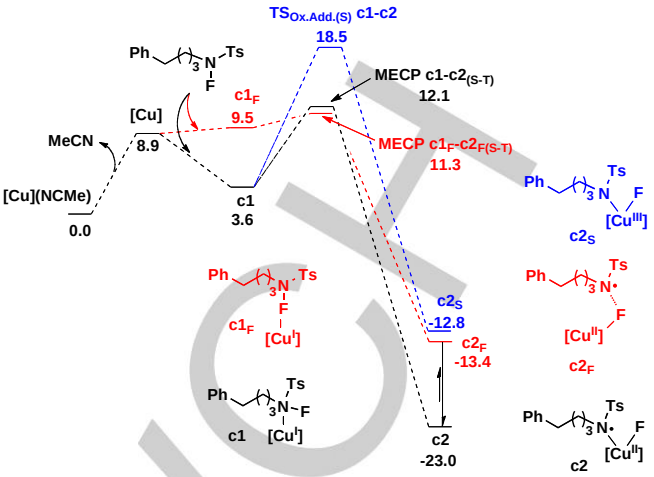
induced lower yields. EPR studies with a mixture of the catalyst Tp$^{iPr2}$Cu(NCMe) and substrate **1k** showed the appearance of a typical resonance for Cu(II) at 3260 Gauss, both at room temperature and 77 K[12, 19] Mass spectrometric studies confirmed the presence of a species of composition [Tp$^{iPr2}$CuF(NCMe)]. Additional control experiments used partially deuterated substrates.[12] Individual reaction rates for substrates **1k** and **1k-d$_2$** with fully deuterated benzylic position showed a relative rate acceleration for compound **1k**, which corresponds to a kinetic isotope effect of 1.7 at 80 ºC. This KIE value is consistent with C–H bond cleavage as the turnover-limiting step.[20] The kinetic data on the transformation of **1k** into **2k** at variable catalyst concentration are consistent with the reaction being first order in catalyst.[12]

The observed superiority of the ancillary Tp$^x$ ligand was further investigated for the formation of diastereomeric



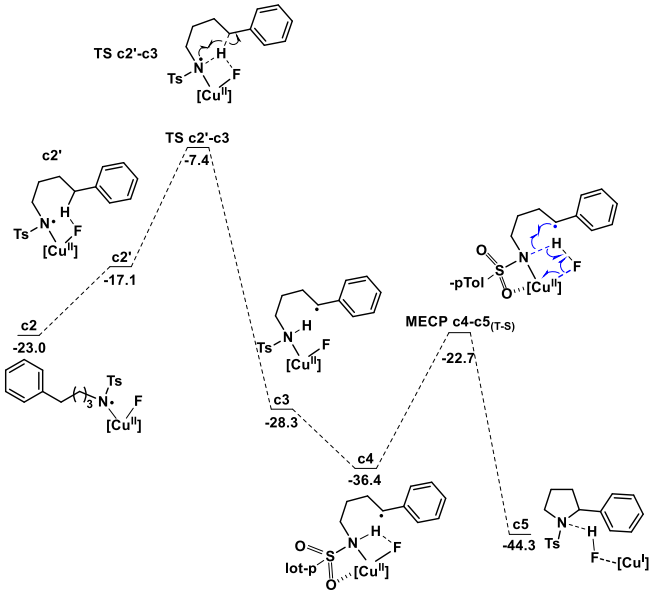

**Scheme 4.** Intramolecular competition experiment for the Cu-catalysis in favor of pyrrolidine synthesis.

pyrrolidines **2m**.[12] While Tp*Cu(NCMe) catalyst gave a 1:1 mixture, bulkier Tp$^x$ ligands such as Tp$^{MS}$ (hydrotris(3-(2,4,6-trimethylphenyl)pyrazolyl)borate)[21] or Tp$^{iPr2}$ provided just slightly higher diastereoselectivities pointing toward a subtle influence of the copper catalysts on the C-N bond formation step.



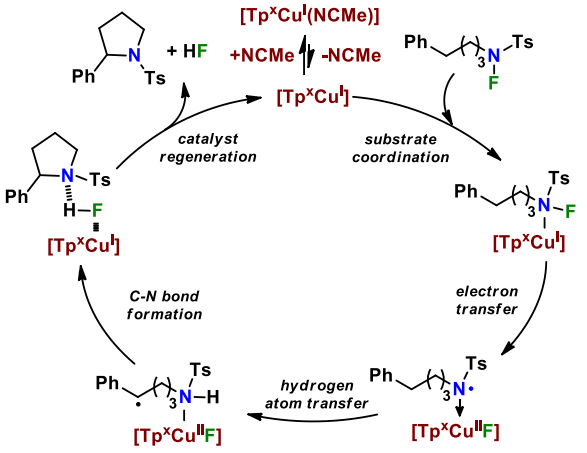

**Scheme 5.** Free energy profile of the N-F activation step of reaction with **1k** as the substrate. Energies in kcal/mol. ([Cu] = Tp*Cu).

DFT calculations were carried out to further analyze the reaction mechanism. All the structures were optimized using the B3LYP-D3 functional,[22] in toluene solution, energies being refined with triple-ζ basis set plus polarization and diffusion shells. All reported energies are free energies. A data set of all computed structures is available in the ioChem-BD repository.[23] Compound **1k** was chosen as the model substrate together with Tp*Cu(NCMe) as the catalyst because of the more limited conformational flexibility and the similar experimental behavior with the optimal catalyst Tp$^{iPr2}$Cu(NCMe) (Table 1, entries 7 and 8). The reaction starts with the coordination of **1k** to the vacant copper site generated from acetonitrile ligand release (Scheme 5). The substrate can be coordinated *via* the nitrogen (**c1**) or the fluorine atom (**c1$_F$**). Single electron transfers from the Cu(I) center to the N-F σ* orbital, either from **c1** (black path) or from **c1$_F$** (red path), results in the cleavage of the N-F bond together with the formation of a new Cu-F bond in intermediate **c2**, which contains a nitrogen centered radical coordinated to a Cu(II) center. These reactions involve a change from singlet to triplet spin state, and are thus characterized by minimum energy crossing points (MECP) instead of transition states.[24] The two processes from either **c1** or **c1$_F$** have similar low barriers of 12.1 kcal/mol and 11.3 kcal/mol, and they are likely to coexist. In contrast, the oxidative addition pathway to yield the Cu(III) intermediate **c2$_S$** (blue path) is 6.4 kcal/mol higher in energy, and thus discarded. This is an important observation taking into account the commonly postulated copper(III) intermediates in related reactions. Results are very similar for the related mesyl-substituted systems, corroborating the experimentally observed related outcome for **2a** and **2c**.[12]




**Scheme 6.** Free energy profile of the C-H activation and cyclization steps of reaction with **1k** as the substrate. Energies in kcal/mol. ([Cu] = Tp*Cu).

Intermediate **c2** undergoes alkyl chain rotation to intermediate **c2'** resulting in fluoride interaction with one of the benzylic C-H bonds (Scheme 6). At this stage, F-assisted hydrogen atom transfer relocates the radical from the nitrogen atom to the benzylic carbon center. According to the calculated mechanism, **TS c2'-c3** is rate-determining with a barrier of 15.6




**Scheme 7.** Mechanistic proposal based on combined experimental and computational data.

kcal/mol. The transition vector in **TS c2'-c3** is localized mainly in the F-H-C moiety, and we confirmed that its relaxation irreversibly yields the protonated amide intermediate **c3**. Once the radical is located in the carbon chain in **c3**, the system undergoes a series of low-barrier rearrangements that end up in the release of the pyrrolidine product and the HF by-product from intermediate **c5**. The overall process from reactants to products is highly exergonic, by 56.5 kcal/mol. The computed mechanism confirms the experimentally observed presence of radical species in the process, reproduces the measured kinetic isotope effect, and hints at the crucial role of the fluorine substituent, as other halogens do not have the same ability to form bonds with copper and abstract protons.

It is noteworthy pointing out that the existence of a putative benzylic cation intermediate deriving from benzylic oxidation at **c4** could not be substantiated by theoretical calculations, as the reductive pathway from **c4** is energetically straightforward. There is indeed an intramolecular electron-transfer between the benzyl radical and the copper(II) centre, but it is coupled with the formation of the C-N bond, without a detectable cationic state being involved.

On the basis of all collected data, the full catalytic cycle for *N*-fluorinated substrates is depicted in Scheme 7. Within the initial N-F cleavage phase, the reaction of the copper catalyst starts with acetonitrile release and substrate N-coordination prior to N-F cleavage via a single electron transfer (SET) from Cu to the N-F bond. Radical transfer from nitrogen to the benzylic carbon by a fluorine-assisted hydrogen atom transfer (HAT) initiates the C-H functionalization phase. The generated Cu(II) intermediate yields the product by a second N-H-F shuttled SET from the benzylic radical to the copper center. In the final cyclization phase, the C-N bond and the HF byproduct are provided within tandem bond formation. Finally, combined dissociation of both product and HF regenerate the active copper(I) catalyst. At variance with Atom Transfer Radical reactions, once the halide is extruded from the substrate, the latter remains coordinated to the metal center instead of becoming a free radical, thus propelling this alternative reaction pathway.

Concerning some catalyst precursors containing Cu(II) centers in Table 1, one could propose a Cu(II)/Cu(III) scheme similar to the Cu(I)/Cu(II) mechanism we have outlined above. However, calculations clearly discard this option, since Cu(II) is unable to release one electron to the organic moiety at the initial stage of the N-F cleavage.[16] At present, this suggests that these precursors react either through the presence of small amounts of Cu(I) or through some alternative mechanism involving an active role for the chloride ligand. More detailed investigation is required to clarify if an involvement of copper(II) catalysts can pose productive pathways for N-F bond activation.

In conclusion, we have developed a catalytic system capable of promoting both N-F and C-H activation processes leading to the formation of heterocycles in moderate to high yields, which is based on a defined copper(I) precatalyst. The resulting copper(I/II) catalysis manifold allows for a rare case of uniform reaction conditions for the one-pot formation of piperidines and pyrrolidines and therefore exemplifies an advanced use of the always challenging class of fluorine derivatives toward practical synthetic applications.

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**Keywords:** amination catalysis • C-H bond activation • C-N bond formation • copper catalysis • DFT calculation

[1] a) C. Djerassi, *Chem. Rev.* **1948**, *43*, 271-317; b) S. Minakata, *Acc. Chem. Res.* **2009**, *42*, 1172–1182.

[2] a) M. E. Wolff, *Chem. Rev.* **1963**, *63*, 55-64; b) R. S. Neale, *Synthesis* **1971**, 1-15; c) L. Stella, *Angew. Chem.* **1983**, *95*, 368-380; *Angew. Chem. Int. Ed.* **1983**, *22*, 337-350.

[3] For recent transition metal based transformations: a) N. Yoshikai, A. Mieczkowski, A. Matsumoto, L. Ilies, E. Nakamura, *J. Am. Chem. Soc.* **2010**, *132*, 5568-5569; b) Y.-F. Wang, H. Chen, X. Zhu, S. Chiba, *J. Am. Chem. Soc.* **2012**, *134*, 11980-11983; c) M. Yang, B. Su, Y. Wang, K. Chen, X. Jiang, Y.-F. Zhang, X.-S. Zhang, G. Chen, Y. Cheng, Z. Cao, Q.-Y. Guo, L. Wang, Z.-J. Shi, *Nat. Commun.* **2014**, *5*, 4707; d) M. Parasram, P. Chuentragool, Y. Wang, Y. Shi, V. Gevorgyan, *J. Am. Chem. Soc.*, **2017**, *139*, 14857-14860; e) Y. Tang, Y. Qin, D. Meng, C. Li, J. Wei, M. Yang, *Chem. Sci.* **2018**, *9*, 6374-6378.

[4] For recent iodine catalyses: a) C. Martínez, K. Muñiz, *Angew. Chem*. **2015**, *127*, 8405; *Angew. Chem. Int. Ed.* **2015**, *54*, 8287-8291; b) P. Becker, T. Duhamel, C. J. Stein, M. Reiher, K. Muñiz, *Angew. Chem*. **2017**, *129*, 8117; *Angew. Chem. Int. Ed.* **2017**, *56*, 8004-8008; c) T. Duhamel, C. J. Stein, C. Martínez, M. Reiher, K. Muñiz, *ACS Catal.* **2018**, *8*, 3918-3925; d) L. M. Stateman, E. A. Wappes, K. M. Nakafuku, K. M. Edwards, D. A. Nagib, *Chem. Sci.* **2019**, *10*, 2693; e) F. Wang, S. S. Stahl, *Angew. Chem.* DOI: 10.1002/ange.201813960; *Angew. Chem. Int. Ed.* DOI: 10.1002/anie.201813960

[5] For a recent bromine catalysis: P. Becker, T. Duhamel, C. Martínez, K. Muñiz, *Angew. Chem.* **2018**, *130*, 5262-5266; Angew. Chem. Int. Ed. **2018**, *57*, 5166-5170.

[6] a) M. D. Kärkäs, *ACS Catal.* **2017**, *7*, 4999-5022; b) D. Sakic, H. Zipse, *Adv. Synth. Catal.* **2016**, *358*, 3983-3991.

[7] T. Xiong, Q. Zhang, *Chem Soc. Rev*. **2016**, *45*, 3069–3087.

[8] J. M. Muñoz-Molina, W. M. C. Sameera, E. Álvarez, F. Maseras, T. R. Belderrain, P. J. Pérez, *Inorg. Chem.* **2011**, *50*, 2458–2467.

[9] E. Clot, O. Eisenstein, N. Jasim, S. A. Macgregor, J. E. Mcgrady, R. N. Perutz, *Acc. Chem. Res.* **2011**, *44*, 333–348.

[10] a) Z. Li, Q. Wang, J. Zhu, *Angew. Chem.* **2018**, *130*, 13472-13476; *Angew. Chem. Int. Ed*. **2018**, *57*, 13288-13292; b) Z. Zhang, L. H. Stateman, D. A. Nagib, *Chem. Sci.* **2019**, *10*, 1207–1211.

[11] a) J. M. Muñoz-Molina, T. R. Belderrain, P. J. Pérez, *Eur. J. Inorg. Chem*. **2011**, 3155–3164; b) J. M. Muñoz-Molina, T. R. Belderrain, P. J. Pérez, *Inorg. Chem.* **2010**, *49*, 642–645; c) J. M. Muñoz-Molina, T. R. Belderrain, P. J. Pérez, *Macromolecules* **2010**, *43*, 3221–3227; d) J. M. Muñoz-Molina, T. R. Belderrain, P. J. Pérez, *Adv. Synth. Catal.* **2008**, *350*, 2365–2372.

[12] See Supporting Information for full description.

[13] X-ray crystallographic data for compound **1a** have been deposited with the Cambridge Crystallographic Data Centre database (http://www.ccdc.cam.ac.uk/) under code CCDC-1900264.

[14] a) D. Meyer, H. Jangra, F. Walther, H. Zipse, P. Renaud, *Nature Comm.* **2018**, *9,* 4888; b) D. S. Timofeeva, A. R. Ofial, H. Mayr, *J. Am. Chem. Soc.* **2018**, *140*, 11474-11486.

[15] C. Pettinari, R. Pettinari, F. Marchetti, *Adv. Organomet. Chem.* **2016**, *65*, 175–260.

[16] See Supporting Information for details.

[17] a) M. Nechab, S. Mondal, M. P. Bertrand, *Chem. Eur. J.* **2014**, *20*, 16034-16059; b) H. Zhang, K. Muñiz, *ACS Catal*. **2017**, *7*, 4122-4125.

[18] a) S. Herold, D. Bafaluy, K. Muñiz, *Green Chem.* **2018**, *20*, 3191-3196; b) X. Hu, G. Zhang, F. Bu, L. Nie, A. Lei, *ACS Catal.* **2018**, *8*, 9370-9375.

[19] P. S. Subramanian, E. Suresh, P. Dastidar, S. Waghmode, D. Srinivas, *Inorg. Chem.* **2001**, *40*, 4291-4301.

[20] E. M. Simmons, J. F. Hartwig, *Angew. Chem.* **2012**, *124,* 3120-3126; *Angew. Chem. Int. Ed.* **2012**, *51*, 3066–3072.

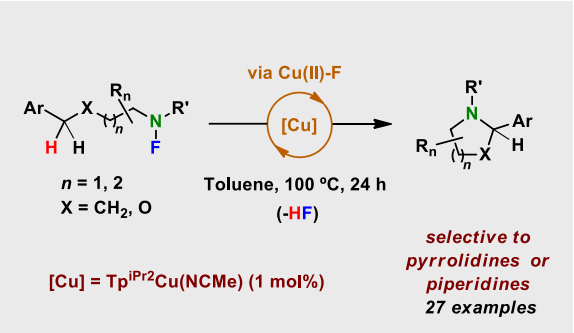
[21] a) S. Trofimenko, *Scorpionates, The Coordination Chemistry of Polypyrazolylborate Ligands*; Imperial College Press, London, **1990**; b) C. Pettinari, *Scorpionates II. Chelating Borate Ligands*, Imperial College Press, London, **2008**.

[22] a) P. J. Stephens, F. J. Devlin, C. F. Chabalowski, M. J. Frisch, *J. Phys. Chem.* **1994**, *98*, 11623–11627; b) S. Grimme, J. Antony, S. Ehrlich, H. Krieg, *J. Chem. Phys.* **2010**, *132*, 154104–154119.

[23] M. Álvarez-Moreno, C. de Graaf, N. López, F. Maseras, J. M. Poblet, C. Bo, *J. Chem. Inf. Model.* **2015**, *55*, 95–103.

[24] MECP were calculated using the software by J. N. Harvey, M. Aschi, H. Schwarz, W. Koch, *Theor. Chem. Acc.* **1998**, *99*, 95–99.

# COMMUNICATION

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**Copper-Catalyzed N-F Bond Activation for Uniform Intramolecular C-H Amination to Pyrrolidines and Piperidines**

A copper-based catalytic protocol involving C-F activation that serves for the synthesis of pyrrolidines and the more challenging piperidines has been developed, which operates through a Cu(I)/Cu(II) cycle.