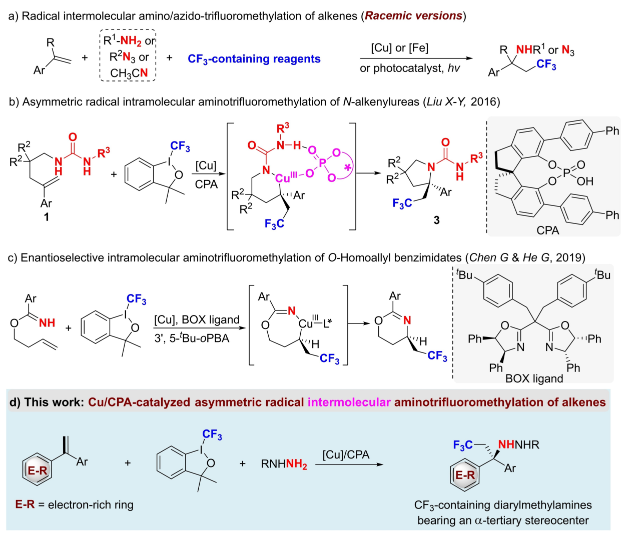
Catalytic Asymmetric Intermolecular Radical Aminotrifluoromethylation of Alkenes with Hydrazines by Cu(I)/CPA Cooperative Catalysis

Zhe Wang+,[a, b] Jiang-Tao Cheng+,[c] Zhichao Shi,[a, b] Na Wang,[c] Feng Zhan,[a, b] Sheng-Peng Jiang,[c] Jin-Shun Lin,*[a, b] Yuyang Jiang,*[b, d] and Xin-Yuan Liu*[c]

A first catalytic enantioselective intermolecular radical aminotrifluoromethylation of alkene with hydrazine and Togni's reagent by Cu(I)/CPA cooperative catalysis has been reported, accessing diversely substituted CF_3-containing enantioenriched diarylmethylamines bearing an α-tertiary stereocenter with high enantioselectivity and excellent chemoselectivity. The highly asymmetric induction of C–N bond formation between hydrazine and the carbocation intermediate was achieved by using a CPA catalyst *via* hydrogen-bonding and ion pair interaction.

Catalytic difunctionalization of unactivated alkenes, simultaneously installing two different functional groups across a double bond in a single step, is a versatile and step-economic strategy for construction of complex molecular architectures from simple and readily available alkene feedstocks.[1] In this context, transition-metal-catalyzed trifluoromethylation of alkenes has attracted considerable attention due to the unique physical and biological properties of trifluoromethyl (CF_3)-containing molecules.[2] Recently, very impressive advances have been achieved in the development of transition-metal-catalyzed radical-involved intra-[3]/intermolecular[4] aminotrifluoromethylation of alkenes with different CF_3-containing reagents, which enable highly efficient and selective incorporation of a CF_3 group and amino/azido group into alkenes, providing an efficient access to diversely CF_3-containing azaheterocycles or β-trifluoromethylamines in racemic fashion (Scheme 1a).[5] Given the increasing importance of chiral CF_3-containing molecules for the development of pharmaceuticals and agrochemicals, it would be of high value to develop enantioselective variants. Our group has recently developed the copper/chiral phosphate as a single-electron-transfer catalyst for the asymmetric radical-involved intramolecular aminotrifluoromethylation of *N*-alkenylurea with Togni's reagent[6] or CF_3SO_2Cl[7] respectively, giving facile access to densely functionalized CF_3-containing azaheterocycles bearing an α-tertiary stereocenter with excellent enantioselectivity (Scheme 1b). In 2019, Chen G & He G *et al.* succeeded in utilizing copper/BOX ligand for asymmetric intramolecular aminotrifluoromethylation of *O*-homoallyl benzimidates with Togni's reagent to afford chiral 1,3-oxazines with high enantioselectivity (Scheme 1c).[8] *Unfortunately, despite these achievements, the catalytic enantioselective radical-involved intermolecular aminotrifluoromethylation of alkenes, to the best of our knowledge, still has not been demonstrated so far.*

Although great endeavors have been devoted to diversely asymmetric variants of radical-involved intermolecular



Scheme 1. Asymmetric radical aminotrifluoromethylation of alkenes.

[a] Z. Wang,+ Z. Shi, F. Zhan, Dr. J.-S. Lin
Department of Chemistry
Tsinghua University
Beijing 100084 (P. R. China)
E-mail: lin.jinshun@sz.tsinghua.edu.cn
[b] Z. Wang,+ Z. Shi, F. Zhan, Dr. J.-S. Lin, Prof. Y. Jiang
The State Key Laboratory of Chemical Oncogenomics
Key Laboratory of Chemical Biology
Tsinghua Shenzhen International Graduate School
Shenzhen, 518055 (P. R. China)
[c] J.-T. Cheng,+ Dr. N. Wang, Dr. S.-P. Jiang, Prof. X.-Y. Liu
Shenzhen Grubbs Institute and Department of Chemistry
Guangdong Provincial Key Laboratory of Catalysis
Southern University of Science and Technology
Shenzhen 518055 (P. R. China)
E-mail: liuxy3@sustech.edu.cn
[d] Prof. Y. Jiang
School of Pharmaceutical Sciences
Tsinghua University
Beijing 100084 (P. R. China)
E-mail: jiangyy@sz.tsinghua.edu.cn
[+] These authors contributed equally to this work.

Supporting information for this article is available on the WWW under https://doi.org/10.1002/cctc.202001398

This publication is part of a Special Collection on "Phosphorus in Catalysis". Please check the ChemCatChem homepage for more articles in the collection.

trifluoromethylation of alkenes, the development of catalytic asymmetric radical-involved intermolecular trifluoromethylation of α-substituted alkene for the efficient construction of chiral quaternary stereocenter *via* tertiary carbon-centered radical still remains a formidable challenge and scarcity. To address this challenge, Liu *et al.* have recently developed the asymmetric Cu/Box-catalyzed radical intermolecular trifluoromethylarylation of α-substituted acrylamides to construct chiral quaternary all-carbon stereocenters.[9] More recently, we have developed an asymmetric intermolecular, three-component radical-involved dicarbofunctionalization of 1,1-diarylalkenes by a Cu(I)/chiral phosphoric acid (CPA) dual-catalysis strategy, affording the chiral heteroaromatic-containing triarylmethanes bearing quaternary all-carbon stereocenters with excellent chemo- and enantioselectivity *via* the cooperative interactions.[10]

In continuation of our efforts in copper-catalyzed asymmetric radical reactions,[6–7,10–11] we were wondering whether our recently developed radical-carbocation crossover together with Cu(I)/CPA cooperative catalysis strategy could enable the enantioselective radical intermolecular aminotrifluoromethylation of alkenes. Considering the intrinsic instability and the high reactivity of tertiary benzylic carbocation, and the long-standing problems associated with tertiary benzylic radical derived from α-substituted styrene, there are several ongoing challenges that have to be faced with, such as (1) achieving steric differentiation between the enantiotopic faces of tertiary benzylic carbocation[12] by electrostatic interactions that lack rigidity in their association and the steric repulsion between the bulky tertiary benzylic cation and amino group in the stereo-induction; (2) selectively controlling promiscuous reaction, such as competitive deprotonation[10] of the tertiary benzylic carbocation and direct C–H trifluoromethylation of arenes.[13] Herein we describe our ongoing efforts toward the development of the first efficient asymmetric intermolecular radical aminotrifluoromethylation of 1,1-diarylalkenes with nitrogen-based nucleophile and Togni's reagent enabled by Cu(I)/CPA cooperative catalysis (Scheme 1d). The success of the strategy would provide a step-economic and practicable approach to construct enantioenriched hydroxy-substituted diarylmethylamines bearing an α-tertiary stereocenter, which represent key structural motifs of a large number of bioactive molecules in medicinal chemistry, such as chiral tetrahydroisoquinoline phenols,[14] 3-(4-hydroxyphenyl)-indolin-2-ones,[15] fluorescein hydrazones,[16] FR-Lys,[17] and (*S*)-HPPH,[18] whose asymmetric construction remains a significant challenge and scarce (Figure 1).

Our study commenced with the examination of 1,1-diarylalkene **1a** bearing *p*-OH-substituted electron-rich arene as the pilot alkene substrate with Togni's reagent **3**[19] and phenylurea **2Aa**,[6] where the urea bearing two acidic N–H may act as both the nucleophile and directing group. Unfortunately, asymmetric intermolecular radical-involved aminotrifluoromethylation in the presence of CuI and CPA (*S*)-**A1** provided the side monofunctionalization product **4bb** in good yield *via* a β-hydride elimination process without any desired product (Scheme 2).[9] Next, we set out to explore other nitrogen-based nucleophiles, such as aniline, $BzNH_2$, $BzNHNH_2$ or $PhSO_2NH_2$. To our delight, $BzNHNH_2$ afforded the desired product **4A** in 56% yield, albeit with poor enantioselectivity (3% ee), presumably due to the appropriate nucleophilicity of the nitrogen for the nucleophilic attacking and cooperative hydrogen-bonding interaction with the CPA, and other nitrogen-based nucleophiles did not result in any formation of the desired products.

Encouraged by the proof-of-principle results, we continued to carry out further systematic optimizations of different reaction parameters (Table 1). To minimize the β-hydride elimination side-reaction and improve the enantioselectivity of the reaction, we screened the reaction temperatures and different copper salts as well as various organic solvents.

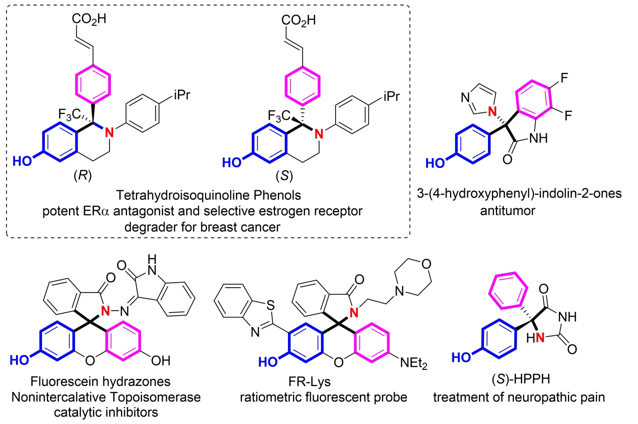
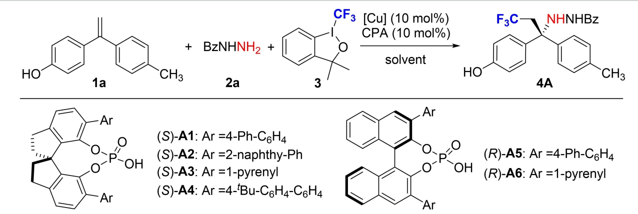


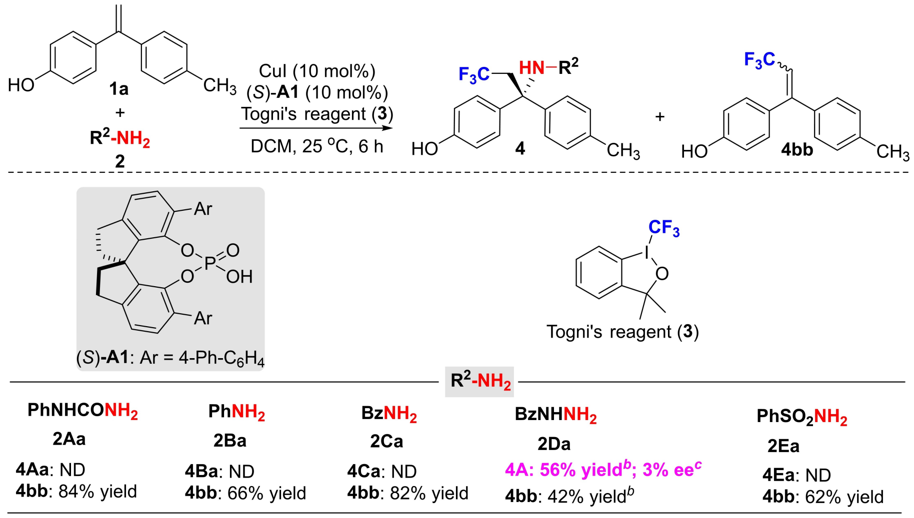
Figure 1. Representative hydroxy-substituted diarylmethylamines bearing an α-tertiary stereocenter.

Table 1. Screening of reaction conditions.[a],[b],[c]



entry	[Cu]	CPA	solvent	T [°C]	yield[b]	ee [%][c]
1	CuI	(*S*)-**A1**	DCM	0	70	48
2	CuI	(*S*)-**A2**	DCM	0	82	41
3	CuI	(*S*)-**A3**	DCM	0	78	14
4	CuI	(*S*)-**A4**	DCM	0	92	55
5	CuI	(*R*)-**A5**	DCM	0	96	19
6	CuI	(*R*)-**A6**	DCM	0	74	1
7	CuI	–	DCM	0	trace	–
8	$Cu(CH_3CN)_4BF_4$	(*S*)-**A4**	DCM	0	81	3
9	Cu_2O	(*S*)-**A4**	DCM	0	58	61
10	$Cu_2(OTf)_2$•Ph	(*S*)-**A4**	DCM	0	53	29
11	CuI	(*S*)-**A4**	DCM	−10	94	72
12	CuI	(*S*)-**A4**	DCM	−20	94	74
13	CuI	(*S*)-**A4**	$CHCl_3$	−20	38	63
14	CuI	(*S*)-**A4**	DCE	−20	90	68
15	CuI	(*S*)-**A4**	PhMe	−20	trace	–
16	–	(*S*)-**A4**	DCM	−20	–	–

[a] Reaction conditions: **1a** (0.05 mmol), **2a** (0.05 mmol), Togni's reagent **3** (0.05 mmol), solvent (2.0 mL) in 25 mL Schlenk tube under argon. [b] Isolated yield based on **1a**. [c] Ee value on HPLC.

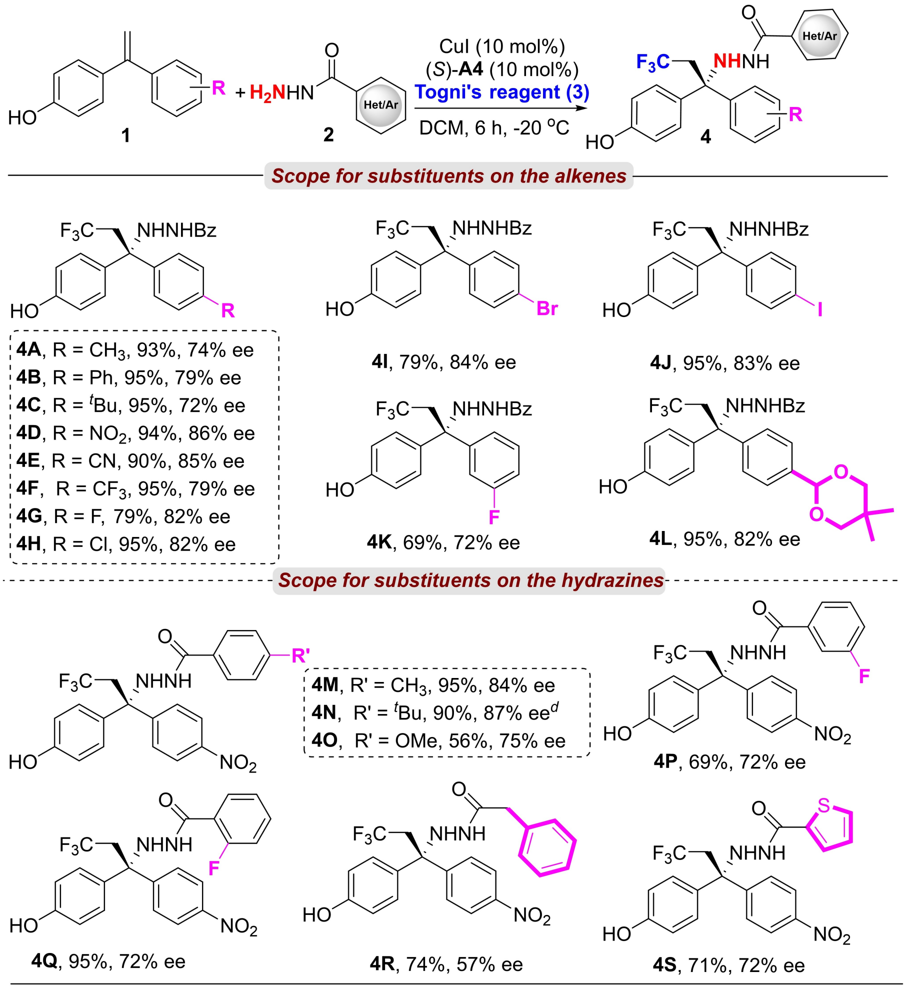


Scheme 2. Evaluation of diverse nitrogen-based nucleophiles.[a],[b],[c] [a] Reaction conditions: **1 a** (0.05 mmol), **2** (0.05 mmol), Togni's reagent **3** (0.05 mmol), CuI (10 mol %), CPA (10 mol %), DCM (1.0 mL) under argon. [b] Isolated yield. [c] ee value on HPLC.

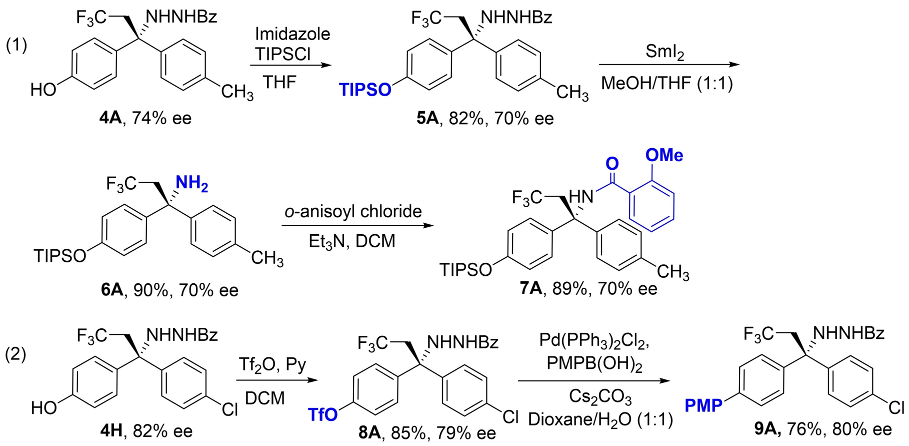
Fortunately, lowering the reaction temperature and decreasing the substrate concentrations were obviously beneficial for the reaction, affording **4A** in 70% yield with 48% ee at 0 °C (entry 1). We then screened diverse SPINOL- and BINOL-derived CPAs (entries 2–8) as well as copper salts, and found that the combination of CuI (10 mol %) and (*S*)-**4A** (10 mol %) with 4-^{t}Bu-C_6H_4-C_6H_4 group at the 3,3′-positions was the best dual-catalyst (entries 2–10). A control experiment revealed that only a trace amount of the desired product was detected in the absence of a CPA catalyst, unambiguously indicating that the dual catalyst is essential as a single-electron catalyst to activate Togni's reagent to generate CF_3 radical (entry 7).[6] Further investigation revealed that lowering the reaction temperature to −20 °C led to an increase in enantioselectivity (entries 11 and 12) but did not affect the chemical yield. Finally, the screening of solvents for chemical reactions did not improve the enantioselectivity (entries 13–15).

Having identified effective conditions, we next investigated the substrate scope of the asymmetric intermolecular radical-involved aminotrifluoromethylation and the results are summarized in Scheme 3. Various diversely functionalized 1,1-diarylalkenes with various substituents on the aromatic ring, including those having aryl groups with strong electron-withdrawing (–NO_2, –CN, –CF_3, –F and –Cl) or electron-donating groups (–Me, –^{t}Bu, and –Ph) at different positions (*meta*, *or para*), were proved to be suitable candidates to afford the expected products **4A**–**4L** in 69–95 % yields with 72–86 % ee. It was found that both the position and electronic nature of the R^1 substituent on the aromatic ring had an obvious effect on the efficiency and enantioselectivity of the reaction. Accordingly, the 1,1-diarylethylenes bearing electron-withdrawing groups on the phenyl ring, performed better than those bearing electron-donating groups on the aromatic ring in term of enantioselectivity, and the substituent (R^1) on the *meta* position of phenyl ring resulted in relatively lower enantioselectivity. Importantly, the halogen atoms (–Br and –I) on the phenyl ring were well-tolerated, leading to the corresponding products **4I** and **4J**, which also provided a versatile pathway for further elaboration of the products. Additionally, the configurationally acid-labile acetal group was well-tolerated and gave the expected products **4L**.[20] Furthermore, a range of substituted hydrazines all underwent the current radical-involved aminotrifluoromethylation smoothly to furnish the expected products **4M**–**4Q** in excellent yields with good enantioselectivity, and the absolute configuration of **4N** has been determined to be *R* by chiroptical methods, wherein ECD spectra were calculated by the DFT method (see Supplementary Information, Figure S1 for details). Remarkably, the protocol could be extended to benzyl- and thiophene-substituted hydrazines, and the corresponding products **4R** and **4S** were obtained in good results, showcasing the good functional group compatibility of the protocol. To further expand the utility of this reaction, the obtained enantioenriched products bearing a quaternary stereocenter can serve as pivotal intermediates for easy access to other medicinally intriguing enantioenriched CF_3-containing diarylmethylamines (Scheme 4). For instance, treatment of the TIPS (triisopropylsilyl) protected product **5A** with SmI_2[21] enables the direct access to the hindered primary amine **6A**, featuring a fully substituted carbon center α to the primary amino functional group, which is synthetically challenging[22] (Scheme 4, eq 1). **6A** could be further transformed to a chiral amide **7A** without erosion of the stereochemical integrity. Moreover, the hydroxy group was readily triflated to afford **8A** (Scheme 4, eq 2), which provided extra synthetic application for further transformation by cross-coupling reaction to provide **9A** with excellent efficiency.[10]

To probe the reaction mechanism, radical trapping experiments with 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) and butylated hydroxytoluene (BHT) were conducted to reveal remarkable inhibition of the desired reaction, and the TEMPO-CF_3 adduct was detected with ^{19}F NMR analysis, (Scheme 5, eq 1, see the Supporting Information for details), suggesting

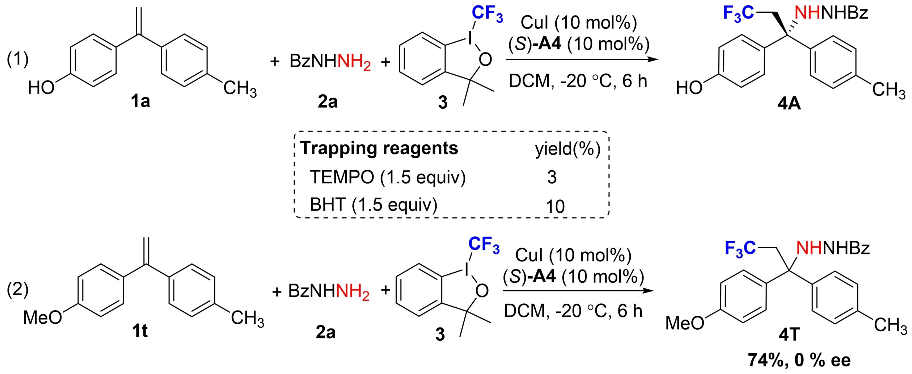


Scheme 3. Substrate scope for alkenes or hydrazines.[a,b,c] [a] All of the reactions were conducted on a 0.1 mmol scale in 25 mL Schlenk tube under argon. [b] Isolated yields based on **1**. [c] Determined by chiral HPLC analysis. [d] Run at 0 °C.



Scheme 4. Representative product transformations

that the generation of the CF_3 radical might be involved in the reaction process *via* a single electron-transfer process. Additionally, no desired product **4A** or trace of *rac*-**4A** was respectively observed in the absence of copper catalysts or CPAs (Table 1, entries 7, and 16), thus indicating that both the Cu(I) salt and CPA are essential for the present transformation. Furthermore,



Scheme 5. Mechanistic study.

only a racemic product **4T** was obtained under otherwise identical conditions using the methoxyl substituted 1,1-diarylalkene **1t** as the substrate (Scheme 5, eq 2), clearly revealing that the alkene with hydroxy group played a pivotal role in asymmetric induction.

Based on the results of the present study and previous reports,[3b,c,e,g,6,10] a possible reaction mechanism is proposed, as shown in Figure 2. Firstly, Togni's reagent **3** reacts with Cu(I) and CPA to generate CF_3 radical species *via* single-electron transfer (SET) and chiral Cu(II) phosphate complex **A**, followed by the addition of CF_3 radical to the alkene **1** to afford α-CF_3 alkyl radical **B**, which could be subsequently trapped by Cu (II) complex **A** to give the corresponding carbocation intermediate **C** *via* single-electron oxidation, wherein the two aryl groups could stabilize this carbocation.[10,23] Subsequently, carbocation intermediate **C** is attacked by hydrazine **2** through intermediate **C**[24] or its *p*-quinone methide resonance structure **D**[25] to give the desired product **4** along with the regeneration of CPA, wherein the good stereoinduction proceeds through both hydrogen-bonding interactions and ion-pair interactions in **C** with the chiral phosphate anion or only hydrogen bonding interactions in **D**.[26]

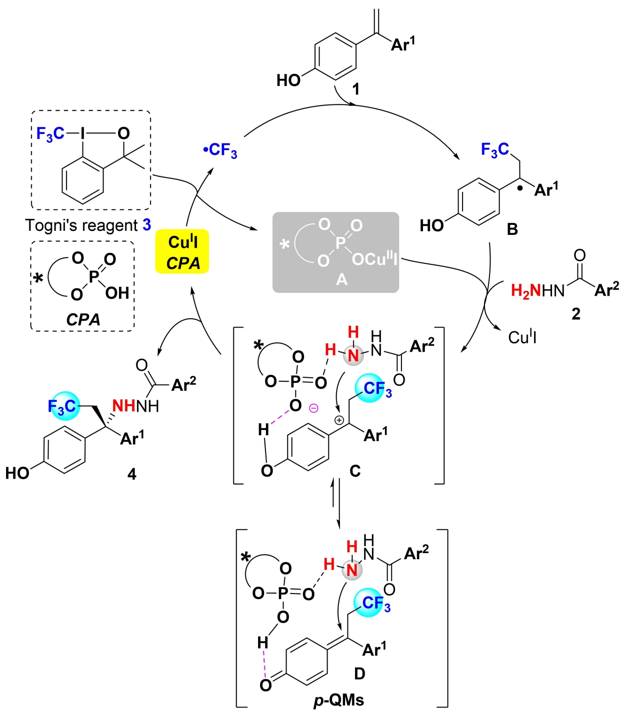


Figure 2. Mechanistic proposal.

In summary, we have developed a highly efficient strategy to enable the first catalytic enantioselective intermolecular radical aminotrifluoromethylation of 1,1-diarylalkenes with hydrazines and Togni's reagent by Cu(I)/CPA cooperative catalysis, delivering an array of diversely substituted CF_3-containing enantioenriched hydroxy-substituted diarylmethylamines bearing an α-tertiary stereocenter with high enantioselectivity and excellent chemoselectivity. Incorporating a convertible hydroxy group as the directing group and using hydrazine as nitrogen-based nucleophile jointly favor the desired radical aminotrifluoromethylation over the otherwise remarkable side reactions. The highly asymmetric induction of C–N bond formation between hydrazine and the carbocation intermediate was achieved by using a CPA catalyst *via* hydrogen-bonding and ion pair interaction. The obtained enantioenriched *p*-OH-diarylmethylamines represent key structural motifs of a large of biologically molecules in medicinal chemistry. Furthermore, the highly enantioenriched products can be easily transformed into other valuable chiral CF_3-containing hindered primary amines. Thus, this synthetic strategy holds significant potential.

Acknowledgements

Financial support from the National Natural Science Foundation of China (No. 21602098), Shenzhen Development and Reform Committee (No. 2019156), Shenzhen Science, Technology and Innovation Commission (No. JCYJ20180306174248782), Department of Science and Technology of Guangdong Province (No. 2017B030314083), and Shenzhen Bay Laboratory Open Funding (No. SZBL2019062801009) is greatly appreciated.

Conflict of Interest

The authors declare no conflict of interest.

Keywords: aminotrifluoromethylation · asymmetric · cooperative catalysis · diarylmethylamine · radical-involved

[1] For selected reviews, see: a) K. H. Jensen, M. S. Sigman, *Org. Biomol. Chem.* **2008**, *6*, 4083; b) R. I. McDonald, G. Liu, S. S. Stahl, *Chem. Rev.* **2011**, *111*, 2981; c) S. Tang, K. Liu, C. Liu, A. Lei, *Chem. Soc. Rev.* **2015**, *44*, 1070; d) G. Yin, X. Mu, G. Liu, *Acc. Chem. Res.* **2016**, *49*, 2413.

[2] For selected recent reviews and examples, see: a) S. Purser, P. R. Moore, S. Swallow, V. Gouverneur, *Chem. Soc. Rev.* **2008**, *37*, 320; b) T. Furuya, A. S. Kamlet, T. Ritter, *Nature* **2011**, *473*, 470; c) J. Nie, H.-C. Guo, D. Cahard, J.-A. Ma, *Chem. Rev.* **2011**, *111*, 455; d) A. Studer, *Angew. Chem. Int. Ed.* **2012**, *51*, 8950; e) T. Liang, C. N. Neumann, T. Ritter, *Angew. Chem. Int. Ed.* **2013**, *52*, 8214; f) E. Merino, C. Nevado, *Chem. Soc. Rev.* **2014**, *43*, 6598; g) H. Egami, M. Sodeoka, *Angew. Chem. Int. Ed.* **2014**, *53*, 8294; h) X. Yang, T. Wu, R. J. Phipps, F. D. Toste, *Chem. Rev.* **2015**, *115*, 826; i) X.-H. Xu, K. Matsuzaki, N. Shibata, *Chem. Rev.* **2015**, *115*, 731; j) T. Li, P. Yu, J.-S. Lin, Y. Zhi, X.-Y. Liu, *Chin. J. Chem.* **2016**, *34*, 490; k) N. Wang, Q.-S. Gu, Y.-F. Cheng, L. Li, Z.-L. Li, Z. Guo, X.-Y. Liu, *Chin. J. Org. Chem.* **2019**, *39*, 200.

[3] For selected recent examples of intramolecular versions, see: a) J.-S. Lin, X.-G. Liu, X.-L. Zhu, B. Tan, X.-Y. Liu, *J. Org. Chem.* **2014**, *79*, 7084; b) J.-S. Lin, Y.-P. Xiong, C.-L. Ma, L.-J. Zhao, B. Tan, X.-Y. Liu, *Chem. Eur. J.* **2014**, *20*, 1332; c) S. Kawamura, H. Egami, M. Sodeoka, *J. Am. Chem. Soc.* **2015**, *137*, 4865; d) Z. Zhang, X. Tang, C. S. Thomoson, W. R. Dolbier, Jr., *Org. Lett.* **2015**, *17*, 3528; e) K. Shen, Q. Wang, *Org. Chem. Front.* **2016**, *3*, 222; f) S. Kawamura, K. Dosei, E. Valverde, K. Ushida, M. Sodeoka, *J. Org. Chem.* **2017**, *82*, 12539; g) Y. Zhang, H.-Y. Zhang, W. Huo, C. Ge, J. Zhao, *Synlett* **2017**, *28*, 962; h) X.-F. Li, J.-S. Lin, X.-Y. Liu, *Synthesis* **2017**, *49*, 4213; i) Y. Zhang, X. Han, J. Zhao, Z. Qian, T. Li, Y. Tang, H. Y. Zhang, *Adv. Synth. Catal.* **2018**, *360*, 2659; j) H. Zhang, X. Mou, G. Chen, G. He, *Acta Chim. Sinica.* **2019**, *77*, 884.

[4] For selected recent examples of intermolecular versions, see: a) Y. Yasu, T. Koike, M. Akita, *Org. Lett.* **2013**, *15*, 2136; b) F. Wang, X. Qi, Z. Liang, P. Chen, G. Liu, *Angew. Chem. Int. Ed.* **2014**, *53*, 1881; c) A. Carboni, G. Dagousset, E. Magnier, G. Masson, *Org. Lett.* **2014**, *16*, 1240; d) G. Dagousset, A. Carboni, E. Magnier, G. Masson, *Org. Lett.* **2014**, *16*, 4340; e) X. Geng, F. Lin, X. Wang, N. Jiao, *Org. Lett.* **2017**, *19*, 4738; f) C.-L. Zhu, C. Wang, Q.-X. Qin, S. Yruegas, C. D. Martin, H. Xu, *ACS Catal.* **2018**, *8*, 5032; g) H. Xiao, H. Shen, L. Zhu, C. Li, *J. Am. Chem. Soc.* **2019**, *141*, 11440; h) P. Wang, S. Zhu, D. Lu, Y. Gong, *Org. Lett.* **2020**, *22*, 1924.

[5] a) Y. Tian, S. Chen, Q.-S. Gu, J.-S. Lin, X.-Y. Liu, *Tetrahedron Lett.* **2018**, *59*, 203; b) H. Egami, S. Kawamura, A. Miyazaki, M. Sodeoka, *Angew. Chem. Int. Ed.* **2013**, *52*, 7841.

[6] J.-S. Lin, X.-Y. Dong, T.-T. Li, N.-C. Jiang, B. Tan, X.-Y. Liu, *J. Am. Chem. Soc.* **2016**, *138*, 9357.

[7] J.-S. Lin, F.-L. Wang, X.-Y. Dong, W.-W. He, Y. Yuan, S. Chen, X.-Y. Liu, *Nat. Commun.* **2017**, *8*, 14841.

[8] X.-Q. Mou, F.-M. Rong, H. Zhang, G. Chen, G. He, *Org. Lett.* **2019**, *21*, 4657.

[9] L. Wu, F. Wang, P. Chen, G. Liu, *J. Am. Chem. Soc.* **2019**, *141*, 1887.

[10] J.-S. Lin, T.-T. Li, J.-R. Liu, G.-Y. Jiao, Q.-S. Gu, J.-T. Cheng, Y.-L. Guo, X. Hong, X.-Y. Liu, *J. Am. Chem. Soc.* **2019**, *141*, 1074.

[11] a) F.-L. Wang, X.-Y. Dong, J.-S. Lin, Y. Zeng, G.-Y. Jiao, Q.-S. Gu, X.-Q. Guo, C.-L. Ma, X.-Y. Liu, *Chem* **2017**, *3*, 979; b) X.-T. Li, Q.-S. Gu, X.-Y. Dong, X. Meng, X.-Y. Liu, *Angew. Chem. Int. Ed.* **2018**, *57*, 7668; c) X.-F. Li, J.-S. Lin, J. Wang, Z.-L. Li, Q.-S. Gu, X.-Y. Liu, *Acta Chim. Sinica.* **2018**, *76*, 878; d) Y. Zeng, X.-D. Liu, X.-Q. Guo, Q.-S. Gu, Z.-L. Li, X.-Y. Chang, X.-Y. Liu, *Sci. China Chem.* **2019**, *62*, 1529; e) X.-Y. Dong, Y.-F. Zhang, C.-L. Ma, Q.-S. Gu, F.-L. Wang, Z.-L. Li, S.-P. Jiang, X.-Y. Liu, *Nat. Chem.* **2019**, *11*, 1158; f) Z.-H. Zhang, X.-Y. Dong, X.-Y. Du, Q.-S. Gu, Z.-L. Li, X.-Y. Liu, *Nat. Commun.* **2019**, *10*, 5689; g) Y.-F. Cheng, J.-R. Liu, Q.-S. Gu, Z.-L. Yu, J. Wang, Z.-L. Li, J.-Q. Bian, H.-T. Wen, X.-J. Wang, X. Hong, X.-Y. Liu, *Nat. Catal.* **2020**, *3*, 401; h) L. Ye, Y. Tian, X. Meng, Q.-S. Gu, X.-Y. Liu, *Angew. Chem. Int. Ed.* **2020**, *59*, 1129; i) Z.-L. Li, G.-C. Fang, Q.-S. Gu, X.-Y. Liu, *Chem. Soc. Rev.* **2020**, *49*, 32; j) C.-J. Yang, C. Zhang, Q.-S. Gu, J.-H. Fang, X.-L. Su, L. Ye, Y. Sun, Y. Tian, Z.-L. Li, X.-Y. Liu, *Nat. Catal.* **2020**, *3*, 539; k) Q.-S. Gu, Z.-L. Li, X.-Y. Liu, *Acc. Chem. Res.* **2020**, *53*, 170; l) X.-T. Li, L. Lv, T. Wang, Q.-S. Gu, G.-X. Xu, Z.-L. Li, L. Ye, X. Zhang, G.-J. Cheng, X.-Y. Liu, *Chem* **2020**, *6*, 1692; m) X.-Y. Dong, J.-T. Cheng, Y.-F. Zhang, Z.-L. Li, T.-Y. Zhan, J.-J. Chen, F.-L. Wang, N.-Y. Yang, L. Ye, Q.-S. Gu, X.-Y. Liu, *J. Am. Chem. Soc.* **2020**, *142*, 9501; n) H.-D. Xia, Z.-L. Li, Q.-S. Gu, X.-Y. Dong, J.-H. Fang, X.-Y. Du, L.-L. Wang, X.-Y. Liu, *Angew. Chem. Int. Ed.* **2020**, DOI:10.1002/anie.202006317; o) M. Zhang, W. Su, *Chin. J. Org. Chem.* **2019**, *39*, 3596.

[12] a) K. Brak, E. N. Jacobsen, *Angew. Chem. Int. Ed.* **2013**, *52*, 534; b) A. E. Wendlandt, P. Vangal, E. N. Jacobsen, *Nature* **2018**, *556*, 447.

[13] X. Chen, L. Ding, L. Li, J. Li, D. Zou, Y. Wu, Y. Wu, *Tetrahedron Lett.* **2020**, *61*, 151538.

[14] J. S. Scott, A. Bailey, R. D. Davies, S. L. Degorce, P. A. MacFaul, H. Gingell, T. Moss, R. A. Norman, J. H. Pink, A. A. Rabow, B. Roberts, P. D. Smith, *ACS Med. Chem. Lett.* **2016**, *7*, 94.

[15] M. K. Christensen, F. Björkling, *Patent WO 2008129075A1* **2008**.

[16] A. F. Rahman, S. E. Park, A. A. Kadi, Y. Kwon, *J. Med. Chem.* **2014**, *57*, 9139.

[17] Q. Wang, L. Zhou, L. Qiu, D. Lu, Y. Wu, X.-B. Zhang, *Analyst* **2015**, *140*, 5563.

[18] J. Riedner, P. Vogel, *Tetrahedron: Asymmetry* **2004**, *15*, 2657.

[19] P. Eisenberger, S. Gischig, A. Togni, *Chem. Eur. J.* **2006**, *12*, 2579.

[20] J.-S. Lin, P. Yu, L. Huang, P. Zhang, B. Tan, X.-Y. Liu, *Angew. Chem. Int. Ed.* **2015**, *54*, 7847.

[21] Y. Hu, Z. Zhang, J. Zhang, Y. Liu, I. D. Gridnev, W. Zhang, *Angew. Chem. Int. Ed.* **2019**, *58*, 15767.

[22] M. C. Nicastri, D. Lehnherr, Y. H. Lam, D. A. DiRocco, T. Rovis, *J. Am. Chem. Soc.* **2020**, *142*, 987.

[23] M. Chen, Y. Han, D. Ma, Y. Wang, Z. Lai, J. Sun, *Chin. J. Chem.* **2018**, *36*, 587.

[24] a) Z. Wang, F. Ai, Z. Wang, W. Zhao, G. Zhu, Z. Lin, J. Sun, *J. Am. Chem. Soc.* **2015**, *137*, 383; b) Z. Wang, Y. F. Wong, J. Sun, *Angew. Chem. Int. Ed.* **2015**, *54*, 13711.

[25] a) W.-J. Bai, J. G. David, Z.-G. Feng, M. G. Weaver, K.-L. Wu, T. R. R. Pettus, *Acc. Chem. Res.* **2014**, *47*, 3655; b) J. Sun, Z. Wang, *Synthesis* **2015**, *47*, 3629.

[26] a) M. Rueping, U. Uria, M.-Y. Lin, I. Atodiresei, *J. Am. Chem. Soc.* **2011**, *133*, 3732; b) K. Brak, E. N. Jacobsen, *Angew. Chem. Int. Ed.* **2013**, *52*, 534; c) M. Mahlau, B. List, *Angew. Chem. Int. Ed.* **2013**, *52*, 518; d) N. Tsuji, J. L. Kennemur, T. Buyck, S. Lee, S. Prevost, P. S. J. Kaib, D. Bykov, C. Fares, B. List, *Science* **2018**, *359*, 1501; e) J.-S. Lin, T.-T. Li, G.-Y. Jiao, Q.-S. Gu, J.-T. Cheng, L. Lv, X.-Y. Liu, *Angew. Chem. Int. Ed.* **2019**, *58*, 7092; f) X. Li, J. Sun, *Angew. Chem. Int. Ed.* **2020**, DOI: 10.1002/anie.202006137.

Manuscript received: August 27, 2020
Revised manuscript received: September 14, 2020
Accepted manuscript online: September 17, 2020
Version of record online: September 30, 2020

