SHORT COMMUNICATION

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Synthesis of 10-Methylacridin-9(10*H*)-ones through Cu-Catalyzed Intramolecular Oxidative C(sp^2)–H Amination of 2-(Methylamino)benzophenones

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An efficient synthesis of a diverse set of 10-methylacridin-9(10*H*)-ones from 2-(methylamino)benzophenones has been developed. The reaction proceeds though Cu-catalyzed intramolecular aromatic C–H amination by using O_2 as the sole oxidant to provide the desired products in moderate to good yields. In addition, 2-allylamino- and 2-(benzylamino)benzophenones as well as unprotected substrates can also undergo the C–H amination reaction to deliver the corresponding cyclization products smoothly. Preliminary mechanistic studies suggest that C–H activation is involved in a rate-limiting step.

Introduction

Nitrogen-containing heterocycles (azaheterocycles) are omnipresent in natural products, drugs, and other biologically active molecules.[1] As a consequence, a substantial amount of synthetic methods have been established to construct azaheterocycles. Among those, transition-metal-catalyzed intramolecular C–N bond-formation reactions starting from aryl or vinyl (pseudo)halides has been recognized as a powerful method for the preparation of azaheterocycles.[2,3] Over the past decade, the direct transformation of C–H bonds into C–N bonds catalyzed by transition metals has emerged as an efficient and environmentally benign alternative to traditional C–N bond-forming methods in the synthesis of azaheterocycles.[4] Notable progress has been made predominantly by using ruthenium-,[5] rhodium-,[6] and palladium-based[7] systems. In most of these cases, stoichiometric or excess amounts of oxidants, such as $Cu(OAc)_2$, AgOAc, BQ, $CeSO_4$, and/or F^+, are inevitable to achieve catalytic turnover.[5–7] The disadvantages associated with these methods include not only the use of expensive transition-metal catalysts, but also the use of a large amount of heavy metal based oxidants, which may limit applications in the synthesis of drugs.

In recent years, much cheaper and less toxic copper salts along with oxygen, an ideal terminal oxidant, have been used in direct C–H/C–N oxidative coupling processes.[8] In the pioneering work of Buchwald's group,[9] they disclosed a novel $Cu(OAc)_2/O_2$ catalytic system for the synthesis of benzimidazoles through intramolecular C–H imidation of *N*-arylamidines. Our group[10] also developed an efficient synthesis of pyrido[1,2-*a*]benzimidazoles through direct aromatic C–H amination of *N*-aryl-2-aminopyridines under an atmosphere of oxygen. Recently, Chiba and coworkers[11] reported an approach for the synthesis of bi- and tricyclic amidines through copper-catalyzed aerobic C–H imidation of *N*-alkenylamidines.

Despite the significant advances of Cu/O_2 catalytic system in C–H amination reactions,[12] the type of azaheterocycles constructed by applying this strategy is still limited. Herein, we report a copper-catalyzed intramolecular C–H amination reaction for the synthesis of a diverse set of 10-methylacridin-9(10*H*)-ones starting from 2-(methylamino)-benzophenones under balloon pressure of O_2.

Acridone is a ubiquitous structural motif that exists in a wide range of biologically active compounds.[13] Methods leading to the construction of this scaffold are mainly based on the acid-promoted annulation of *N*-phenylanthranilic acids or the intramolecular nucleophilic substitution of 2-amino-2′-halobenzophenones (Scheme 1, path a).[14] Recently, Larock[15a] and Shi[15b] described novel approaches to acridones through tandem reactions involving intermolecular coupling of benzoates or benzamides with arynes generated from silylaryl triflate precursors in the presence of CsF (Scheme 1, path b). However, the methods developed thus far suffer from tedious workup procedures and have a limited substrate scope and/or unsatisfactory yields. Inspired by the recent advances in Cu-catalyzed C–H func-

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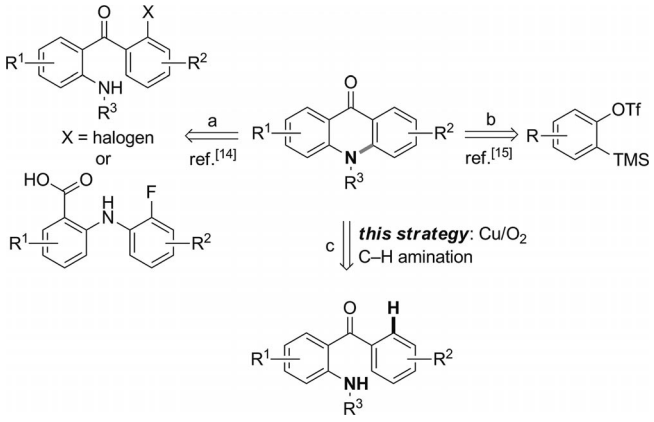
tionalization processes,[12] we envisaged[16] that the acridone nucleus could also be constructed by direct intramolecular C–H amination reactions of readily available 2-(methylamino)benzophenones[17] (Scheme 1, path c).

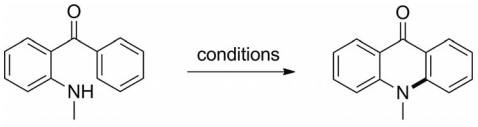


Scheme 1. Major approaches to acridone derivatives.

Results and Discussion

To test the idea, we began our investigation with 2-(methylamino)benzophenone (**1a**) as a substrate, and the results are summarized in Table 1. The reaction afforded desired annulation product **2a** in 20% yield, as determined by NMR spectroscopy, when CuBr (20 mol-%) was used as the catalyst in DMF at 130 °C under balloon pressure of oxygen (Table 1, entry 1). Screening of various copper salts revealed that the yield of **2a** could be improved to 35% by using CuTc (Table 1, entries 2 and 3). Switching the solvent from DMF to DMA and DMSO identified DMSO as the optimum solvent. Copper(II) sources such as $Cu(OAc)_2$ and $Cu(OTf)_2$ were also effective in this transformation (Table 1, entries 7 and 8), although the products were obtained in lower yields. To our delight, the yield of **2a** was improved to 79% (Table 1, entry 9) when pivalic acid (10 mol-%) was used as an additive. However, alteration of the amount of pivalic acid (from 10 to 50 mol-%) did not improve the yield of **2a** further (Table S1, Supporting Information). When pivalic acid was replaced by trifluoroacetic acid, only a trace amount of **2a** was detected (Table 1, entry 10). On the contrary, basic additives including KOAc and K_2CO_3 gave poor results (Table 1, entries 11 and 12). Next, several ligands such as 1,10-phenanthroline, 2,2-bipyridine, TMEDA, and PPh_3 were screened (Table 1, entries 13–16). It was found that the ligands alone (without pivalic acid) did not enhance the reaction efficiency; in these cases, **2a** was afforded in 52–73% yield. Lowering the catalyst loading (10 mol-%) led to a less efficient formation of **2a** (74%). A synergistic effect was observed by combining PPh_3 and PivOH in the catalytic system (84%; Table 1, entry 17). Notably, when the reaction was performed under an atmosphere of argon, no reaction was observed and **1a** was recovered in 73%, which suggests that O_2 plays a vital role in the catalytic cycle (Table 1, entry 18).

Table 1. Optimization of the reaction conditions.[a]



1a **2a**

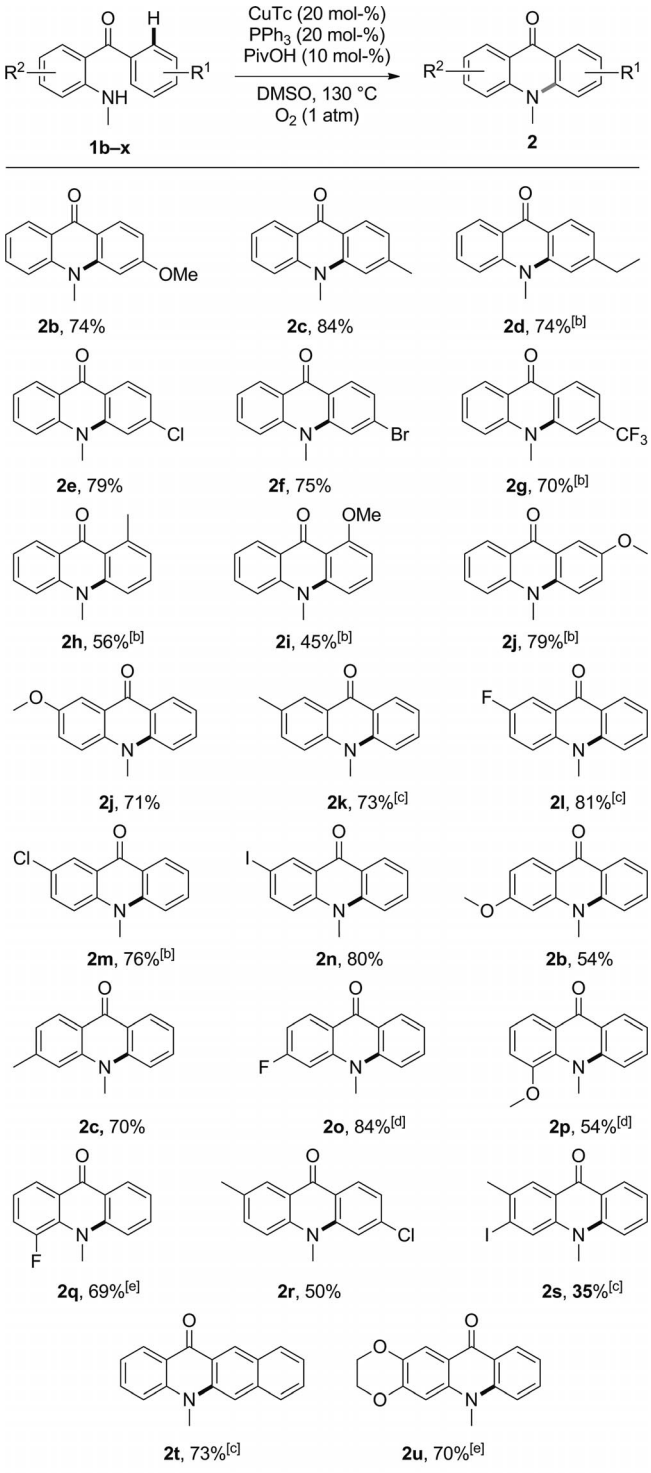
Entry	Cat.	Solvent	Ligand	Additive	Yield [%][b]
1	CuBr	DMF	–	–	20[c]
2	CuI	DMF	–	–	30
3	CuTc	DMF	–	–	35
4	CuTc	DMA	–	–	<10[c]
5	CuI	DMSO	–	–	55
6	CuTc	DMSO	–	–	63
7	$Cu(OAc)_2$	DMSO	–	–	49[c]
8	$Cu(OTf)_2$	DMSO	–	–	40[c]
9	CuTc	DMSO	–	PivOH	79
10	CuTc	DMSO	–	TFA	trace
11	CuTc	DMSO	–	KOAc[d]	36[c]
12	CuTc	DMSO	–	K_2CO_3	<5
13	CuTc	DMSO	phen	–	52[c]
14	CuTc	DMSO	bipy	–	70[c]
15	CuTc	DMSO	TMEDA	–	73
16	CuTc	DMSO	PPh_3	–	70[c]
17	CuTc	DMSO	PPh_3	PivOH	84 (74)[e]
18	CuTc	DMSO	PPh_3	PivOH	0[f]

[a] The reactions were carried out at 130 °C in O_2 (1 atm) with **1a** (0.2 mmol), catalyst (0.04 mmol), ligand (0.04 mmol), and additive (0.02 mmol) in solvent (2 mL) for 23 h. CuTc = copper(I) thiophene-2-carboxylate, DMA = dimethylacetamide, 1,10-phen = 1,10-phenanthroline, bipy = 2,2-bipyridine, TMEDA = tetramethylethylenediamine, PivOH = trimethylacetic acid, TFA = trifluoroacetic acid. [b] Isolated yield. [c] Determined by NMR spectroscopy by using 4-iodoanisole as an internal standard. [d] 1.0 equiv. of KOAc was used. [e] 10 mol-% of CuTc was used. [f] The reaction was carried out under an Ar atmosphere, 73% of **1a** was recovered.

With the optimal reaction conditions in hand, the scope of the substrates (Table 2) was investigated as illustrated in Scheme 1. The amination reaction displayed good functional group tolerance and proved to be a quite general approach to a diverse set of acridones. Substrates bearing electron-donating (Me, MeO, Et) or electron-withdrawing (Cl, Br, CF_3) groups in the *para* position of the non-aniline aryl ring of 2-(methylamino)benzophenones **1** cyclized efficiently in good yields (i.e., **2b**–**g**), with a slight preference for electron-rich substrates. Unlike Cheng's catalytic system,[16a] no regioisomeric byproducts were observed. Notably, *meta*-methoxy-substituted substrate **1j** reacted regioselectively at the less sterically hindered C–H bond to furnish **2j** exclusively in 79% yield. However, substituents in the *ortho* position hampered the reaction for steric hindrance reasons (i.e., for **2h** and **2i**). Substituent effects of the aniline ring were also examined. The reaction proceeded more efficiently for substrates in which the aniline ring contained an electron-withdrawing group (R^2 = F, Cl, I) than for substrates in which the aniline ring contained an electron-donating group (R^2 = OMe, Me) in the same position. To access products such as **2b**, **2c**, and **2j**, higher yields were obtained by placing the electron-donating group in the non-aniline moiety. Notably, the aryl iodide in **1n** and **1s** was

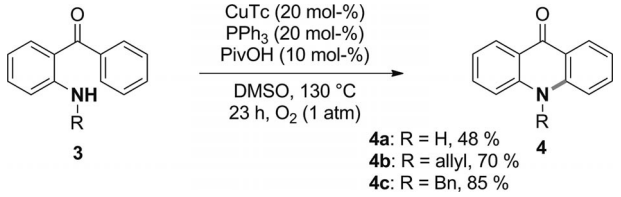
compatible with the reaction conditions, and this provides the opportunity to elaborate the scaffold further. Although the presence of substituents *ortho* to the *N*-methylamino group retarded the cyclization, the corresponding products were inaccessible by connecting the C–N bond on the other side, which enabled the synthesis of 4-substituted acidones **2p** and **2q** by applying this strategy. In addition, substrates **2r**–**u** containing fused-rings or polysubstituted groups were also suitable for the oxidative annulation reaction.

Table 2. Scope of CuTc-catalyzed intramolecular C(sp^2)–H amination.[a]



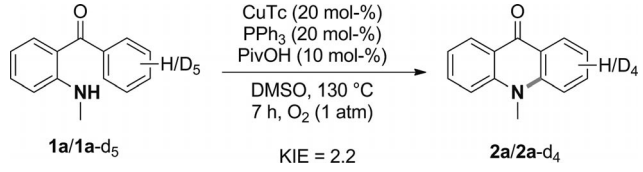
[a] Reaction conditions: **1** (0.2 mmol), CuTc (0.04 mmol), PivOH (0.02 mmol), PPh_3 (0.04 mmol), DMSO (2 mL), 130 °C, O_2 (1 atm), 23 h, isolated yields. [b] 26 h. [c] 29 h. [d] 45 h. [e] 48 h.

NH-free acridone **4a** can also be prepared in lower yield by applying the same protocol starting from unprotected 2-aminobenzophenone (**3a**, Scheme 2). 2-Allylamino- (**3b**) and 2-(benzylamino)benzophenones (**3c**) gave corresponding products **4b** and **4c**, respectively, in good yields. Nevertheless, electron-withdrawing groups such as Ac, Ts, and Boc on the nitrogen atom failed to afford the corresponding products.



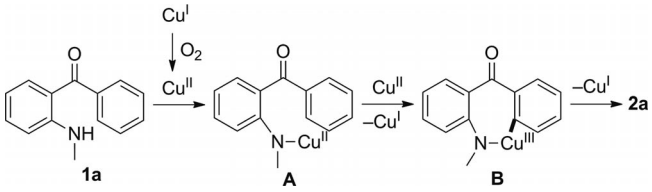
Scheme 2. Preparation of acridones with substituents on the nitrogen atom.

To gain insight into the reaction mechanism, radical-trapping experiments were carried out by using 2,2,6,6-tetramethylpiperidine *N*-oxide (TEMPO) or 1,1-diphenylethylene (1 equiv.), which are known as radical scavengers. The reactions were not greatly suppressed under otherwise identical conditions (Table S2, Supporting Information), and this suggests that radical intermediates are likely not involved in the catalytic cycle, whereas a radical-involved mechanism was proposed by Cheng.[16a] In addition, the kinetic isotope effect (KIE) was measured by parallel reactions with using **1a** and deuterated analogue **1a**-d_5 (Scheme 3). The KIE (2.2) indicates that C–H activation is a rate-limiting step.[18]



Scheme 3. KIE study.

On the basis of the mechanistic studies and literature reports,[19] we propose the reaction mechanism in Scheme 4. Initially, coordination of the substrate with the Cu^{II} species generated from Cu^{I} by oxidation of O_2 delivers intermediate **A**, followed by ligand-assisted rate-limiting C–H bond activation. The presence of catalytic amounts of PivOH has been reported to promote C–H activation.[19c,20] The resulting aryl–Cu^{II} intermediate could be further oxidized to Cu^{III} by disproportionation of another Cu^{II} species before reductive elimination via **B**. Direct reductive elimination from the aryl–Cu^{II} intermediate cannot be ruled out at the current stage.



Scheme 4. Proposed reaction mechanism.

Conclusions

In summary, we have developed an efficient approach for the preparation of acridones through intramolecular C(sp^2)–H amination by using molecular oxygen as an oxidant. A variety of functional groups are compatible with the catalytic system and a diverse set of acridones were obtained in moderate to good yields. A reaction mechanism involving rate-limiting C–H activation was proposed. The new methodology not only serves as an alternative approach for the synthesis of acridones but also broadens the application of Cu-catalyzed C–H activation reactions in the preparation of nitrogen-containing heterocycles.

Experimental Section

General Procedure for the Synthesis of *N*-Methyl Acridones 2: To a solution of 2-(methylamino)benzophenone **1** (0.2 mmol) in DMSO (2 mL) was added CuTc (0.04 mmol), PivOH (0.02 mmol), and PPh_3 (0.04 mmol). The reaction mixture was then stirred at 130 °C under an O_2 atmosphere until the starting material was consumed (23–48 h). After cooling to ambient temperature, the reaction mixture was quenched with a concentrated solution of ammonia (5 mL) and extracted with EtOAc (3 × 5 mL). The combined organic extracts were washed with brine (3 × 5 mL), dried with Na_2SO_4, and concentrated under vacuum. The residue was purified by column chromatography on silica gel to give cyclized products **2**.

Supporting Information (see footnote on the first page of this article): Experimental details and copies of the ^1H NMR and ^{13}C NMR spectra of all new compounds.

Acknowledgments

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[1] a) N. K. Boaen, M. A. Hillmyer, *Chem. Soc. Rev.* **2005**, *34*, 267; b) M. A. Koch, A. Schuffenhauer, M. Scheck, S. Wetzel, M. Casaulta, A. Odermatt, P. Ertl, H. Waldmann, *Proc. Natl. Acad. Sci. USA* **2005**, *102*, 17272; c) R. Hili, A. K. Yudin, *Nat. Chem. Biol.* **2006**, *2*, 284; d) J. S. Carey, D. Laffan, C. Thomson, M. T. Williams, *Org. Biomol. Chem.* **2006**, *4*, 2337; e) R. Tohme, N. Darwiche, H. Gali-Muhtasib, *Molecules* **2011**, *16*, 9665.

[2] a) F. Paul, J. Patt, J. F. Hartwig, *J. Am. Chem. Soc.* **1994**, *116*, 5969; b) A. S. Guram, S. L. Buchwald, *J. Am. Chem. Soc.* **1994**, *116*, 7901; c) S. V. Ley, A. W. Thomas, *Angew. Chem.* **2003**, *115*, 5558; *Angew. Chem. Int. Ed.* **2003**, *42*, 5400; d) D. Ma, Q. Cai, *Acc. Chem. Res.* **2008**, *41*, 1450.

[3] a) A. R. Muci, S. L. Buchwald, *Top. Curr. Chem.* **2002**, *219*, 131; b) J. F. Hartwig, *Acc. Chem. Res.* **2008**, *41*, 1534; c) D. S. Surry, S. L. Buchwald, *Angew. Chem.* **2008**, *120*, 6438; *Angew. Chem. Int. Ed.* **2008**, *47*, 6338.

[4] For reviews on direct C–H bond amination/amidation, see: a) H. M. L. Davies, M. S. Long, *Angew. Chem.* **2005**, *117*, 3584; *Angew. Chem. Int. Ed.* **2005**, *44*, 3518; b) H. M. L. Davies, J. R. Manning, *Nature* **2008**, *451*, 417; c) F. Collet, R. H. Dodd, P. Dauban, *Chem. Commun.* **2009**, 5061; d) A. Armstrong, J. C. Collins, *Angew. Chem.* **2010**, *122*, 2332; *Angew. Chem. Int. Ed.* **2010**, *49*, 2282.

[5] For recent examples of ruthenium-catalyzed C–H amination/amidation, see: a) D. Intrievi, M. Mariani, A. Caselli, F. Ragaini, E. Gallo, *Chem. Eur. J.* **2012**, *18*, 10487; b) D. G. Musaer, S. B. Blakey, *Organometallics* **2012**, *31*, 4950; c) W. Xiao, C.-Y. Zhou, C.-M. Che, *Chem. Commun.* **2012**, *48*, 5871; d) H. Dong, R. T. Latka, T. G. Driver, *Org. Lett.* **2011**, *13*, 2726; e) E. Milczek, N. Boudet, S. Blakey, *Angew. Chem.* **2008**, *120*, 6931; *Angew. Chem. Int. Ed.* **2008**, *47*, 6825; f) T. Uchida, Y. Tamura, M. Ohba, T. Katsuki, *Tetrahedron Lett.* **2003**, *44*, 7965.

[6] For recent examples of rhodium-catalyzed C–H amination/amidation, see: a) K. Takashi, D. Yamaguchi, J. Ishihara, *Org. Lett.* **2012**, *14*, 1644; b) K.-H. Ng, Z. Zhou, W.-Y. Yu, *Org. Lett.* **2012**, *14*, 272; c) J. Ryu, K. Shin, S. Park, S. Chang, *Angew. Chem.* **2012**, *124*, 10042; *Angew. Chem. Int. Ed.* **2012**, *51*, 9904; d) K. Sun, S. Liu, P. M. Bec, T. G. Driver, *Angew. Chem.* **2011**, *123*, 1740; *Angew. Chem. Int. Ed.* **2011**, *50*, 1702; e) J. Du Bois, *Org. Process Res. Dev.* **2011**, *15*, 758; f) S. Kang, J. Han, E. S. Lee, *Org. Lett.* **2012**, *14*, 4184; g) K. W. Fiori, C. G. Espino, B. H. Brodsky, J. Du Bois, *Tetrahedron* **2009**, *65*, 3042; h) F. Collet, R. H. Dodd, P. Dauban, *Org. Lett.* **2008**, *10*, 5473; i) M. Shen, B. E. Leslie, T. G. Driver, *Angew. Chem.* **2008**, *120*, 5134; *Angew. Chem. Int. Ed.* **2008**, *47*, 5056; j) H. Lebel, K. Huard, *Org. Lett.* **2007**, *9*, 639.

[7] For recent examples of palladium-catalyzed C–H amination/amidation, see: a) T. Xiang, Y. Li, L. Mao, Q. Zhang, Q. Zhang, *Chem. Commun.* **2012**, *48*, 2246; b) Á. Iglesias, R. Álvarez, Á. R. de Lera, K. Muñiz, *Angew. Chem.* **2012**, *124*, 2268; *Angew. Chem. Int. Ed.* **2012**, *51*, 2225; c) X.-Y. Liu, P. Gao, Y.-W. Shen, Y.-M. Liang, *Org. Lett.* **2011**, *13*, 4196; d) K. Sun, Y. Li, T. Xiong, J. Zhang, Q. Zhang, *J. Am. Chem. Soc.* **2011**, *133*, 1694; e) J. Pan, M. Su, S. L. Buchwald, *Angew. Chem.* **2011**, *123*, 8806; *Angew. Chem. Int. Ed.* **2011**, *50*, 8647; f) G. Yin, Y. Wu, G. Liu, *J. Am. Chem. Soc.* **2010**, *132*, 11978; g) G. Liu, G. Yin, L. Wu, *Angew. Chem.* **2008**, *120*, 4811; *Angew. Chem. Int. Ed.* **2008**, *47*, 4733; h) S. Chiba, L. Zhang, S. Sanjaya, G. Y. Ang, *Tetrahedron* **2010**, *66*, 5692; i) T. Xiong, Y. Lv, Q. Zhang, *Chem. Commun.* **2010**, *46*, 6831.

[8] For recent examples of copper-catalyzed C-H amination/amidation with O_2 as an oxidant, see: a) X. Chen, X.-S. Hao, C. E. Goodhue, J.-Q. Yu, *J. Am. Chem. Soc.* **2006**, *128*, 6790; b) T. Uemura, S. Imoto, N. Chatani, *Chem. Lett.* **2006**, *35*, 842; c) T. Hamada, X. Ye, S. S. Stahl, *J. Am. Chem. Soc.* **2008**, *130*, 833; d) Q. Wang, S. L. Schreiber, *Org. Lett.* **2009**, *11*, 5178; e) D. Monguchi, T. Fujiwara, H. Furukawa, A. Mori, *Org. Lett.* **2009**, *11*, 1607; f) T. Kawano, K. Hirano, T. Satoh, M. Miura, *J. Am. Chem. Soc.* **2010**, *132*, 6900; g) Y. Li, Y. Xie, R. Zhang, J. Kun, X. Wang, C. Duan, *J. Org. Chem.* **2011**, *76*, 5444; h) S. Guo, B. Qian, Y. Xie, C. Xia, H. Huang, *Org. Lett.* **2011**, *13*, 522; i) T. M. U. Ton, C. Tejo, D. L. Y. Tiong, P. W. H. Chan, *J. Am. Chem. Soc.* **2012**, *134*, 7344; j) D. N. Barman, K. M. Nicholas, *Chem. Eur. J.* **2012**, *18*, 908; k) G.-R. Qu, L. Liang, H.-Y. Niu, W.-H. Rao, H.-M. Guo, J. S. Fossey, *Org. Lett.* **2012**, *14*, 4494.

[9] G. Brasche, S. L. Buchwald, *Angew. Chem.* **2008**, *120*, 1958; *Angew. Chem. Int. Ed.* **2008**, *47*, 1932.

[10] H. Wang, Y. Wang, C. Peng, J. Zhang, Q. Zhu, *J. Am. Chem. Soc.* **2010**, *132*, 13217.

[11] Y.-F. Wang, X. Zhu, S. Chiba, *J. Am. Chem. Soc.* **2012**, *134*, 3679.

[12] For recent reviews on metal-catalyzed reactions with O_2 as the oxidant, see: a) Z. Shi, C. Zhang, C. Tang, N. Jiao, *Chem. Soc. Rev.* **2012**, *41*, 3381; b) A. N. Campbell, S. S. Stahl, *Acc. Chem. Res.* **2012**, *45*, 851; c) C. Zhang, C. Tang, N. Jiao, *Chem. Soc. Rev.* **2012**, *41*, 3464; d) W. Wu, H. Jiang, *Acc. Chem. Res.* **2012**, *45*, 1736; e) A. E. Wendlandt, A. M. Suess, S. S. Stahl, *Angew. Chem.* **2011**, *123*, 11256; *Angew. Chem. Int. Ed.* **2011**, *50*, 11062.

[13] a) O. Tabarrini, G. Manfroni, A. Fravolini, V. Cecchetti, S. Sabatini, E. De Clercq, J. Rozenski, B. Canard, H. Dutartre, J. Paeshuyse, J. Neyts, *J. Med. Chem.* **2006**, *49*, 2621; b) R. J. Harrison, A. P. Reszka, S. M. Haider, B. Romagnoli, J. Morrell, M. A. Read, S. M. Gowan, C. M. Incles, L. R. Kellandc, S. Neidle, *Bioorg. Med. Chem. Lett.* **2004**, *14*, 5845; c) Y. Nishihama, Y. Ishikawa, S. Nishiyama, *Tetrahedron Lett.* **2009**, *50*, 2801; d) P. Singh, J. Kaur, P. Kaur, S. Kaur, *Bioorg. Med. Chem.* **2009**, *17*, 2423; e) C. Pal, M. K. Kundu, U. Bandyopadhyay, S. Adhikari, *Bioorg. Med. Chem. Lett.* **2011**, *21*, 3563.

[14] a) J. H. Gorvin, P. D. Whalley, *J. Chem. Soc. Perkin Trans. 1* **1979**, 1364; b) R. Nishio, S. Wessely, M. Sugiura, S. Kobayashi, *J. Comb. Chem.* **2006**, *8*, 459; c) J. R. Goodell, A. A. Madhok, H. Hiasa, D. M. Ferguson, *Bioorg. Med. Chem.* **2006**, *14*, 5467; d) D. G. Pintori, M. F. Greaney, *Org. Lett.* **2010**, *12*, 168; e) G. Manfroni, J. Paeshuyse, S. Massari, S. Zanoli, B. Gatto, G. Maga, O. Tabarrini, V. Cecchetti, A. Fravolini, J. Neyts, *J. Med. Chem.* **2009**, *52*, 3354; f) A. Stankiewicz-Drogń, B. Dörner, T. Erker, A. M. Boguszewska-Chachulska, *J. Med. Chem.* **2010**, *53*, 3117; g) Z. R. Woydziak, L. Fu, B. R. Peterson, *J. Org. Chem.* **2012**, *77*, 473.

[15] a) J. Zhao, R. C. Larock, *J. Org. Chem.* **2007**, *72*, 583; b) Y. Fang, D. C. Rogness, R. C. Larock, F. Shi, *J. Org. Chem.* **2012**, *77*, 6262.

[16] During the preparation of the manuscript, Cheng and Deng independently reported two similar catalytic systems for the synthesis of acridones, see: a) P.-C. Huang, K. Parthasarathy, C.-H. Cheng, *Chem. Eur. J.* **2013**, *19*, 460; b) W. Zhou, Y. Liu, Y. Yang, G.-J. Deng, *Chem. Commun.* **2012**, *48*, 10678.

[17] a) Y. Wu, B. Li, F. Mao, X. Li, F. Y. Kwong, *Org. Lett.* **2011**, *13*, 3258; b) P. Fang, M. Li, H. Ge, *J. Am. Chem. Soc.* **2010**, *132*, 11898.

[18] a) E. M. Simmons, J. F. Hartwig, *Angew. Chem.* **2012**, *124*, 3120; *Angew. Chem. Int. Ed.* **2012**, *51*, 3066; b) E. J. Hennessy, S. L. Buchwald, *J. Am. Chem. Soc.* **2003**, *125*, 12084.

[19] a) L. M. Huffman, A. Casitas, M. Font, M. Canta, M. Costas, X. Ribas, S. S. Stahl, *Chem. Eur. J.* **2011**, *17*, 10643; b) B. Chen, X.-L. Hou, Y.-X. Li, Y.-D. Wu, *J. Am. Chem. Soc.* **2011**, *133*, 7668; c) J. Zhao, Q. Zhang, L. Liu, Y. He, J. Li, J. Li, Q. Zhu, *Org. Lett.* **2012**, *14*, 5362, and references cited therein.

[20] a) M. Lafrance, S. I. Gorelsky, K. Fagnou, *J. Am. Chem. Soc.* **2007**, *129*, 14570; b) C. Tsukano, M. Okuno, Y. Takemoto, *Angew. Chem.* **2012**, *124*, 2817; *Angew. Chem. Int. Ed.* **2012**, *51*, 2763; c) C.-Y. He, Q.-Q. Min, X. Zhang, *Organometallics* **2012**, *31*, 1335.

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