EurJOC
European Journal of Organic Chemistry

A Journal of
ChemPubSoc Europe

Accepted Article

Title: Facile synthesis of substituted acridines via a palladium-catalyzed condensation/cyclization/tautomerization sequence

Authors: Xiangui Chen, Yanjun Xie, Cheng Li, Fuhong Xiao, and Guo-Jun Deng

To be cited as: *Eur. J. Org. Chem.* 10.1002/ejoc.201601553

Link to VoR: http://dx.doi.org/10.1002/ejoc.201601553

Supported by
ACES Asian Chemical Editorial Society

WILEY-VCH

10.1002/ejoc.201601553

WILEY-VCH

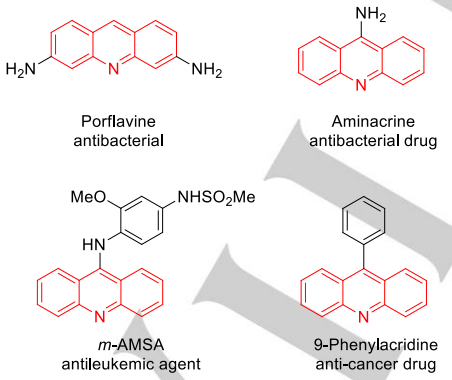
Facile synthesis of substituted acridines *via* a palladium-catalyzed condensation/cyclization/tautomerization sequence

Xiangui Chen,[a] YanjunXie,[a] Cheng Li, [a] Fuhong Xiao, [a]* Guo-Jun Deng[a],[b]*

Abstract: An efficient strategy for 9-aryl-substituted acridine synthesis from cyclohexanones and 2-aminobenzophenones under palladium-catalyzed conditions has been developed. Using molecular oxygen as the green oxidant, various cyclohexanones were acted as aryl source to construct the nitrogen-containing heterocycles *via* condensation/cyclization/tautomerization sequence.

Introduction

Acridines comprise an important class of nitrogen-containing heterocycles that have been widely used as antibacterial, antileukemic, antimalarial and anticancer agents (Scheme 1).[1] Certain 9-amino-substituted acridines have been successfully used as RNA and DNA intercalating agents.[2] Substituted acridines have long been used as dyes and pigments; recently, however, these chemicals have been gradually utilized as key building blocks for electronic application because of their rigid conjugated structure.[3] Consequently, interest in developing an efficient approach to produce various substituted acridine derivatives has been increasing.[4] The classic Brenthsen reaction which uses diphenylamines and carboxylic acids as starting materials in the presence of excess Lewis acids at 200-270 °C, is the earliest practical synthetic method. [5] In recent years, numerous novel synthetic routes for generating substituted acridines under relative mild reaction conditions have been successfully developed. Buchwald et al. established an intramolecular Heck-type reaction from 2-chloroaniline and 2-bromostyrene to produce an acridine derivative.[6] Larock et al. synthesized an acridine derivative from 2-aminoaryl ketones and arynes in the presence of CsF.[7] 2-Halobenzaldehydes or 2-formyl-phenyl triflate could be smoothly reacted with anilines to produce unsymmetrical acridine derivatives.[8] Ellman et al. developed an Rh-catalyzed [3+3] annulation of aromatic imines and aromatic azides to provide various substituted acridine derivatives in reasonable yields.[9] The reaction of *o*-acylanilines with diaryliodonium salts *via* tandem arylation/Friedel-Crafts procedures offers an efficient alternative approach for rapidly preparing substituted acridines.[10] The direct C-H bond functionalization of acridine motif achieves an efficient synthetic approach, particularly for preparing 9-aryl-substituted acridine derivatives.[11] Although several methods are already available,[12] efficient synthetic methods for preparing substituted acridines under mild conditions are still highly sought-after.



Scheme 1. Representative bioactive acridines.

Cyclohexanones are cheap, readily available and easy to handle. These compounds could be easily dehydrogenated to yield cyclohexenones or phenols.[13] Recently, we and others developed various methods using these six-membered cyclic ketones as the aryl source *via* the dehydrogenation-tautomerization process.[14] Cyclohexanones and their reactive intermediates can be trapped to form C-C,[15] C-hetero bonds,[16] and heterocycles.[17] Reaction selectivity can be easily controlled when cyclohexanones are used as cyclization partners to synthesize heterocycles because the reactivities of the carbonyl group and its *ortho*-position carbon are relatively different. Therefore, using cyclohexanone as a two carbon unit and as an aryl source for synthesizing heterocycles exhibits considerable advantage, particularly for selectivity control. In this paper, we report a facile 9-aryl-substituted acridine synthesis from 2-aminobenzophenones and cyclohexanones *via* a palladium-catalyzed condensation/cyclization/aromatization sequence as a continuation of our effort to use cyclohexanones as an aryl source for synthesizing heterocycles. During our investigation on mechanistic study and the preparation of this manuscript, a report about acridine synthesis under metal-free conditions is reported by Wang and coworkers.[18]

Results and Discussion

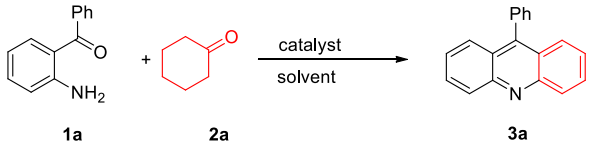
We began the investigation of the reaction of 2-aminobenzophenone (**1a**) and cyclohexanone (**2a**) under palladium catalysis reaction conditions using oxygen as the hydrogen acceptor at 160 °C (Table 1). The corresponding 9-phenylacridine (**3a**) was observed in 25% yield, as determined by gas chromatography analysis when $PdCl_2$/xanthphos was used as the catalyst system and toluene was used as the solvent (entry 1). A brief solvent screening process showed that 1,1,2,2-tetrachloroethane (TCE) is a suitable reaction medium

[a] Key Laboratory of Environmentally Friendly Chemistry and Application of Ministry of Education, College of Chemistry, Xiangtan University, Xiangtan 411105, China. E-mail: fhxiao@xtu.edu.cn; gjdeng@xtu.edu.cn

[b] Beijing National Laboratory for Molecular Sciences and CAS Key Laboratory of Molecular Recognition and Function Institute of Chemistry, Chinese Academy of Sciences (CAS) Beijing 100190 (P.R. China)

Supporting information for this article is given via a link at the end of the document.

Table1. Optimization of the reaction conditions.[a]



1a **2a** **3a**

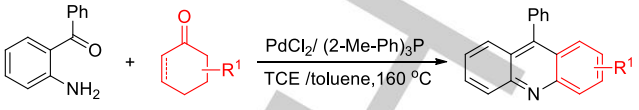
Entry	Catalyst	Ligand	Solvent	Yield [%][b]
1	$PdCl_2$	Xanthphos	toluene	25
2	$PdCl_2$	Xanthphos	PhCl	20
3	$PdCl_2$	Xanthphos	TCE	60
4	$PdCl_2$	$(4\text{-Me-Ph})_3P$	TCE	52
5	$PdCl_2$	$(3\text{-Me-Ph})_3P$	TCE	58
6	$PdCl_2$	$(2\text{-Me-Ph})_3P$	TCE	68
7	$PdCl_2$	DMAP	TCE	43
8	$PdCl_2$	Bipyridine	TCE	65
9	$PdCl_2$	1,10-Phen	TCE	13
10	$Pd(OAc)_2$	$(2\text{-Me-Ph})_3P$	TCE	49
11	$Pd(TFA)_2$	$(2\text{-Me-Ph})_3P$	TCE	35
12	$Pd(OH)_2$	$(2\text{-Me-Ph})_3P$	TCE	13
13	$Pd(MeCN)_2Cl_2$	$(2\text{-Me-Ph})_3P$	TCE	29
14	$PdCl_2$	$(2\text{-Me-Ph})_3P$	TCE/toluene (6/1)	51
15	$PdCl_2$	$(2\text{-Me-Ph})_3P$	TCE/toluene (3/1)	69
16	$PdCl_2$	$(2\text{-Me-Ph})_3P$	TCE/toluene (2/1)	52
17[c]	$PdCl_2$	$(2\text{-Me-Ph})_3P$	TCE/toluene (3/1)	85
18[c,d]	$PdCl_2$	$(2\text{-Me-Ph})_3P$	TCE/toluene (3/1)	90
19[c,d, e]	$PdCl_2$	$(2\text{-Me-Ph})_3P$	TCE/toluene (3/1)	86

[a] Conditions : **1a** (0.2 mmol), **2a** (0.3 mmol), catalyst (5 mol%), ligand (10 mol %), 1,1,2,2-tetrachloroethane (TCE, 0.6 mL), 160 °C under oxygen for 24 h. [b] Determined by GC using trimethylbenzene as an internal standard. [c] **1a** (0.4 mmol), **2a** (0.2 mmol). [d] Catalyst (10 mol%). [e] At 150 °C.

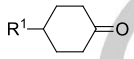
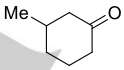
for this type of transformation (entry 2). Several phosphine ligands were investigated using TCE as the solvent, and (2- Me-Ph)$_3$P exhibited the best efficiency (entries 3-6). A few nitrogen-containing ligands were also tested, and good yield was achieved when bipyridine was used (entry 8). Other palladium salts were less efficient than $PdCl_2$ and lower yields were obtained (entries 10-13). The reaction yield was slightly increased when a mixture of TCE/toluene (*v*/*v* = 3/1) was used as the solvent (entry 15). When the excess of **1a** was used, **3a** was obtained in 85% yield (entry 17). Reaction yield was further increased to 90% when 10 mol% of $PdCl_2$ was used (entry 18). Reaction efficiency was significantly reduced when the reaction temperature was decreased (entry 19).

Given these optimized conditions, a variety of cyclohexanones were examined under optimized reaction conditions, as summarized in (Table 2). Various cyclohexanones with electron-donating groups at the *para* position of the carbonyl group were able to react efficiently with **1a** to provide 9-phenyl-substituted acridines in good yields (entries 2-7). The reaction yield slightly

Table2. Reactions of 2-Aminobenzophenone (**1a**) with Cyclohexanones and Cyclohexenone.[a]



1a **2** **3**

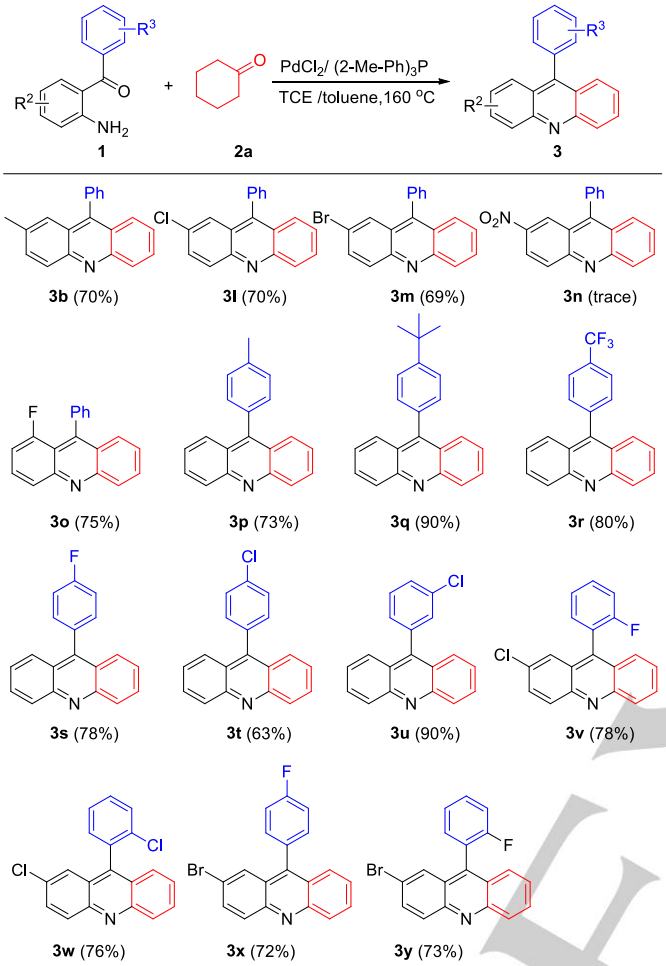
Entry	Cyclohexanone or Cyclohexenone	Product	Yiield [%][b]
			
1	R^1 = H **2a**	**3a**	82
2	R^1 = Me **2b**	**3b**	71
3	R^1 = Et **2c**	**3c**	86
4	R^1 = propyl **2d**	**3d**	86
5	R^1 = *tert*-butyl **2e**	**3e**	72
6	R^1 = *n*-pentyl **2f**	**3f**	62
7	R^1 = *tert*-pentyl **2g**	**3g**	72
8	R^1 = Ph **2h**	**3h**	50
9	R^1 = CO_2Et **2i**	**3i**	51
10	 **2j**	**3j**	38
11	 **2k**	**3k**	62
12[c]	 **2l**	**3a**	55
13	 **2m**	**3a**	66

[a] Reaction conditions: **1a** (0.4 mmol), **2** (0.2 mmol), $PdCl_2$ (10 mol%), t *ortho*-tolylphosphine (10 mol%),1,1,2,2-tetrachloroethane (TCE, 0.6 mL toluene (0.2 mL), 160 °C, 24 h, under oxygen atmosphere. [b] Isolated yie based on **2**. [c] 36 hours.

decreased when a bulky or long chain alkyl substituent was present (entries 5-7). The presence of a phenyl group at the *para* position significantly decreased reaction yield to 50% (entry 8). A similar yield was obtained when an ester functional group was present (entry 9). The position of the substituent profoundly affected reaction yields. When 2-methylcyclohexanone (**2j**) and 3-methylcyclohexanone (**2k**) were used, **3j** and **3k** were obtained in 38% and 62% yields, respectively (entries 10 and 11). When 2-chlorocyclohexanone (**2l**) was used, **3a** was obtained as the only product *via* the cleavage of the C-Cl bond (entry 12). Interestingly, a considerably lower yield was obtained when more reactive cyclohexenone (**2m**) was used (entry 13).

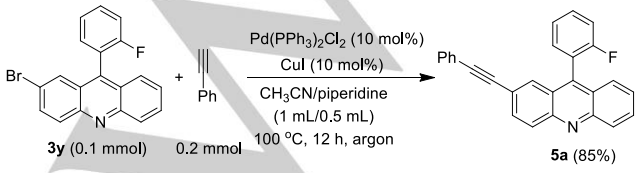
After screening various cyclohexanones for this type of reaction, we then investigated different 2- aminobenzophenones to further explore reaction scope and limitations (Table 3). Several substituents at the *para* position of the amino group were investigated under the aforementioned conditions, and good yields were obtained when methyl, chloro and bromo

Table 3. Reactions of various 2-aminobenzophenones (**1**) with cyclohexanone (**2a**) [a]



[a] Conditions : **1** (0.4 mmol), **2a** (0.2 mmol), $PdCl_2$ (10 mol%), tri-*ortho*-tolylphosphine (10 mol%), 1,1,2,2-tetrachloroethane (TCE, 0.6 mL), toluene (0.2 mL), 160 °C, 24 h, under oxygen atmosphere. [b] Isolated yield based on **2a**.

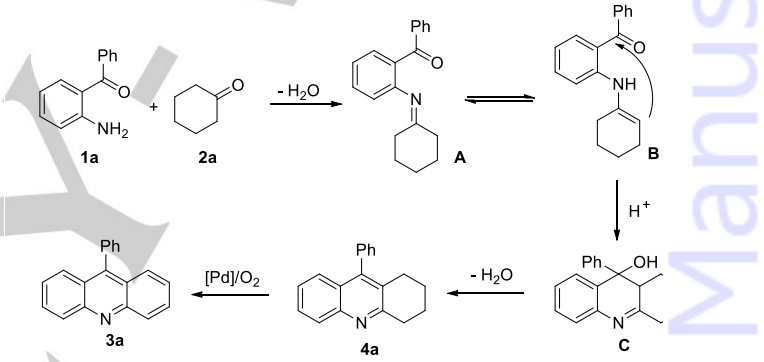
substituents were employed (**3b**-**3m**). However, reaction was inefficient when a strong electron-withdrawing nitro group was present (**3n**). When a fluoro group was present at the *meta* position of the amino group, the desired product **3o** was obtained in 75% yield. The effect of the substituent under different phenyl rings was also investigated. Good yield was obtained when a methyl group existed to provide **3p** in 73% yield. Interestingly, product **3q** was obtained in 90% yield when a more steric *tert*-butyl substituent was used. Halogen groups such as fluoro and chloro were compatible to give the desired products **3r**-**3t** with good yields. The desired product **3u** was obtained in



Scheme 2. Alkynylation of **3y** under palladium-catalysis conditions.

90% yield when a chloro was located at the *meta* position of the carbonyl group. Interestingly, when two halogen substituents existed in both rings of 2-aminobenzophenone, the corresponding functionalized products which could be easily converted further into other useful compounds could be obtained in good yields (**3v**-**3y**). Furthermore, 2-bromo-9-(2-fluorophenyl)acridine (**3y**) could smoothly couple with phenylacetylene under palladium catalyzed reaction conditions to provide 9-(2-fluorophenyl)-2-(phenylethynyl)acridine (**5a**) in 85% yield (Scheme 2).

A plausible reaction pathway to rationalize this reaction is illustrated in (Scheme 3). The condensation reaction of 2-aminobenzophenone (**1a**) with cyclohexanone (**2a**) yields an imine intermediate **A**, which can further isomerize into an enamine intermediate **B**. The cyclization of **B** under acidic reaction conditions[19] affords **C** to convert into **4a** *via* dehydration.[8a,20] A dehydrogenative-tautomerization sequence under palladium-catalyzed conditions used oxygen as the oxidant to achieve the final product **3a**.[15a,17c, 21,]



Scheme 3 . Plausible reaction mechanism.

Conclusions

In summary, we developed a novel approach for 9-aryl-substituted acridines from 2-aminobenzophenones and cyclohexanones *via* a sequence of condensation/cyclization/aromatization procedure. Cheap and readily available cyclohexanones were used as the aryl source *via* dehydrogenation/tautomerization process in an oxygen atmosphere. The significant reactivity difference between the carbonyl group and the ortho carbon in cyclohexanone provided a simple selectivity control process. This method offered an efficient alternative approach for rapidly synthesizing of 9-aryl-substituted acridines from aromatic and non-aromatic substrates

Experimental Section

General information: All reactions were carried out under an atmosphere of oxygen unless otherwise noted. Column chromatography was performed using silica gel 48-75 μm. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker-AV (400 and 100 MHz, respectively) instrument internally referenced to tetramethylsilane (TMS) or chloroform signals.

Mass spectra were measured on Agilent 5975 GC-MS instrument (EI). High-resolution mass spectra were recorded at the Institute of Chemistry, Chinese Academy of Sciences. The structures of known compounds were further corroborated by comparing their ^{1}H NMR, ^{13}C NMR data and MS data with those of literature. Most reagents were obtained from commercial suppliers and used without further purification.

General procedure for the synthesis of 3a: 2-Aminobenzophenone (80 mg, 0.4 mmol) , 1,1,2,2-tetrachloroethane (0.6 mL) were added to a 10 mL oven-dried reaction vessel. The reaction vessel was purged with oxygen for three times and was added cyclohexanone (21.0 μL, 0.2 mmol) and toluene (0.2 mL) by syringe. The sealed reaction vessel was stirred at 160 °C for 24 h. After cooling to room temperature, the reaction was diluted with ethyl acetate (5 mL) and washed with saturated sodium hydroxide solution. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate for three times. The combined organic layer was dried over sodium sulfate, the volatiles were removed under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 95:5) to yield the desired product **3a** as yellow solid (41.8 mg, 82% yield), mp 182-183 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.31 (d, *J* = 8.8 Hz, 2H), 7.81-7.76 (m, 2H), 7.73-7.70 (m, 2H), 7.63-7.58 (m, 3H), 7.46-7.41 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 148.8, 147.2, 135.9, 130.4, 129.9, 129.6, 128.4, 128.3, 126.8, 125.6, 125.1; MS (EI) m/z (%) 255 (100), 226, 113, 88, 77.

Acknowledgements

This work was supported by the National Natural Science Foundation of China (21372187, 21502160, 21572194), the Program for Innovative Research Cultivation Team in University of Ministry of Education of China (1337304), and the Hunan Provincial Innovative Foundation for Postgraduate (CX2015B202).

Keywords: acridines; cyclohexanones; 2-aminobenzophenones; palladium; dehydrogenation.

[1] a) H. Singh, S. Sharma, *Heterocycles* **2015**, *91*, 2043; b) M. Galdino-Pitta, M. Pitta, M. Lima, S. Galdino, I. Pitta, *Mini. Rev. Med. Chem.* **2013**, *13*, 1256; c) G. Cholewiński, K. Dzierzbicka, A. M. Kolodziejczyk, *Pharmacol. Rep.* **2011**, *63*, 305; d) R. M. Acheson, *Acridines*, *2nd ed.*, John Wiley & Sons, New York, **1973**; e) Acrisorcinum, acriflavinium chloride and proflavine are examples of FDA-approved drugs containing an acridine motif. f) P. Liu, Y. J. Hu, J. X. Chen Q. Yang, *Rapid Commun. Mass Spectrom.* **2015**, *29*, 1328.

[2] a) T. Mahmood, A. Paul, S. J. Ladame, *Org. Chem.* **2010**, *75*, 204; b) L. Janovec, M. Kozurková, D. Sabolová, H. Ungvarský, J. Plsíková, Z. Vantová, J. Imrich, *Bioorg. Med. Chem.* **2011**, *19*, 1790; c) G. W. Collie, S. Sparapani, G. N. Parkinson, S. Neidle, *J. Am. Chem. Soc.* **2011**, *133*, 3780; d) L. A. Howell, R. Gulam, A. Mueller, A. O'Connell, M. Searcey, *Bioorg. Med. Chem. Lett.* **2010**, *20*, 6956. e) E. Kuruvilla, P. C. Nandajan, G. B.Schuster, D. Ramaiah, *Org. Lett.*. **2008**,*10(19)*, 4285.

[3] a) J. A. Seo, K. Sang, J. Y. Lee, *Org. Electron*. **2016**, *34*, 33; b) X. Y. Liu, F. Liang, L. Ding, Q. Li, Z. Q. Jiang, L. S. Liao, *Dyes Pigments* **2016**, *126*, 131; c) L. Ding, S. C. Dong, Z. Q. Jiang, H. Chen, L. S. Liao, *Adv. Funct. Mater.* **2015**, *25*, 645; d) M. Uoyama, K.; Shizu, K. Goushi, H. Nomura, C. Adachi, *Nature* **2012**, *492*, 234; e) G. Méhes, H. Normura, Q. Zhang, T. Nakagawa, C. Adachi, *Angew. Chem. Int. Ed.* **2012**, *51*, 11311.

[4] A. Schmidt, M. Liu, *Adv. Heterocycl. Chem.* **2015**, *115*, 287.

[5] a) A. Bernthsen, *Justus Liebigs Ann. Chem.* **1878**, *192*, 1; b) A. Bernthsen,*Justus Liebigs Ann. Chem.* **1884**, *224*, 1.

[6] D. Tsvelikhovsky, S. L. Buchwald, *J. Am. Chem. Soc*. **2010**, *132*, 14048.

[7] D. C. Rogness, R. C. Larock, *J. Org. Chem*. **2010**, *75*, 2289.

[8] a) H. M. Guo, R. Z. Mao, Q. T. Wang, H. Y. Niu, M. S. Xie, *Org. Lett.* **2013**, *15*, 5460; b) Q. Su, P. Li, M. He, Q. L. Wu, L. He, Y. Mu, *Org. Lett.* **2014**, *16*, 18; c) T. J. Wang, W. W. Chen, M. H. Xu, *Org. Biomol. Chem.* **2015**, *13*, 6580.

[9] Y. J. Lian, J. R. Hummel, R. G. Bergman, J. A. Ellman, *J. Am. Chem. Soc.* **2013**, *135*, 12548.

[10] X. L. Pang, Z. B. Lou, M. Li, L. R. Wen, C. Chen, *Eur. J. Org. Chem.* **2015**, 3361.

[11] I. Hyodo, M. Tobisu, N. Chatani, *Chem. Commun*. **2012**, *48*, 308.

[12] a) R. Morioka, K. Hirano, T. Satoh, M. Miura, *Chem. Eur. J.* **2014**, *20*,12720; b) Y. Y. Shan, W. D. Yan, *Tetrahedron Lett.* **2016**, *57*, 2905; c) T. Godet, P. Belmont, *Synlett* **2008**, *16*, 2513; d) J. J. Wu, D. Talwar, S. Johnston, M. Yan, J. L. Xiao, *Angew. Chem. Int. Ed.* **2013**, *52*, 6983 e) Z. S. Zheng, L. Y. Dian, Y. C. Yuan, D. Zhang-Negrerie, Y. F. Du, K. Zhao, *J. Org. Chem*. **2014**, *79*, 7451; f) X. J. Cui, Y. H. Li, S. Bachmann, M. Scalone, A. Surkus, K. Junge, C. Topf, M. Beller, *J. Am. Chem. Soc.* **2015**, *137*, 10652; g) Z. X. Huang, Y. Yang, Q. Xiao, Y. Zhang, J. B. Wang, *Eur. J. Org. Chem*. **2012**, 6586.

[13] a) Y. Izawa, D. Pun, S. S. Stahl, *Science* **2011**, 333, 209; b) T. Diao, S. S. Stahl, *J. Am. Chem. Soc*. **2011**, *133*, 14566.

[14] For a recent review on catalytic dehydrogenative aromatization of cyclohexanones, see: S. Girard, H. W. Huang, F. Zhou, G. J. Deng, C. J. Li, *Org. Chem. Front*. **2015**, *2*, 279.

[15] a) S. P. Chen, Y. F. Liao, F. Zhao, H. R. Qi, S. W. Liu, G. J. Deng, *Org. Lett.* **2014**, *16*, 1618; b) F. Zhou, M. Simon, C. J. Li, *Chem.-Eur. J.* **2013** *19*, 7151.

[16] a) Y. J. Xie, S. W. Liu, Y. Liu, W. Chen, G. J. Deng, *Org. Lett.* **2012**, *14*, 1692; b) S. Girard, X. Hu, T. Knauber, F. Zhou, M. Simon, G. J. Deng, C. J. Li, *Org. Lett.* **2012**, *14*, 5606; c) A. Hajra, Y. Wei, N. Yoshika, *Org. Lett.* **2012**, *14*, 5488; d) M. Barros, S. Dey, C. Maycock, P. Rodrigues, *Chem. Commun.* **2012**, *48*, 10901; e) J. Zhao, H. W. Huang, W. Q. Wu, H. J. Chen, H. F. Jiang, *Org. Lett*. **2013**, *15*, 2604; f) M. Simon, S. A. Girard, C. J. Li, *Angew. Chem., Int. Ed.* **2012**, *51*, 7537; g) Y. F. Liao, P. C. Jiang, S. P. Chen, H. R. Qi, G. J. Deng, *Green Chem.* **2013**, *15*, 3302; h) W. Ge, X. Zhu, Y. Y. Wei, *Adv. Synth. Catal*. **2013**, *355*, 3014.

[17] a) F. H. Xiao, Y. F. Liao, M. Y. Wu, G. J. Deng, *Green Chem*. **2012**, *14*, 3277; b) X. X. Cao, X. F. Cheng, Y. Bai, S. W. Liu, G. J. Deng, *Green Chem*. **2014**, *16*, 4644; c) Y. F. Liao, Y. Peng, H. R. Qi, G. J. Deng, H. Gong, C. J. Li, *Chem. Commun.* **2015**, *51*, 1031; d) J. J. Chen, G. Z. Li Y. J. Xie, Y. F. Liao, F. H. Xiao, G. J. Deng, *Org. Lett.* **2015**, *17*, 5870; f) Y. J. Xie, J. Wu, X. Z. Che, Y. Chen, H. W. Huang, G. J. Deng, *Green Chem*. **2016**, *18*, 667.

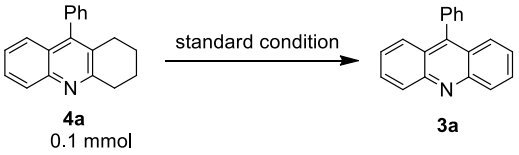
[18] G. C. Senadi, G. K. Dhandabani, W. Hu, J. Wang, *Green Chem.,* 2016, **18**, 6242.

[19] After completion of the reaction, the pH value of the reaction mixture is about 2.

[20] Y. Kuninobo, T. Tatsuzaki, T. Matsuki, K. Takai, *J. Org. Chem.* **2011**, *76* 7005.

[21] Control experiment showed that **4a** was formed even in the absence of palladium catalyst. Intermediate 4acould be isolated from the reaction mixture and further converted into the desired product **3a** in only 23% yield under the standard reaction conditions. However, more than 85% conversion could be observed when added **4a** into a reaction mixture in the presence of starting materials such as **1a** and **2c** (**3a** and **3c** were obtained in high yields). This means the presence of original starting materials could significantly promote the conversion of **4a** into the desired product **3a**.

10.1002/ejoc.201601553



4a
0.1 mmol

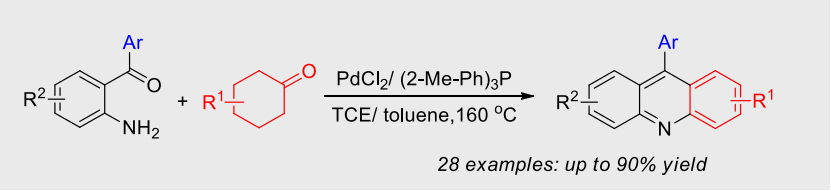
3a

1) conversion 23%
2) with **1a** (0.2 mmol), **2c** (0.1 mmol) conversion > 85%

.

Entry for the Table of Contents (Please choose one layout)

COMMUNICATION



An efficient strategy for 9-aryl-substituted acridine synthesis from cyclohexanones and 2-aminobenzophenones under palladium-catalyzed conditions has been developed. Using molecular oxygen as the green oxidant, various cyclohexanones were acted as aryl source to construct the nitrogen-containing heterocycles *via* condensation/cyclization/tautomerization sequence.

Condensation, cyclization

Xiangui Chen, YanjunXie, Cheng Li, Fuhong Xiao, Guojun Deng.

Page No. – Page No.

Facile synthesis of substituted acridines *via* a palladium-catalyzed condensation/cyclization/tautomerizat-ion sequence