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Synthesis of Polysubstituted Quinolines via Transition-Metal-Free Oxidative Cycloisomerization of *o*-Cinnamylanilines

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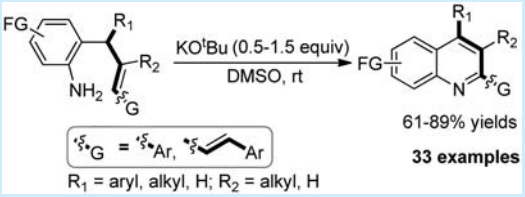
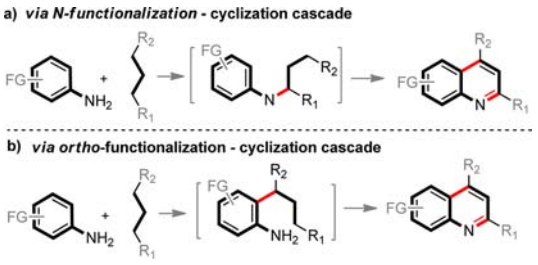
Supporting Information

ABSTRACT: An efficient synthesis of 2-aryl 4-substituted quinolines from stable and readily available *o*-cinnamylanilines, prepared from anilines and cinnamylalcohols, has been developed. The reaction occurred via a regioselective 6-*endo*-*trig* intramolecular oxidative cyclization using KO^{t}Bu as a mediator and DMSO as an oxidant at rt. The reaction showed a broad substrate scope with good to excellent yields.



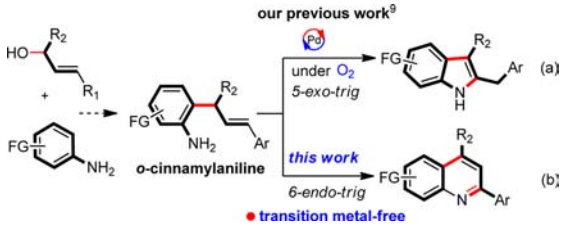
The quinoline skeleton is a key structural unit in a large number of natural products, pharmaceuticals, and agrochemicals.[1] Functionalized quinolines are also widely used as materials[2] and catalysts for asymmetry synthesis.[3] For this reason, the development of synthetic protocols for functionalized quinolines has always been an active area of research.[4,5] The most prevalent strategies for constructing quinoline rings are the classic annulation reactions, including the Combes synthesis,[6a−c] Skraup synthesis,[6d−f] Gould−Jacobs reaction,[6g] Conard−Limpach synthesis,[6h,i] Doebner−von Miller reaction,[6j,k] and Povarov reaction,[6l−n] where commercially available anilines are still a common substrate.[4] Strategically, in the above cases, N-alkylation of anilines followed by cyclization occurs to provide the corresponding quinolines (Scheme 1a). Recently, considerable attention has been focused toward the development of strategies concerning the *ortho*-functionalization of anilines followed by a cyclization reaction (Scheme 1b).[7] Despite these significant advances, the synthesis of such starting materials remains a challenging task in many cases. In this context, the development of a new synthetic protocol for the rapid construction of highly functionalized quinolines with high efficiency from easily available *ortho*-functionalized anilines would be a significant contribution.

Scheme 1. Strategies for the Synthesis of Substituted Quinolines from Anilines



Driven by the fact that a wide variety of highly substituted *o*-cinnamylanilines[8] and their analogues are readily available from cinnamyl alcohols and commercially available anilines, we recently reported a methodology for the synthesis of 2-benzyl indoles from such *o*-cinnamyl anilines (Scheme 2a).[9] In an effort to pursue the diversified application of such *o*-cinnamyl anilines, we have turned our attention toward the possibility of achieving the synthesis of functionalized quinolines from the same (Scheme 2b). Herein, we report a transition-metal-free oxidative cycloisomerization methodology using simple and economical KO^{t}Bu in DMSO at room temperature. Functionalized quinolines were synthesized in high yields and with excellent chemoselectivities. Nevertheless, from the standpoint of sustainability and green chemistry, the development of transition-metal-free reaction conditions has always been an attractive strategy.[10]

Scheme 2. Oxidative Cyclization of *o*-Cinnamylanilines



The 2-arylquinoline moiety is commonly found in a wide range of bioactive molecules such as antimalarials, antitumor agents, and P-selectin antagonists (Figure 1).[11] On the other hand, 2-styrylquinolines are also important scaffolds having considerable biological significance (Figure 1).[12] However, there are limited methods available for the synthesis of such scaffolds.[13]

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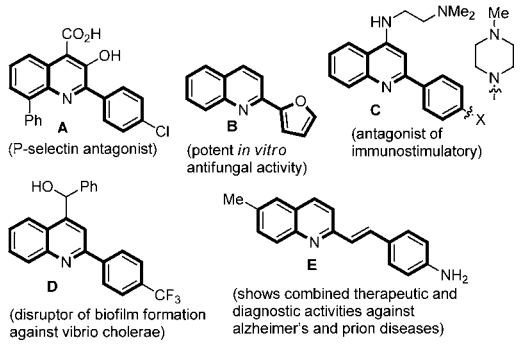
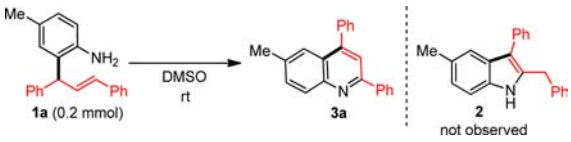


Figure 1. Biologically active quinoline skeleton containing a 2-aryl and 2-styryl substitutions.

Our studies began with (*E*)-2-(1,3-diphenylallyl)-4-methylaniline **1a** (Table 1). When a solution of **1a** in dimethyl sulfoxide

Table 1. Optimization of the Reaction Conditions[a]



entry	base (0.5 equiv)	solvent	**3a** (%)[b]
1	carbonates[c]	DMSO	–
2	LiOH	DMSO	–
3	NaOH	DMSO	22
4	KOH	DMSO	25
5	NaH	DMSO	58
6	KO^{t}Bu	DMSO	83
7	KO^{t}Bu	DMF	53
8	KO^{t}Bu	1,4-dioxane	–
9	KO^{t}Bu	Et_2O	16
10	KO^{t}Bu	THF	12
11	KO^{t}Bu	MeOH	–
12	KO^{t}Bu	EtOAc	12
13	KO^{t}Bu	CH_2Cl_2	–

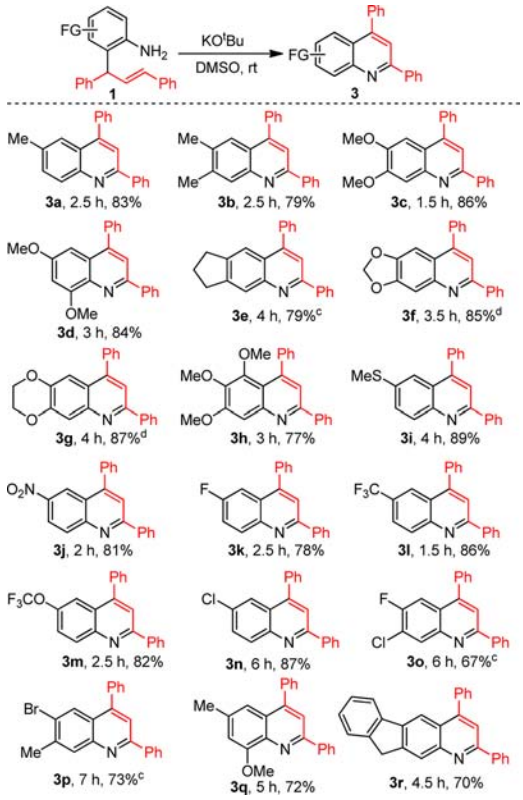
[a]The reaction was carried out with **1a** (0.2 mmol), base (0.5 equiv), 4 h, 1 mL solvent, under an argon atmosphere. [b]The isolated yields. [c]Carbonates such as Na_2CO_3, K_2CO_3, Cs_2CO_3 are used.

(DMSO) was stirred at rt in the presence of a catalytic amount of various bases (such as Na_2CO_3, K_2CO_3, $CsCO_3$, LiOH, NaOH, KOH, NaH, and KO^{t}Bu, entries 1–6, respectively), it was observed that KO^{t}Bu provided the desired 2,4-diphenylquinoline **3a** (entry 6) in 83% isolated yield, which is found to be the best among all the considered bases.

When the same reaction was carried out in other solvents such as DMF,1,4-dioxane, Et_2O, THF, MeOH, EtOAc, and CH_2Cl_2, the reactivity of KO^{t}Bu remained less efficient than in DMSO (entries 7–13, respectively). Further, various diamine ligands were added in addition to KO^{t}Bu, aimed at increasing the yields of the reaction; however, the desired improvement was not observed (see Supporting Information for details). In any case, we could not observe the formation of the indole **2**.

The results summarized in Scheme 3 demonstrate that the oxidative cyclization protocol is a robust one. We examined the scope of the present reaction of *o*-allylanilines with substitution on the aniline moiety. Electron-donating groups including 6-methyl (**3a**), 6,7-dialkyl (**3b**, **3e**), 6,7-dialkoxy (**3c**, **3f**–**g**), 6,8-dimethoxy (**3d**), 5,6,7-trimethoxy (**3h**), and 6-methylthio (**3i**)

Scheme 3. Variation of Aryl Amine[a,b]



[a]Reaction conditions: *o*-allyl aniline **1** (0.20 mmol), KO^{t}Bu (0.5–1.5 equiv), DMSO (1 mL). [b]Isolated yields after column chromatography. [c]1.0 equiv of KO^{t}Bu was used. [d]1.5 equiv of KO^{t}Bu was used.

on the aryl moiety were effectively converted to the corresponding 2,4-diphenyl quinoline in good to excellent yields (77–89%). Electron-withdrawing substituents such as 6-nitro (**3j**), 6-fluoro (**3k**, **3o**), 6-trifluoromethyl (**3l**), and 6-trifluoromethoxy (**3m**) groups are also compatible with the present reaction conditions and proceeded smoothly to afford the desired quinolines. Even sensitive halogens such as bromo- and chloro-substitutions on the aryl ring, which are sensitive to KO^{t}Bu, were also nicely tolerated to afford the desired halogenated quinolines (**3n**–**p**). Substitution *ortho* to the NH_2-group of 2-allyl aniline did not affect the reactivity (for example, in case of **3q**). Another type of aryl group, such as 9*H*-fluorene-2-allyl-1-amine, was equally applicable to provide a fused tetracyclic **3r** quinoline in good yield (70%). In the case of quinolines **3e**–**g** and **3o**–**p**, further addition of KO^{t}Bu was required to achieve the complete consumption of the starting material.

In Scheme 4, the oxidative cyclization of *o*-allylanilines containing substitutions on the allyl counterpart is summarized. Various symmetrically substituted 1′,3′-diaryl allyls such as *p*-methyl, *p*-chloro-, and *p*-bromo-phenyls attached to anilines at *ortho*-position reacted smoothly to provide the desired quinolines (**5a**–**c**, respectively) in moderate yields (80%, 76%, and 77%, respectively). Similar reactivity was found with *o*-allylaniline having the 2-thiophenyl as well as 1-naphthyl group as an aryl counterpart on the allyl moiety (**5d** and **5e**, respectively). Additionally, 2-aryl 4-alkyl quinolines (**5f** and **5g**) were also successfully synthesized using the present protocol. Besides, 4-unsubstituted 2-aryl quinoline **5h** was synthesized in 70% yield using the current strategy. Simple 2-allyl aniline is also reacted to

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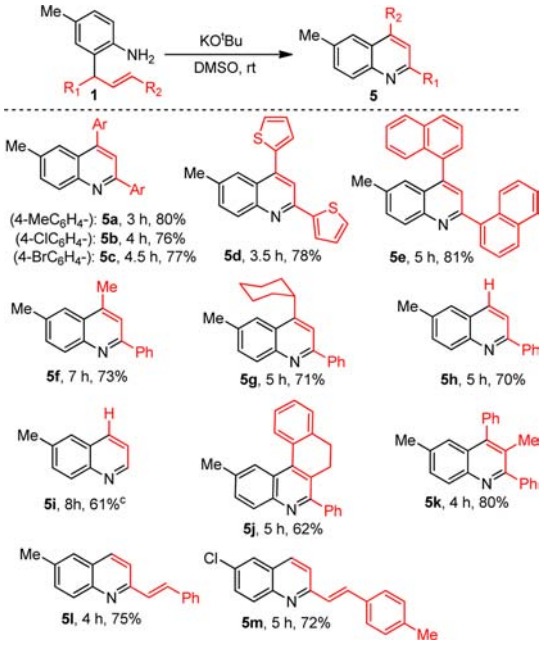
Scheme 4. Variation of Allyl Counterpart[a,b]

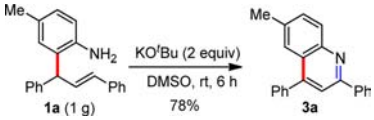


[a]Reaction conditions: *o*-allyl aniline **1** (0.20 mmol), KO^{t}Bu (1.5 equiv), DMSO (1 mL). [b]Isolated yields. [c]Reaction at 80 °C.

provide the desired unsubstituted quinoline (**5i**), except that a slight increase in reaction temperature (80 °C) was needed. Not only substitutions at the 2- and 4- position of quinolines but also a simultaneous substitution at the 2,3- and 4-position could also be achieved using this approach as shown in the case of **5j** and **5k**. Notably, 2-styrylquinoline **5l** and **5m** that are difficult to prepare using other strategies are also synthesized using our methodology.

Further, the reaction of **1a** was scaled 17-fold (1 g, 3.35 mmol) under similar reaction conditions, resulting in a good yield (78%) of the desired product as shown in Scheme 5.

Scheme 5. Gram Scale Synthesis

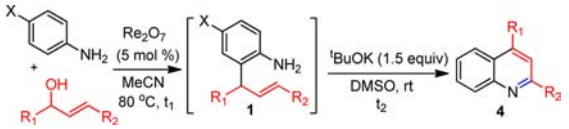


Finally, a one-pot, sequential FC-allylation of anilines with allylalcohols using Re_2O_7 as the catalyst followed by ^{t}BuOK/DMSO mediated cyclization to provide 2,4-disubstituted quinolines have been demonstrated (see Table 2). Although, moderate yields are obtained, nevertheless, the one-pot methodology is expected to be of high synthetic utility.

A tentative mechanism for the current oxidative cyclization reaction is proposed in Scheme 6. The initial step involves KO^{t}Bu/DMSO mediated oxidation[14] of 2-cinnamylaniline **1** to generate intermediate **II** which undergoes 6π-electrocyclization[15] to provide the quinolane **III**.

Subsequent oxidation of intermediate **III** using KO^{t}Bu/DMSO afforded product **3** or **5**. In general, catalytic KO^{t}Bu (0.5 equiv) is sufficient when R is an aryl group (as exemplified in Scheme 3). However, the requirement of excess KO^{t}Bu is realized when R is an alkyl or electron-rich aryl group (as exemplified in Scheme 4); otherwise, a prolonged reaction time

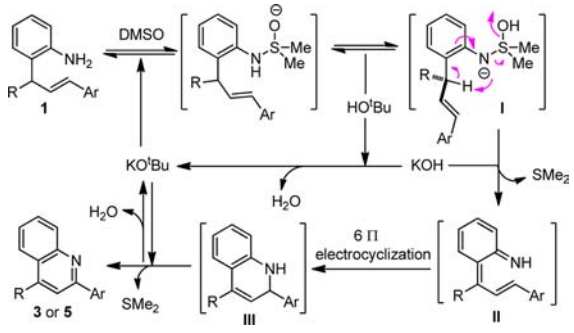
Table 2. One-Pot Protocol: Sequential Process[a]



	X	R_1	R_2	t_1 (h)	t_2 (h)	yield[b]
1	$-CH_3$	C_6H_5	C_6H_5	10	4	53
2	$-SCH_3$	C_6H_5	C_6H_5	8	4	56
3	$-CH_3$	*p*-$CH_3C_6H_4$	*p*-$CH_3C_6H_4$	12	5	51
4	$-CH_3$	*p*-ClC_6H_4	*p*-ClC_6H_4	10	4	54

[a]Reaction conditions: (i) alcohol (0.20 mmol), aniline (0.24 mmol), Re_2O_7 (5 mol %) in CH_3CN; (ii) KO^{t}Bu (1.2 equiv), DMSO (1 mL). [b]Isolated yields after column chromatography.

Scheme 6. Proposed Mechanism for Current Oxidative Cyclization



is observed. We reasoned that the pK_a values of the allylic C−H bond (as shown in intermediate **I**) are responsible for such a display of reactivity.

In summary, we have developed a novel and environmentally benign method for the preparation of 2-arylquinoline and 2-styrylquinolines from readily available *o*-cinnamylanilines using ^{t}BuOK/DMSO as an economical and commercially available reagent. A sequential synthesis of *o*-cinnamylaniline, starting from corresponding anilines and substituted cinnamyl alcohols, followed by oxidative cycloannulation has also been demonstrated. The reaction displays a broad substrate scope and good tolerance to a variety of substituents including aryl, alkyl, and heterocyclic groups. 2-Arylquinoline and 2-styrylquinolines are important compounds with potential applications in medicinal chemistry[11,12] that are now accessible via this inexpensive and transition-metal-free approach. Extension of the present reaction demonstrated toward the synthesis of related heterocyclic moieties, and detailed mechanistic investigations are currently in progress in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedures, characterization data, and copies of NMR spectra for all products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) For bioactivity of quinolines: (a) Michael, J. P. *Nat. Prod. Rep.* **2007**, *24*, 223. (b) Kaur, K.; Jain, M.; Reddy, R. P.; Jain, R. *Eur. J. Med. Chem.* **2010**, *45*, 3245. (c) Ahmed, N.; Brahmbhatt, K. G.; Sabde, S.; Mitra, D.; Singh, I. P.; Bhutani, K. K. *Bioorg. Med. Chem.* **2010**, *18*, 2872. (d) Musiol, R.; Serda, M.; Hensel-Bielowka, S.; Polanski. *J.Curr. Med. Chem.* **2010**, *17*, 1960. (e) Solomon, V. R.; Lee, H. *Curr. Med. Chem.* **2011**, *18*, 1488. (f) Afzal, O.; Kumar, S.; Haider, M. R.; Ali, M. R.; Kumar, R.; Jaggi, M.; Bawa, S. *Eur. J. Med. Chem.* **2014**, DOI: 10.1016/j.ejmech.2014.07.044.

(2) Ligands for the preparation of OLED materials: (a) Kim, J. L.; Shin, I. S.; Kim, H. *J. Am. Chem. Soc.* **2005**, *127*, 1614. (b) Tao, S.; Li, L.; Yu, J.; Jiang, Y.; Zhou, Y.; Lee, C. S.; Lee, S. T.; Zhang, X.; Kwon, O. *Chem. Mater.* **2009**, *21*, 1284. (c) Bhalla, V.; Vij, V.; Kumar, M.; Sharma, P. R.; Kaur, T. *Org. Lett.* **2012**, *14*, 1012.

(3) Quinoline moiety as an organocatalyst: (a) Biddle, M. M.; Lin, M.; Scheidt, K. A. *J. Am. Chem. Soc.* **2007**, *129*, 3830. (b) Zhang, Y.; Sigman, M. S. *J. Am. Chem. Soc.* **2007**, *129*, 3076. (c) Tan, B.; Shi, Z.; Chua, P. J.; Zhong, G. *Org. Lett.* **2008**, *10*, 3425.

(4) For recent reviews on the quinoline synthesis: (a) Madapa, S.; Tusi, A.; Batra, S. *Curr. Org. Chem.* **2008**, *12*, 1116. (b) Marco-Contelles, J.; Perez-Mayoral, E.; Samadi, A.; Carreiras, M. C.; Soriano, E. *Chem. Rev.* **2009**, *109*, 2652.

(5) Selected recent protocols for the quinoline synthesis: (a) Matsubara, Y.; Hirakawa, S.; Yamaguchi, Y.; Yoshida, Z.-I. *Angew. Chem., Int. Ed.* **2011**, *50*, 7670. (b) Batchu, H.; Bhattacharyya, S.; Batra, S. *Org. Lett.* **2012**, *14*, 6330. (c) Zhang, X.; Liu, B.; Shu, X.; Gao, Y.; Lv, H.; Zhu, J. *J. Org. Chem.* **2012**, *77*, 501. (d) Ji, X.; Huang, H.; Li, Y.; Chen, H.; Jiang, H. *Angew. Chem., Int. Ed.* **2012**, *51*, 7292. (e) Yan, R.; Liu, X.; Pan, C.; Zhou, X.; Li, X.; Kang, X.; Huang, G. *Org. Lett.* **2013**, *15*, 4876. (f) Wang, Y.; Chen, C.; Peng, J.; Li, M. *Angew. Chem., Int. Ed.* **2013**, *52*, 5323. (g) Zhang, L.; Zheng, L.; Guo, B.; Hua, R. *J. Org. Chem.* **2014**, *79*, 11541. (h) Wu, K.; Huang, Z.; Liu, C.; Zhang, H.; Lei, A. *Chem. Commun.* **2015**, *51*, 2286. (i) Gao, Q.; Liu, S.; Wu, X.; Wu, A. *Org. Lett.* **2014**, *16*, 4582. (j) Zhao, P.; Yan, X.; Yin, H.; Xi, C. *Org. Lett.* **2014**, *16*, 1120.

(6) For Combes synthesis: (a) Combes, A. *Bull. Soc. Chim. Fr.* **1888**, *49*, 89. (b) Born, J. L. *J. Org. Chem.* **1972**, *37*, 3952. (c) Johnson, W. S.; Mathews, F. J. *J. Am. Chem. Soc.* **1944**, *66*, 210. For Skraup synthesis: (d) Skraup, Z. H. *Chem. Ber.* **1880**, *13*, 2086. (e) Manske, R. H. *Chem. Rev.* **1942**, *30*, 113. (f) Warren, M. *Tetrahedron* **1964**, *20*, 2773. For Gould−Jacobs synthesis: (g) Gould, R. G.; Jacob, W. A. *J. Am. Chem. Soc.* **1939**, *61*, 2890. For Conard−Limpach synthesis: (h) Conrad, M.; Limpach, L. *Chem. Ber.* **1887**, *20*, 944. (i) Misani, F.; Bogert, M. T. *J. Org. Chem.* **1945**, *10*, 347. For Doebner−Von Miller synthesis: (j) Doebner, O.; Miller, W. V. *Chem. Ber.* **1881**, *14*, 2812. (k) Doebner, O.; Miller, W. V. *Chem. Ber.* **1883**, *16*, 1664. For Povarov synthesis: (l) Povarov, L. S. *Ser. Khim.* **1963**, 953. (m) Povarov, L. S.; Mikhailov, B. M. *Izv. Akad. Nauk SSSR Ser. Khim.* **1963**, 953. (n) Kouznetsov, V. V. *Tetrahedron* **2009**, *65*, 2721.

(7) For cyclization of *ortho*-substituted anilines: from 2-acylaniline: (a) Gabriele, B.; Mancuso, R.; Salerno, G.; Lupinacci, E.; Ruffolo, G.; Costa, M. *J. Org. Chem.* **2008**, *73*, 4971. (b) Lekhok, K. C.; Prajapati, D.; Boruah, R. C. *Synlett* **2008**, 655. (c) Gabriele, B.; Mancuso, R.; Salerno, G.; Ruffolo, G.; Plastina, P. *J. Org. Chem.* **2007**, *72*, 6873. (d) Kong, L.; Zhou, Y.; Huang, H.; Yang, Y.; Liu, Y.; Li, Y. *J. Org. Chem.* **2015**, *80*, 1275. (e) Jia, C.-S.; Zhang, Z.; Tu, S.-J.; Wang, G.-W. *Org. Biomol. Chem.* **2006**, *4*, 104. (f) Wu, J.; Xia, H.-G.; Gao, k. *Org. Biomol. Chem.* **2006**, *4*, 126. (g) Khong, S.; Kwon, O. *J. Org. Chem.* **2012**, *77*, 8257. From 2-formyl aniline: (h) Patil, N. T.; Raut, V. S. *J. Org. Chem.* **2010**, *75*, 6961. (i) Stone, M. T. *Org. Lett.* **2011**, *13*, 2326. (j) Patil, N. T.; Raut, V. S.; Shinde, V. S.; Gayatri, G.; Sastry, G. N. *Chem.—Eur. J.* **2012**, *18*, 5530. (k) Bañón-Caballero, A.; Guillena, G.; Nájera, C. *J. Org. Chem.* **2013**, *78*, 5349. (l) Selig, P.; Raven, W. *Org. Lett.* **2014**, *16*, 5192. From 2-alkynyl aniline: (m) Sakai, N.; Annaka, K.; Konakahara, T. *J. Org. Chem.* **2006**, *71*, 3653. (n) Toh, K. K.; Sanjaya, S.; Sahnoun, S.; Chong, S. Y.; Chiba, S. *Org. Lett.* **2012**, *14*, 2290. (o) Liu, B.; Gao, H.; Yu, Y.; Wu, W.; Jiang, H. *J. Org. Chem.* **2013**, *78*, 10319. From 2-boryl aniline: (p) Horn, J.; Marsden, S. P.; Nelson, A.; House, D.; Weingarten, G. G. *Org. Lett.* **2008**, *10*, 4117. From 2-hydroxyalkyl aniline: (q) Zhang, Z.; Tan, J.; Wang, Z. *Org. Lett.* **2008**, *2*, 173. (r) Martíne, R.; Ramón, D. J.; Yus, M. *J. Org. Chem.* **2008**, *73*, 9778. From 2-hydroxypropargyl aniline: (s) Gabriele, B.; Mancuso, R.; Salerno, G.; Lupinacci, E.; Ruffolo, G.; Costa, M. *J. Org. Chem.* **2008**, *73*, 4971. (t) Ali, S.; Zhu, H.-T.; Xia, X.-F.; Ji, K.-G.; Yang, Y.-F.; Song, X.-R.; Liang, Y.-M. *Org. Lett.* **2011**, *13*, 2598. From 2-allylaniline: (u) Beller, M.; Thiel, O. R.; Trauthwein, H.; Hartung, C. G. *Chem.—Eur. J.* **2000**, *6*, 2513. From 2-haloaniline: (v) Stone, M. T. *Org. Lett.* **2011**, *13*, 2326.

(8) Recent synthesis of *ortho*-cinnamylanilines: (a) Chen, K.; Li, Y. X.; Pullarkat, S. A.; Leung, P. H. *Adv. Synth. Catal.* **2012**, *354*, 83. (b) Chen, K.; Chen, H. J.; Wong, J.; Yang, J.; Pullarkat, S. A. *ChemCatChem* **2013**, *5*, 3882. (c) Nallagonda, R.; Mohammad, R.; Ghorai, P. *J. Org. Chem.* **2014**, *79*, 2934.

(9) Nallagonda, R.; Mohammad, R.; Ghorai, P. *Org. Lett.* **2014**, *16*, 4786.

(10) Metal-free pathway: (a) Liu, W.; Cao, H.; Zhang, H.; Zhang, H.; Chung, K. H.; He, C.; Wang, H.; Kwong, F. Y.; Lei, A. *J. Am. Chem. Soc.* **2010**, *132*, 16737. (b) Sun, C.-L.; Li, H.; Yu, D.-G.; Yu, M.; Zhou, X.; Lu, X.-Y.; Huang, K.; Zheng, S.-F.; Li, B.-J.; Shi, Z.-J. *Nat. Chem.* **2010**, *2*, 1044. (c) Shirakawa, E.; Zhang, X.; Hayashi, T. *Angew. Chem., Int. Ed.* **2011**, *50*, 4671. (d) Zhang, H.; Shi, R.; Ding, A.; Lu, L.; Chen, B.; Lei, A. *Angew. Chem., Int. Ed.* **2012**, *51*, 12542. (e) Cuthbertson, J.; Gray, V. J.; Wilden, J. D. *Chem. Commun.* **2014**, *50*, 2575. (f) Zhou, S.; Anderson, G. M.; Mondal, B.; Doni, E.; Ironmonger, V.; Kranz, M.; Tuttle, T.; Murphy, J. A. *Chem. Sci.* **2014**, *5*, 476.

(11) (a) Klingenstein, R.; Melnyk, P.; Leliveld, S. R.; Ryckebusch, A.; Korth, C. *J. Med. Chem.* **2006**, *49*, 5300. (b) Kaila, N.; Janz, K.; Huang, A.; Moretto, A.; DeBernardo, S.; Bedard, P. W.; Tam, S.; Clerin, V.; Keith, J. C., Jr; Tsao, D. H. H.; Sushkova, N.; Shaw, G. D.; Camphausen, R. T.; Schaub, R. G.; Wang, Q. *J. Med. Chem.* **2007**, *50*, 40. (c) Chan, S. H.; Chui, C. H.; Chan, S. W.; Kok, S. H. L.; Chan, D.; Tsoi, M. Y. T.; Leung, P. H. M.; Lam, A. K. Y.; Chan, A. S. C.; Lam, K. H.; Tang, J. C. O. *Med. Chem. Lett.* **2013**, *4*, 170.

(12) For 2-styrylquinolines: Staderini, M.; Aulić, S.; Bartolini, M.; Tran, H. N. A.; González-Ruiz, V.; Pérez, D. I.; Cabezas, N.; Martínez, A.; Martín, M. A.; Andrisano, V.; Legname, G.; Menéndez, J. C.; Bolognesi, M. L. *Med. Chem. Lett.* **2013**, *4*, 225.

(13) (a) Yan, Y.; Xu, K.; Fang, Y.; Wang, Z. *J. Org. Chem.* **2011**, *76*, 6849. (b) Qian, B.; Xie, P.; Xie, Y.; Huang, H. *Org. Lett.* **2011**, *13*, 2580. (c) Wang, Z.; Li, S.; Yu, B.; Wu, H.; Wang, Y.; Sun, X. *J. Org. Chem.* **2012**, *77*, 8615. (d) Leon, B.; Fong, J. C. N.; Peach, K. C.; Wong, W. R.; Yildiz, F. H.; Linington, R. G. *Org. Lett.* **2013**, *15*, 1234.

(14) For such a dipolar association followed by oxidation: (a) Epstein, W. W.; Sweat, F. W. *Chem. Rev.* **1967**, *67*, 247. (b) Martin, H. D.; Weise, A.; Niclas, H.-J. *Angew. Chem., Int. Ed.* **1967**, *6*, 318.

(15) For such 6π-electrocyclization: (a) Jiang, Y.; Park, C.-M.; Loh, T.-P. *Org. Lett.* **2014**, *16*, 3432. Cyclization occurring at rt: (b) Winter, A.; Risch, N. *Synlett* **2003**, 1959.

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