

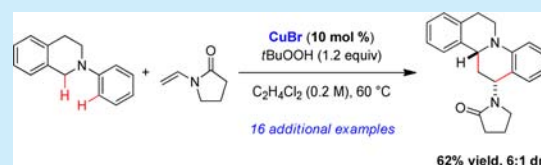
Dual C–H Functionalization of *N*-Aryl Amines: Synthesis of Polycyclic Amines via an Oxidative Povarov Approach

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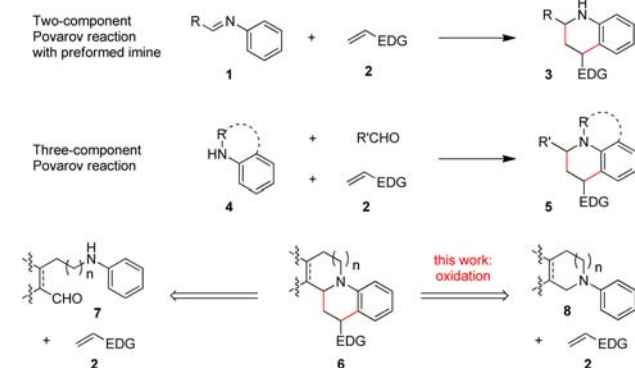
S Supporting Information

ABSTRACT: Iminium ions generated in situ via copper(I) bromide catalyzed oxidation of *N*-aryl amines readily undergo [4 + 2] cycloadditions with a range of dienophiles. This method involves the functionalization of both a C(sp³)–H and a C(sp²)–H bond and enables the rapid construction of polycyclic amines under relatively mild conditions.



First reported in 1963,¹ the Povarov reaction comprises a formal [4 + 2] cycloaddition of an electron-rich dienophile and a 2-azadiene, typically an *N*-aryl imine or iminium ion.² This transformation generally requires a Lewis or Brønsted acid catalyst or promoter and provides an efficient route to tetrahydroquinolines (Scheme 1).³ Povarov reactions are

Scheme 1. Variants of the Povarov Reaction

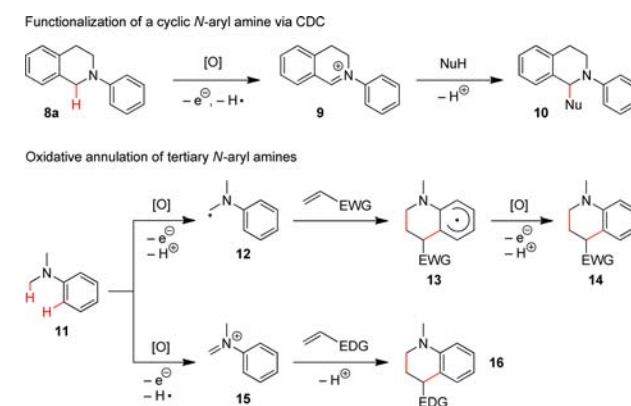


commonly performed as two-component transformations in which a preformed imine **1** engages an electron-rich dienophile **2** to form tetrahydroquinoline product **3**. Three-component variants are also popular and involve the condensation of an amine **4** with an aldehyde (or a ketone) and a dienophile **2**.² While the two-component method is limited to imines derived from primary amines, the three-component approach is also applicable to secondary *N*-aryl amines, including cyclic amines.⁴ The latter enables the formation of polycyclic products **5** in which two rings are fused to the same aryl group. In contrast, the classic Povarov reaction is not readily applicable to the synthesis of polycyclic amines of type **6**. A typical two-component Povarov approach to these compounds would require an aminoaldehyde **7**, species that are not readily accessible. Other approaches to polycyclic frameworks related to **6** typically require *ortho*-functionalized *N*-aryl amines and/or

additional steps. These methods include intramolecular redox transformations,⁵ oxidative couplings,⁶ C–N bond formation via Pd-catalysis⁷ or benzyne intermediates,⁸ and Bischler–Napieralski reactions followed by reduction.⁹ As part of our continuing efforts to develop practical methods for the C–H functionalization of amines,¹⁰ herein we report an alternate Povarov approach to polycyclic tetrahydroquinolines **6** that utilizes the in situ oxidation of readily available *N*-aryl amines **8**.

The oxidative C–H functionalization of amines has a venerable history and was greatly popularized by the pioneering studies of the Murahashi¹¹ and Li¹² groups, who advanced the applicability of catalytic approaches. Oxidative reactions in which a C–H bond is replaced with a functional group are now widely referred to as cross-dehydrogenative coupling reactions (CDC reactions).^{13,14} A typical CDC reaction involves the oxidation of a tertiary amine such as **8a** to an iminium ion (e.g., **9**), followed by capture of **9** with a nucleophilic species (NuH) to form product **10** (Scheme 2).^{15,16} The vast majority of these

Scheme 2. Examples of Oxidative Amine C–H Functionalizations



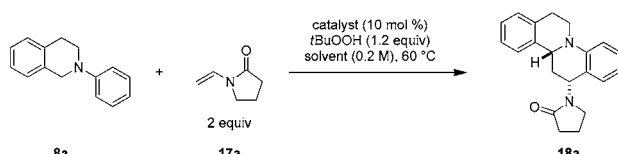
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transformations employ *N*-aryl tetrahydroisoquinolines and lead to the monofunctionalization of the benzylic α -position of these substrates. Few transformations of *N*-aryl amines have been reported that, in addition to α -functionalization, simultaneously result in the functionalization of an *ortho* aryl C–H bond. An example of such a process is the oxidation of **11** to radical **12** which subsequently engages an electron-deficient olefin to give product **14** via the oxidation of radical intermediate **13**.¹⁷ With regard to the proposed oxidative Povarov reaction, to our knowledge such a process has only been realized with *N,N*-dimethylanilines (e.g., **11**),¹⁸ giving relatively simple *N*-alkyl tetrahydroquinoline derivatives **16** (via iminium ion **15**), products that are also accessible via classic Povarov reactions that utilize *N*-methyl aniline as the substrate.^{2,4,19}

The title reaction was first evaluated using *N*-phenyl 1,2,3,4-tetrahydroisoquinoline (**8a**) and 1-vinylpyrrolidin-2-one (**17a**) as model substrates (Table 1). A preliminary survey of various

Table 1. Reaction Development^a



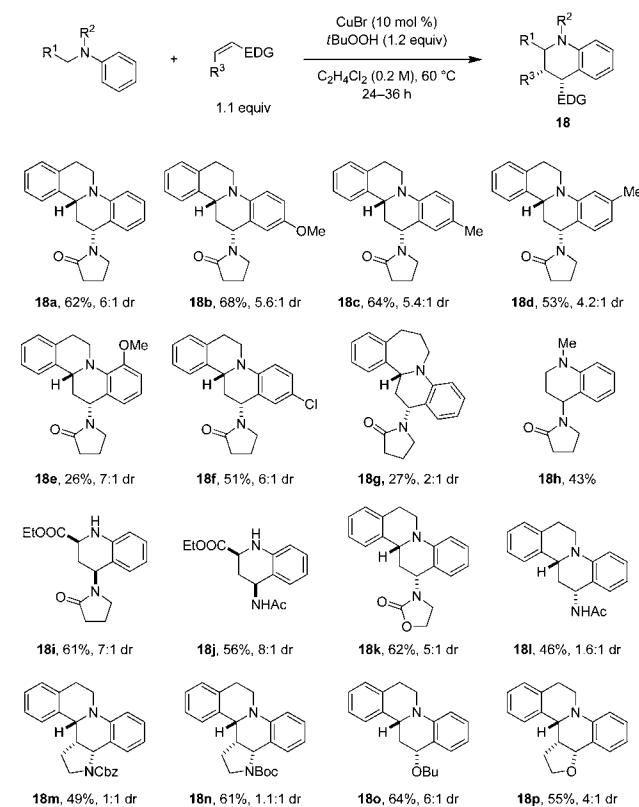
entry ^a	catalyst	solvent	time [h]	dr ^b	yield ^c (%)
1	CuCl	CH ₃ CN	24	10:1	60
2	CuBr	CH ₃ CN	24	8.7:1	65
3	CuBr ₂	CH ₃ CN	24	10:1	50
4	CuCl ₂	CH ₃ CN	10	12:1	27
5	CuI	CH ₃ CN	24	7:1	49
6	Cu(OTf) ₂	CH ₃ CN	24	1:1	26
7	CuBr	THF	24	5:1	49
8	CuBr	C ₂ H ₄ Cl ₂	24	5.8:1	81
9	CuBr	dioxane	24	5.2:1	59
10	CuBr	MeOH	32	4.6:1	49
11	CuBr	CHCl ₃	32	3:1	60
12	CuBr	PhMe	32	2.7:1	20
13	CuBr	—	24	ND	13
14 ^d	CuBr	C ₂ H ₄ Cl ₂	24	6:1	80 (62 ^e)

^aReactions were performed with 0.2 mmol of **8a**, 0.4 mmol of **17a**, 0.02 mmol of catalyst, and 0.24 mmol of *t*BuOOH (5.5 M in decane) in 1 mL of solvent. ^bThe dr was determined by ¹H NMR of the crude reaction mixture. ^cYield was determined by ¹H NMR with an internal standard. ^d1.1 equiv of **17a** was used. ^eIsolated yield.

methods for amine oxidation (including aerobic conditions) led to the identification of *tert*-butyl hydroperoxide (TBHP) as the most promising terminal oxidant.²⁰ Out of a number of copper salts that were tested as catalysts in reactions performed in acetonitrile solution, copper(I) bromide provided the best results (entry 2). With regard to product yield, 1,2-dichloroethane was found to be superior to acetonitrile and other solvents such as tetrahydrofuran, dioxane, methanol, chloroform, and toluene. A reaction performed under neat conditions resulted in a dramatically reduced yield of **18a** (entry 13). Decreasing the amount of **17a** from two to 1.1 equiv had no adverse effects on the reaction outcome (entry 14). Under these optimized conditions, **18a** was obtained in 62% isolated yield and with a dr of 6:1 in favor of the endo-product.

The scope of the oxidative Povarov reaction was evaluated on a set of amine/dienophile combinations (Scheme 3). A range of

Scheme 3. Scope of the Reaction^a



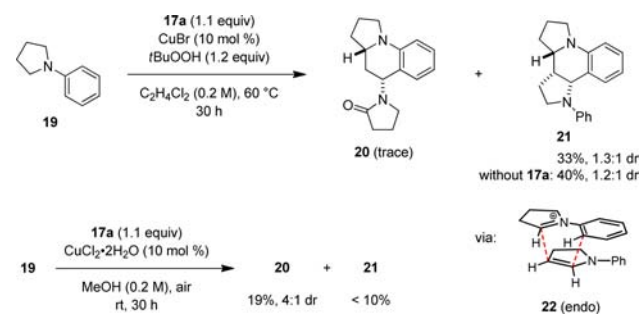
^aReactions were performed with 0.5 mmol of the amine, 0.55 mmol of the dienophile, 0.05 mmol of CuBr, and 0.6 mmol of *t*BuOOH (5.5 M in decane) in 2.5 mL of C₂H₄Cl₂. All yields are combined isolated yields of both diastereomers.

tetrahydroisoquinolines with different substituents on the *N*-aryl ring readily underwent cycloaddition with 1-vinylpyrrolidin-2-one (**17a**) to produce the corresponding products **18** in moderate to good yields. However, *ortho*-substituents on the *N*-aryl ring proved problematic, presumably due to developing A_{1,3}-type strain in the transition state of this reaction. As a consequence, product **18e** was isolated in only a 26% yield. Although low-yielding, *N*-phenyl tetrahydroazepine also engaged in a reaction with **17a** to form polycyclic product **18g**. To our knowledge, this represents the first example of a tetrahydroazepine derivative undergoing a CDC-type reaction.

In order to explore the generality of the method, two acyclic aniline derivatives were tested. *N,N*-Dimethylaniline, upon reacting with **17a**, provided the expected product **18h** in 43% yield. An *N*-phenylglycine ester was also found to be a suitable substrate, giving cyclic amino acid derivative **18i**, in 61% yield. This illustrates the potential utility of this method in the direct C–H functionalization of peptide derivatives.²¹ Finally, the scope of the oxidative Povarov reaction was explored with regard to the dienophile. Various acyclic and cyclic enol ethers and enamides readily underwent the title reaction to provide polycyclic products in moderate to good yields. The diastereoselectivity for some of these reactions was rather poor.

An attempt to extend the scope of the oxidative Povarov reaction to *N*-phenyl pyrrolidine (**19**) as the amine initially only led to the formation of trace amounts of the expected product **20** (Scheme 4). Instead, oxidation of **19** in the presence of **17a** resulted in the formation of **21** as a 1.3:1 mixture of diastereomers in 33% yield. The yield of **21**

Scheme 4. Oxidative Functionalization of *N*-Phenylpyrrolidine



increased to 40% when the reaction was conducted in the absence of **17a**. This substrate dimerization (i.e., via **22**) is easily rationalized, as the iminium ion resulting from the oxidation of **19** is expected to exist in equilibrium with its corresponding enamine.²² As was observed previously with cyclic enecarbamates, the diastereoselectivity of this process was found to be low.

In order to obtain the desired product **20**, a number of other conditions were evaluated. Gratifyingly, **20** was obtained, albeit in only 19% yield, in a reaction that was conducted in methanol, using copper(II) chloride dihydrate as the catalyst and air as the terminal oxidant. In this instance, dimerization product **21** was obtained in less than 10% yield. This change in product distribution may be rationalized on the basis that the intermediate iminium ion can be captured by methanol to form the corresponding *N,O*-acetal which in turn could act as a reservoir for the iminium ion, thus reducing the concentration of the *N*-phenyl pyrrolidine enamine.

In summary, we have reported oxidative Povarov reactions of various *N*-aryl amines as a method to rapidly access polycyclic amines. These reactions feature the dual functionalization of both a C(sp³)-H and a C(sp²)-H bond and are likely amenable to enantioselective catalysis.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedures and characterization data, including an X-ray crystal structure of product **18k** (CIF). 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) Povarov, L. S.; Mikhailov, B. M. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1963**, 955.
- (2) Selected recent reviews on the Povarov reaction: (a) Glushkov, V. A.; Tolstikov, A. G. *Russ. Chem. Rev.* **2008**, 77, 137. (b) Kouznetsov, V. V. *Tetrahedron* **2009**, 65, 2721. (c) Sridharan, V.; Suryavanshi, P. A.; Menendez, J. C. *Chem. Rev.* **2011**, 111, 7157. (d) Masson, G.; Lalli, C.;

Benohoud, M.; Dagousset, G. *Chem. Soc. Rev.* **2013**, 42, 902. (e) Jiang, X. X.; Wang, R. *Chem. Rev.* **2013**, 113, 5515. (f) Fochi, M.; Caruana, L.; Bernardi, L. *Synthesis* **2014**, 46, 135.

(3) Selected recent reports on the Povarov reaction: (a) Ishitani, H.; Kobayashi, S. *Tetrahedron Lett.* **1996**, 37, 7357. (b) Sundararajan, G.; Prabakaran, N.; Varghese, B. *Org. Lett.* **2001**, 3, 1973. (c) Akiyama, T.; Morita, H.; Fuchibe, K. *J. Am. Chem. Soc.* **2006**, 128, 13070. (d) Liu, H.; Dagousset, G.; Masson, G.; Retailleau, P.; Zhu, J. P. *J. Am. Chem. Soc.* **2009**, 131, 4598. (e) Xie, M. S.; Chen, X. H.; Zhu, Y.; Gao, B.; Lin, L. L.; Liu, X. H.; Feng, X. M. *Angew. Chem., Int. Ed.* **2010**, 49, 3799. (f) Dagousset, G.; Zhu, J. P.; Masson, G. *J. Am. Chem. Soc.* **2011**, 133, 14804. (g) Caruana, L.; Fochi, M.; Ranieri, S.; Mazzanti, A.; Bernardi, L. *Chem. Commun.* **2013**, 49, 880. (h) Chen, Z. L.; Wang, B. L.; Wang, Z. B.; Zhu, G. Y.; Sun, J. W. *Angew. Chem., Int. Ed.* **2013**, 52, 2027. (i) Luo, C. S.; Huang, Y. *J. Am. Chem. Soc.* **2013**, 135, 8193.

(4) Selected examples of Povarov reactions with secondary *N*-aryl amines: (a) Shono, T.; Matsumura, Y.; Inoue, K.; Ohmizu, H.; Kashimura, S. *J. Am. Chem. Soc.* **1982**, 104, 5753. (b) Katritzky, A. R.; Gordeev, M. F. *J. Org. Chem.* **1993**, 58, 4049. (c) Beifuss, U.; Ledderhose, S. *J. Chem. Soc., Chem. Commun.* **1995**, 2137. (d) Chen, R.; Qian, C. *Synth. Commun.* **2002**, 32, 2543. (e) Muhuhi, J.; Spaller, M. R. *J. Org. Chem.* **2006**, 71, 5515. (f) Dehnhardt, C. M.; Espinal, Y.; Venkatesan, A. M. *Synth. Commun.* **2008**, 38, 796. (g) Min, C.; Mittal, N.; Sun, D. X.; Seidel, D. *Angew. Chem.* **2013**, 52, 14084.

(5) Selected recent reviews on intramolecular redox transformations: (a) Matyus, P.; Elias, O.; Tapolsanyi, P.; Polonka-Balint, A.; Halasz-Dajka, B. *Synthesis* **2006**, 2625. (b) Platonova, A. Y.; Glukhareva, T. V.; Zimovets, O. A.; Morzherin, Y. Y. *Chem. Heterocycl. Compd.* **2013**, 49, 357. (c) Peng, B.; Maulide, N. *Chem.—Eur. J.* **2013**, 19, 13274. (d) Wang, L.; Xiao, J. *Adv. Synth. Catal.* **2014**, 356, 1137. (e) Haibach, M. C.; Seidel, D. *Angew. Chem., Int. Ed.* **2014**, 53, DOI: 10.1002/anie.201306489.

(6) (a) Richter, H.; Mancheno, O. G. *Eur. J. Org. Chem.* **2010**, 4460. (b) Chen, D.-F.; Han, Z.-Y.; He, Y.-P.; Yu, J.; Gong, L.-Z. *Angew. Chem., Int. Ed.* **2012**, 51, 12307. (c) Gwon, S. H.; Kim, S. G. *Tetrahedron: Asymmetry* **2012**, 23, 1251. (d) Zhang, G.; Wang, S.; Ma, Y.; Kong, W.; Wang, R. *Adv. Synth. Catal.* **2013**, 355, 874. (e) Nie, S.-z.; Sun, X.; Wei, W.-t.; Zhang, X.-j.; Yan, M.; Xiao, J.-l. *Org. Lett.* **2013**, 15, 2394.

(7) Harada, R.; Nishida, N.; Uchiito, S.; Onozaki, Y.; Kurono, N.; Senboku, H.; Masao, T.; Ohkuma, T.; Orito, K. *Eur. J. Org. Chem.* **2012**, 2012, 366.

(8) (a) Kametani, T.; Terui, T.; Fukumoto, K. *Yakugaku Zasshi* **1968**, 88, 1388. (b) Kano, S.; Yokomatsu, T.; Shibuya, S. *Chem. Pharm. Bull.* **1975**, 23, 1089.

(9) Ohba, M.; Shinbo, Y.; Toda, M.; Fujii, T. *Chem. Pharm. Bull.* **1992**, 40, 2543.

(10) (a) Zhang, C.; De, C. K.; Mal, R.; Seidel, D. *J. Am. Chem. Soc.* **2008**, 130, 416. (b) Zhang, C.; Murarka, S.; Seidel, D. *J. Org. Chem.* **2009**, 74, 419. (c) Murarka, S.; Zhang, C.; Konieczynska, M. D.; Seidel, D. *Org. Lett.* **2009**, 11, 129. (d) Murarka, S.; Deb, I.; Zhang, C.; Seidel, D. *J. Am. Chem. Soc.* **2009**, 131, 13226. (e) Deb, I.; Seidel, D. *Tetrahedron Lett.* **2010**, 51, 2945. (f) Zhang, C.; Seidel, D. *J. Am. Chem. Soc.* **2010**, 132, 1798. (g) Zhang, C.; Das, D.; Seidel, D. *Chem. Sci.* **2011**, 2, 233. (h) Haibach, M. C.; Deb, I.; De, C. K.; Seidel, D. *J. Am. Chem. Soc.* **2011**, 133, 2100. (i) Deb, I.; Das, D.; Seidel, D. *Org. Lett.* **2011**, 13, 812. (j) Deb, I.; Coiro, D. J.; Seidel, D. *Chem. Commun.* **2011**, 47, 6473. (k) Das, D.; Richers, M. T.; Ma, L.; Seidel, D. *Org. Lett.* **2011**, 13, 6584. (l) Zhang, C.; De, C. K.; Seidel, D. *Org. Synth.* **2012**, 89, 274. (m) Ma, L.; Chen, W.; Seidel, D. *J. Am. Chem. Soc.* **2012**, 134, 15305. (n) Das, D.; Sun, A. X.; Seidel, D. *Angew. Chem., Int. Ed.* **2013**, 52, 3765. (o) Dieckmann, A.; Richers, M. T.; Platonova, A. Y.; Zhang, C.; Seidel, D.; Houk, K. N. *J. Org. Chem.* **2013**, 78, 4132. (p) Richers, M. T.; Deb, I.; Platonova, A. Y.; Zhang, C.; Seidel, D. *Synthesis* **2013**, 45, 1730. (q) Richers, M. T.; Zhao, C. F.; Seidel, D. *Beilstein J. Org. Chem.* **2013**, 9, 1194. (r) Das, D.; Seidel, D. *Org. Lett.* **2013**, 15, 4358. (s) Chen, W.; Wilde, R. G.; Seidel, D. *Org. Lett.* **2014**, 16, 730. (t) Seidel, D. *Org. Chem. Front.* **2014**, 1, DOI: 10.1039/C4QO00022F. (u) Chen, W.; Kang, Y.; Wilde, R. G.; Seidel, D. *Angew.*

Chem., Int. Ed. **2014**, 53, DOI: 10.1002/anie.201311165. (v) Richers, M. T.; Breugst, M.; Platonova, A. Y.; Ullrich, A.; Dieckmann, A.; Houk, K. N.; Seidel, D. *J. Am. Chem. Soc.* **2014**, 136, 6123.

(11) (a) Murahashi, S.-I.; Komiya, N.; Terai, H.; Nakae, T. *J. Am. Chem. Soc.* **2003**, 125, 15312. (b) Murahashi, S.-I.; Komiya, N.; Terai, H. *Angew. Chem., Int. Ed.* **2005**, 44, 6931. (c) Murahashi, S.-I.; Zhang, D. *Chem. Soc. Rev.* **2008**, 37, 1490. (d) Murahashi, S.-I.; Nakae, T.; Terai, H.; Komiya, N. *J. Am. Chem. Soc.* **2008**, 130, 11005.

(12) (a) Li, Z. P.; Li, C. J. *J. Am. Chem. Soc.* **2004**, 126, 11810. (b) Li, Z.; Li, C.-J. *Eur. J. Org. Chem.* **2005**, 3173. (c) Li, Z.; Li, C.-J. *J. Am. Chem. Soc.* **2005**, 127, 3672. (d) Li, Z. P.; Li, C. J. *J. Am. Chem. Soc.* **2005**, 127, 6968. (e) Li, Z. P.; Bohle, D. S.; Li, C. J. *Proc. Natl. Acad. Sci. U.S.A.* **2006**, 103, 8928.

(13) Selected reviews on the CDC reaction: (a) Li, C.-J. *Acc. Chem. Res.* **2009**, 42, 335. (b) Scheuermann, C. J. *Chem.—Asian J.* **2010**, 5, 436. (c) Yoo, W. J.; Li, C. J. *Top. Curr. Chem.* **2010**, 292, 281. (d) Yeung, C. S.; Dong, V. M. *Chem. Rev.* **2011**, 111, 1215. (e) Liu, C.; Zhang, H.; Shi, W.; Lei, A. W. *Chem. Rev.* **2011**, 111, 1780. (f) Cho, S. H.; Kim, J. Y.; Kwak, J.; Chang, S. *Chem. Soc. Rev.* **2011**, 40, 5068. (g) Klussmann, M.; Sureshkumar, D. *Synthesis* **2011**, 353. (h) Zhang, C.; Tang, C. H.; Jiao, N. *Chem. Soc. Rev.* **2012**, 41, 3464. (i) Girard, S. A.; Knauber, T.; Li, C.-J. *Angew. Chem., Int. Ed.* **2014**, 53, 74.

(14) Other selected reviews on amine C—H functionalization: (a) Murahashi, S.-I. *Angew. Chem., Int. Ed. Engl.* **1995**, 34, 2443. (b) Campos, K. R. *Chem. Soc. Rev.* **2007**, 36, 1069. (c) Jazzar, R.; Hitce, J.; Renaudat, A.; Sofack-Kreutzer, J.; Baudoin, O. *Chem.—Eur. J.* **2010**, 16, 2654. (d) Wendlandt, A. E.; Suess, A. M.; Stahl, S. S. *Angew. Chem., Int. Ed.* **2011**, 50, 11062. (e) Sun, C. L.; Li, B. J.; Shi, Z. J. *Chem. Rev.* **2011**, 111, 1293. (f) Pan, S. C. *Beilstein J. Org. Chem.* **2012**, 8, 1374. (g) Mitchell, E. A.; Peschiulli, A.; Lefevre, N.; Meerpoel, L.; Maes, B. U. W. *Chem.—Eur. J.* **2012**, 18, 10092. (h) Jones, K. M.; Klussmann, M. *Synlett* **2012**, 23, 159. (i) Qin, Y.; Lv, J.; Luo, S. *Tetrahedron Lett.* **2014**, 55, 551.

(15) Selected recent examples of CDC reactions: (a) Basle, O.; Li, C. *J. Org. Lett.* **2008**, 10, 3661. (b) Sureshkumar, D.; Sud, A.; Klussmann, M. *Synlett* **2009**, 1558. (c) Ghobrial, M.; Harhammer, K.; Mihovilovic, M. D.; Schnurch, M. *Chem. Commun.* **2010**, 46, 8836. (d) Su, W. K.; Yu, J. B.; Li, Z. H.; Jiang, Z. J. *J. Org. Chem.* **2011**, 76, 9144. (e) Zhang, G.; Zhang, Y.; Wang, R. *Angew. Chem., Int. Ed.* **2011**, 50, 10429. (f) Boess, E.; Sureshkumar, D.; Sud, A.; Wirtz, C.; Farès, C.; Klussmann, M. *J. Am. Chem. Soc.* **2011**, 133, 8106. (g) Alagiri, K.; Devadig, P.; Prabhu, K. R. *Chem.—Eur. J.* **2012**, 18, 5160. (h) Xie, J.; Li, H.; Zhou, J.; Cheng, Y.; Zhu, C. *Angew. Chem., Int. Ed.* **2012**, 51, 1252. (i) Boess, E.; Schmitz, C.; Klussmann, M. *J. Am. Chem. Soc.* **2012**, 134, 5317. (j) Zhang, G.; Ma, Y.; Wang, S.; Zhang, Y.; Wang, R. *J. Am. Chem. Soc.* **2012**, 134, 12334. (k) Ratnikov, M. O.; Xu, X. F.; Doyle, M. P. *J. Am. Chem. Soc.* **2013**, 135, 9475. (l) Nobuta, T.; Tada, N.; Fujiya, A.; Kariya, A.; Miura, T.; Itoh, A. *Org. Lett.* **2013**, 15, 574. (m) Dhineshkumar, J.; Lamani, M.; Alagiri, K.; Prabhu, K. R. *Org. Lett.* **2013**, 15, 1092. (n) Muramatsu, W.; Nakano, K.; Li, C.-J. *Org. Lett.* **2013**, 15, 3650.

(16) Selected examples of related photoredox processes: (a) Condie, A. G.; Gonzalez-Gomez, J. C.; Stephenson, C. R. J. *J. Am. Chem. Soc.* **2010**, 132, 1464. (b) Rueping, M.; Zhu, S. Q.; Koenigs, R. M. *Chem. Commun.* **2011**, 47, 8679. (c) Hari, D. P.; Koenig, B. *Org. Lett.* **2011**, 13, 3852. (d) McNally, A.; Prier, C. K.; MacMillan, D. W. C. *Science* **2011**, 334, 1114. (e) Freeman, D. B.; Furst, L.; Condie, A. G.; Stephenson, C. R. J. *Org. Lett.* **2012**, 14, 94. (f) Rueping, M.; Vila, C.; Bootwicha, T. *ACS Catal.* **2013**, 3, 1676. (g) Zhong, J. J.; Meng, Q. Y.; Wang, G. X.; Liu, Q.; Chen, B.; Feng, K.; Tung, C. H.; Wu, L. Z. *Chem.—Eur. J.* **2013**, 19, 6443. (h) Xue, Q.; Xie, J.; Jin, H.; Cheng, Y.; Zhu, C. *Org. Biomol. Chem.* **2013**, 11, 1606. (i) Bergonzini, G.; Schindler, C. S.; Wallentin, C.-J.; Jacobsen, E. N.; Stephenson, C. R. J. *Chem. Sci.* **2014**, 5, 112. (j) Zhong, J.-J.; Meng, Q.-Y.; Liu, B.; Li, X.-B.; Gao, X.-W.; Lei, T.; Wu, C.-J.; Li, Z.-J.; Tung, C.-H.; Wu, L.-Z. *Org. Lett.* **2014**, 16, 1988.

(17) (a) Araneo, S.; Fontana, F.; Minisci, F.; Recupero, F.; Serri, A. *Tetrahedron Lett.* **1995**, 36, 4307. (b) Nishino, M.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2011**, 76, 6447. (c) Zhu, S.; Das, A.; Bui,

L.; Zhou, H.; Curran, D. P.; Rueping, M. *J. Am. Chem. Soc.* **2013**, 135, 1823.

(18) (a) Murata, S.; Miura, M.; Nomura, M. *J. Org. Chem.* **1989**, 54, 4700. (b) Murahashi, S. I.; Naota, T.; Miyaguchi, N.; Nakato, T. *Tetrahedron Lett.* **1992**, 33, 6991. (c) Yang, X. H.; Xi, C. J.; Jiang, Y. F. *Molecules* **2006**, 11, 978. (d) Huang, L.; Zhang, X.; Zhang, Y. *Org. Lett.* **2009**, 11, 3730.

(19) For oxidative Povarov-type reactions of N-aryl glycine derivatives that generate quinolines, see: (a) Huang, H.; Jiang, H.; Chen, K.; Liu, H. *J. Org. Chem.* **2009**, 74, 5476. (b) Richter, H.; García Mancheño, O. *Org. Lett.* **2011**, 13, 6066. (c) Jia, X.; Peng, F.; Qing, C.; Huo, C.; Wang, X. *Org. Lett.* **2012**, 14, 4030. (d) Liu, P.; Wang, Z.; Lin, J.; Hu, X. *Eur. J. Org. Chem.* **2012**, 1583. (e) Rohlmann, R.; Stopka, T.; Richter, H.; García Mancheño, O. *J. Org. Chem.* **2013**, 78, 6050. (f) Jia, X.; Wang, Y.; Peng, F.; Huo, C.; Yu, L.; Liu, J.; Wang, X. *J. Org. Chem.* **2013**, 78, 9450.

(20) For further details see the Supporting Information.

(21) (a) Zhao, L.; Li, C. J. *Angew. Chem., Int. Ed.* **2008**, 47, 7075. (b) Zhao, L.; Basle, O.; Li, C. J. *Proc. Natl. Acad. Sci. U.S.A.* **2009**, 106, 4106. (c) Zhu, S.; Rueping, M. *Chem. Commun.* **2012**, 48, 11960.

(22) This type of Povarov dimerization has previously been reported with iminium ions/enamines that were generated by alternate means: (a) Swan, G. A.; Wilcock, J. D. *J. Chem. Soc., Perkin Trans. 1* **1974**, 885. (b) Kerr, G. H.; Meth-Cohn, O.; Mullock, E. B.; Suschitzky, H. *J. Chem. Soc., Perkin Trans. 1* **1974**, 1614. (c) Anastasiou, D.; Campi, E. M.; Chaouk, H.; Fallon, G. D.; Jackson, W. R.; McCubbin, Q. J.; Trnacek, A. E. *Aust. J. Chem.* **1994**, 47, 1043. (d) Buswell, M.; Fleming, I. *Chem. Commun.* **2003**, 202. (e) Fustero, S.; Bello, P.; Miro, J.; Sanchez-Rosello, M.; Maestro, M. A.; Gonzalez, J.; Pozo, C. d. *Chem. Commun.* **2013**, 49, 1336. (f) Brown, P. D.; Willis, A. C.; Sherburn, M. S.; Lawrence, A. L. *Angew. Chem., Int. Ed.* **2013**, 52, 13273.