Organic LETTERS

Letter

Cite This: Org. Lett. XXXX, XXX, XXX−XXX

pubs.acs.org/OrgLett

Pd/TiO_2-Photocatalyzed Self-Condensation of Primary Amines To Afford Secondary Amines at Ambient Temperature

Lyu-Ming Wang,[†] Kensuke Kobayashi,[†] Mitsuhiro Arisawa,[‡] Susumu Saito,*[,†] and Hiroshi Naka*[,§]

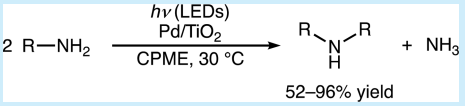
[†]Graduate School of Science, Nagoya University, Chikusa, Nagoya 464-8602, Japan

[‡]Graduate School of Pharmaceutical Sciences, Osaka University, Yamada-oka 1-6, Suita, Osaka 565-0871, Japan

[§]Research Center for Materials Science, Nagoya University, Chikusa, Nagoya 464-8602, Japan

Supporting Information

ABSTRACT: Symmetric secondary amines were synthesized by the self-condensation of primary amines over a palladium-loaded titanium dioxide (Pd/TiO_2) photocatalyst. The reactions afforded a series of secondary amines in moderate to excellent isolated yields at ambient temperature (30 °C, in cyclopentyl methyl ether). Applicability for one-pot pharmaceutical synthesis was demonstrated by a photocatalytic reaction sequence of self-condensation of an amine followed by N-alkylation of the resulting secondary amine with an alcohol.



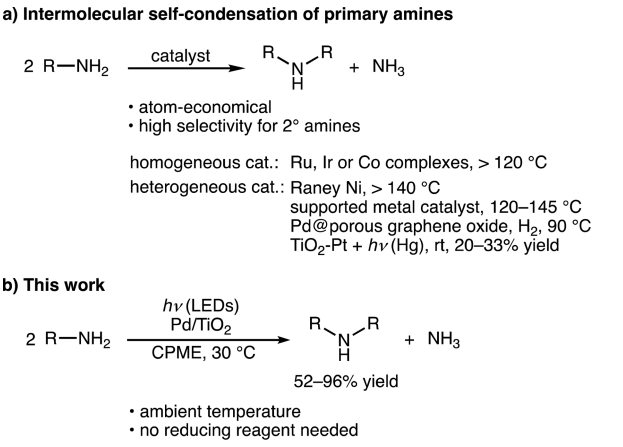
Symmetric secondary amino groups (R_2N) are fundamental structures present in various pharmaceuticals, agrochemicals, and molecular catalysts.[1] Figure 1 illustrates selected examples of such functional molecules bearing symmetric secondary amino groups. These molecules have most frequently been synthesized from the parent secondary amines (R_2NH).[2,3]

Intermolecular self-condensation of primary amines (RNH_2) is one of the most efficient methods for the synthesis of symmetric secondary amines (R_2NH, Scheme 1a).[4−10] The beauty of this clean reaction scheme is illustrated by the highly atom-economical and selective production of the target secondary amine and the coproduction of ammonia as the only byproduct. The self-condensation process is free from the problem of organic waste formation involved in the conventional N,N-dialkylation of primary carboxamides or sulfonamides followed by cleavage of the amide moieties.[11] Moreover, the selectivity for a secondary amine over a tertiary amine is generally higher than in the analogous alkylation of primary amines using alkyl halides[12] or alcohols.[2,13−16]

The self-condensation of primary amines could be effectively catalyzed by both molecular and heterogeneous catalysts. Ru and Ir complexes have frequently been used to achieve the self-condensation of amines at 150−185 °C, affording the desired products in moderate to good yields.[5,6] A cobalt complex catalyzes this reaction at 120 °C.[7] Heterogeneous catalysts such as Raney Ni, Pt−Sn/γ-Al_2O_3, Cu/Al_2O_3, $NiCuFeO_x$, and Pd_3Pb/Al_2O_3 effectively promote this transformation at 120−145 °C.[8] The self-condensation can be carried out at 90 °C with Pd on a porous graphene oxide catalyst under a H_2 atmosphere.[9] These methods provide efficient access to various symmetric secondary amines. However, the development of self-condensation of primary amines at ambient temperature has remained elusive.

During the course of our studies on the photocatalytic conversion of amines and alcohols by metal-loaded titania-

Scheme 1. Approaches for Self-Condensation of Primary Amines to Secondary Amines



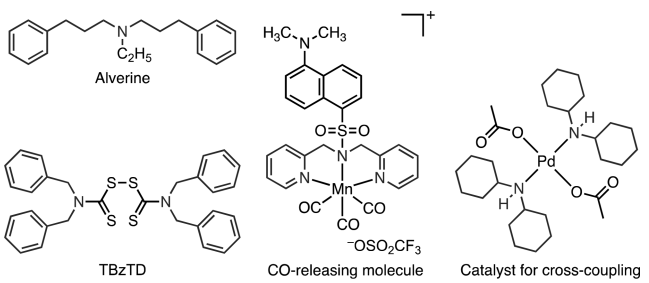


Figure 1. Functional molecules with symmetric secondary amino moieties.

Received: October 13, 2018

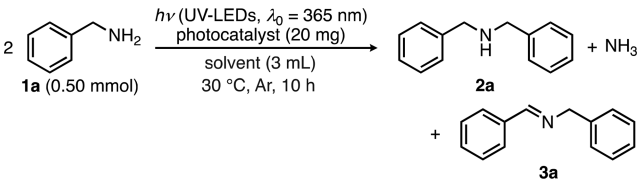
DOI: 10.1021/acs.orglett.8b03271
Org. Lett. XXXX, XXX, XXX−XXX

based photocatalysts,[2,14c,17] we noticed that the self-condensation of benzylamines competes with alkylation with alcohols. In addition, it was reported that the self-condensation of primary amines proceeds under light irradiation in the presence of a Pt-modified TiO_2 photocatalyst[10a] or a polycrystalline CdS photocatalyst,[10b] albeit the substrate scope of the intermolecular condensation was limited to three substrates (ethylamine, propylamine, and benzylamine) and the yields were poor (20−33%). Inspired by our observations and these preceding reports, we herein report the first photocatalytic self-condensation of primary amines at ambient temperature that enables scalable synthesis of symmetric secondary amines (Scheme 1b).

We selected benzylamine (**1a**) as a model substrate (Table 1). Cyclopentyl methyl ether (CPME) was used as a solvent because of its favorable properties in sustainable chemistry.[18] Among the tested photocatalysts, Pd/TiO_2 proved to be the best, affording dibenzylamine (**2a**) in 98% GC yield and 96% isolated yield under light irradiation (UV-LEDs, λ_0 = 365 nm) for 10 h (entry 1). The Pd/TiO_2 photocatalyst was prepared as previously described using $PdCl_2(CH_3CN)_2$, TiO_2 (Aeroxide P25), and $NaBH_4$ [see Supporting Information (SI) for details].[2b,17c] The presence of palladium nanoparticles ($[Pd]_n$, mean particle size = 3.3 nm ±0.6 nm [based on the analysis of 100 $[Pd]_n$ nanoparticles]) on TiO_2 was also established.[2b] GC monitoring of the reaction progress every hour indicated the clean formation of **2a** from **1a** (Figure S1 in SI). We could not detect any side products such as imine **3a** throughout the reaction. This preliminary kinetic study indicated that the reaction is subjected to a zero order with respect to the concentration of **1a** (Figure S1). The reaction hardly proceeded in the dark, indicating that it is driven by light irradiation (entry 2). Platinum is a privileged cocatalyst on heterogeneous photocatalysts for hydrogen evolution from water and alcohols.[19] In fact, Pt/TiO_2 showed good reactivity for the formation of imine **3a**, but almost no catalytic ability for further hydrogenation to the desired secondary amine **2a** (entry 3). Other photocatalysts such as Au/TiO_2,[17c] Ag/TiO_2,[14c] Cu/TiO_2,[2a] a Cu/TiO_2−Au/TiO_2 mixture,[2a] and pristine TiO_2 poorly promoted the reaction leading to **2a** and **3a** (entries 4−8). The Pd/TiO_2-mediated photocatalytic self-condensation also proceeded selectively in THF (entry 9). Other solvents such as acetonitrile, ethyl acetate, and toluene could be used, but a small amount of **3a** was formed (entries 10−12).

Having established the optimized conditions, the scope of this Pd/TiO_2-mediated photocatalytic self-condensation of primary amines was clarified (Scheme 2). This reaction could be operated on a 10 mmol scale using a Xe lamp (λ = 300−470 nm), affording **2a** in 95% yield (940.1 mg) after 25-h irradiation. Benzylamines with electron-donating groups, such as methyl and methoxy groups, gave the corresponding secondary amines (**2b** and **2c**) in good to excellent yields. The presence of a fluoro group on the aromatic ring was well tolerated, and the desired secondary amine **2d** was obtained in 96% yield. The reactions of benzylamines bearing more reducible chloro-, bromo-, or nitro groups on the aromatic rings were sluggish (see Scheme S1 in SI). A substrate with a strongly electron-withdrawing CF_3 group was less reactive than **2a**−**d**, yet still gave the product **2e** in a fair yield. Moreover, the present method for the first time offers salt-free access to amines with biphenyl, 1-naphthyl, and 2-/3-pyridyl functionalities (**2f**−**2i**), which are frequently incorporated in the metal ligands of molecular catalysts (**2f** and **2h**).[3b,20] 2-Phenethylamines and a long-chain alkyl amine also underwent the self-condensation reaction, affording the secondary amines **2j**−**l** in

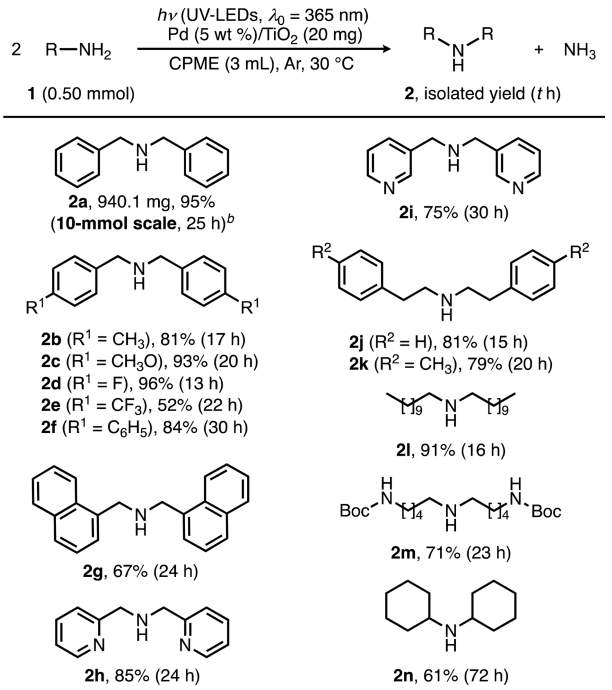
Table 1. Photocatalytic Self-Condensation of 1a to 2a[a]



entry	photocatalyst [metal (mol %)]	solvent	yield (%)[b] 2a	3a
1	Pd/TiO_2 [Pd (1.7)]	CPME	98 (96)	<1
2[c]	Pd/TiO_2 [Pd (1.7)]	CPME	<1	<1
3	Pt/TiO_2 [Pt (1.0)]	CPME	<1	78
4	Au/TiO_2 [Au (0.9)]	CPME	<1	22
5	Ag/TiO_2 [Ag (1.5)]	CPME	<1	<1
6	Cu/TiO_2 [Cu (2.9)]	CPME	<1	20
7[d]	Au/TiO_2 + Cu/TiO_2	CPME	1	26
8	TiO_2	CPME	<1	<1
9	Pd/TiO_2 [Pd (1.7)]	THF	75	<1
10	Pd/TiO_2 [Pd (1.7)]	CH_3CN	88	9
11	Pd/TiO_2 [Pd (1.7)]	$AcOC_2H_5$	88	4
12	Pd/TiO_2 [Pd (1.7)]	toluene	90	3

[a]32 W UV-LEDs λ_0 = 365 nm. Metal content (Pd: 5 wt %; Pt: 5 wt %; Cu: 5 wt %; Ag: 4 wt %; Au: 5 wt %) was determined by ICP-AES. [b]GC/MS yields using *n*-decane as an internal standard, isolated yield in parentheses. [c]In the dark. [d]10 mg each of photocatalyst [Au (0.5 mol %), Cu (1.5 mol %)].

Scheme 2. Self-Condensation of Primary Amines to Secondary Amines Catalyzed by a Pd/TiO_2[a]



[a]Conditions were similar to those in Table 1, entry 1. [b]**1a** (10 mmol), Pd/TiO_2 (300 mg, 1.3 mol % Pd), CPME (20 mL), 300 W Xe lamp with a UV-cold mirror (λ = 300−470 nm).

DOI: 10.1021/acs.orglett.8b03271
Org. Lett. XXXX, XXX, XXX−XXX

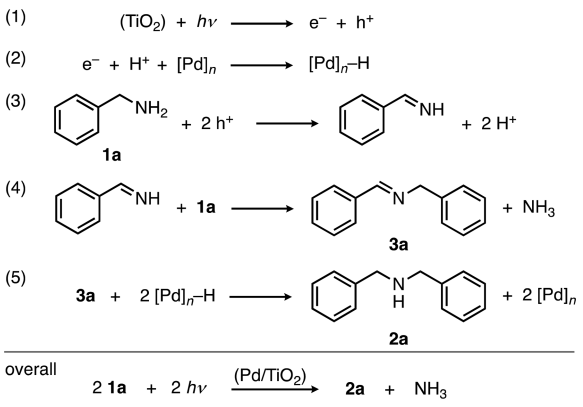
high yields. The condensation of a Boc-protected amine took place selectively at the free amino moiety and gave the desired Boc-diprotected triamine **2m** in 71% yield. Cyclohexanamine was considerably less reactive than primary amines, but the sterically congested dicyclohexylamine (**2n**) was obtained in an acceptable yield after prolonged irradiation.

Furthermore, the Pd/TiO_2 photocatalyst was found to be recyclable at least 4 times without losing its photocatalytic activity (96–98% yields, Table S1).

Coproduction of ammonia (0.19 mmol, 75%) was detected by ^1H NMR analysis in dimethylsulfoxide-d_6 on self-condensation of **1l** after trapping with HCl in methanol (see SI for details).[21] This result confirms that the light-induced conversion of **1** to **2** involves formation of ammonia as a stoichiometric byproduct (Scheme 1b).

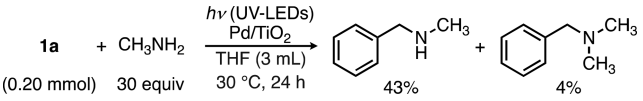
In order to obtain further mechanistic insight, the self-condensation of **1a** to **2a** in the presence of impurities was examined (Table S2). The desired reaction proceeded well (**2a**, 82%) in the presence of chlorobenzene, but 17% of imine **3a** formed (Table S2, entry 1). This tendency was stronger in the case of bromobenzene, and **3a** (80%) was obtained as a major product, together with **2a** (18%) and recovered bromobenzene (60%, Table S2, entry 2). More reducible iodobenzene or nitrobenzene stopped the reaction at the imine stage without formation of any desired **2a**, yet the **3a** was formed in 39% and 77% yields and the impurities were recovered in 87% and 70% yields, respectively (Table S2, entries 3 and 4). These results imply the participation of the borrowing hydrogen mechanism[13] promoted by light irradiation of the photocatalyst (Scheme 3).[10a] The proposed

Scheme 3. Proposed Mechanism



mechanism involves (1) formation of an electron–hole pair on Pd/TiO_2 by irradiation and their separation ($e^- + h^+$); (2) production of $[Pd]_n$–H species on the photocatalyst surface from electrons, protons, and Pd nanoparticles ($[Pd]_n$); (3) oxidation of primary amine **1a** by holes on the photocatalyst surface leading to benzaldimine and protons; (4) amine–imine exchange (transamination) between **1a** and benzaldimine to give imine **3a** and ammonia; and (5) reduction of imine **3a** to secondary amine **2a** by the $[Pd]_n$–H species. The overall reaction is summarized in the bottom of Scheme 3. The presence of reducible impurities lowered the yield of **2a** and increased the yield of **3a** (Table S2) by retarding the reduction of **3a**. The high reactivity of $[Pd]_n$–H for the reduction of **3a** to **2a** accounts for the higher selectivity of Pd/TiO_2 for producing **2a** over **3a**, compared with other metal/TiO_2 analogues (Table 1, entry 1 vs entries 3–7). Hydrogenation of **3a** in the presence of Pd/TiO_2 under H_2 (1 atm) proceeded both under light irradiation and in the dark (Scheme S2).

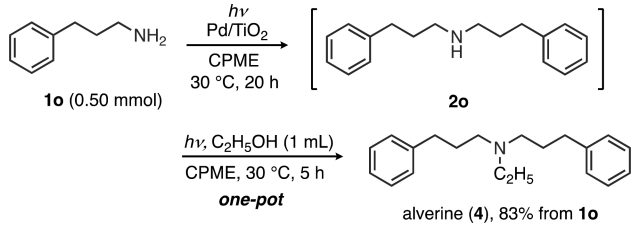
Scheme 4. Cross-Condensation



Next, we tested the cross-condensation of two different amines.[4] Whereas reactions of **1a** with *n*-butyl or *n*-octylamine gave complex mixtures, reasonable amounts of cross-condensation products were obtained in the reaction of methylamine with **1a**; *N*-methylbenzylamine formed in 43% yield together with *N*,*N*-dimethylbenzylamine (4%, Scheme 4).

Finally, the current protocol was extended to a one-pot photocatalytic pharmaceutical synthesis (Scheme 5). Alverine

Scheme 5. One-Pot Photocatalytic Synthesis of Alverine at Ambient Temperature



(**4**), a drug used for irritable bowel syndrome, was synthesized through sequential photocatalytic amine self-condensation of **1o** to **2o** followed by photocatalytic N-ethylation of **2o** with ethanol.[2] These two photocatalytic reactions were both promoted by Pd/TiO_2 and coproduce only ammonia and water as byproducts, respectively. Thus, the present method for the first time enabled the synthesis of alverine in high yield without stoichiometric salt-waste formation.

In summary, we have developed an efficient photocatalytic method for the self-condensation of primary amines to symmetric secondary amines at room temperature. We expect this method will serve as an economical and environmentally friendly complement to existing methods for secondary amine synthesis.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.8b03271.

Supplementary tables, figure, and schemes; experimental procedures, spectroscopic data, and NMR charts (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: saito.susumu@f.mbox.nagoya-u.ac.jp.
*E-mail: h_naka@nagoya-u.jp.

ORCID

Mitsuhiro Arisawa: 0000-0002-7937-670X
Susumu Saito: 0000-0003-0749-2020
Hiroshi Naka: 0000-0002-1198-6835

DOI: 10.1021/acs.orglett.8b03271
Org. Lett. XXXX, XXX, XXX–XXX

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors wish to thank Professors R. Noyori (Nagoya U.), A.E.H. Wheatley (U. Cambridge), and A. Kudo (Tokyo U. of Science) for fruitful discussions and warm encouragement. This work was supported by the JGC-S Scholarship Foundation (to H.N.), Fusion Emergent Research Program from IRCCS (to H.N. and M.A.), and JSPS KAKENHI Grant Numbers JP26410115 (to H.N.) and JPA16H010260 and JP16H01012 (to M.A. and S.S., respectively for Precisely Designed Catalysts with Customized Scaffolding).

■ REFERENCES

(1) *Amines: Synthesis, Properties, and Applications*; Lawrence, S. A., Ed.; Cambridge University: Cambridge, 2006.

(2) (a) Wang, L.-M.; Morioka, Y.; Jenkinson, K.; Wheatley, A. E. H.; Saito, S.; Naka, H. *Sci. Rep.* **2018**, *8*, 6931. (b) Wang, L.-M.; Jenkinson, K.; Wheatley, A. E. H.; Kuwata, K.; Saito, S.; Naka, H. *ACS Sustainable Chem. Eng.* **2018**, *6*, 15419−15424.

(3) (a) Li, T.-T.; Song, X.-H.; Wang, M.-S.; Ma, N. *RSC Adv.* **2014**, *4*, 40054−40060. (b) G, U. P.; Axthelm, J.; Hoffmann, P.; Taye, N.; Gläser, S.; Görls, H.; Hopkins, S. L.; Plass, W.; Neugebauer, U.; Bonnet, S.; Schiller, A. *J. Am. Chem. Soc.* **2017**, *139*, 4991−4994. (c) Tao, B.; Boykin, D. W. *J. Org. Chem.* **2004**, *69*, 4330−4335.

(4) (a) Larock, R. C.; Pletnev, A. A. In *Comprehensive Organic Transformations: A Guide to Functional Group Preparations*, 3rd ed.; Larock, R. C., Ed.; John Wiley & Sons, Inc.: Hoboken, NJ, 2018; Vol. 2, pp 1558−1559. (b) Guillena, G.; Ramón, D. J.; Yus, M. *Chem. Rev.* **2010**, *110*, 1611−1641.

(5) (a) Bui-The-Khai; Concilio, C.; Porzi, G. *J. Organomet. Chem.* **1981**, *208*, 249−251. (b) Hollmann, D.; Bähn, S.; Tillack, A.; Beller, M. *Angew. Chem., Int. Ed.* **2007**, *46*, 8291−8294. (c) Bähn, S.; Hollmann, D.; Tillack, A.; Beller, M. *Adv. Synth. Catal.* **2008**, *350*, 2099−2103. (d) Arachchige, P. T. K.; Lee, H.; Yi, C. S. *J. Org. Chem.* **2018**, *83*, 4932−4947.

(6) (a) Prades, A.; Corberán, R.; Poyatos, M.; Peris, E. *Chem. - Eur. J.* **2008**, *14*, 11474−11479. (b) Lorentz-Petersen, P. L.; Jensen, P.; Madsen, R. *Synthesis* **2009**, *24*, 4110−4112. (c) Saidi, O.; Blacker, A. J.; Farah, M. M.; Marsden, S. P.; Williams, J. M. *Angew. Chem., Int. Ed.* **2009**, *48*, 7375−7378. (d) Yamashita, M.; Moroe, Y.; Yano, T.; Nozaki, K. *Inorg. Chim. Acta* **2011**, *369*, 15−18. (e) Valencia, M.; Pereira, A.; Müller-Bunz, B. H.; Belderraín, T.; Pérez, P. J.; Albrecht, M. *Chem. - Eur. J.* **2017**, *23*, 8901−8911.

(7) Yin, Z.; Zeng, H.; Wu, J.; Zheng, S.; Zhang, G. *ACS Catal.* **2016**, *6*, 6546−6550.

(8) (a) De Angelis, F.; Grgurina, I.; Nicoletti, R. *Synthesis* **1979**, *1979*, 70. (b) He, W.; Wang, L.; Sun, C.; Wu, K.; He, S.; Chen, J.; Wu, P.; Yu, Z. *Chem. - Eur. J.* **2011**, *17*, 13308−13317. (c) Kim, I.; Itagaki, S.; Jin, X.; Yamaguchi, K.; Mizuno, N. *Catal. Sci. Technol.* **2013**, *3*, 2397−2430. (d) Liu, H.; Chuah, G.-K.; Jaenicke, S. *J. Catal.* **2015**, *329*, 262−268. (e) Cui, X.; Dai, X.; Deng, Y.; Shi, F. *Chem. - Eur. J.* **2013**, *19*, 3665−3675. (f) Furukawa, S.; Suga, A.; Komatsu, T. *Chem. Commun.* **2014**, *50*, 3277−3280.

(9) Su, C.; Tandiana, R.; Balapanuru, J.; Tang, W.; Pareek, K.; Nai, C. T.; Hayashi, T.; Loh, C. T. *J. Am. Chem. Soc.* **2015**, *137*, 685−690.

(10) (a) Nishimoto, S.-i.; Ohtani, B.; Yoshikawa, T.; Kagiya, T. *J. Am. Chem. Soc.* **1983**, *105*, 7180−7182. (b) Mitkina, T.; Stanglmair, C.; Setzer, W.; Gruber, M.; Kisch, H.; König, B. *Org. Biomol. Chem.* **2012**, *10*, 3556−3561.

(11) Kan, T.; Fukuyama, T. *Chem. Commun.* **2004**, 353−359.

(12) (a) *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Ed.; Pergamon: U.K., 1991. (b) Singh, C. B.; Kavala, V.; Samal, A. K.; Patel, B. K. *Eur. J. Org. Chem.* **2007**, *2007*, 1369−1377.

(13) (a) Hamid, M. H. S. A.; Slatford, P. A.; Williams, J. M. *Adv. Synth. Catal.* **2007**, *349*, 1555−1575. (b) Bähn, S.; Imm, S.; Neubert, L.; Zhang, M.; Neumann, H.; Beller, M. *ChemCatChem* **2011**, *3*, 1853−1864. (c) Gunanathan, C.; Milstein, D. *Science* **2013**, *341*, 249−260. (d) Yang, Q.; Wang, Q.; Yu, Z. *Chem. Soc. Rev.* **2015**, *44*, 2305−2329. (e) Shimizu, K.-i. *Catal. Sci. Technol.* **2015**, *5*, 1412−1427.

(14) (a) Zhao, Y.; Foo, S. W.; Saito, S. *Angew. Chem., Int. Ed.* **2011**, *50*, 3006−3009. (b) Du, Y.; Oishi, S.; Saito, S. *Chem. - Eur. J.* **2011**, *17*, 12262−12267. (c) Tsarev, V. N.; Morioka, Y.; Caner, J.; Wang, Q.; Ushimaru, R.; Kudo, A.; Naka, H.; Saito, S. *Org. Lett.* **2015**, *17*, 2530−2533.

(15) (a) Kawahara, R.; Fujita, K.-i.; Yamaguchi, R. *Adv. Synth. Catal.* **2011**, *353*, 1161−1168. (b) Shimizu, K.-i.; Imaiida, N.; Kon, K.; Siddiki, S. M. A. H.; Satsuma. *ACS Catal.* **2013**, *3*, 998−1005. (c) Yan, T.; Feringa, B. L.; Barta, K. *Nat. Commun.* **2014**, *5*, 5602. (d) Dang, T. T.; Ramalingam, B.; Seayad, A. M. *ACS Catal.* **2015**, *5*, 4082−4088. (e) Rösler, S.; Ertl, M.; Irrgang, T.; Kempe, R. *Angew. Chem., Int. Ed.* **2015**, *54*, 15046−15050. (f) Rawlings, A. J.; Diorazio, L. J.; Wills, M. *Org. Lett.* **2015**, *17*, 1086−1089. (g) Pan, H.-J.; Ng, T. W.; Zhao, Y. *Chem. Commun.* **2015**, *51*, 11907−11910. (h) Zou, Q.; Wang, C.; Smith, J.; Xue, D.; Xiao, J. *Chem. - Eur. J.* **2015**, *21*, 9656−9661. (i) Elangovan, S.; Neumann, J.; Sortais, J.-B.; Junge, K.; Darcel, C.; Beller, M. *Nat. Commun.* **2016**, *7*, 12641. (j) Furukawa, S.; Suzuki, R.; Komatsu, T. *ACS Catal.* **2016**, *6*, 5946−5953. (k) Hikawa, H.; Ijichi, Y.; Kikkawa, S.; Azumaya, I. *Eur. J. Org. Chem.* **2017**, *2017*, 465−468.

(16) (a) Ohtani, B.; Osaki, H.; Nishimoto, S.-i.; Kagiya, T. *J. Am. Chem. Soc.* **1986**, *108*, 308−310. (b) Shiraishi, Y.; Fujiwara, K.; Sugano, Y.; Ichikawa, S.; Hirai, T. *ACS Catal.* **2013**, *3*, 312−320. (c) Zhang, L.; Zhang, Y.; Deng, Y.; Shi, F. *Catal. Sci. Technol.* **2015**, *5*, 3226−3234.

(17) (a) Liu, Z.; Caner, J.; Kudo, A.; Naka, H.; Saito, S. *Chem. - Eur. J.* **2013**, *19*, 9452−9456. (b) Caner, J.; Liu, Z.; Takada, Y.; Kudo, A.; Naka, H.; Saito, S. *Catal. Sci. Technol.* **2014**, *4*, 4093−4098. (c) Shibata, M.; Nagata, R.; Saito, S.; Naka, H. *Chem. Lett.* **2017**, *46*, 580−582. (d) Takada, Y.; Caner, J.; Kaliyamoorthy, S.; Naka, H.; Saito, S. *Chem. - Eur. J.* **2017**, *23*, 18025−18032. (e) Takada, Y.; Caner, J.; Naka, H.; Saito, S. *Pure Appl. Chem.* **2018**, *90*, 167−174.

(18) Watanabe, K.; Yamagiwa, N.; Torisawa, Y. *Org. Process Res. Dev.* **2007**, *11*, 251−258.

(19) Kudo, A.; Miseki, Y. *Chem. Soc. Rev.* **2009**, *38*, 253−278.

(20) Fang, Y.-Q.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2008**, *130*, 5660−5661.

(21) Wickramasinghe, L. A.; Ogawa, T.; Schrock, R. R.; Müller, P. *J. Am. Chem. Soc.* **2017**, *139*, 9132−9135.

DOI: 10.1021/acs.orglett.8b03271
Org. Lett. XXXX, XXX, XXX−XXX