Organic LETTERS

Letter

pubs.acs.org/OrgLett

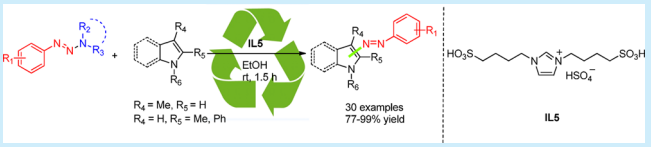
Ionic Liquid Promoted Diazenylation of *N*-Heterocyclic Compounds with Aryltriazenes under Mild Conditions

Dawei Cao, Yonghong Zhang,* Chenjiang Liu,* Bin Wang, Yadong Sun, Ablimit Abdukadera, Haiyan Hu, and Qiang Liu

The Key Laboratory of Oil and Gas Fine Chemicals, Ministry of Education & Xinjiang Uygur Autonomous Region, Urumqi Key Laboratory of Green Catalysis and Synthesis Technology, School of Chemistry and Chemical Engineering, Physics and Chemistry Detecting Center, Xinjiang University, Urumqi 830046, P. R. China

Supporting Information

ABSTRACT: An efficient, mild, and metal-free approach to direct diazenylation of *N*-heterocyclic compounds with aryltriazenes using Brønsted ionic liquid as a promoter has been developed for the first time. Many *N*-heterocyclic azo compounds were synthesized in good to excellent yields at room temperature under an open atmosphere. Notably, the promoter 1,3-bis(4-sulfobutyl)-1*H*-imidazol-3-ium hydrogen sulfate could be conveniently recycled and reused with the same efficacies for at least four cycles.

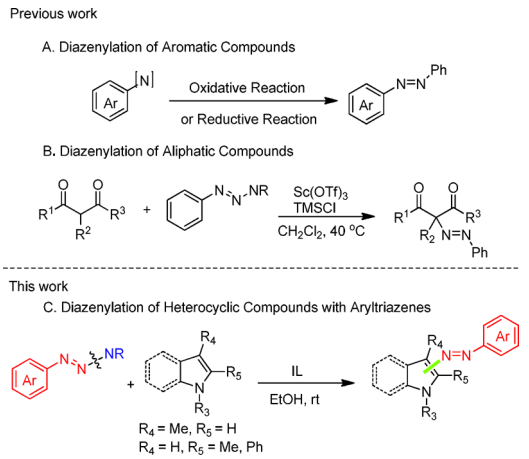


Azo compounds have widespread applications in medicinal chemistry and materials science, such as therapeutic agents, food additives, and textile fibers.[1,2] In particular, those with aromatic or heterocyclic substituents as directing groups, initiators, dyes, nonlinear optics, and photochemical switches have attracted considerable attention in the field of chemistry.[3] Therefore, intensive research has been directed toward the development of simple and efficient methods for the synthesis of azo derivatives.

The synthesis of azo derivatives is often performed by the coupling reactions of the diazonium salts and Mills coupling of aromatic nitroso compounds with aromatic amines.[4,5] Symmetrical azo compounds can also be obtained by oxidation reaction of amines/hydrazines or reduction reaction of nitroaromatic compounds (Scheme 1, A).[6] In addition, there are other methods for preparing azo compounds, such as the Wallach rearrangement of azoxy derivatives, dimerization reaction of the diazonium salts, and pyrolysis of azides.[7] However, these methods often suffer from harsh reaction conditions, such as anaerobic anhydrous conditions, high temperature, and pressure. In particular, some reactions involve reducing agents and oxidizing agents containing heavy metal ions and use toxic solvents, which do not meet the concept of green chemistry. Furthermore, the limited substrate scope of some traditional strategies involving only arenes impedes their applications, and heterocyclic compounds have rarely been studied. Therefore, the development of mild and convenient methods for the diazenylation of heterocyclic compounds is still in high demand.

Aryltriazenes have emerged as highly powerful building blocks in a variety of synthetic transformations,[8] which attracted extensive attention due to the advantages of good reactivity and stability. Aryltriazenes as masked diazonium ions have been widely utilized in the construction of C−C and C−heteroatom bonds by transition-metal-catalyzed cross-coupling reactions.[9,10] However, the applications of triazenes in diazenylation reactions have rarely been reported. Recently, Luo[11] reported a $Sc(OTf)_3$-catalyzed method for the synthesis of aliphatic azo compounds with triazenes in the presence of TMSCl (Scheme 1, B), which successfully solved the problem of instability of the diazonium salts in the reaction process. The diazenylation of heterocyclic compounds with triazenes has never been reported so far.

Scheme 1. Traditional and IL-Promoted Methods for the Synthesis of Diazenylation Derivatives



Ionic liquids (ILs) have been widely used as an environmentally acceptable reaction medium or catalyst in green synthesis over the past decade owing to their advantages of

Received: March 3, 2016

DOI: 10.1021/acs.orglett.6b00605
Org. Lett. XXXX, XXX, XXX−XXX

nonvolatility, thermal stability, recyclability, and tunable chemistry.[12] In particular, the application of task-specific ILs including Brønsted or Lewis acid ILs in the preparation of heterocyclic compounds has become an attractive field in organic synthesis (Figure 1).[13] With this background in mind,

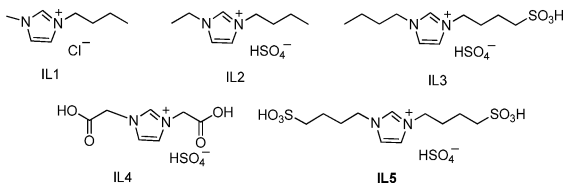


Figure 1. ILs examined in this work.

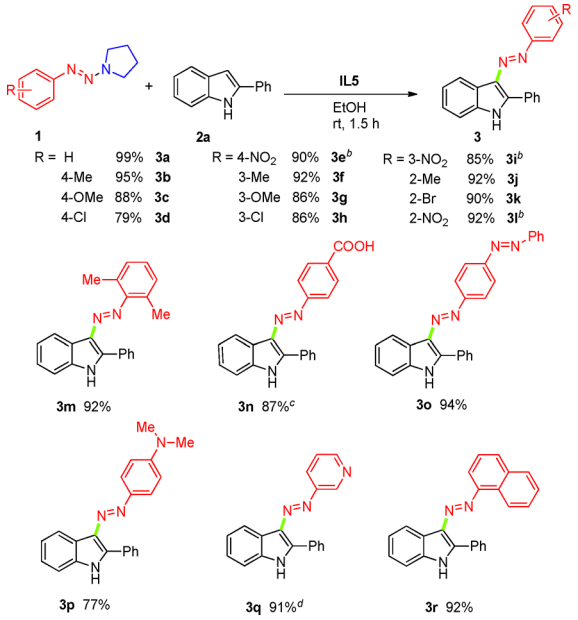
we report that a Brønsted acid IL promoted diazenylation reaction of *N*-heterocyclic compounds with aryl triazenes at room temperature under air (Scheme 1, C).

We commenced our study using 1-phenyltriazenes (**1**) and 2-phenylindole (**2a**) as model substrates (Table S1). Initially, we examined the influence of the ILs for the reaction (Table S1, entries 1−5). 1,3-Bis(4-sulfobutyl)-1*H*-imidazol-3-ium hydrogen sulfate (**IL5**) was found to be superior to the others (Table S1, entry 5), which produced the desired product **3a** in 96% isolated yield. However, reducing the amount of **IL5** led to a relatively lower yield (Table S1, entry 6). Gratifyingly, among the organic solvents tested (Table S1, entries 7−15), green solvent ethanol was found to be the best one. However, the yield of product **3a** was greatly decreased with water as solvent or under solvent-free conditions, which might be due to the insolubility of substrates (Table S1, entries 16−17). We next examined the effect of leaving group of the 1-aryltriazene compounds. For cyclic substitution, the ring size exhibited almost no influence on yield (Table S1, entries 18 and 19), and the substrates with various linear chains, such as ethyl, allyl, and ethoxyl, could produce the desired compound in more than 87% yields (Table S1, entries 20−22). Consequently, the reaction was carried out with 1 equiv of **IL5** as the promoter in EtOH (1 mL) at 25 °C for 1.5 h.

With the optimized conditions established, the scope of aromatic triazo reagents was examined (Scheme 2). A variety of electron-rich and electron-poor groups at the para-position of the aromatic ring readily reacted to give the corresponding products in good to excellent yields. For example, methyl-, methoxy-, and halogen-substituted products were isolated in 79%−96% yields (compounds **3a**−**d**). In particular, the strong electron-withdrawing group of nitro-substituted triazene can be involved well in the reaction (compound **3e**). It is important to note that the above groups whether in ortho- or meta- also reacted smoothly (compounds **3f**−**l**). To our gratification, the multisubstituted substrate could be transformed well with good yield (compound **3m**). Surprisingly, the carboxyl-substituted substrate furnished the corresponding product **3n** in good yield. In addition, some special groups were also tolerated in this transformation, such as sensitive groups azo, alkaline group *N*,*N*-dimethyl, condensed ring, and heteroaromatic groups (entries **3o**−**r**).

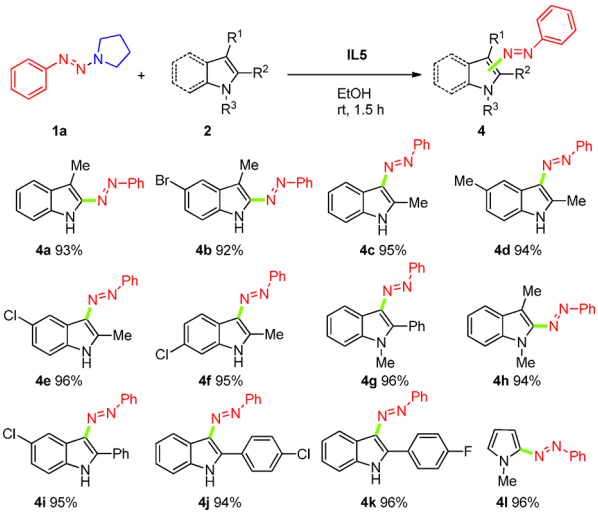
The substrate scope of a series of *N*-heterocyclic derivatives was next expanded to explore the generality of this reaction under the optimized reaction conditions, and the results are summarized in Scheme 3. This protocol was found to be general, affording the desired products in excellent yields. First, 3-methylindole and 5-bromo-3-methylindole can be transformed into the corresponding 2-position diazenylation products in excellent yields (compounds **4a**,**b**). Next, a series of 2-methyl-substituted indoles, whether with electron-rich or electron-poor groups, proceeded smoothly to produce the desired compounds in more than 93% yields (compounds **4c**−**f**). Furthermore, *N*-substituted indoles could furnish the corresponding products in excellent yields (compounds **4g**,**h**). To our delight, the aromatic ring moiety or 2-aryl of indoles with electron-withdrawing groups (e.g., 4-Cl, 4-F) led to compounds **4i**−**k** smoothly. Interestingly, 1-methylpyrrole could also be transformed in this reaction (compound **4l**).

Scheme 2. Scope of Diazenylation of Aromatic Triazenes and 2-Phenylindole[a]



[a]General conditions: **1** (0.2 mmol), **2a** (0.2 mmol), and **IL5** (0.2 mmol) at 25 °C for 1.5 h in the EtOH (1 mL) under air. [b]At 50 °C for 5 h. [c]Direct filtration. [d]At 80 °C for 8 h.

Scheme 3. Scope of Diazenylation of Triazophenyl Reagent and *N*-Heterocyclic Compounds[a]



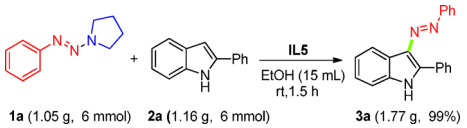
[a]General conditions: **1a** (0.2 mmol), **2** (0.2 mmol), and **IL5** (0.2 mmol) at 25 °C for 1.5 h in the EtOH (1 mL) under air.

DOI: 10.1021/acs.orglett.6b00605
Org. Lett. XXXX, XXX, XXX−XXX

However, other heterocycle substrates, such as thiophene, 2,6-dimethylthiophene, benzothiophene, and benzofuran, did not deliver the desired products.

In order to further demonstrate the potential industrial application of current protocol, a gram-scale experiment of **1a** and **2a** was carried out in 15 mL of EtOH at 25 °C for 1.5 h in the presence of 45 mol % of **IL5**. The result is shown in Scheme 4. As the **IL5** is highly water-soluble, it could be

Scheme 4. Gram-Scale Reaction



removed by filtration with water, and the product **3a** was obtained after drying in vacuo. It is noted that the purity of **3a** was achieved without requiring chromatographic purification or recrystallization.

To further develop a recyclable catalytic system, the recycling of the **IL5** was investigated under the optimized conditions (Figure 2). Following each cycle, water and ethyl acetate were

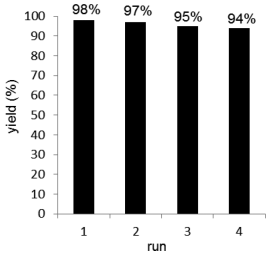


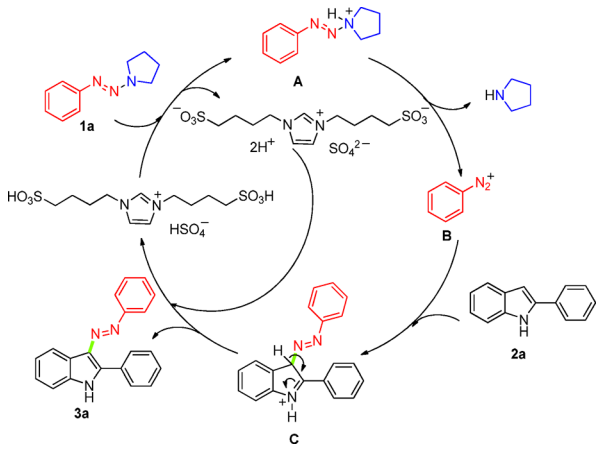
Figure 2. Recycling of **IL5** in the synthesis (*E*)-2-phenyl-3-(phenyldiazenyl)-1*H*-indole.

added, and the **IL5** was recovered from the water layer and recycled for the next reaction after drying in vacuo. For the first run, the activity of **IL5** remained the same. In the subsequent two cycles, the desired products were still reached with 100% conversions and high yields by extension of the reaction time from 1.5 to 3 and 5 h. In the fourth cycle, even if the reaction time was prolonged to 24 h, the conversion could not reach 100%. However, the corresponding product was afforded in 94% yield after addition of another 5 mol % of **IL5** and then reacted for 8 h. The decrease of promoter activity may be because the acidity of **IL5** is affected by tetrahydropyrrole generated during the reaction.

According to the above result and previous reports,[14] a plausible mechanism is depicted in Scheme 5. First, the aryltriazene **1a** was activated by promoter **IL5** to give the tetrahydropyrrolyl cation **A**, which was then transformed into azo cation **B** through the release of tetrahydropyrrole. Subsequently, the intermediate **C** was afforded via electrophilic addition of diazonium species **B** to 2-phenylindole **2a**. Finally, the product **3a** was generated by deprotonation of **C**.

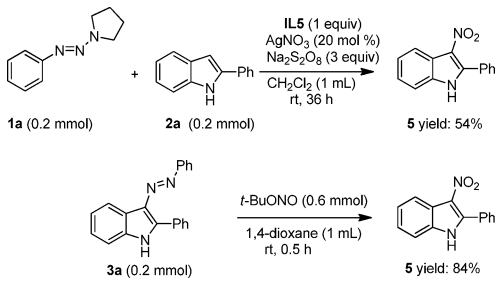
We found that this reaction is useful in the synthesis of 3-nitroindole. 3-Nitroindoles are useful precursors in the preparation of novel antidiabetic agents.[15] They are also the key building block in the formation of amino acid derivatives.[16] Therefore, the compound 2-phenyl-3-nitroindole can be synthesized by **IL5** as promoter, $AgNO_3$ as the catalyst, and $Na_2S_2O_8$ as the oxidant in CH_2Cl_2 at 25 °C after 36 h of

Scheme 5. Plausible Reaction Mechanism



reaction in 54% yield. Meanwhile, the same product was obtained in the presence of *tert*-butyl nitrite using 1,4-dioxane as solvent under air at room temperature for 0.5 h in 84% yield. The results are shown in Scheme 6.

Scheme 6. Derivatization Reactions



In summary, we have found a Brønsted acidic IL-promoted diazenylation reaction of *N*-heterocyclic derivatives with triazenes. This system can provide some advantages, such as being metal-free, providing excellent yields, avoiding the use of highly toxic organic solvents, and using mild conditions. Most importantly, the promoter is very easy to handle and can be recycled and reused for four runs with no significant loss of activity. Furthermore, the protocol can be used as an economical synthetic method for the diazenylation reaction of *N*-heterocyclic derivatives.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b00605.

Experimental procedure, NMR spectra, and analytical data for all new compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: pxylcj@126.com.
*E-mail: zhzhzyh@126.com.

Notes

The authors declare no competing financial interest.

DOI: 10.1021/acs.orglett.6b00605
Org. Lett. XXXX, XXX, XXX−XXX

■ ACKNOWLEDGMENTS

We are grateful to Key Laboratory of Xinjiang Uyghur Autonomous Region (2015KL014), NSFC (21572195, 21502162, 21262035, and 21162025), the Program for Outstanding Youth Science and Technology Innovation Talents Training in Xinjiang Uygur Autonomous Region (2014721004), and the Natural Science Foundation of Xinjiang University (BS110133 and BS150230) for financial support of this research.

■ REFERENCES

(1) (a) Hunger, K. In *Industrial Dyes: Chemistry, Properties, Applications*; Wiley−VCH: Weinheim, 2003. (b) Bandyopadhyay, A.; Higuchi, M. *Eur. Polym. J.* **2013**, *49*, 1688.

(2) (a) Ikeda, T.; Tsutsumi, O. *Science* **1995**, *268*, 1873. (b) Banerjee, I. A.; Yu, L. T.; Matsui, H. *J. Am. Chem. Soc.* **2003**, *125*, 9542. (c) Yu, Y. L.; Nakano, M.; Ikeda, T. *Nature* **2003**, *425*, 145. (d) Cisnetti, F.; Ballardini, R.; Credi, A.; Gandolfi, M. T.; Masiero, S.; Negri, F.; Pieraccini, S.; Spada, G. P. *Chem. - Eur. J.* **2004**, *10*, 2011. (e) Venkataramani, S.; Jana, U.; Dommaschk, M.; Sönnichsen, F. D.; Tuczek, F.; Herges, R. *Science* **2011**, *331*, 445. (f) Szymański, W.; Beierle, J. M.; Kistemaker, H. A. V.; Velema, W. A.; Feringa, B. L. *Chem. Rev.* **2013**, *113*, 6114.

(3) (a) DiCesare, N.; Lakowicz, J. R. *Org. Lett.* **2001**, *3*, 3891. (b) Wang, Q.; Yi, L.; Liu, L. L.; Zhou, C. Z.; Xi, Z. *Tetrahedron Lett.* **2008**, *49*, 5087. (c) Wang, J.; Ha, C. S. *Tetrahedron* **2009**, *65*, 6959. (d) Isaad, J.; Perwuelz, A. *Tetrahedron Lett.* **2010**, *51*, 5810. (e) Li, H. J.; Li, P. H.; Wang, L. *Org. Lett.* **2013**, *15*, 620. (f) Xiong, F.; Qian, C.; Lin, D. G.; Zeng, W.; Lu, X. X. *Org. Lett.* **2013**, *15*, 5444. (g) Song, H. Y.; Chen, D.; Pi, C.; Cui, X. L.; Wu, Y. J. *J. Org. Chem.* **2014**, *79*, 2955. (h) Wang, H.; Yu, Y.; Hong, X. H.; Tan, Q. T.; Xu, B. *J. Org. Chem.* **2014**, *79*, 3279. (i) Jia, X. F.; Han, J. *J. Org. Chem.* **2014**, *79*, 4180. (j) Zhang, D.; Cui, X. L.; Zhang, Q. Q.; Wu, Y. J. *J. Org. Chem.* **2015**, *80*, 1517. (k) Son, J. Y.; Kim, S.; Jeon, W. H.; Lee, P. H. *Org. Lett.* **2015**, *17*, 2518.

(4) (a) Albar, H.; Shawali, A. S.; Abdaliah, M. A. *Can. J. Chem.* **1993**, *71*, 2144. (b) Hunter, C. A.; Sarson, L. D. *Tetrahedron Lett.* **1996**, *37*, 699. (c) Haghbeen, K.; Tan, E. W. *J. Org. Chem.* **1998**, *63*, 4503. (d) Desroches, C.; Parola, S.; Vocanson, F.; Ehlinger, N.; Miele, P.; Lamartine, R.; Bouix, J.; Eriksson, A.; Lindgren, M.; Lopes, C. *J. Mater. Chem.* **2001**, *11*, 3014. (e) Lhoták, P.; Morávek, J.; Stibor, I. *Tetrahedron Lett.* **2002**, *43*, 3665. (f) Merrington, J.; James, M.; Bradley, M. *Chem. Commun.* **2002**, 140. (g) Otutu, J. O. *Curr. Res. Chem.* **2012**, *4*, 119. (h) González, A.; Granell, J.; López, C.; Bosque, R.; Rodríguez, L.; Font-Bardia, M.; Calvet, T.; Solans, X. *J. Organomet. Chem.* **2013**, *726*, 21. (i) Babür, B.; Seferoğlu, N.; Aktan, E.; Hökelek, T.; Şahin, E.; Seferoğlu, Z. *J. Mol. Struct.* **2015**, *1081*, 175.

(5) (a) Boyer, J. H. In *The Chemistry of the Nitro and Nitroso Groups*; Interscience: New York, 1969; Part 1. (b) Davey, M. H.; Lee, V. Y.; Miller, R. D.; Marks, T. J. *J. Org. Chem.* **1999**, *64*, 4976. (c) Hamon, F.; Djedaini-Pilard, F.; Barbot, F.; Len, C. *Tetrahedron* **2009**, *65*, 10105. (d) Bellotto, S.; Reuter, R.; Heinis, C.; Wegner, H. A. *J. Org. Chem.* **2011**, *76*, 9826. (e) Kubitschke, J.; Näther, C.; Herges, R. *Eur. J. Org. Chem.* **2010**, *2010*, 5041. (f) Merino, E. *Chem. Soc. Rev.* **2011**, *40*, 3835.

(6) (a) Grirrane, A.; Corma, A.; García, H. *Science* **2008**, *322*, 1661. (b) Zhu, H. Y.; Ke, X. B.; Yang, X. Z.; Sarina, S.; Liu, H. W. *Angew. Chem., Int. Ed.* **2010**, *49*, 9657. (c) Guo, X. N.; Hao, C. H.; Jin, G. Q.; Zhu, H.-Y.; Guo, X.-Y. *Angew. Chem., Int. Ed.* **2014**, *53*, 1973. (d) Liu, X.; Li, H.-Q.; Ye, S.; Liu, Y.-M.; He, H.-Y.; Cao, Y. *Angew. Chem., Int. Ed.* **2014**, *53*, 7624. (e) Lu, W. C.; Xi, C. J. *Tetrahedron Lett.* **2008**, *49*, 4011. (f) Zhang, C.; Jiao, N. *Angew. Chem., Int. Ed.* **2010**, *49*, 6174. (g) Zhu, Y. G.; Shi, Y. A. *Org. Lett.* **2013**, *15*, 1942. (h) Jiang, B.; Ning, Y.; Fan, W.; Tu, S.-J.; Li, G. G. *J. Org. Chem.* **2014**, *79*, 4018. (i) Li, H.-Q.; Liu, X.; Zhang, Q.; Li, S.-S.; Liu, Y.-M.; He, H.-Y.; Cao, Y. *Chem. Commun.* **2015**, *51*, 11217.

(7) (a) Buncel, E. *Acc. Chem. Res.* **1975**, *8*, 132. (b) Cohen, T.; Lewarchik, R. J.; Tarino, J. Z. *J. Am. Chem. Soc.* **1974**, *96*, 7753. (c) Scriven, E. F. V.; Suschitzky, H.; Garner, G. V. *Tetrahedron Lett.* **1973**, *14*, 103.

(8) (a) Gampbell, T. W.; Day, B. F. *Chem. Rev.* **1951**, *48*, 299. (b) Vaughan, K.; Stevens, M. F. G. *Chem. Soc. Rev.* **1978**, *7*, 377. (c) Julliard, M.; Vernin, G.; Metzger, J. *Helv. Chim. Acta* **1980**, *63*, 456. (d) Kimball, D. B.; Haley, M. M. *Angew. Chem., Int. Ed.* **2002**, *41*, 3338. (e) Přikryl, J.; Macháček, V.; Jansa, P.; Svobodová, M.; Růžička, A.; Nachtigall, P.; Černý, M. *Eur. J. Org. Chem.* **2008**, *2008*, 3272. (f) Zhang, Y. H.; Cao, D. W.; Liu, W. B.; Hu, H. Y.; Zhang, X. M.; Liu, C. J. *Curr. Org. Chem.* **2015**, *19*, 151.

(9) (a) Sengupta, S.; Sadhukhan, S. K. *Tetrahedron Lett.* **1998**, *39*, 715. (b) Bräse, S.; Schroen, M. *Angew. Chem., Int. Ed.* **1999**, *38*, 1071. (c) Saeki, T.; Son, E. C.; Tamao, K. *Org. Lett.* **2004**, *6*, 617. (d) Nan, G. M.; Ren, F.; Luo, M. M. *Beilstein J. Org. Chem.* **2010**, *6*, 1. (e) Saeki, T.; Matsunaga, T.; Son, E. C.; Tamao, K. *Adv. Synth. Catal.* **2004**, *346*, 1689. (f) Wang, R.; Falck, J. R. *Org. Chem. Front.* **2014**, *1*, 1029. (g) Hafner, A.; Bräse, S. *Angew. Chem., Int. Ed.* **2012**, *51*, 3713. (h) Hafner, A.; Bräse, S. *Adv. Synth. Catal.* **2013**, *355*, 996.

(10) (a) Zhu, C.; Yamane, M. *Org. Lett.* **2012**, *14*, 4560. (b) Ku, H.; Barrio, J. R. *J. Org. Chem.* **1981**, *46*, 5239. (c) Satyamurthy, N.; Barrio, J. R.; Schmidt, D. G.; Kammerer, C.; Bida, G. T.; Phelps, M. E. *J. Org. Chem.* **1990**, *55*, 4560. (d) Döbele, M.; Vanderheiden, S.; Jung, N.; Bräse, S. *Angew. Chem., Int. Ed.* **2010**, *49*, 5986. (e) Li, Q.; Jin, C. S.; Petukhov, P. A.; Rukavishnikov, A. V.; Zaikova, T. O.; Phadke, A.; LaMunyon, D. H.; Lee, M. D.; Keana, J. F. W. *J. Org. Chem.* **2004**, *69*, 1010. (f) Romanato, P.; Duttwyler, S.; Linden, A.; Baldridge, K. K.; Siegel, J. S. *J. Am. Chem. Soc.* **2010**, *132*, 7828. (g) Romanato, P.; Duttwyler, S.; Linden, A.; Baldridge, K. K.; Siegel, J. S. *J. Am. Chem. Soc.* **2011**, *133*, 11844. (h) Kirk, M. L.; Shultz, D. A.; Stasiw, D. E.; Lewis, G. F.; Wang, G. B.; Brannen, C. L.; Sommer, R. D.; Boyle, P. D. *J. Am. Chem. Soc.* **2013**, *135*, 17144. (i) Liu, C. Y.; Knochel, P. *J. Org. Chem.* **2007**, *72*, 7106. (j) Yang, W. J.; Xu, L. J.; Chen, Z. K.; Zhang, L. L.; Miao, M. Z.; Ren, H. J. *Org. Lett.* **2013**, *15*, 1282. (k) Trost, B. M.; Pearson, W. H. *J. Am. Chem. Soc.* **1981**, *103*, 2483. (l) Zhang, Y. H.; Li, Y. M.; Zhang, X. M.; Jiang, X. F. *Chem. Commun.* **2015**, *51*, 941.

(11) Liu, C.; Lv, J.; Luo, S. Z.; Cheng, J.-P. *Org. Lett.* **2014**, *16*, 5458.

(12) (a) Wasserscheid, P.; Keim, W. *Angew. Chem., Int. Ed.* **2000**, *39*, 3772. (b) Dupont, J.; de Souza, R. F.; Suarez, P. A. Z. *Chem. Rev.* **2002**, *102*, 3667. (c) Pârvulescu, V. I.; Hardacre, C. *Chem. Rev.* **2007**, *107*, 2615. (d) Xin, B. W.; Hao, J. C. *Chem. Soc. Rev.* **2014**, *43*, 7171.

(13) (a) Zhang, Q. H.; Zhang, S. G.; Deng, Y. Q. *Green Chem.* **2011**, *13*, 2619. (b) Taheri, A.; Liu, C. H.; Lai, B. B.; Cheng, C.; Pan, X. J.; Gu, Y. L. *Green Chem.* **2014**, *16*, 3715. (c) Isambert, N.; Duque, M. M. S.; Plaquevent, J. C.; Génissoń, Y.; Rodriguez, J.; Constantieux, T. *Chem. Soc. Rev.* **2011**, *40*, 1347. (d) Rizzo, C.; D'Anna, F.; Marullo, S.; Noto, R. *J. Org. Chem.* **2014**, *79*, 8678. (e) Martins, M. A. P.; Frizzo, C. P.; Tier, A. Z.; Moreira, D. N.; Zanatta, N.; Bonacorso, H. G. *Chem. Rev.* **2014**, *114*, PR1.

(14) (a) Shang, X. B.; Chen, W. Z.; Yao, Y. M. *Synlett* **2013**, *24*, 851. (b) Shiri, M. *Chem. Rev.* **2012**, *112*, 3508. (c) Khazaei, A.; Kazem-Rostami, M.; Moosavi-Zare, A. R.; Bayat, M.; Saednia, S. *Synlett* **2012**, *23*, 1893. (d) Liu, C. Y.; Gavryushin, A.; Knochel, P. *Chem. - Asian J.* **2007**, *2*, 1020.

(15) Bahekar, R. H.; Jain, M. R.; Goel, A.; Patel, D. N.; Prajapati, V. M.; Gupta, A. A.; Jadav, P. A.; Patel, P. R. *Bioorg. Med. Chem.* **2007**, *15*, 3248.

(16) Urwyler, S.; Floersheim, P.; Roy, B. L.; Koller, M. *J. Med. Chem.* **2009**, *52*, 5093.

DOI: 10.1021/acs.orglett.6b00605
Org. Lett. XXXX, XXX, XXX−XXX