Organic LETTERS

Letter

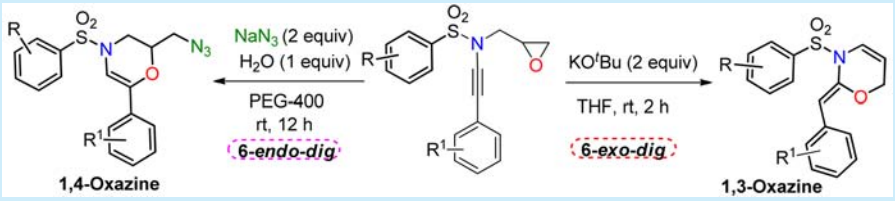
pubs.acs.org/OrgLett

Transition Metal-Free Cascade Cyclization of Epoxy-Ynamides: To Go for 1,3-Oxazines or 1,4-Oxazines?

A. Leela Siva Kumari, Alla Siva Reddy, and K. C. Kumara Swamy*

School of Chemistry, University of Hyderabad, Hyderabad-500046, Telangana, India

Supporting Information

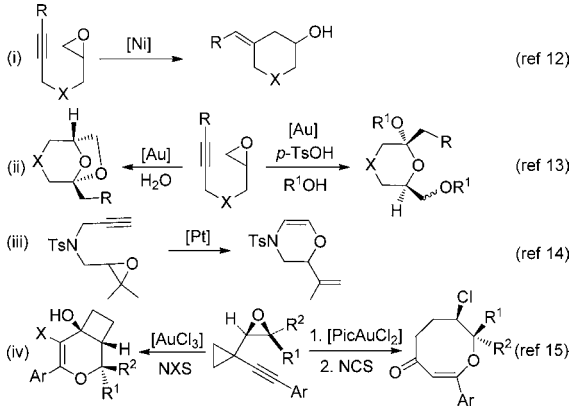


ABSTRACT: An approach to both 1,3- and 1,4-oxazines is developed by the cascade cyclization of epoxy ynamides under transition metal-free conditions. Thus, while 1,3-oxazines are obtained in a regio- and stereoselective manner by using base, cyclization of epoxy ynamides with sodium azide as a nucleophile results in 1,4-oxazines. Deuterium-labeling experiment demonstrates the role of water as a proton source in the formation of 1,4-oxazines. Epoxy tethered alkyne precursors provide 1,4-oxazines that undergo click reaction.

Ynamides constitute an important subgroup of alkynes because of the versatile reactivity of carbon−carbon triple bond directly attached to the nitrogen atom.[1,2] Cyclization reactions using ynamide substrates generally lead to products with very high regio- and stereoselectivity.[3,4] Most of the cyclization reactions of ynamides involve the α-carbon of the alkyne connected to the nitrogen atom.[5] The cyclization at the β-position of ynamides are, however, rarely explored.[6]

Ynamides with an epoxy functional group are attractive substrates for intramolecular[7] or intermolecular cyclization reactions by virtue of highly strained three-membered epoxide ring.[8] In particular, ring expansion reactions of epoxides are of considerable interest since multitudes of carbocycles or oxygen containing heterocycles can be generated.[9−11] Illustrative recent examples of novel transformations involving epoxide substrates containing an alkyne skeleton are shown in Scheme 1.[12−15] In the first example, generation of carbo- or heterocycles by the reductive coupling of substrates having both the epoxide and alkyne moieties using [Ni]-catalysts is shown.[12] The second reaction involves [Au]-catalyzed cycloisomerization of epoxy alkynes resulting in ketal skeleton in highly regio- and diastereoselective manner using water or alcohol as the nucleophilic source.[13] The report from Fang's group involves the [Pt]-catalyzed isomerization of alkynyl epoxides to cyclic allyl vinyl ethers.[14] The last report deals with ring expansion of 1-epoxy-1-alkynyl cyclopropanes using [Au]-catalytic systems under the influence of halonium ions.[15]

Scheme 1. Selected Transformations of Epoxy Alkynes



In all the above reactions, both the alkyne and epoxide participated in the cyclization process under transition metal catalysis. In this context, we anticipated that ynamides appended with epoxide functionality are versatile synthons. Such epoxide tagged ynamide substrates **1** can undergo varied ring-expansion reactions. The resulting cyclic products possess both nitrogen and oxygen in their core structure that is present in numerous biological active compounds.[16,17]

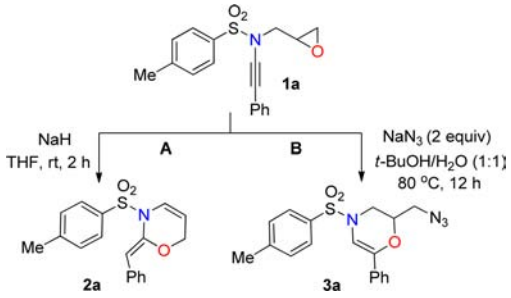
Thus, in continuation of our interest in the reactivity of functionalized ynamides,[18] herein we report the synthesis of 1,3- and 1,4-oxazines via ***6-exo-*** and ***6-endo-dig*** cyclization of epoxy ynamides using a base and NaN_3 nucleophile, respectively, in the absence of any transition metal catalyst.

Initially, we performed the reaction of the epoxy ynamide **1a** (see Supporting Information for its synthesis) with NaH (2 equiv) in THF. Surprisingly, the ring expanded product **2a** was isolated in 26% yield (Scheme 2A). In an interesting contrast, the reaction between **1a** and NaN_3 (2 equiv) in *t*-BuOH/H_2O (1:1) mixture at 80 °C for 12 h gave the cyclized product **3a** in 20%

Received: October 11, 2016
Published: October 26, 2016

DOI: 10.1021/acs.orglett.6b03047
Org. Lett. 2016, 18, 5752−5755

Scheme 2. Contrasting Ring Expansion Reactions of Epoxy Ynamide 1a Leading to 1,3-Oxazines or 1,4-Oxazines



yield, again, in the absence of a transition metal catalyst (Scheme 2B). It should be noted that the first reaction leads to 1,3-oxazine, while the second one affords 1,4-oxazine.

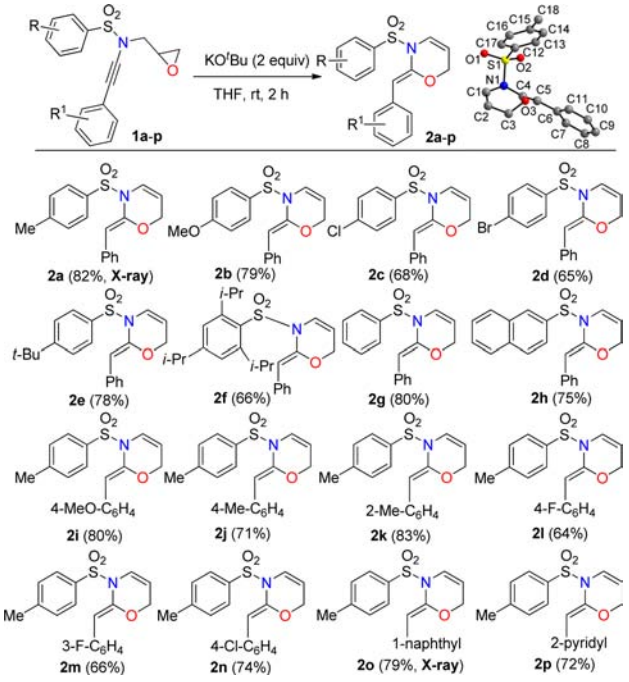
For the reaction shown in Scheme 2A, the product yield did not improve by changing the solvent from THF to $(EtO)_2CO$ (cf. Table S1, SI). Use of bases such as $NaNH_2$, NaOH, K_2CO_3, NaO^{t}Bu, and LiO^{t}Bu did not give the desired product. To our delight, the reaction proceeded very smoothly with 2 equiv of KO^{t}Bu as the base in THF at rt (25 °C) within 2 h affording the desired product **2a** in 82% yield with excellent regio- and stereoselectivity. We also tried to use a catalytic amount of KO^{t}Bu (10−20 mol %), but the yield was negligible. Thus, the optimal reaction conditions for this ring expansion reaction were: **1a** (1.0 equiv) in THF with KO^{t}Bu (2 equiv) as the base at rt for 2 h.

For the reaction shown in Scheme 2B, use of *t*-BuOH alone afforded only a trace amount of the desired product (cf. Table S2, SI), probably because of the low solubility of the azide, but the cyclized product was not observed by using only H_2O. Other polar protic and polar aprotic solvents provided only traces of the cyclized compound **3a**.The reaction proceeded very smoothly in PEG-400 providing the desired product **3a** in 70% yield with excellent regioselectivity. Later, we found that cyclization occurred even at rt (25 °C) and delivered the desired product **3a** in 72% yield within 12 h. For entries 4−16 (cf. Table S2), it should be noted that 1 equiv of H_2O was used as a reagent. Among the solvent mixtures checked, EtOH + PEG-400 system gave better yield of the product. Thus, the best reaction conditions were: **1a** (1.0 equiv), NaN_3 (2.0 equiv), and H_2O (1 equiv) in PEG-400 solvent at rt for 12 h.

As can be seen from Schemes 3 and 4, the substrate scope for both the reactions is excellent. Both electron-donating (**2a−b**, **2e**; **3a−b**, **3e**) and electron-withdrawing groups (**2c−d**; **3c−d**) on sulfonyl attached benzene ring gave good yields, and electron withdrawing groups (−Cl, −Br) marginally reduced the yield. The presence of bulky 1,3,5-triisopropyl-phenyl group on sulfonyl is well-tolerated, affording the desired product **2f** or **3f** in decent yield. The reaction using diverse substituents on alkyne attached aryl group of the epoxy ynamide was very clean and afforded 1,3-oxazines **2i−n** in 64−83% yields and 1,4-oxazines **3i−n** in 52−70% yields in a highly regioselective manner. Epoxy ynamide **1p** with a 2-pyridyl motif attached to the alkyne also produced a good yield of the cyclized product **2p**. The structures of the ring expansion products **2a**, **2o**, **3f**, and **3g** were confirmed by single crystal X-ray diffraction (Figures S1−S4).

In a control experiment, the ring expansion reaction of alkyne-free epoxy sulfonamide **4** in the presence of the base KO^{t}Bu (2 equiv) in THF (2 mL) led to product **5** in 46% yield (Scheme 5a). This part is consistent with a literature report.[19] The reaction

Scheme 3. Atom Economic Synthesis of 1,3-Oxazines (2a−p) from Epoxy Ynamides (1a−p)[a]



[a]Standard conditions: epoxy ynamide (0.3 mmol) in THF (2 mL) and KO^{t}Bu (0.6 mmol) at rt for 1−2 h. Isolated yields are given in parentheses.

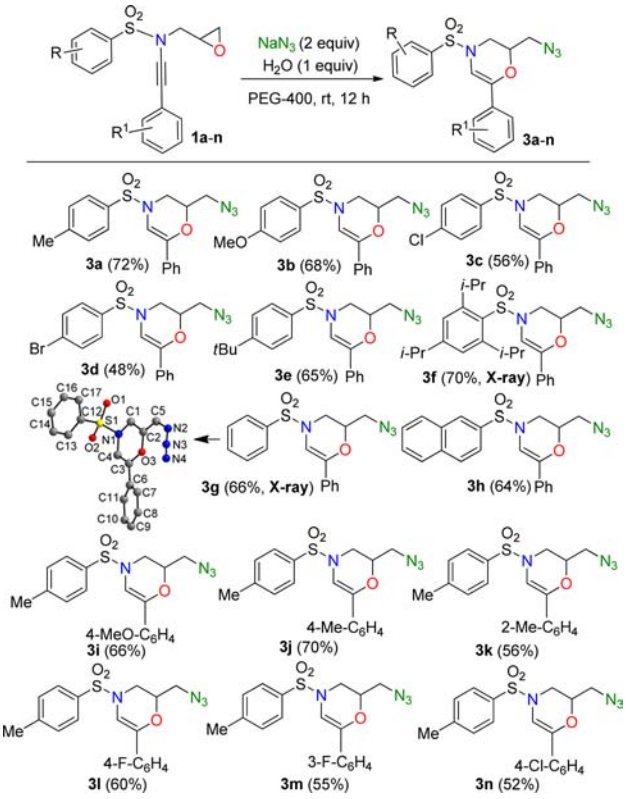
of epoxy ynamide **1a** with LDA or *n*-BuLi at −78 °C for 0.5 h resulted in isomeric allyl alcohols (*E* + *Z*)-**6** (ca. 95% purity; Scheme 5b); at 0 °C and above, the reaction gave a complex mixture. Thus, the base abstracts a proton from the carbon atom adjacent to the nitrogen atom of epoxy ynamide **1a** resulting in carbanion **I** that undergoes epoxide ring opening, initially affording allyloxide anion **I′**, which may be in equilibrium with **I″** (Scheme 5c and Scheme S1). A similar *E*/*Z* equilibrium is proposed in a reaction of *N*-allyl-ynamides.[6c] Species **I″** can be in resonance with keteniminium species **I‴**.[1a−c] Subsequent nucleophilic attack of allyloxide anion at the α-position of keteniminium species **I‴** followed by protonation provides the product **2a** via intermediate **II**. Upon formation of the **2a**, more of **I′** may be transformed to **I″**, which leads to more product.[20]

Deuterium-labeling experiment in the reaction of epoxy ynamide **1a** with NaN_3 in PEG-400 + D_2O mixture (5:1) furnished compound **3a′** (Scheme 6a) that exhibited ∼80% deuterium incorporation at the alkenyl C-*H* position. This result clearly suggests the key role of water as a proton source in the cyclization process. Based on this, we propose that initial intermolecular nucleophilic attack of azide onto the less hindered side of epoxide group of epoxy ynamide leads to species **III** (Scheme 6b and Scheme S2). Subsequent ***6-endo-dig*** attack of oxide ion on the ynamide results in intermediate **IV**. Protonation of **IV** delivers the cyclized product **3a**.

Interestingly, epoxy tethered alkyne substrates **7a−d** that contain $NCH_2-C\equiv C$ moiety also underwent isomerization followed by ***6-endo-dig*** cyclization with sodium azide affording the 1,4-oxazines **8a−d** in good yields (Scheme 7). The azides **3j** and **8b** possessing 1,4-oxazine moiety underwent click reaction readily resulting in the triazolo appended 1,4-oxazines **9** and **10** (Scheme 8). This result proves the structure of **8b**. As regards the reaction pathway, we believe that an intermediate of type **V**[21] that

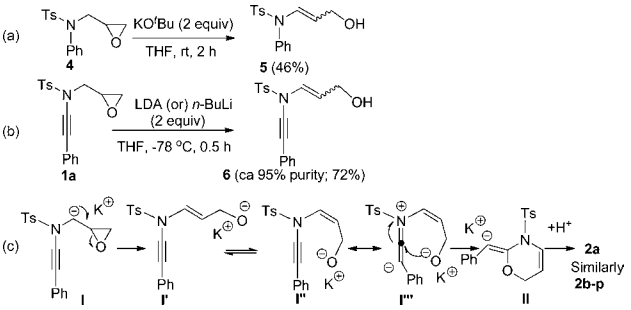
DOI: 10.1021/acs.orglett.6b03047
Org. Lett. 2016, 18, 5752−5755

Scheme 4. Transition Metal-Free Synthesis of 1,4-Oxazines (3a–n) from Epoxy Ynamides (1a–n)[a,b]

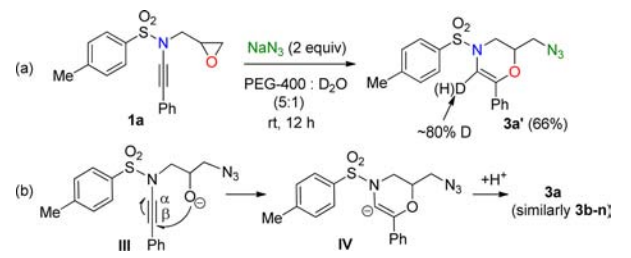


[a]Reaction conditions: epoxy ynamide (0.3 mmol), NaN_3 (0.6 mmol), H_2O (0.3 mmol), PEG-400 (2 mL) at rt for 12 h. [b]Isolated yields are given in parentheses.

Scheme 5. Control Experiments and Possible Pathway for the Formation of 2a (Similarly for 2b–p)

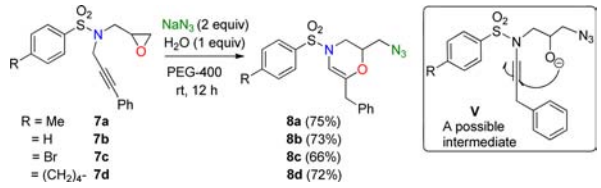


Scheme 6. Deuterium-Labeling Experiment and Possible Pathway for the Formation of 1,4-Oxazine 3a

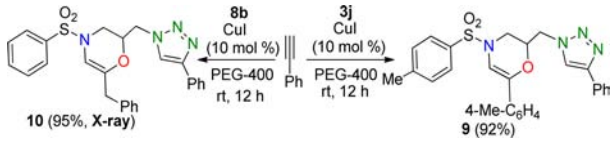


is formed by isomerization of the initially formed azido anion (see Scheme S3 in SI for more details) is involved in this ***6-endo-dig*** cyclization.

Scheme 7. Synthesis of 1,4-Oxazines (8a–d) from Epoxy Alkynes (7a–d)



Scheme 8. Click Reaction of 3j and 8b with PhC≡CH



In conclusion, we have developed a highly efficient and expedient way for the regio- and stereoselective synthesis of 1,3-oxazines in an *atom economic* approach by a base-assisted intramolecular ***6-exo-dig*** closure of epoxy ynamides. The main attractive feature of our methodology is that the ring expansion of an epoxide is performed in the absence of a transition metal catalyst. In contrast, ***6-endo-dig*** cyclization of epoxy ynamides with sodium azide provided highly regioselective synthesis of 1,4-oxazines. Deuterium-labeling experiment supported the important role of water as a proton source. This protocol was further elaborated to epoxy tethered alkynes. We have also reported click chemistry of azido substituted 1,4-oxazines. The cyclization of an epoxide and alkyne has been carried out using an environmentally benign PEG-400 solvent and simple sodium azide as a nucleophilic source under the transition metal-free conditions.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b03047.

Experimental details; X-ray data (CCDC nos. 1488891–1488892 and 1500789–1500791); ORTEPS of **2a**, **2o**, **3f**, **3g**, and **10**; $^1H/^{13}C$ NMR spectra (PDF)
Combined X-ray data (CIF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: kckssc@uohyd.ac.in or kckssc@yahoo.com.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank DST and UGC (both New Delhi) for support. A.L.S.K. and A.S.R. thank UGC for fellowship. K.C.K. thanks DST for the J. C. Bose fellowship and UGC for a one-time grant.

■ REFERENCES

(1) (a) Zificsak, C. A.; Mulder, J. A.; Hsung, R. P.; Rameshkumar, C.; Wei, L.-L. *Tetrahedron* **2001**, *57*, 7575. (b) Dekorver, K. A.; Li, H.; Lohse, A. G.; Hayashi, R.; Lu, Z.; Zhang, Y.; Hsung, R. P. *Chem. Rev.* **2010**, *110*, 5064. (c) Evano, G.; Coste, A.; Jouvin, K. *Angew. Chem., Int. Ed.* **2010**, *49*, 2840. (d) Lu, T.; Hsung, R. P. *ARKIVOC* **2014**, *i*, 127.
(2) (a) Saito, N.; Ichimaru, T.; Sato, Y. *Org. Lett.* **2012**, *14*, 1914. (b) Frischmuth, A.; Knochel, P. *Angew. Chem., Int. Ed.* **2013**, *52*, 10084.

DOI: 10.1021/acs.orglett.6b03047
Org. Lett. 2016, 18, 5752–5755

(c) Wang, X.-N.; Yeom, H.-S.; Fang, L.-C.; He, S.; Ma, Z.-X.; Kedrowski, B. L.; Hsung, R. P. *Acc. Chem. Res.* **2014**, *47*, 560. (d) Theunissen, C.; Métayer, B.; Henry, N.; Compain, G.; Marrot, J.; Martin-Mingot, A.; Thibaudeau, S.; Evano, G. *J. Am. Chem. Soc.* **2014**, *136*, 12528. (e) Okitsu, T.; Nakata, K.; Nishigaki, K.; Michioka, N.; Karatani, M.; Wada, A. *J. Org. Chem.* **2014**, *79*, 5914.

(3) (a) Zhang, Y.; Hsung, R. P.; Zhang, X.; Huang, J.; Slafer, B. W.; Davis, A. *Org. Lett.* **2005**, *7*, 1047. (b) Ghosh, N.; Nayak, S.; Sahoo, A. K. *Chem. - Eur. J.* **2013**, *19*, 9428. (c) Fujino, D.; Yorimitsu, H.; Osuka, A. *J. Am. Chem. Soc.* **2014**, *136*, 6255. (d) Karad, S. N.; Liu, R. − S. *Angew. Chem., Int. Ed.* **2014**, *53*, 9072.

(4) (a) Walker, P. R.; Campbell, C. D.; Suleman, A.; Carr, G.; Anderson, E. A. *Angew. Chem., Int. Ed.* **2013**, *52*, 9139. (b) Kiruthika, S. E.; Nandakumar, A.; Perumal, P. T. *Org. Lett.* **2014**, *16*, 4424. (c) Jadhav, A. M.; Pagar, V. V.; Huple, D. B.; Liu, R. − S. *Angew. Chem., Int. Ed.* **2015**, *54*, 3812. (d) Tokimizu, Y.; Wieteck, M.; Rudolph, M.; Oishi, S.; Fujii, N.; Hashmi, A. S. K.; Ohno, H. *Org. Lett.* **2015**, *17*, 604. (e) Lecomte, M.; Evano, G. *Angew. Chem., Int. Ed.* **2016**, *55*, 4547. (f) Chen, L.; Yu, L.; Deng, Y.; Zheng, Z.-J.; Xu, Z.; Cao, J.; Xu, L.-W. *Adv. Synth. Catal.* **2016**, *358*, 480.

(5) (a) Oppenheimer, J.; Johnson, W. L.; Tracey, M. R.; Hsung, R. P.; Yao, P.-Y.; Liu, R.; Zhao, K. *Org. Lett.* **2007**, *9*, 2361. (b) Yao, P.-Y.; Zhang, Y.; Hsung, R. P.; Zhao, K. *Org. Lett.* **2008**, *10*, 4275. (c) Dooleweerdt, K.; Ruhland, T.; Skrydstrup, T. *Org. Lett.* **2009**, *11*, 221. (d) Couty, S.; Liegault, B.; Meyer, C.; Cossy, J. *Org. Lett.* **2004**, *6*, 2511. (e) Marion, F.; Courillon, C.; Malacria, M. *Org. Lett.* **2003**, *5*, 5095. (f) Garcia, P.; Harrak, Y.; Diab, L.; Cordier, P.; Ollivier, C.; Gandon, V.; Malacria, M.; Fensterbank, L.; Aubert, C. *Org. Lett.* **2011**, *13*, 2952. (g) Dateer, R. B.; Pati, K.; Liu, R.-S. *Chem. Commun.* **2012**, *48*, 7200. (h) Kong, Y.; Jiang, K.; Cao, J.; Fu, L.; Yu, L.; Lai, G.; Cui, Y.; Hu, Z.; Wang, G. *Org. Lett.* **2013**, *15*, 422.

(6) (a) Witulski, B.; Alayrac, C.; Tevzadze-Saeftel, L. *Angew. Chem., Int. Ed.* **2003**, *42*, 4257. (b) Istrate, F. M.; Buzas, A. K.; Jurberg, A. D.; Odabachian, Y.; Gagosz, F. *Org. Lett.* **2008**, *10*, 925. (c) Gati, W.; Rammah, M. M.; Rammah, M. B.; Couty, F.; Evano, G. *J. Am. Chem. Soc.* **2012**, *134*, 9078. (d) Gati, W.; Couty, F.; Boubaker, T.; Rammah, M. M.; Rammah, M. B.; Evano, G. *Org. Lett.* **2013**, *15*, 3122.

(7) Lin, G.-Y.; Li, C.-W.; Hung, S.-H.; Liu, R.-S. *Org. Lett.* **2008**, *10*, 5059 (only one example with ynamide).

(8) (a) Morten, C. J.; Byers, J. A.; Van Dyke, A. R.; Vilotijevic, I.; Jamison, T. F. *Chem. Soc. Rev.* **2009**, *38*, 3175. (b) Huang, C. − Y.; Doyle, A. G. *Chem. Rev.* **2014**, *114*, 8153. (c) Rotstein, B. H.; Zaretsky, S.; Rai, V.; Yudin, A. K. *Chem. Rev.* **2014**, *114*, 8323. (d) Zhu, Y.; Wang, Q.; Cornwall, R. G.; Shi, Y. *Chem. Rev.* **2014**, *114*, 8199. (e) He, J.; Ling, J.; Chiu, P. *Chem. Rev.* **2014**, *114*, 8037. (f) Wang, C.; Luo, L.; Yamamoto, H. *Acc. Chem. Res.* **2016**, *49*, 193.

(9) (a) Movassaghi, M.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 2456. (b) Bartoli, G.; Bosco, M.; Carlone, A.; Locatelli, M.; Melchiorre, P.; Sambri, L. *Org. Lett.* **2005**, *7*, 1983. (c) Church, T. L.; Byrne, C. M.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2007**, *129*, 8156. (d) Bao, W.; Liu, Y.; Lv, X.; Qian, W. *Org. Lett.* **2008**, *10*, 3899. (e) Liu, Y.; Bao, W. *Org. Biomol. Chem.* **2010**, *8*, 2700. (f) Mack, D. J.; Njardarson, J. T. *ACS Catal.* **2013**, *3*, 272. (g) Li, H.; Spannenberg, A.; Neumann, H.; Beller, M.; Wu, X.-F. *Chem. Commun.* **2014**, *50*, 2114.

(10) (a) Taber, D. F.; He, Y.; Xu, M. *J. Am. Chem. Soc.* **2004**, *126*, 13900. (b) Lin, M.-Y.; Maddirala, S. J.; Liu, R.-S. *Org. Lett.* **2005**, *7*, 1745. (c) Yoshida, M.; Hayashi, M.; Shishido, K. *Org. Lett.* **2007**, *9*, 1643. (d) Shu, X.-Z.; Liu, X.-Y.; Xiao, H.-Q.; Ji, K.-G.; Guo, L.-N.; Qi, C.-Z.; Liang, Y.-M. *Adv. Synth. Catal.* **2007**, *349*, 2493. (e) Wen, S. − G.; Liu, W.-M.; Liang, Y.-M. *J. Org. Chem.* **2008**, *73*, 4342. (f) Blanc, A.; Tenbrink, K.; Weibel, J.-M.; Pale, P. *J. Org. Chem.* **2009**, *74*, 5342. (g) Iwata, A.; Inuki, S.; Oishi, S.; Fujii, N.; Ohno, H. *J. Org. Chem.* **2011**, *76*, 5506. (h) Gronnier, C.; Kramer, S.; Odabachian, Y.; Gagosz, F. *J. Am. Chem. Soc.* **2012**, *134*, 828. (i) Shiroodi, R. K.; Koleda, O.; Gevorgyan, V. *J. Am. Chem. Soc.* **2014**, *136*, 13146. (j) Hoffmann, M.; Weibel, J.-M.; de Frémont, P.; Pale, P.; Blanc, A. *Org. Lett.* **2014**, *16*, 908.

(11) (a) Piotti, M. E.; Alper, H. *J. Org. Chem.* **1997**, *62*, 8484. (b) Hashmi, A. S. K.; Sinha, P. *Adv. Synth. Catal.* **2004**, *346*, 432. (c) Wang, L.; Maddess, M. L.; Lautens, M. *J. Org. Chem.* **2007**, *72*, 1822. (d) Cordonnier, M.-C.; Blanc, A.; Pale, P. *Org. Lett.* **2008**, *10*, 1569. (e) Blanc, A.; Tenbrink, K.; Weibel, J.-M.; Pale, P. *J. Org. Chem.* **2009**, *74*, 4360. (f) Miura, T.; Shimada, M.; de Mendoza, P.; Deutsch, C.; Krause, N.; Murakami, M. *J. Org. Chem.* **2009**, *74*, 6050. (g) Trenkle, J. D.; Jamison, T. F. *Angew. Chem., Int. Ed.* **2009**, *48*, 5366. (h) Kang, J. Y.; Connell, B. T. *J. Org. Chem.* **2011**, *76*, 2379. (i) Sau, M.; Rodriguez-Escrich, C.; Pericas, M. A. *Org. Lett.* **2011**, *13*, 5044. (j) Li, S.; Wu, J. *Chem. Commun.* **2012**, *48*, 8973.

(12) (a) Molinaro, C.; Jamison, T. F. *J. Am. Chem. Soc.* **2003**, *125*, 8076. (b) Woodin, K. S.; Jamison, T. F. *J. Org. Chem.* **2007**, *72*, 7451. (c) Beaver, M. G.; Jamison, T. F. *Org. Lett.* **2011**, *13*, 4140.

(13) (a) Dai, L.-Z.; Qi, M.-J.; Shi, Y.-L.; Liu, X.-G.; Shi, M. *Org. Lett.* **2007**, *9*, 3191. (b) Dai, L.-Z.; Shi, M. *Chem. - Eur. J.* **2008**, *14*, 7011.

(14) Wang, Z.; Lin, X.; Luck, R. L.; Gibbons, G.; Fang, S. *Tetrahedron* **2009**, *65*, 2643.

(15) (a) Yang, C.-Y.; Lin, M.-S.; Liao, H.-H.; Liu, R.-S. *Chem. - Eur. J.* **2010**, *16*, 2696. (b) Liao, H.-H.; Liu, R.-S. *Chem. Commun.* **2011**, *47*, 1339.

(16) (a) Joo, J.-E.; Lee, K.-Y.; Pham, V.-T.; Tian, Y.-S.; Ham, W.-H. *Org. Lett.* **2007**, *9*, 3627. (b) Thompson, A. M.; Sutherland, H. S.; Palmer, B. D.; Kmentova, I.; Blaser, A.; Franzblau, S. G.; Wan, B.; Wang, Y.; Ma, Z.; Denny, W. A. *J. Med. Chem.* **2011**, *54*, 6563. (c) Palmer, B. D.; Sutherland, H. S.; Blaser, A.; Kmentova, I.; Franzblau, S. G.; Wan, B.; Wang, Y.; Ma, Z.; Denny, W. A.; Thompson, A. M. *J. Med. Chem.* **2015**, *58*, 3036. (d) Park, S.-H.; Jin, X.; Kang, J.-C.; Jung, C.; Kim, S.-S.; Kim, S.-S.; Lee, K.-Y.; Ham, W.-H. *Org. Biomol. Chem.* **2015**, *13*, 4539. (e) Park, S.-H.; Kim, J.-Y.; Kim, J.-S.; Jung, C.; Song, D.-K.; Ham, W. H. *Tetrahedron: Asymmetry* **2015**, *26*, 657.

(17) (a) Urbanski, T.; Radzikowski, Cz.; Ledochowski, Z.; Czarnocki, W. *Nature* **1956**, *178*, 1351. (b) Urbanski, T.; Gurne, D.; Slopek, S.; Mordarska, H.; Mordarski, M. *Nature* **1960**, *187*, 426. (c) Chylińska, J. B.; Urbański, T.; Mordarski, M. *J. Med. Chem.* **1963**, *6*, 484. (d) de Poel, H. V.; Guillaumet, G.; Viaud-Massuard, M. − C. *Tetrahedron Lett.* **2002**, *43*, 1205. (e) Jin, Z.; Wang, X.; Huang, H.; Liang, X.; Ye, J. *Org. Lett.* **2011**, *13*, 564.

(18) (a) Siva Reddy, A.; Nagarjuna Reddy, M.; Kumara Swamy, K. C. *RSC Adv.* **2014**, *4*, 28359. (b) Siva Reddy, A.; Kumara Swamy, K. C. *Org. Lett.* **2015**, *17*, 2996. (c) Siva Reddy, A.; Leela Siva Kumari, A.; Saha, S.; Kumara Swamy, K. C. *Adv. Synth. Catal.* **2016**, *358*, 1625.

(19) Brown, J. A.; Chudasama, V.; Giles, M. E.; Gill, D. M.; Keegan, P. S.; Kerr, W. J.; Munday, R. H.; Griffin, K.; Watts, A. *Org. Biomol. Chem.* **2012**, *10*, 509.

(20) Since this is an equilibrium process, consumption of **I″** would lead to the conversion of more of **I′** to **I″**.

(21) (a) Katritzky, A. R.; Ramer, W. H. *J. Org. Chem.* **1985**, *50*, 852. (b) Huang, J.; Xiong, H.; Hsung, R. P.; Rameshkumar, C.; Mulder, J. A.; Grebe, T. P. *Org. Lett.* **2002**, *4*, 2417.

DOI: 10.1021/acs.orglett.6b03047
Org. Lett. 2016, 18, 5752−5755