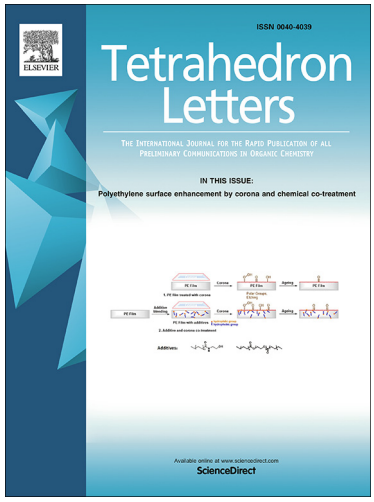
Accepted Manuscript



$PhI(OAc)_2$-Mediated Alkoxyoxygenation of β,γ-Unsaturated Ketoximes: Preparation of Isoxazolines Bearing Two Contiguous Tetrasubstituted Carbons

Chenghao Ye, Xuezhen Kou, Guoqiang Yang, Jiefeng Shen, Wanbin Zhang

PII: S0040-4039(19)30263-1
DOI: https://doi.org/10.1016/j.tetlet.2019.03.046
Reference: TETL 50687

To appear in: *Tetrahedron Letters*

Received Date: 22 January 2019
Revised Date: 17 March 2019
Accepted Date: 18 March 2019

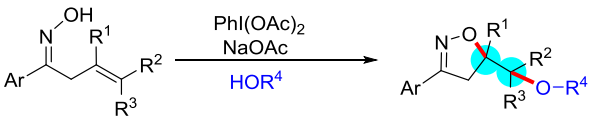
Please cite this article as: Ye, C., Kou, X., Yang, G., Shen, J., Zhang, W., $PhI(OAc)_2$-Mediated Alkoxyoxygenation of β,γ-Unsaturated Ketoximes: Preparation of Isoxazolines Bearing Two Contiguous Tetrasubstituted Carbons, *Tetrahedron Letters* (2019), doi: https://doi.org/10.1016/j.tetlet.2019.03.046

Graphical Abstract

PhI(OAc)$_2$-Mediated Alkoxyoxygenation of β,γ-Unsaturated Ketoximes: Preparation of Isoxazolines Bearing Two Contiguous Tetrasubstituted Carbons

Chenghao Ye, Xuezhen Kou, Guoqiang Yang, Jiefeng Shen, Wanbin Zhang

Leave this area blank for abstract info.



- Contiguous Tetrasubstituted Carbons
- Etherification
- Operationally Simple

24 examples
36~96% yield

Tetrahedron Letters
journal homepage: www.elsevier.com

$PhI(OAc)_2$-Mediated Alkoxyoxygenation of β,γ-Unsaturated Ketoximes: Preparation of Isoxazolines Bearing Two Contiguous Tetrasubstituted Carbons

Chenghao Ye,[a] Xuezhen Kou,[a] Guoqiang Yang,[a] Jiefeng Shen,[b,*] and Wanbin Zhang[a,b,*]

Shanghai Key Laboratory of Molecular Engineering for Chiral Drugs, [a]School of Chemistry and Chemical Engineering, [b]School of Pharmacy, Shanghai Jiao Tong University, 800 Dongchuan Road, Shanghai 200240, P. R. China

ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
$PhI(OAc)_2$
dioxygenation
oximes
isoxazoline

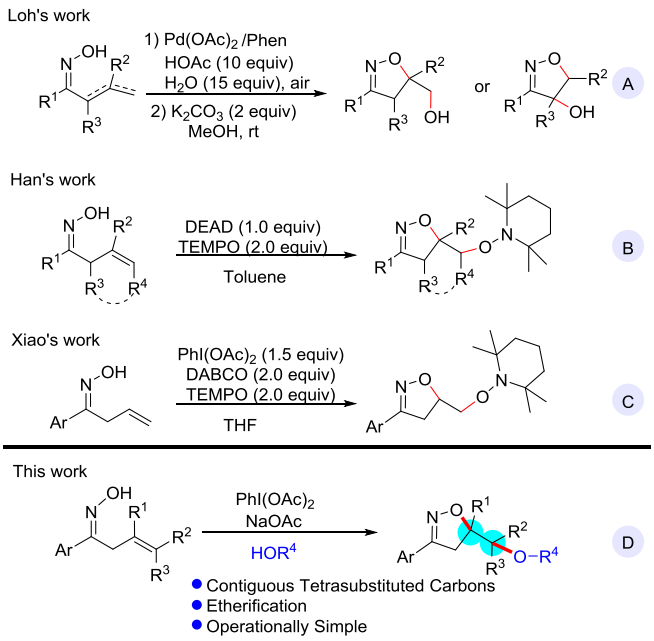
ABSTRACT

A $PhI(OAc)_2$-promoted dioxygenation of allyl oximes, including one alkoxylation, has been developed. This reaction can give isoxazoline products bearing two contiguous tetrasubstituted carbons. Various oximes substrates bearing different aryl groups and tetrasubstituted-olefin moieties were compatible with the mild reaction conditions. A two-electron oxidation pathway was proposed based on results of preliminary mechanistic studies.

1. Introduction

The difunctionalization of olefins is an important transformation for the synthesis of complex molecular skeletons.[1] Dioxygenation is one of such reactions that has attracted much attention due to the abundance of vicinal diol compounds and other derivatives in natural and pharmaceutical products.[2] Great advances have occurred in this area using transition-metal-catalysts, primarily Os and Pd.[3] However, these methodologies suffer from high cost or high toxicity and the requirement of harsh reaction conditions. Recently, the use of hypervalent iodine (III) reagents has become popular due to their use in the functionalization of C-H bonds and C=C bonds. [4] Hypervalent reagent-mediated or catalyzed difunctionalizations of C=C bonds, including diacetoxylation,[5] aminoacetoxylation[6] and diamination[7] have been reported by several groups. However, the difunctionalization of olefins, including alkoxylation, has not been widely reported, especially for the generation of tetrasubstituted carbons. [8]

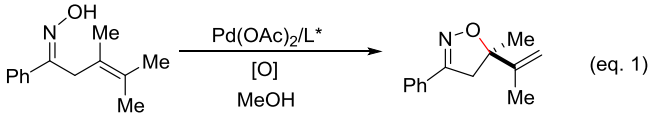
Isoxazolines are commonly found in natural and pharmaceutical compounds. [9] This skeleton has also been used as chiral ligands in asymmetric catalysis. [10] Therefore, efficient syntheses of these types of heterocycle are greatly desired. The classic method for the preparation of such skeletons consists of a 1,3-dipolar cycloaddition of nitrile oxides with alkenes. [11] However, different methods are still required to compliment the limited substrate scope of the 1,3-dipolar cycloadditions. Recently, the cyclization of allylic oximes has been well-studied (with and without the aid of metal-catalysts) via the hydroxylation, oxyamination and dioxygenation of olefins.[12] It should be mentioned that in 2010, the Loh group reported a Pd-catalyzed dioxygenation of alkenes using oxime substrates with 1 atm of air as the sole oxidant (Scheme 1, A).[12b] In 2012, the Han group developed a radical cyclization of allylic oximes using astoichiometric amount of TEMPO, giving the corresponding dioxygenation products



Scheme 1 Methodologies for dioxygenation of allyl oxime

(Scheme 1, B).[12c] The Xiao group has also described a $PhI(OAc)_2$-mediated dioxygenation cyclization of allylic oximes, again using a stoichiometric amount of TEMPO (Scheme 1, C).[12e] The generation of two contiguous tetrasubstituted carbons

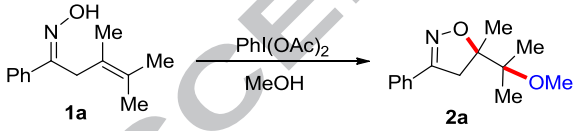
is a challenging in organic synthesis due to the congested substitution. There is no example of generation of two contiguous tetrasubstituted carbons via the aforementioned methodologies, maybe due to steric hindrance of tetrasubstituted olefins. Furthermore, an alkoxyoxygenation cyclization for the preparation of isoxazolines is still desired. Previously, our group developed a series of methodologies for the synthesis of various heterocycles, [13] including aminooxygenation cyclizations. [14] In continuation of our efforts in this area, we herein report an $PhI(OAc)_2$-mediated alkoxyoxygenation of alkenyl oximes for the preparation of isoxazolines bearing two contiguous tetrasubstituted carbon atoms (Scheme 1, D).



(eq. 1)

Our initial goal was to develop an asymmetric Wacker-type reaction of allyl oximes (Eq. 1).[15] During the screening of the reaction conditions, we found that the oxidant $PhI(OAc)_2$ could give the dioxygenation product with a methyl ether bond being formed. Then we turned our attention to this interesting reaction. The reaction conditions were optimized to improve the yield of the dioxygenation product (Table 1). Control experiments showed that $Pd(OAc)_2$ was not necessary for this reaction (entry 2 vs 1). A better yield could be obtained by increasing the reaction temperature to 50 °C from 25 °C (entry 3). Shorter and longer reaction times led to nearly full conversion but lower yields (entries 4 and 5). It appeared reducing or increasing the amount of $PhI(OAc)_2$ was not beneficial to the reaction yield (entries 6 and 7). Reaction using NaOAc or DABCO as a base considerably improved the yield (entries 8 and 9). However, use of base with a prolonged reaction still gave the dioxygenation product in lower yield (entry 10), possibly due to the decomposition of **2a** into some unidentified byproducts. Reaction in diluted methanol solution gave the desired product in a similar yield (entry 11). When the reaction with base additive was carried out at lower temperature or shorter reaction time, lower yields was observed (entries 12 and 13). The optimized reaction conditions are operationally simple since there is no need of metal catalyst, inert atmosphere protection, and anhydrous solvent.

Table 1 Optimization of reaction conditions[a]

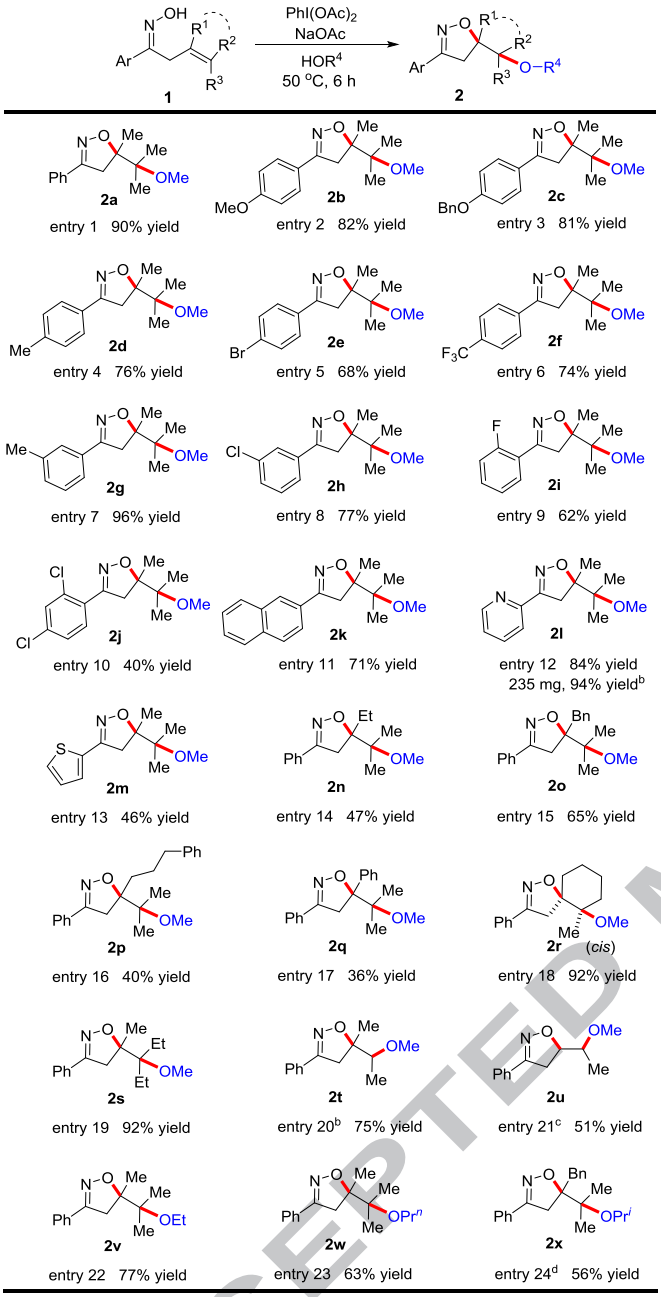


Entry	Additive	Temp. (°C)	Time (h)	Yield (%)
1[b]	-	25	6	41
2	-	25	6	44
3	-	50	6	73
4	-	50	2	56
5	-	50	12	65
6[c]	-	50	6	35
7[d]	-	50	6	38
8	**NaOAc**	**50**	**6**	**90**
9	DABCO	50	6	88
10	NaOAc	50	12	72
11[e]	NaOAc	50	6	87
12	NaOAc	50	2	73
13	NaOAc	25	2	51

[a] Reaction conditions: substrate **1a** (0.2 mmol, 1 equiv), $PhI(OAc)_2$ (0.4 mmol, 2 equiv), with or without NaOAc (0.2 mmol, 1 equiv), in MeOH (2 mL), at a certain temperature for a certain time.
[b] with $Pd(OAc)_2$ (0.02 mmol).
[c] $PhI(OAc)_2$ (0.2 mmol, 1 equiv).
[d] $PhI(OAc)_2$ (0.6 mmol, 3 equiv). [d] $PhI(OAc)_2$ (0.6 mmol, 3 equiv).
[e] MeOH (4 mL).

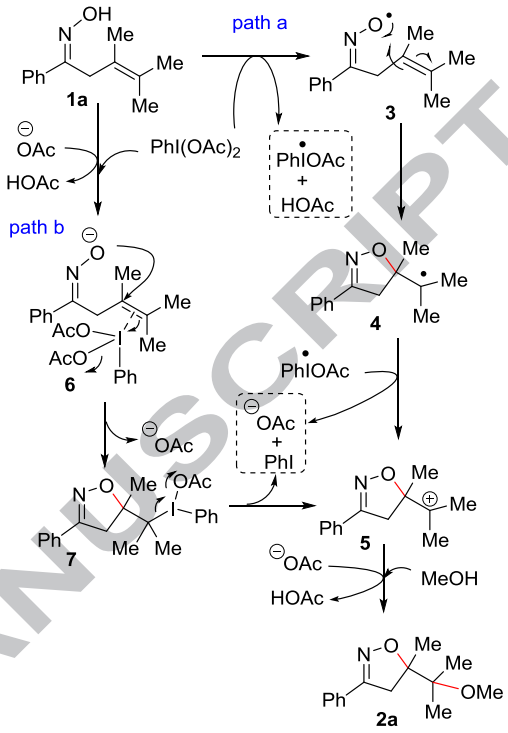
With the optimized reaction conditions in hand, the dioxygenation of different allyl oximes and alcohols was conducted (Table 2). An electron neutral phenyl-substituted substrate gave the desired product in higher yield than *para*-substituted electron-rich and electron-deficient compounds (entries 1 vs 2-6). The dioxygenation of substrates bearing electron-donating groups on the benzene ring afforded the corresponding products with better yields than those bearing electron-withdrawing groups (entries 2-4 vs 5-6, 7 vs 8). The presence of methyl groups at the *meta* position led to an increase in yield, giving the dioxygenation product with the highest yield (entry 7). The dioxygenation of *ortho*-substituted substrates provided the corresponding products in lower yields (entries 9 and 10). A substrate bearing a *β*-naphthyl group afforded the desired product in 71% yield (entry 11). To our delight, 2-pyridinyl and 2-thineyl-substituted compounds were also amenable to the reaction conditions, giving their corresponding products in moderate to good yields (entries 12 and 13). Product **2l** may be used as a ligand in organometallic catalysis, as an analogue of the widely-used pyridine-oxazoline (Pyrox) ligand.[16] We have also carried out a 1 mmol scale reaction for the producing of **2l**, which was obtained in excellent yield.

Table 2 Substrate scope[a]



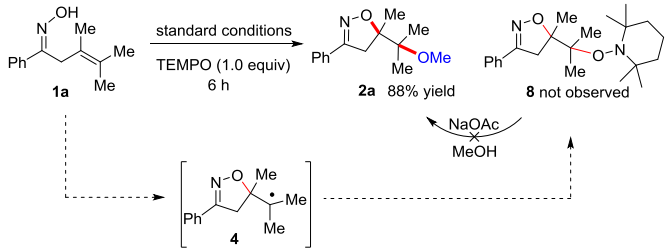
[a] Reaction conditions: substrate **1** (0.2 mmol, 1 equiv), $PhI(OAc)_2$ (0.4 mmol, 2 equiv), NaOAc (0.2 mmol, 1 equiv), in alcohol (2 mL), at 50 °C for 6 h.
[b] Reaction scale is 1.04 mmol (212 mg substrate **1l**).
[c] From (*E*)-olefin substrate.
[d] 80 °C for 5 d.

Substrates with different R^1 groups at the olefin could also be dioxygenated under our system, giving the corresponding products with poor to moderate yields (entries 14-17). We have also prepared an endo-cyclic olefin substrate bearing a six-membered ring. This substrate could react with $PhI(OAc)_2$ and MeOH to afford product *cis*-**2r** in excellent yield (entry 18). Substrate bearing two ethyl groups as R^2 and R^3 could give the corresponding product **2s** in excellent yield (entry 19). We have also tested the dioxygenation reaction of tri- and disubstituted olefin substrates (entries 20 and 21). The results indicate that less substituent on the olefin led to lower yield. Different alcohols were also tested under our dioxygenation conditions. Under the standard reaction conditions, linear alcohols successfully gave their corresponding products (entries 22 and 23). However, the sterically hindered alcohol, isopropanol, showed lower reactivity for the reaction. Therefore, a longer reaction time at higher temperature was needed in order to obtain **2x** in acceptable yield. We have also attempted to prepare six-membered or even larger sized ring product using this methodology, however, those reaction failed to give any detectable products.



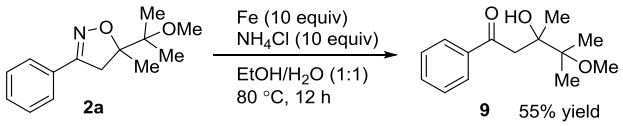
Scheme 2 Proposed mechanism.

We have proposed two possible mechanisms for this reaction, path a and b (Scheme 2). For path a, the reaction proceeds via a radical mechanism. The oxime is oxidized by $PhI(OAc)_2$ to form an oxime radical **3**,[11c,e] which undergoes radical cyclization to generate isoxazoline **4** bearing a tertiary radical. The tertiary radical is further oxidized to tertiary cation **5**. The first step for path b is the coordination of the olefin with the iodine atom of $PhI(OAc)_2$.[5b,5c,5d,6a] Subsequently, the oxygen of the oxime attacks the activated olefin to form intermediate **7**. The C-I bond can undergo a heterolytic cleavage to generate tertiary cation **5**. The desired product **2a** is obtained via the nucleophilic attack of methanol on intermediate **5**. Then we carried out an experiment using 1 equivalent of TEMPO as a radical trap, **2a** was still obtained in 88% of yield (Scheme 3), without the formation of Han's TEMPO-attacked dioxygenation product (Scheme 1, B). Since using TEMPO as an additive has only a slight effect on the yield but the use of the basic additive NaOAc is able to give the desired products in higher yield, path b appears to be the more plausible mechanism for this dioxygenation reaction. Besides, another possible explanation of the result using TEMPO as additive is that the TEMPO-captured intermediate **8** reacts with MeOH to yield the desired product **2a** in high yield. Therefore, we prepared the TEMPO-tethered compound **8** and carried out the substitution reaction of **8** with MeOH in the presence of NaOAc. The result indicates that the TEMPO cannot be replaced by MeOH, further ruling out the possibility of the presence of intermediate **4**.



Scheme 3 Reaction with TEMPO as additive.

Finally, the isoxazoline product **2a** could be transformed to acyclic β-hydroxyl-γ-methoxyl ketone **9** bearing two contiguous tetrasubstituted carbons (Eq. 2).



Scheme 4 Transformation of **2a** to acyclic compound.

2. Conclusions

In conclusion, we have developed a $PhI(OAc)_2$-promoted dioxygenation of allyl oximes, including one alkoxylation. This reaction can give isoxazoline products bearing two contiguous tetrasubstituted carbons under mild and simple conditions. Various oximes bearing different aryl groups and olefins were compatible with our reaction conditions. Preliminary mechanistic studies suggest a two-electron oxidation pathway.

Acknowledgments

We thank the The National Natural Science Foundation of China (Nos. 21302124, 21620102003, 21772119), Science and Technology Commission of Shanghai Municipality (No. 15JC1402200), and Shanghai Municipal Education Commission (No. 201701070002E00030) for financial support.

References and notes

1. For selected reviews, see: (a) Niloy, D.; Reiser, O. *Adv. Synth. Catal.* **2002**, *344*, 1169. (b) Hong, S.; Marks, T. J. *Acc. Chem. Res.* **2004**, *37*, 673. (c) Muniz, K. *Chem. Soc. Rev.* **2004**, *33*, 166. (d) Muller, T. E.; Hultzsch, K. C.; Yus, M.; Foubelo, F.; Tada, M. *Chem. Rev.* **2008**, *108*, 3795. (e) Chemler, S. R.; *Org. Biomol. Chem.* **2009**, *7*, 3009. (f) Cardona, F.; Goti, A. *Nat. Chem.* **2009**, *1*, 269. (g) de Figueiredo, R. M.; *Angew. Chem., Int. Ed.* **2009**, *48*, 1190. (h) McDonald, R. I.; Liu, G.; Stahl, S. S. *Chem. Rev.* **2011**, *111*, 2981. (i) Donohoe, T. J.; Callens, C. K.; Flores, A.; Lacy, A. R.; Rathi, A. H. *Chem. - Eur. J.* **2011**, *17*, 58. (j) Beccalli, E. M.; Broggini, G.; Fasana, A.; Rigamonti, M.; J. *Organomet. Chem.* **2011**, *696*, 277. (k) Ramirez, T. A.; Zhao, B.; Shi, Y. *Chem. Soc. Rev.* **2012**, *41*, 931. (l) Wolfe, J. P. *Angew. Chem., Int. Ed.* 2012, *51*, 10224. (m) Chen, P.; Liu, G. *Eur. J. Org. Chem.* **2015**, *2015*, 4295. (n) Serguchev, Y. A.; Ponomarenko, M. V.; Ignat'ev, N. V. *J. Fluorine Chem.* **2016**, *185*, 1.
2. (a) Giglio, B. C.; Schmidt, V. A.; Alexanian, E. J. J. *Am. Chem. Soc.* **2011**, *133*, 13320. (b) Lu, Q.; Liu, Z.; Luo, Y.; Zhang, G.; Huang, Z.; Wang, H.; Liu, C.; Miller, J. T.; Lei, A. *Org. Lett.* **2015**, *17*, 3402. (c) Xia, X.-F.; Zhu, S.-L.; Gu, Z.; Wang, H.; Li, W.; Liu, X.; Liang, Y.-M. J. *Org. Chem.* **2015**, *80*, 5572. (d) Alamillo-Ferrer, C.; Karabourniotis-Sotti, M.; Kennedy, A. R.; Campbell, M.; Tomkinson, N. C. O. *Org. Lett.* **2016**, *18*, 3102. (e) Wdowik, T.; Chemler, S. R. *J. Am. Chem. Soc.* **2017**, *139*, 9515.
3. For examples of alkene dioxygenation using osmium catalysis, see: (a) Schröder, M. *Chem. Rev.* **1980**, *80*, 187. (b) Jacobsen, E. N.; Marko, I.; Mungall, W. S.; Schroeder, G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1988**, *110*, 1968. (c) Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483. For examples of alkene dioxygenation using palladium catalysis, see: (a) Schultz, M. J.; Sigman, M. S. *J. Am. Chem. Soc.* **2006**, *128*, 1460. (b) Zhang, Y.; Sigman, M. S. *J. Am. Chem. Soc.* **2007**, *129*, 3076. (c) Li, Y.; Song, D.; Dong, V. M.; *J. Am. Chem. Soc.* **2008**, *130*, 2962. (d) Wang, A.; Jiang, H.; Chen, H. *J. Am. Chem. Soc.* **2009**, *131*, 3846; (e) Wang, W.; Wang, F.; Shi, M. *Organometallics* **2010**, *29*, 928. (f) Park, C. P.; Lee, J. H.; Yoo, K. S.; Jung, K. W. *Org. Lett.* **2010**, *12*, 2450. (g) Neufeldt, S. R.; Sanford, M. S. *Org. Lett.* **2013**, *15*, 46. (h) Huang, J.; Li, J.; Zheng, J.; Wu, W.; Hu, W.; Ouyang, L.; Jiang, H. *Org. Lett.* **2017**, *19*, 3354.
4. For selected reviews, see: (a) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2002**, *102*, 2523. (b) Wirth, T. *Angew. Chem., Int. Ed.* **2005**, *44*, 3656. (c) Deprez, N. R.; Sanford, M. S. *Inorg. Chem.* **2007**, *46*, 1924. (d) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2008**, *108*, 5299. (e) Moriarty, R. M.; Prakash, O., Eds.; *Hypervalent Iodine in Organic Chemistry: Chemical Transformations*; Wiley-Interscience, New York, 2008. Dohi, T.; Kita, Y. *Chem. Commun.* **2009**, 2073. (f) Liang H.; Ciufolini, M. A. *Angew. Chem., Int. Ed.* **2011**, *50*, 11849. (g) Romero, R. M.; Woste, T. H.; Muniz, K. *Chem. - Asian J.* **2014**, 9, 972. (h) Wang, X.; Studer, A. *Acc. Chem. Res.* **2017**, 50, 1712.
5. (a) Boye, A. C.; Meyer, D.; Ingison, C. K.; French, A. N.; Wirth, T. *Org. Lett.* **2003**, *5*, 2157. (b) Fujita, M.; Yoshida, Y.; Miyata, K.; Wakisaka, A.; Sugimura, T. *Angew. Chem., Int. Ed.* **2010**, *49*, 7068. (c) Kang, Y.-B.; Gade, L. H. *J. Am. Chem. Soc.* **2011**, *133*, 3658. (d) Zhong, W.; Yang, J.; Meng, X.; Li, Z. *J. Org. Chem.* **2011**, *76*, 9997. (e) Zhong, W.; Liu, S.; Yang, J.; Meng, X.; Li, Z. *Org. Lett.* **2012**, *14*, 3336. (f) Gelis, C.; Dumoulin, A.; Bekkaye, M.; Neuville, L.; Masson, G. *Org. Lett.* **2017**, *19*, 278.
6. (a) Lovick, H. M.; Michael, F. E. *J. Am. Chem. Soc.* **2010**, *132*, 1249. (b) Wardrop, D. J.; Bowen, E. G.; Forslund, R. E.; Sussman, A. D.; Weerasekera, S. L. *J. Am. Chem. Soc.* **2010**, *132*, 1188. (c) Chen, H.; Kaga, A.; Chiba, S. *Org. Lett.* **2014**, *16*, 6136.
7. (a) Röben, C.; Souto, J. A.; González, Y.; Lishchynskyi, A.; Muñiz, K. *Angew. Chem., Int. Ed.* **2011**, *50*, 9478. (b) Kim, H. J.; Cho, S. H.; Chang, S. *Org. Lett.* **2012**, *14*, 1424. (c) Röben, C.; Souto, J. A.; Escudero-Adán, E. C.; Muñiz, K. *Org. Lett.* **2013**, *15*, 1008. (d) Romero, R. M.; Souto, J. A.; Muñiz, K. *J. Org. Chem.* **2016**, *81*, 6118.
8. (a) Xu, H.-C.; Moeller, K. D. *J. Am. Chem. Soc.* **2008**, *130*, 13542. (b) Liskin, D. V.; Sibbald, P. A.; Rosewall, C. F.; Michael, F. E. *J. Org. Chem.* **2010**, *75*, 6294. (c) Zhou, L.; Tan, C. K.; Zhou, J.; Yeung, Y. Y. *J. Am. Chem. Soc.* **2010**, *132*, 10245. (d) Xu, H.-C.; Moeller, K. D. *J. Am. Chem. Soc.* **2010**, *132*, 2839. (e) Nakanishi, M.; Minard, C.; Retailleau, P.; Cariou, K.; Dodd, R. H. *Org. Lett.* **2011**, *13*, 5792. (f) Herrera-Leyton, C.; Madrid-Rojas, M.; López, J. J.; Cañete, A.; Hermosilla-Ibáñez, P.; Pérez, E. G. *ChemCatChem* **2016**, *8*, 2015. (g) Sun, H.; Cui, B.; Duan, L.; Li, Y.-M. *Org. Lett.* **2017**, *19*, 1520.
9. (a) Groutas, W. C.; Venkataramam, R.; Chong, L. S.; Yoder, J. E.; Epp, J. B.; Stanga, M. A.; Kim, E.-H. *Bioorg. Med. Chem.* **1995**, *3*, 125. (b) Schaller, C.; Demange, R.; Picasso, S.; Vogel, P. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 277. (c) Varshney, V.; Mishra, N. N.; Shukla, P. K.; Sahu, D. P. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 3573. (d) Rakesh; Sun D.; Lee, R. B.; Tangallapally, R. P.; Lee, R. E. *Eur. J. Med. Chem.* **2009**, *44*, 460. (e)f Kaur, K.; Kumar, V.; Sharma, A. K.; Gupta, G. K. *Eur. J. Med. Chem.* **2014**, *77*, 121. (f) Prajapti, S. K.; Shrivastava, S.; Bihade, U.; Gupta, A. K.; Naidu, V. G. M.; Banerjee, U. C.; Babu, B. N. *Med. Chem. Comm.* **2015**, *6*, 839.
10. See ref. 15d and 15k.
11. For selected examples, see: (a) Vaughan, W. R.; Spencer, J. L. *J. Org. Chem.* **1960**, *25*, 1160. (b) Jäger, V. *The Chemistry of Heterocyclic Compounds*, Volume 59: *Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products*, (Ed. A. Padwa, W. H.Pearson), Wiley, 2002, Chapter 6. (c) Cecchi, L.; De Sarlo, F.; Machetti, F. *Eur. J. Org. Chem.* **2006**, 4852. (d) Cecchi, L.; De Sarlo, F.; Machetti, F. *Chem. - Eur. J.* **2008**, *14*, 7903. (e) Beleńkii, L. I. *in Nitrile Oxides, Nitrones and Nitronates in Organic Synthesis: Novel Strategies in Synthesis*, 2nd ed. (Ed.: H. Feuer), Wiley, Hoboken, 2008, pp.1–127. (f) Mendelsohn, B. A.; Lee, S.; Kim, S.; Teyssier, F.; Aulakh, V. S.; Ciufolini, M. A. *Org. Lett.* **2009**, *11*, 1539. (g) Lee, C. C.; Fitzmaurice, R. J.; Caddick, S. *Org. Biomol. Chem.* **2009**, *7*, 4349. (h) Spiteri, C.; Sharma, P.; Zhang, F.;

Macdonald, S. J. F.; Keeling, S.; Moses, J. E. *Chem. Commun*. **2010**, *46*, 1272. (i) Crossley, J. A.; Browne, D. L. *J. Org. Chem.* **2010**, *75*, 5414. (jj) Jen, T.; Mendelsohn, B. A.; Ciufolini, M. A. *J. Org. Chem.* **2011**, *76*, 728. (k) Minakata, S.; Okumura, S.; Nagamachi, T.; Takeda, Y. *Org. Lett.* **2011**, *13*, 2966. (l) Kawai, H.; Sugita, Y.; Tokunaga, E.; Shibata, N. Eur. *J. Org. Chem.* **2012**, 1295. (m) Yoshimura, A.; Middleton, K. R.; Todora, A. D.; Kastern, B. J.; Koski, S. R.; Maskaev, A. V.; Zhdankin, V. V. *Org. Lett*. **2013**, *15*, 4010. (n) Li, C.; Deng, H.; Li, C.; Jia, X.; Li, J. *Org. Lett.* **2015**, *17*, 5718. (o) Okusu, S.; Tokunaga, E.; Shibata, N. *Org. Lett*. **2015**, *17*, 3802. (p) Wang, G.-W.; Cheng, M.-X.; Ma, R.-S.; Yang, S.-D. *Chem. Commun.* **2015**, *51*, 6308. (q) Gao, M.; Li, Y.; Gan, Y.; Xu, B. *Angew. Chem., Int. Ed.* **2015**, *54*, 8795. (r) Kesornpun, C.; Aree, T.; Mahidol, C.; Ruchirawat, S.; Kittakoop, P. *Angew. Chem., Int. Ed*. **2016**, *55*, 3997.

12. For selected examples, see: (a) Jiang, D.; Peng, J.; Chen, Y. *Org. Lett.* **2008**, *10*, 1695. (b) Zhu, M.-K.; Zhao, J.-F.; Loh, T.-P. *J. Am. Chem. Soc*. **2010**, *132*, 6284. (c) Han, B.; Yang, X.-L.; Fang, R.; Yu, W.; Wang, C.; Duan, X.-Y.; Liu, S. *Angew. Chem., Int. Ed.* **2012**, *51*, 8816. (d) Li, W.; Jia, P.; Han, B.; Li, D.; Yu, W.; *Tetrahedron* **2013**, *69*, 3274. (e) Hu, X.-Q.; Feng, G.; Chen, J.-R.; Yan, D.-M.; Zhao, Q.-Q.; Wei, Q.; Xiao, W.-J. *Org. Biomol. Chem.* **2015**, *13*, 3457. (f) Hu, X.-Q.; Chen, J.; Chen, J.-R.; Yan, D.-M. Xiao, W.-J. *Chem. - Eur. J.* **2016**, *22*, 14141. (g) Liu, R.; Wei, D.; Han, B.; Yu, W. *ACS Catal.* **2016**, 6, 6525. (h) Chen, F.; Yang, X.; Wu, Z.; Han, B. *J. Org. Chem*. **2016**, 81, 3042. (i) Chen, F.; Zhu, F.; Zhang, M.; Liu, R.; Yu, W.; Han, B. *Org. Lett*. **2017**, 19, 3255 (j) Peng, X.; Wei, D.; Han, W.; Chen, F.; Yu, W.; Han, B. *ACS Catal*. **2017**, 7, 7830 (k) Chen, H.; Wei, D.; Zhang, J.; Li, C.; Yu, W.; Han, B. *Org. Lett*. **2018**, 20, 2906 (l) Han, W.; Wang, Y.; Zhang, J.; Chen, F.; Zhou, B.; Han, B. *Org*. *Lett*. **2018**, 20, 2960;

13. (a) Jiang, F.; Wu, Z.; Zhang, W. *Tetrahedron Lett.* **2010**, *51*, 5124. (b) Jiang, F.; Wu, Z.; Zhang, W. *Tetrahedron* **2011**, *67*, 1501. (b) Yang, G.; Shen, C.; Zhang, W. *Angew. Chem., Int. Ed.* **2012**, *51*, 9141. (c) Yang, G.; Zhang, W. *Org. Lett.* **2012**, *14*, 268. (d) Wu, Z.; Zhang, J.; Li, Y.; Zhang, W.; *Tetrahedron Lett*. **2017**, *58*, 2640. (e) Wu, Z.; Wen, K.; Zhang, J.; Zhang, W. *Org*. *Lett*. **2017**, *19*, 2813. (f) Ye, C.; Kou, X.; Xia, J.; Yang, G.; Kong, L.; Wei, Q.; Zhang, W. *Chem. - Asian J*. **2018**, *13*, 1897. (g) Kou, X.; Shao, Q.; Ye, C.; Yang, G.; Zhang, W. *J. Am. Chem. Soc.* **2018**, *140*, 7587. (h) Ling, Z.; Xie, F.; Gridnev, I. D.; Terada, M. Zhang, W. *Chem. Commun.* **2018**, *54*, 9446.

14. (a) Wang, X.; Wu, Z.; Zhu, X.; Ye, C.; Jiang, F.; Zhang, W.; *Chin. J. Chem.* **2013**, *31*, 132. (b) Kou, X.; Li, Y.; Wu, L.; Zhang, X.; Yang, G.; Zhang, W. *Org. Lett.* **2015**, *17*, 5566. (c) Wen, K.; Wu, Z.; Chen, B.; Chen, J.; Zhang, W. *Org. Biomol. Chem.* **2018**, *16*, 5618. (d) Wen, K.; Wu, Z.; Huang, B.; Ling, Z.; Gridnev, I. D.; Zhang, W. *Org. Lett.* **2018**, *20*, 1608.

15. (a) Uozumi, Y.; Kato, K.; Hayashi, T. *J. Am. Chem. Soc*. **1997**, *119*, 5063. (b) Uozumi, Y.; Kato, K.; Hayashi, T. *J. Org. Chem.* **1998**, *63*, 5071. (c) Uozumi, Y.; Kyota, H.; Kato, K.; Ogasawara, M.; Hayashi, T. *J. Org. Chem.* **1999**, *64*, 1620. (d) Arai, M. A.; Kuraishi, M.; Arai, T.; Sasai, H. *J. Am. Chem. Soc*. **2001**, *123*, 2907. (e) Trend, R. M.; Ramtohul, Y. K.; Ferreira, E. M.; Stoltz, B. M. *Angew. Chem., Int. Ed*. **2003**, *42*, 2892. (f) Hayashi, T.; Yamasaki, K.; Mimura, M.; Uozumi, Y. *J. Am. Chem. Soc*. **2004**, *126*, 3036. (g) Trend, R. M.; Ramtohul, Y. K.; Stoltz, B. M. *J. Am. Chem. Soc*. **2005**, *127*, 17778. (h) Zhang, Y. J.; Wang, F.; Zhang, W.; *J. Org. Chem.* **2007**, *72*, 9208. (i) Wang, F.; Zhang, Y. J.; Wei, H.; Zhang, J.; Zhang, W. *Tetrahedron Lett.* **2007**, *48*, 4083. (j) Wang, F.; Yang, G.; Zhang, Y. J.; Zhang, W. *Tetrahedron* **2008**, *64*, 9413. (k) Takenaka, K.; Mohanta, S. C.; Patil, M. L.; Rao, C. V. L.; Takizawa, S.; Suzuki, T.; Sasai, H. *Org. Lett*. **2010**, *12*, 3480. (l) Liu, Q.; Wen, K.; Zhang, Z.; Wu, Z.; Zhang, Y. J.; Zhang, W. *Tetrahedron* **2012**, *68*, 5209.

16. Yang, G.; Zhang, W. *Chem. Soc. Rev*. **2018**, *47*, 1783.

Supplementary Material

YES (Supplementary material is prepared and provided as a separate electronic file and submitted along with the manuscript)

Highlights

1. $PhI(OAc)_2$-promoted dioxygenation of allyl oximes, including one alkoxylation.
2. Giving isoxazoline products bearing two contiguous tetrasubstituted carbons.
3. Mild conditions and operationally simple.