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Zhuyong Zhang, Weidong Chen, Junfei Luo

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## **Graphical Abstract**

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# 1,1,1,3,3,3-Hexafluoroisopropanol as an Efficient Medium for the Room Temperature Oxidation of Styrenes to Benzaldehydes

Zhuyong Zhang<sup>a</sup>, Weidong Chen<sup>a</sup> and Junfei Luo<sup>a,</sup> \*

<sup>a</sup> School of Materials Science and Chemical Engineering, Ningbo University, Ningbo, Zhejiang, 315211, China

### ARTICLE INFO

ABSTRACT

Article history: Received Received in revised form Accepted Available online A room temperature N-hydroxyphthalimide-catalyzed oxidation of styrene derivatives to the corresponding aldehydes has been developed. The use of 1,1,1,3,3,3-hexafluoroisopropanol as the solvent was determined as being key for efficient oxidation. The incorporated oxygen atom originates from molecular dioxygen.

*Keywords:* 1,1,1,3,3,3-Hexafluoroisopropanol Mild conditions Oxidation Olefins Aldehydes 2009 Elsevier Ltd. All rights reserved.

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\* Corresponding author: Junfei Luo, e-mail: luojunfei@nbu.edu.cn.

Alkene cleavage is an important transformation in organic synthesis to obtain carbonyl compounds.<sup>1</sup> The ozonolysis of olefins is often utilised for the generation of carbonyls, but suffers from safety issues and inconvenient operation.<sup>2</sup> While methods synthetic using other  $OsO_4,^4$ stoichiometric oxidants, such as KMnO<sub>4</sub>,<sup>3</sup> chromium(VI) reagents,<sup>5</sup> hypervalent iodine,<sup>6</sup> and metachloroperoxybenzoic acid7 have been reported, they often involve large amounts of waste production and overoxidation. Thus, increased focus has been placed on the use of metal catalysts in combination with benign oxidants.8 Most notably, RuCl<sub>3</sub>-NaIO<sub>4</sub> in the mixed solvent system CCl<sub>4</sub>-CH<sub>3</sub>CN-H<sub>2</sub>O (2:2:3) was discovered by Sharpless and co-workers,9 and many other elegant methods based on ruthenium catalysts have also been reported.<sup>10</sup> For instance, Bera and co-workers demonstrated a highly efficient method for the selective oxidation of olefins to aldehydes catalysed by a NHC-Ru(II) complex.<sup>11</sup> Methods based on photocatalysis, enzymatic conversion, and electrochemistry have also been reported.12

The development of catalytic methods using abundant and green molecular oxygen as the terminal oxidant is of upmost interest as it is inexpensive and, ideally, forms H<sub>2</sub>O as a benign side-product.<sup>13</sup> However, to the best of our knowledge, methods for the catalytic aerobic oxidation of olefins to the corresponding aldehydes are rarely reported. In this regard, the palladium-catalysed oxidation of olefins to aldehydes under acidic conditions has been reported under high temperature and oxygen pressure.<sup>14</sup> Metal porphyrin complexes<sup>15</sup> have been reported as suitable catalysts for the scission of olefins but resulted in low selectivity.



Scheme 1. Representative methods for the oxidation of styrenes to aldehyde derivatives.

An iron-*N*-hydroxyphthalimide system was also proven competent using an atmospheric pressure of oxygen, although the oxidation was unselective.<sup>16</sup> The selectivity issue was solved by Xiao and co-workers who used a combination of an iron catalyst for the copper complex catalysed cleavage of olefins were also reported.<sup>18</sup> These examples further emphasized the importance of aerobic oxidation in this area.

Organic radicals show similar behaviour to high-valent metals, and have attracted attention in catalytic aerobic oxidation.19 In this regard, Jiao and co-workers reported a NHPIcatalysed scission of olefins to obtain aldehyde products at elevated temperature.<sup>20</sup> This method was generally limited to disubstituted alkenes: only one example of a mono-substituted olefin was reported in low yield (26%) in the presence of stoichiometric acetone oxime. Later on, Jiao and co-workers reported the 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO)catalysed selective cleavage of olefins in the presence of 1.5 equivalents of TMSN<sub>3</sub> under oxygen.<sup>21</sup> The aerobic oxidative cleavage of gem-disubstituted alkenes catalyzed by 2,2azobis(isobutyronitrile) (AIBN) was also reported.<sup>22</sup> On the basis of these reports, the development of a methodology for the room temperature, aerobic organo-catalysed scission of olefins, in particular for mono-substituted alkenes, would represent a useful contribution for this area. Herein, we report a NHPI-catalysed aerobic oxidation of olefins to the corresponding aldehydes. The use of HFIP (1,1,1,3,3,3-hexafluoroisopropanol) as the solvent is key to this reaction, allowing the transformation of styrenes to benzaldehydes in a highly selective and efficient manner.

#### 2. Results and Discussion

We first examined the model oxidation of *p-tert*-butylstyrene (1a) under the conditions discovered by Jiao and co-workers,<sup>20</sup> and found that this mono-substituted styrene resulted in very poor yield, with only 5% of the benzaldehyde product 2a being obtained (Entry 1). We then tested different solvents for this transformation, and it was interesting to find that the fluorinated solvent HFIP, exhibited superior reactivity for the oxidation of styrene, with 83% yield of the corresponding aldehyde 2a being produced without any other additive (Entries 2-8). However, the non-fluorinated alcohol, propan-2-ol was much less efficient, leading to only 20% yield of 2a (Entry 9). 2,2,2-Trifluoroethanol was also tested and 46% yield was obtained (Entry 10). Finally, the control reactions demonstrated that this conversion did not proceed without the NHPI catalyst or oxygen (Entries 11 and 12). Satisfyingly, the oxidation reaction could be carried out at room temperature without a decrease in the yield (Entry 13). The reaction showed high selectivity, without any epoxide, radical coupling products or carboxylic acid being observed.

Table 1. Optimization of the reaction conditions.<sup>a</sup>

		NHPI (X	( mol %)	0
	<sup>t</sup> Bu 1a	Solvent T (°C), (	(0.1 M) <sup>t</sup> Bu D <sub>2</sub> , 24 h <b>2a</b>	
Entry	NHPI	T (°C)	Solvent	Yield <b>2a</b> (%)
1	10 mol %	80	DMA	5
2	10 mol %	80	DCE	20
3	10 mol %	80	1,4-dioxane	12
4	10 mol %	80	THF	28
5	10 mol %	80	EtOAc	15
6	10 mol %	80	$H_2O$	0
7	10 mol %	80	MeCN	34
8	10 mol %	80	HFIP	83

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10	10 mol %	80	TFE	46
11	-	80	HFIP	0
12ь	10 mol %	80	HFIP	trace
13	10 mol %	25	HFIP	82

[a] Unless otherwise noted, the reactions were performed using 0.2 mmol of 1a in 1.0 mL of solvent under air for 24 h. Isolated yields. NHPI = N-hydroxyphthalimide.

[b] The reaction was performed under N<sub>2</sub>.

We then turned our attention to probe the scope of the NHPIcatalysed oxidation of olefins with differently decorated styrenes. In general, the electron-rich styrenes were more reactive than the electron-poor substrates in this oxidation process. In detail, the substrate with a strong electron-donating methoxy group substituted at the para-position was well tolerated, giving 83% vield (2b). The weak electron-donating methyl substituted styrene and non-substituted styrene also proceeded efficiently, although prolonged reaction times were required (2c and 2d). 4-Halogenated (-F, -Cl, -Br) styrenes, on the other hand, resulted in relatively low yields under the standard conditions. However, the oxidation of 4-halogenated styrenes could be significantly promoted by the addition of cobalt acetate (2e-g). Substrates with the strong electron-withdrawing nitro and trifluoromethyl groups were less reactive, affording 45% and 56% yield, respectively (2h and 2i). In this case, the addition of cobalt acetate did not improve the yields. Substrates bearing the hydroxyl functionality were unreactive, and the reaction with amine-substituted substrates led to decomposition (1j and 1k). However, acyl protection of the amine/hydroxyl groups resulted in a successful transformation (21 and 2m). The carboxyl group substituted styrene 1n reacted sufficiently without requiring protection. m-Methylstyrene 1j and o-methylstyrene 1k were chosen to test the effect of the substituent position, with lower reactivity observed compared to p-methylstyrene, although the yields could be improved by the addition of cobalt acetate. Di-substituted olefins were also tested to investigate the reaction scope. Both cis- and anti-1,2-diphenylethene (11 and 1m) were found to be compatible, leading to the same product benzaldehyde 2d in 76% and 78% yield, respectively. 1,1-Disubstituted olefins (1n and 10) were less reactive in comparison to the mono-substituted and 1,2-disubstituted olefins, giving the corresponding ketones in moderated yields. Selected hetero-aromatic alkenes were also investigated. Although 3-vinylpyridine (1u) only afforded 17% of the desired product 2u, N-methyl-3-vinylindole (1v) gave the corresponding aldehyde 2v in moderate yield.

Table 2. Scope of the oxidation of styrenes.<sup>a</sup>







[a] Unless otherwise noted, the reactions were performed using 0.2 mmol of 1 in 1.0 mL of HFIP at room temperature for 24 h under 1 atm. of  $O_2$ . Isolated yields;

[b] The reactions were performed for 48 h;

[c] 5 mol % of  $Co(OAc)_2$  was added.

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Control reactions were carried out to help understand the reaction mechanism. The oxidation did not proceed without the NHPI catalyst or oxygen (Scheme 2a and b) The addition of 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) completely stopped the reaction which suggested that a radical initiation pathway is possible (Scheme 2c). This also explained why the substrates containing phenol or aniline moieties significantly decreased the reactivity. Finally, the formation of <sup>18</sup>O labelled aldehyde **20'** in the presence of <sup>18</sup>O<sub>2</sub> indicated that the oxygen atom originated from molecular dioxygen (Scheme 2d). Finally, the reaction was compatible with the addition of acid but did not tolerate the addition of base, suggesting the acidic character of HFIP is important.



Scheme 2 Preliminary mechanism study.

On the basis of the above observations and previous reports, we suggest the reaction is triggered by the formation of PINO radical (I) from NHPI.<sup>19a,19b,23</sup> In the case of the reaction with cobalt acetate, the reaction could begin with the oxidation of Co(II) by molecular oxygen to afford Co(III) complexes, which promotes the transformation from NHPI to PINO radical,<sup>24</sup> consequently enhancing the reactivity in some cases. The PINO radical reacts with styrene to give carbon radical II, which is followed by the trapping of molecular oxygen to furnish peroxyl radical III. The cleavage of III gives the aldehyde product, possibly through a dioxetane intermediate, while simultaneously

(Scheme 3). A previous report by Jiao and co-workers was generally limited to the reaction of di-substituted alkenes, which are able to better stabilise the radical intermediate (*c.f.* **II** and **II**'). In our case, we are able to engage less reactive monosubstituted alkenes. Thus, the superior performance of the reaction in HFIP may be attributed to a stabilizing affect of HFIP on the intermediate radical species.<sup>25</sup> Based on the results in Table 1, entries 8-10, the more acidic HFIP could also promote the generation of PINO from NHPI since the transformation proceeded easily under acidic conditions.<sup>26</sup> Additionally, HFIP and the benzaldehyde product may form a H-bond adduct, preventing over-oxidation to the carboxylic acid.<sup>27</sup> Detailed examination of the reaction mechanism is still ongoing in our lab.



Scheme 3. Putative reaction mechanism

#### 3. Conclusion

We have developed a room temperature NHPI-catalyzed oxidation of styrenes to benzaldehydes. This method allows mono-substituted alkenes to be efficiently converted into the corresponding aldehydes. Aromatic alkenes containing a variety functional groups such as alkyl, alkoxyl, halogen, nitro, ester, amide and carboxyl, were all found to be compatible in the oxidation reactions.

#### **Conflicts of interest**

There are no conflicts to declare.

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Ref

(a) W. N. Oloo, R. Banerjee, J. D. Lipscomb and L. Que, J. Am. Chem. Soc. 2017, 139, 17313-17326;

(b) M. Mu, Y. Wang, Y. Qin, X. Yan, Y. Li, and L.-G. Chen, ACS Appl. Mater. Interfaces 2017, 9, 22856-22863;

(c) D. T. Bregante and D. W. Flaherty, J. Am. Chem. Soc. 2017, 139, 6888-6898:

- (d) J.-Q. Yu and E. J. Corey. Org. Lett. 2002, 4, 2727-2730.
- 2 (a) C. T. T. Wong, H. Y. Lam and X. Li, Org. Biomol. Chem. 2013, 11, 7616-7620:

(b) D. Ray, J. K'E. Malongwe and P. Klan, Environ. Sci. Technol. 2013, 47, 6773-6780.

- 3. (a) S. Bhatia, S. Singh, R. Kumar, A. Kumar, C. E. Olson and A. K. Prasad, Indian J. Chem. 2013, 52, 379-386; (b) S. Lai and D. G. Lee, Synthesis. 2001, 11, 1645-1648.
- (a) S. R. Hart, D. C. Whitehead, B. R Travis and B. Borhan, Org. Biomol. Chem. 2011, 9, 4741-4744; (b) B. R. Travis, R. S. Narayan and B. Borhan, J. Am. Chem. Soc. 2002,
- 124, 3824-3825. 5. W. B. Sheats, L. K. Olli, R. Stout, J. T. Lundeen, R. Justus and W. G. Nigh, J. Org. Chem. 1979, 44, 4075-4078.
- (a) T. E Nielsen and M. Meldal, Org. Lett. 2005, 7, 2695-2698; 6. (b) D. A. Chaudhari and R. A. Fernandes, J. Org. Chem. 2016, 81,
- 2113-2121. (a) K. Miyamoto, Y. Sei, K. Yamaguchi and M. Ochiai, J. Am. Chem. 7.
- Soc. 2009, 131, 1382-1383; (b) F. V. Singh, H. M. S. Milagre, M. N. Eberlin and H. A. Stefani,
  - Tetrahedron Lett. 2009, 50, 2312-2316.
- (a) A. Rajagopalan, M. Lara and W. Kroutil, Adv. Synth. Catal. 2013, 8. 355, 3321-3335:
  - (b) A. Dhaksshinamoorthy and K. Pitchumani, Tetrahedron Lett. 2006, 62.9911-9918:
  - (c) H. Kitahara, H. Sakurai, Chem. Lett. 2012, 41, 1328-1330;
  - (d) D. Xing, B. Guan, G. Cai, Z. Fang, L. Yang and Z. Shi, Org. Lett. 2006, 8, 693-696.
- 9. P. H. J. Carlsen, T. Katsuki, V. S. Martin and K. B. Sharpless, J. Org. Chem. 1981, 46, 3936-3938.
- 10. (a) D. Yang and C. Zhang, J. Org. Chem. 2001, 66, 4814-4818; (b) W.-P. Yip, W.-Y. Yu, N. Zhu and C.-M. Che, J. Am. Chem. Soc. 2005, 127, 14239-14249; (c) D. D. Joarder, S. Gayen, R. Sarkar, R. Bhattacharya, S. Roy and D. K. Maiti, J. Org. Chem. 2019, 84, 8468-8480;

(d) V. Kogan, M. M. Quintal and R. Neumann, Org. Lett. 2005, 7, 5039-5042.

- 11. P. Daw, R. Petakamsetty, A. Sarbajna, S. Laha, R. Ramapanicker and J. K. Bera, J. Am. Chem. Soc. 2014, 136, 13987-13990.
- 12. (a) H. Kotani, K. Ohkubo and S. Fukuzumi, J. Am. Chem. Soc. 2004, 126, 15999-16006;
  - (b) X. Wu, A. P. Davis and A. J. Fry, Org. Lett. 2007, 9, 5633-5636;
  - (c) M. Lara, F. G. Mutti, S. M. Glueck and W. Kroutil, J. Am. Chem. Soc. 2009. 131. 5368-5369:
  - (d) A. K. Singh, R. Chawla and L. D. S. Yadav, Tetrahedron Lett. 2015, 56.653-656:
  - (e) W. Yu and Z. Zhao, Org. Lett. 2019, 21, 7726-7730.
- 13. (a) K. X. Chen, P. F. Zhang, Y. Wang and H. R. Li, Green. Chem. 2014, 16, 2344-2374;
  - (b) T. Mallat and A. Baiker, Chem. Rev. 2004, 104, 3037-3058;
  - (c) T. Punniyamurthy, S. Velusamy and J. Iqbal, Chem. Rev. 2005, 105, 2329-2363:
  - (d) Z. Z. Shi, C. Zhang, C. H. Tang and N. Jiao, Chem. Soc. Rev. 2012, 41, 3381-3430;
- (e) W. Q. Wu and H. F. Jiang, Acc. Chem. Res. 2012, 45, 1736-1748.
- A. Wang, H. Jiang, J. Org. Chem. 2010, 75, 2321-2326. 14.
- 15. (a) X. Zhou and H. Ji, Chin. J. Chem. 2012, 30, 2103-2108;

## **Declaration of interests**

 $\boxtimes$  The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

- Pninalocya. 2006, 10, 942-947. 16. A. Dhakshinamoorthy, M. Alvaro and H. Garcia, ACS. Catal. 2011, 1, 836-840.
- A. Gonzalez-de-Castro and J. Xiao, J. Am. Chem. Soc. 2015, 137, 8206-17. 8218.
- (a) A. Rubinstein, P. Jiménez-Lozanao, J. J. Carbó, J. M. Poblet and R. 18. Neumann, J. Am. Chem. Soc., 2014, 136, 10941-10948; (b) M. M. Hossain and S.-G. Shyu, Tetrahedron, 2014, 70, 251-255; (c) Y. Liu, D. Xue, C. Li, J. Xiao and C Wang, Catal. Sci. Technol. 2017. 7. 5510-5514:
- 19. (a) Y. Ishii, S. Sakaguchi and T. Iwahama, Adv. Synth. Catal. 2001, 343, 393-427; (b) F. Recupero and C. Punta, Chem. Rev. 2007, 107, 3800-3842; (c) J. Luo and J. Zhang, J. Org. Chem. 2016, 81, 9131-9137; (d) L. Vanoye, M. Abdelaal, K. Grundhauser, B. Guicheret, P.
  - Fongarland, C. D. Bellefon and A. Favre-Réguillon, Org. Lett. 2019, 21, 10134-10138;
  - (e) M. Bietti, O. Lanzalunga, A. Lapi, T. Martin, M. Mazzonna, M. Polin and M. Salamone, J. Org. Chem. 2017, 82, 5761-5768.
- 20. R. Lin, F. Chen and N. Jiao, Org. Lett. 2012, 14, 4158-4161.
- 21. T. Wang and N. Jiao, J. Am. Chem. Soc. 2013, 135, 11692-11695.
- 22. G.-Zu Wang, X.-L. Li, J.-J. Dai and H.-J. Xu, J. Org. Chem. 2014, 79, 7220-7225.
- 23. (a) Y. Lv, X. Wang, H. Cui, K. Sun, W. Pu, G. Li, Y. Wu, J. He, X. Ren, RSC. Adv. 2016, 6, 74917-74920; (b) X.-F. Xia, S.-L. Zhu, Z. Gu, H. Wang, W. Li, X. Liu, Y.-M. Liang, J. Org. Chem. 2015, 80, 5572-5580.
- 24. (a) T. Hara, T. Iwahama, S. Sakaguchi, Y. Ishii, J. Org. Chem. 2001, 66, 6425-6431:

(b) Y. Yoshino, Y. Hayashi, T. Iwahama, S. Sakaguchi, Y. Ishii, J. Org. Chem. 1997, 62, 6810-6813;

(c) D. P. Hruszkewycz, K. C. Miles, O. R. Thielb, S. S. Stahl, Chem. Sci. 2017, 8, 1282-1287;

- (d) T. Iwahama, S. Sakaguchi, Y. Ishii, Chem. Commun. 2000, 613-614. 25. (a) I. Colomer, A. E. R. Chamberlain, M. B. Haughey, T. J. Donohoe, Nat. Rev. Chem. 2017, 1, 0088; (b) J. Wencel-Delord, F. Colobert, Org. Chem. Front. 2016, 3, 394-400; (c) S. K. Sinha, T. Bhattacharya and D. Maiti, React. Chem. Eng. 2019, 4. 1492-1492: (d) A. Kirste, M. Nieger, I. M. Malkowsky, F. Stecker, A. Fischer and S. R. Waldvogel, Chem. Eur. J. 2009, 15, 2273-2277; (e) T. Dohi, N. Yamaoka, Y. Kita, Tetrahedron 2010, 66, 5775-5785; (f) M. Arisawa, N. G. Ramesh, M. Nakajima, H. Tohma, Y. Kita, J. Org. Chem. 2001, 66, 59-65; (g) Y. Kita, H. Tohma, K. Hatanaka, T. Takada, S. Fujita, S. Mitoh, H. Sakurai, S. Oka, J. Am. Chem. Soc. 1994, 116, 3684-3691; (h) T. Dohi, A. Maruyama, N. Takenage, K. Senami, Y. Minamitsuji, H. Fujioka, S. B. Caemmerer, Y. Kita, Angew. Chem., Int. Ed. 2008, 47, 3787-3790;
- (i) J. Saha, I. Das, Adv. Synth. Catal. 2020, 362, 609-617.
- 26 (a) Y. Ishii, T. Iwahama, S. Sakaguchi, K. Nakayama, Y. Nishiyama, J. Org. Chem. 1996, 61, 4520-4526; (b) A. Shibamoto, S. Sakaguchi, Y. Ishii, Org. Process Res. Dev. 2000,
- 4, 505-508.
- 27. E. Gaster, S. Kozuch, and D. Pappo, Angew. Chem. Int. Ed. 2017, 56, 5912.

#### **Supplementary Material**

Supplementary material that may be helpful in the review process should be prepared and provided as a separate electronic file. That file can then be transformed into PDF format and submitted along with the manuscript and graphic files to the appropriate editorial office.

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:



# Highlights

- Discovered a NHPI-catalyzed oxidation of styrenes to benzaldehyde derivatives.
- Practical convenience and highly functional group tolerance.
- Mild reaction conditions and low-cost reagents.