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Metal-Free Direct C (sp³)–H Cyanation Reaction with Cyanobenziodoxolones

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ARTICLE

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A metal-free protocol of direct $C(sp^3)$ -H cyanation with cyanobenziodoxolones functioning as both a cyanating reagent and oxidant was developed. Unactivated substrates, such as alkanes, ethers and tertiary amines, were thereby transformed to the corresponding nitriles in moderate to high yields. Mechanistic studies indicated that the cyanation proceeded with two potential pathways, which is highly depend on the substrates: (1) a free radical case for alkanes and ethers; (2) an oxidative case for tertiary amines.

Introduction

The cyano group is an important motif among natural products, pharmaceuticals, functional materials, agrochemicals and holds a critical position within synthetic chemistry.¹ Various methodologies have been developed to introduce a cyano group into different organic skeletons.² In this regard, the direct $C(sp^3)$ -H cyanation reaction provides a concise, efficient atom economy access to nitriles, and represents an important research topic in this field. For instance, the electrophilic cyanation was generally attained under strong basic conditions, wherein the cyanating reagents containing a heteroatom-CN bond serve as synthetic equivalents of [⁺CN] synthon, such as cyanogen halides, p-toluenesulfonyl cyanide (TsCN) or 1-cyanobenzotriazole.^{3a,3b} By following such a stratage, α -C(sp³)–H cyanation of specific carbonyl compound or silyl enol ethers was reached under mild conditions and the enantioselective conversion was also investigated.^{3c-3j} In comparison, cyanation of hydrocarbons through a free radical strategy was rarely reported and only few cases are available up to now (Scheme 1B),⁴ which involves the formation of carbon centred radical intermediates with excess oxidant or under photoinduced conditions. Besides, transition metalcatalyzed oxidative α -C(sp³)–H cyanation of tertiary amines represents the third case (Scheme 1C),⁵ which underwent the formation of an iminium ion intermediate followed by

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nucleophilic addition of cyanide anion ($^{-}$ CN). A series of metal catalyst/peroxidant systems has been developed for such a transformation. Although great progress has been achieved with respect to the direct C(sp³)–H cyanation of organic substrates, development of novel methodology that operates under metal-free conditions for a broad scope of substrates is desirable.

Scheme 1 Direct C (sp³) -H cyanation.

Previous work: (A) Electrophilic Cyana

(A) Electrophilic Cyanation
H
$$R^1$$
 \downarrow base $R^1 \bigcirc [^{+}CN]$

$$\begin{array}{ccc} & & & \\ & & & \\ R^2 \end{array} \xrightarrow{\text{Dase}} & R^1 \xrightarrow{\text{Const}} R^3 \xrightarrow{\text{R}^1} \xrightarrow{\text{R}^2} R^3 \xrightarrow{\text{R}^1} \xrightarrow{\text{R}^3} R^3 \xrightarrow{\text{R}^3} R^2 \xrightarrow{\text{R}^3} R^2 \xrightarrow{\text{R}^3} R^2 \xrightarrow{\text{R}^3} R^3 \xrightarrow{\text{R}^3} R^2 \xrightarrow{\text{R}^3} R^3 \xrightarrow{$$

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[⁺CN] = XCN (X = Cl, Br, I), TsCN, 1-cyanobenzotriazole, cyanobenziodoxolones *et al.*

(B) Free Radical Cyanation

$$\underset{R^{1}}{\overset{H}{\underset{R^{2}}}} \underset{or photoinduced}{\overset{excess [0]}{\underset{r r botoinduced}{\overset{}}}} \underset{R^{1}}{\overset{R^{2}}{\underset{r r s CN}{\overset{}}}} \underset{or r s CN}{\overset{CN}{\underset{r r s CN}{\overset{}}}} \underset{R^{1}}{\overset{CN}{\underset{r r s CN}{\overset{}}}} \underset{R^{2}}{\overset{CN}{\underset{r r s CN}{\overset{}}}} \underset{r r s CN}{\overset{CN}{\underset{r r s CN}{\overset{}}}} \underset{R^{2}}{\overset{CN}{\underset{r r s CN}{\overset{}}}} \underset{r r s CN}{\overset{CN}{\underset{r r s CN}{\overset{}}}}$$

(C) Oxidative Cyanation

$$R^{1}-N \xrightarrow{H} R^{2} \xrightarrow{\text{cat. } [M]} R^{1}-N \xrightarrow{R^{2}} \xrightarrow{\text{TMSCN}} R^{1}-N \xrightarrow{R^{2}} CN$$

$$[O] = H_2O_2, O_2, \text{ peroxidant et al.}$$



TBPB: *tert*-butyl-peroxybenzoate

Cyclic hypervalent iodine reagents exhibited excellent reactivity and enhanced stability, which have been widely

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ARTICLE

employed in various functional-group transfer reactions,⁶ such trifluoromethylas trifluoromethylation,⁷ azidation,⁸ thiolation,⁹ and ethynylation.¹⁰ Electrophilic cyanation using cyanobenziodoxolones as the cyano-transfer reagent has been extensively explored.^{3c,3i} Interestingly, recent studies on the photocatalyzed decarboxylative cyanation and cyanation of thiols with cyanobenziodoxolones demonstrated a novel cyanation process,¹¹ wherein the iodine centred radical species was formed as a key intermediate. Noteworthily, Zhdankin and co-workers reported a metal-free case of direct azidation of organic substrates, such as dimethylanilines, alkanes, and alkenes, with azidobenziodoxoles functioning as not only the azide reagent but also an oxidant.8a A free radical chain mechanism was proposed by their priliminary studies, wherein the propagation steps after initiation stage involves the azide abstraction of azidobenziodoxoles by alkyl radicals and the hydrogen abstraction of substrates by the in-situ generated 2iodobenzoate radical (a kind of iodine centred radical species). We, therefore, speculated that this protocol could also be employed for the direct $C(sp^3)$ -H cyanation of hydrocarbons with cyanobenziodoxolones, which has not been studied yet. Herein, we report a metal-free case of direct C(sp³)-H cyanation of organic substrates with cyanobenziodoxolones using catalytic amount of tert-butyl-peroxybenzoate (TBPB) as the initiator. It shows a wide substrates tolerance. Not only alkanes and tertiary amines but also ethers were transformed to the corresponding nitriles under mild conditions with satisfactory yields. Most importantly, mechanistic studies indicated that the functionalization of tertiary amines proceeded with an oxidative pathway rather than the supposed free radical pathway.

Results and discussion

We started with a model reaction of 1-cyano-1,2-benziodoxole (2a, 0.1 mmol) with cyclohexane (1a, 10.0 equiv.), which was conducted in PhCF₃ (0.3 mL) at 110 °C in the presence of stochiometric amount of tert-butyl-peroxybenzoate (TBPB, 1.0 equiv.). The desired product cyclohexanecarbonitrile (3a) was directly formed with 64% yield (Table 1, entry 1). Consequently, reaction conditions varing the cyano reagents, solvents and amounts of oxidant were examined. Hypervalent iodine(III) reagents other than 2a exhibited reduced activity (entries 1~3). Besides, the highly reactive p-toluenesulfonyl cyanide (TsCN, 2d) was also employed, but leading to 3a with a poor yield of 30% under identical conditions (entry 4). We also found the performance of TBPB is the best as compared with those of the other four oxidants screened (entry 1 vs. entries 5~8). Inspection of the reaction solvents (Table S1) suggested that nonpolar ones, such as PhCF₃, 1,2-dichloroethane (DCE) and ethyl acetate (EtOAc), are more efficient than polar ones, such as CH₃OH, CH₃CN and acetone, wherein EtOAc provided a relatively good yield of 3a (78%). On the other hand, the reactivity is highly thermo-dependent, which was found remarkably dropped when the temperature was reduced to 90 ^oC (48%, Table S1). Suprisingly, further improvement of the reactivity was achieved upon diluting the reaction solution to a

proper extent. As a result, the yield of nitrile product was increased up to 91% from 78% when the amount of solvent was doubled (entry 9 vs. 10). It could be attributed to but not limited to the increased solubility of **2a** in the reaction solution. Most importantly, a catalytic amount of TBPB is equally effective (entries 12~16), suggesting it therein functions as an initiator rather than a terminal oxidant. It is necessary to note that only traces of **3a** could be detected in the absence of TBPB (entry 17). Under optimized conditions, **1a** (10 equiv.) smoothly reacted with **2a** (0.1 mmol) in the presence of TBPB (20 mol%) at 110 °C for 16 h to provide **3a** in a high yield of 90% (entry 14).

Table 1Conditions optimization for the cyanation ofcyclohexane (1a) a



^a General conditions: **1a** (1.0 mmol, 10 equiv.), **2** (0.1 mmol), oxidant (1.0 equiv.), solvent (0.3 mL), 110 °C, under argon, Yield determined by GC using cyclohexanone as the internal standard; ^b solvent (0.6 mL); ^c solvent (1.0 mL).

The scope of alkane substrates tolerance was next examined (Scheme 2). Alkanes (1a~1f) were successfully converted into the corresponding nitriles with yields ranging

from 20% to 90% under the optimized conditions. For instance, 3b originated from cyclooctane (1b) was obtained with satisfactory 75% yield. The reaction involving adamantane (1c) was conducted under a modified ratio of two substrates (1c: 2a = 2) because of the poor solubility of 1c in the reaction solution. The oxidative cyanation proceeded well and provided 3c with 76% yield. Alkanes with benzyl substutents were also examined (1d~1f), which bears active $C(sp^3)$ -H at the benzylic position towards oxidation in principle. However, the yield of each cyanation product was remarkably decreased, especially in the case of an acyclic case (1f). Besides, varied products including the corresponding dimers and those upon dehydrogenation were detected by GC-MS analysis.

This newly developed system can also be extended to the oxidative C(sp³)–H cyanation of ether at oxygen-ortho-position (Scheme 2), which was sporadically reported so far.^{4b,4c,12} We found that 5-membered cyclic ether (1g) was well tolerated, thus leading to the desired product (3g) with 90% yield. In comparison, reduced reactivity was observed for 6-membered ones (1h~1k) under standard reaction conditions. Specifically, in the case of reaction involving 1k, only one nitrile product (3k) with functionalization at the benzylic position was obtained. Besides the cyclic ethers, two acyclic ones (11 and 1m) were also employed as the substrates in the reaction with 2a, each leading to the corresponding nitrile with a moderate yield.

Scheme 2 Substrate scope of alkanes and ethers.^c



^a Yield determined by GC using cyclohexanone as the internal standard. ^b 1c (2 equiv.); ^c Yield determined by ¹H NMR using CH₂Br₂ as internal standard; Isolated vield is shown in the parentheses.

With the success in cyanation of both alkanes and ethers, we turned our attention to tertiary amines bearing reactive $C(sp^{3})$ -H bonds adjacent to the nitrogen (Scheme 3). It was observed that electronic variation of the substituents at the phenyl moiety of N,N-dimethylaniline significantly affected the reaction efficiency. The cyanation of non-substituted N,Ndimethylaniline (4a) and thoes substituted with electronwithdrawing groups (-CN (4b) and -COOMe (4c)) at the para

position underwent guite well with leading to the desired cyno products in high yields. In comparison, the corresponding cyano products substituted with a methoxyl (5e) and methyl (5f) group at the *para*-position were obtained with relatively lower yields. However, the situation for N,N-dimethylaniline bearing electron-withdrawing aldehyde group (4d) is complicated: a low yield of 5d (72%) was detected by ¹H NMR analysis along with a multitude of unrecognizable products, which may be attributed to the high reactivity of aldehyde group under oxidative conditions. Additionally, it exhibited equally effective when the phenyl group in 4a was replaced with a naphthalenyl one (4g). When two otho-positions in 5f was further blocked by methyl group, the yield of the corresponding nitrile (5h) was decreased, suggesting a negative effect of steric hindrance. In addition, we found that 6-membered cyclic tertiary amines (4i) were well tolerated, and the desired nitrile product was obtained with moderate 40% yield. No regioisometric product with cyano group at the methyl position has been observed. The yield was not decreased by replacing the methyl group in 4i with more electron-deficient groups, such as phenyl (Ph, 4j) and (tertbutoxy)carbonyl (BOC, 4k). And it led to a slightly increased performance by introducing benzo group to the 6-membered ring (4I vs. 4k). Unexpectedly, the reaction of 4m bearing an α -C(sp³)–H locating at the benzyl position gave the desired nitrile 5m in a very high yield of 88%, which is different with the observation for alkanes (3d~3f vs. 3a) and ethers (3k vs. 3h). Finally, the performance of 5-membered tertiary amines (4n and 4o) was also studied, thereby offering the corresponding nitriles with satisfactory yields.



To elucidate the oxidative cyanation pathway with respect to different R-H substrate, the spin-trapping technique was introduced to detect the involved but short-lived radicals,

ARTICLE

wherein the N-*tert*-butyl- α -(4-pyridyl-1-oxide) nitrone (4-POBN) was used as the spin-trap reagent (Scheme 4). The cyanation reaction involving either alkane (1a) or ether (1k) was completely supressed in the presence of 1.5 molar equivalent of 4-POBN. Meanwhile, the positive mode ESI-MS analysis of the reaction solution shows peaks at m/z 277.1946 (assigned to 4-POBN-1a) and 327.1776 (assigned to 4-POBN-1k), each being assigned to the corresponding radical adduct with 4-POBN (Scheme S2 and S3), suggesting a radical pathway. To our surprise, a moderate yield of cyanide product (5m) was obtained from the reaction of tertiary amine 4m with 2a in the presence of 4-POBN (1.5 equiv.) with no radical adduct (6m) being detected by ESI-MS analysis, thus disfavoring a similar radical pathway as that of alkanes and ethers. Instead, it raises another parallel mechanistic possibility of an oxidative cyanation progress, wherein iminium cations were mainly formed rather than α -C(sp³) radicals followed by neucleophic addition by the in-situ generated cyanide anion.¹³ To clarify this hypothesis, a competition experiment between the present cyanation and oxidative trifluoromethylation¹⁴ towards tertiary amine was consequently designed (Scheme 4D). The cyanation of 4m with 2a was conducted in the pesence of excess TMSCF₃ (3.0 equiv.) and CsF (2.0 equiv.), wherein not only nitrile (5m, 42%) but also trifluoromethylated (7m, 9%) product was obtained. In addition, further oxidative dehydrogenation was detected towards 7m, thereby offering 7m' with 21% yield. These results demonstrated the iminium cation was indeed formed during the oxidation, thereby rendering nucleophilic addition of trifluoromethyl anion possible.

Scheme 4 Investigation of the reaction mechanism.



On the basis of literatures¹¹ and our experimental results, a mechanistic proposal for the direct cyanation of alkanes, ethers and tertiary amines with cyanobenziodoxolone (**2a**) is presented in Scheme 5. The reaction pathway is highly dependent on the structure of substrates launched, which was categorized into two types (**A** and **B**). Specifically, **A** represents



Scheme 5 Plausible mechanisms.



Conclusions

In conclusion, we have developed a metal-free cyanation method for the direct transformation of unactivated alkanes, ethers and tertiary amines with cyanobenziodoxolones functioning as both cyanating reagent and oxidant. A range of nitrile products could be obtained thereby in moderate to high

Journal Name

yields under mild conditions. Mechanistic studies indicated that the cyanation proceeded with two potential pathways, which is highly depend on the substrates: (1) a free radical case for alkanes and ethers; (2) an oxidative case for tertiary amines. The present results may hold promise for further development of novel structures of hypervalent iodine(III) reagents in the functional group transfer reactions under metal-free conditions.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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Notes and references

- (a) D. Enders and J. P. Shilvock, *Chem. Soc. Rev.*, 2000, 29, 359; (b) F. F. Fleming, *Nat. Prod. Rep.*, 1999, 16, 597; (c) F. F. Fleming, L. Yao, P. C. Ravikumar, L. Funk and B. C. Shook, *J. Med. Chem.*, 2010, 53, 7902; (d) N. Otto and T. Opatz, *Chemistry*, 2014, 20, 13064.
- (a) S. Tang, Y. L. Deng, J. Li, W. X. Wang, Y. C. Wang, Z. Z. Li, L. Yuan, S. L. Chen and R. L. Sheng, Chem. Commun., 2016, 52, 4470; (b) A. Pradal and G. Evano, Chem. Commun., 2014, 50, 11907; (c) S. Tang, S.-H. Li, Z.-H. Li, D. Zhou and R.-L. Sheng, *Tetrahedron Lett.*, 2015, 56, 1423; (d) P. Anbarasan, H. Neumann and M. Beller, *Chem. – Eur. J.*, 2010, 16, 4725; (e) K. Ding, D. Wang, L. Kuang and Z. Li, *Synlett*, 2008, 2008, 69; (f) A. L. Fuentes de Arriba, E. Lenci, M. Sonawane, O. Formery and D. J. Dixon, *Angew. Chem., Int. Ed.*, 2017, 56, 3655; (g) T. J. Gong, B. Xiao, W. M. Cheng, W. Su, J. Xu, Z. J. Liu, L. Liu and Y. Fu, *J. Am. Chem. Soc.*, 2013, 135, 10630; (h) J. Li, Z. Wang, N. Wu, G. Gao and J. You, *Chem. Commun.*, 2014, 50, 15049.
- Electrophilic cyanation: (a) T. V. Hughes and M. P. Cava, J. Org. Chem., 1999, 64, 313; (b) R. Akula, Y. Xiong and H. Ibrahim, RSC Adv., 2013, 3, 10731; (c) Y. F. Wang, J. Qiu, D. Kong, Y. Gao, F. Lu, P. G. Karmaker and F. X. Chen, Org. Biomol. Chem, 2015, 13, 365; (d) K. Kiyokawa, T. Nagata and S. Minakata, Angew. Chem., Int. Ed., 2016, 55, 10458; (e) J. S. Qiu, Y. F. Wang, G. R. Qi, P. G. Karmaker, H. Q. Yin and F. X. Chen, Chem.-Eur. J., 2017, 23, 1775; (f) J. Schörgenhumer and M. Waser, Org. Chem. Front., 2016, 3, 1535; (g) T. Nagata, H. Matsubara, K. Kiyokawa and S. Minakata, Org. Lett., 2017, 19, 4672; (h) J. Qiu, D. Wu, P. G. Karmaker, G. Qi, P. Chen, H. Yin and F. X. Chen, Org. Lett., 2017, 19, 4018; (i) M. Chen, Z. T. Huang and Q. Y. Zheng, Org. Biomol. Chem,

2015, 13, 881; (j) B. Ma, X. Lin, L. Lin, X. Feng and X. Liu, J. Org. Chem., 2017, **82**, 701.

- Free radical cyanation: (a) Wen Zhang, Fei Wang, Scott D. McCann, Dinghai Wang, Pinhong Chen, Shannon S. Stahl and Guosheng Liu, *Science*, 2016, **353**, 1014; (b) S. Kamijo, T. Hoshikawa and M. Inoue, *Org. Lett.*, 2011, **13**, 5928; (c) M. Inoue, T. Hoshikawa, S. Yoshioka and S. Kamijo, *Synthesis*, 2013, **45**, 874.
- Oxidative cyanation: (a) K. Alagiri and K. R. Prabhu, Org. Biomol. Chem, 2012, 10, 835; (b) N. Sakai, A. Mutsuro, R. Ikeda and T. Konakahara, Synlett, 2013, 24, 1283; (c) Y. Zhang, H. Peng, M. Zhang, Y. Cheng and C. Zhu, Chem. Commun., 2011, 47, 2354; (d) W. Han and A. R. Ofial, Chem. Commun., 2009, 5024; (e) M. North, Angew. Chem., Int. Ed., 2004, 43, 4126; (f) S.-I. Murahashi, N. Komiya and H. Terai, Angew. Chem., Int. Ed., 2005, 117, 7091; (g) M. Rueping, S. Zhu and R. M. Koenigs, Chem. Commun., 2011, 47, 12709; (h) A. M. Nauth, N. Otto and T. Opatz, Adv. Synth. Catal., 2015, 357, 3424.
- (a) Y. Li, D. P. Hari, M. V. Vita and J. Waser, *Angew. Chem.*, *Int. Ed.*, 2016, **55**, 4436; X. Wang and A. Studer, *Acc. Chem. Res.*, 2017, **50**, 1712.
- Trifluoromethylation: (a) Y. T. He, L. H. Li, Y. F. Yang, Z. Z. Zhou, H. L. Hua, X. Y. Liu and Y. M. Liang, *Org. Lett.*, 2014, 16, 270; (b) Z. Liang, F. Wang, P. Chen and G. Liu, *J. Fluorine Chem.*, 2014, 167, 55; (c) P. Xu, J. Xie, Q. Xue, C. Pan, Y. Cheng and C. Zhu, *Chem.-Eur. J.*, 2013, 19, 14039.
- Azidation: (a) V. V. Zhdankin, A. P. Krasutsky, C. J. Kuehl, A. J. Simonsen, J. K. Woodward, B. Mismash and J. T. Bolz, J. Am. Chem. Soc., 1996, **118**, 5192; (b) Q.-H. Deng, T. Bleith, H. Wadepohl, L. H. Gade, J. Am. Chem. Soc. 2013, **135**, 5356.
 (c) Y. Wang, G.-X. Li, G. Yang, G. He and G. Chen, Chem. Sci., 2016, **7**, 2679.
- (a) X. Wang, T. Yang, X. Cheng, Q. Shen, *Angew. Chem. Int. Ed.* 2013, **52**, 12860; (b) X. Shao, X. Wang, T. Yang, L. Lu and Q. Shen, *Angew. Chem. Int. Ed.*, 2013, **52**, 3457.
- Ethynylation: (a) H. Wang, F. Xie, Z. Qi and X. Li, Org. Lett., 2015, **17**, 920; (b) A. Nierth and M. A. Marletta, Angew. Chem., Int. Ed., 2014, **53**, 2611; (c) S. Mukherjee, R. A. Garza-Sanchez, A. Tlahuext-Aca and F. Glorius, Angew. Chem., Int. Ed., 2017, **56**, 14723; (d) F. Le Vaillant, T. Courant and J. Waser, Angew. Chem., Int. Ed., 2015, **54**, 11200; (e) C. C. Chen and J. Waser, Chem. Commun., 2014, **50**, 12923.
- (a) F. Le Vaillant, M. D. Wodrich and J. Waser, *Chem. Sci.*, 2017, **8**, 1790; (b) R. Frei, T. Courant, M. D. Wodrich and J. Waser, *Chem.-Eur. J.*, 2015, **21**, 2662; (c) F. L. Vaillant and J. Waser, Chimia (Aarau), 2017, 71, 226.
- 12. S. Kong, L. Zhang, X. Dai, L. Tao, C. Xie, L. Shi and M. Wang, *Adv. Synth. Catal.*, 2015, **357**, 2453.
- M. O. Ratnikov and M. P. Doyle, J. Am. Chem. Soc., 2013, 135, 1549.
- 14. L. Chu and F. L. Qing, Chem. Commun., 2010, 46, 6285.

Metal-Free Direct C (sp³)–H Cyanation Reaction:

Cyanobenziodoxolones as a Cyanating Reagent and Oxidant

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TBPB: tert-butyl-peroxybenzoate