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# Direct synthesis of 2,3-diaryloxirane-2,3-dicarbonitriles from aroyl chlorides using potassium hexacyanoferrate(II) as an eco-friendly cyanide source

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ABSTRACT

A direct synthetic method for 2,3-diaryloxirane-2,3-dicarbonitriles from aroyl chlorides using potassium hexacyanoferrate(II) as an eco-friendly cyanide source, triphenylphosphine as a promoter, and triethylamine as a catalyst is described. This protocol has the features of no use of strong toxic cyanating agents, high yield, and simple work-up procedure.

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## 1. Introduction

2,3-Diaryloxirane-2,3-dicarbonitriles are well known as important synthetic intermediates.[1] The reported synthetic methods for 2,3-diaryloxirane-2,3-dicarbonitriles utilized aroyl cyanides as cyanide sources.[2] However, the commercially available aroyl cyanides are limited and comparatively expensive. Especially, synthesis of aroyl cyanides also had to use strong toxic reagents as original cyanide sources, such as HgCN,[3] NaCN,[4] CuCN,[5] KCN,[6] and TMSCN,[7] which render the reactions unsafe and environmentally unfriendly. Therefore, there is a need to explore environmentally benign cyanating agents and simple procedure for the synthesis of 2,3-diaryloxirane-2,3-dicarbonitriles.

Potassium hexacyanoferrate(II), $K_4[Fe(CN)_6]$, is non-toxic and is even used in the food industry for metal precipitation. In addition, it has been described as an antiagglutinating auxiliary for table salt (NaCl). $K_4[Fe(CN)_6]$ is commercially available on a ton scale and is even cheaper than KCN. Very recently, $K_4[Fe(CN)_6]$ has been proved to be an efficient cyanide source for the cyanation of aryl halides,[8] benzyl chlorides,[9] and indoles[10] to corresponding nitriles, the cyanation of aroyl chlorides to aroyl cyanides,[11] the cyanoaroylation of aldehydes to cyanohydrin esters,[12] the Strecker reactions to α-aminonitriles,[13] the arylcyanation of internal alkynes to β-arylalkenylnitriles,[8d] and the nucleophilic addition–elimination of α,α-dibromoacetophenones to 2-aryl-3,3-dibromoacrylonitriles.[14]

Herein, we report the direct synthesis of 2,3-diaryloxirane-2,3-dicarbonitriles from aroyl chlorides using potassium hexacyanoferrate(II) as an environmentally benign cyanide source, triphenylphosphine as a promoter, and triethylamine as a catalyst.

## 2. Results and discussion

Initially, the direct synthesis of 2,3-diaryloxirane-2,3-dicarbonitriles was attempted using benzoyl chloride and potassium hexacyanoferrate(II) as typical substrates. It was found that no corresponding product was observed in the absence of a promoter and a catalyst (Table 1, entry 1). The later research was found that the reaction could not proceed using either a promoter, such as trimethylphosphine, tributylphosphine, and triphenylphosphine, or a catalyst, such as trimethylamine, triethylamine, pyridine, 1,4-diazabicyclo-[2.2.2]octane (DABCO), and *N*,*N*-dimethylaminopyridine (DMAP) (Table 1, entries 2–9). Fortunately, in the presence of both a promoter and a catalyst the reaction could be taken place efficiently (Table 1, entries 10–24). Among them, the combination of triphenylphosphine and triethylamine gave the corresponding product in highest yield (Table 1, entry 15).

The further research showed that solvents also played an important role in the reaction. It was found that no 2,3-diphenyloxirane-2,3-dicarbonitrile was observed in some solvents such as $Et_2O$ and DMF. However, the reactions in THF, MeCN, PhMe, MeOH, EtOH, and $CH_2Cl_2$ could give the desired product in moderate to high yield. Especially the reaction in $CH_2Cl_2$ afforded 2,3-diphenyloxirane-2,3-dicarbonitrile in highest yield (Table 2).

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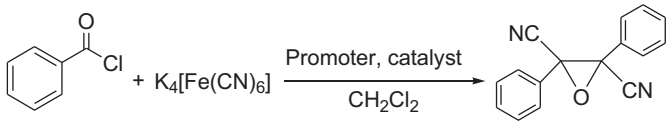
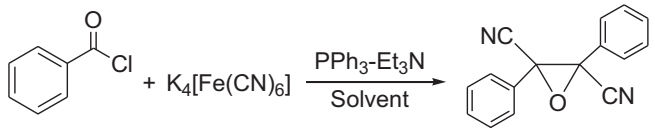
**Table 1**
The effect of promoters and catalysts on the yield of 2,3-diphenyloxirane-2,3-dicarbonitrile[a]




| Entry | Promoter | Catalyst | Yield[b] (%) |
|---|---|---|---|
| 1 | — | — | 0 |
| 2 | $PMe_3$ | — | 0 |
| 3 | $P^nBu_3$ | — | 0 |
| 4 | $PPh_3$ | — | 0 |
| 5 | — | $NMe_3$ | 0 |
| 6 | — | $NEt_3$ | 0 |
| 7 | — | Pyridine | 0 |
| 8 | — | DABCO | 0 |
| 9 | — | DMAP | 0 |
| 10 | $PMe_3$ | $NMe_3$ | 51 |
| 11 | $P^nBu_3$ | $NMe_3$ | 60 |
| 12 | $PPh_3$ | $NMe_3$ | 73 |
| 13 | $PMe_3$ | $NEt_3$ | 58 |
| 14 | $P^nBu_3$ | $NEt_3$ | 67 |
| 15 | $PPh_3$ | $NEt_3$ | 80 |
| 16 | $PMe_3$ | Pyridine | 45 |
| 17 | $P^nBu_3$ | Pyridine | 49 |
| 18 | $PPh_3$ | Pyridine | 56 |
| 19 | $PMe_3$ | DABCO | 52 |
| 20 | $P^nBu_3$ | DABCO | 31 |
| 21 | $PPh_3$ | DABCO | 35 |
| 22 | $PMe_3$ | DMAP | 40 |
| 23 | $P^nBu_3$ | DMAP | 58 |
| 24 | $PPh_3$ | DMAP | 43 |

[a] Reaction condition: benzoyl chloride (1 mmol), potassium hexacyanoferrate(II) (0.2 mmol), promoter (0.5 mmol), and catalyst (0.02 mmol) in 10 mL of $CH_2Cl_2$ for 8 h.
[b] The isolated yield.

**Table 2**
The effect of solvents on the yield of 2,3-diphenyloxirane-2,3-dicarbonitrile[a]




| Entry | Solvent | Reaction time (h) | Yield[b] (%) |
|---|---|---|---|
| 1 | $Et_2O$ | 16 | 0 |
| 2 | DMF | 16 | 0 |
| 3 | PhMe | 8 | 35 |
| 4 | THF | 8 | 20 |
| 5 | MeCN | 8 | 25 |
| 6 | $CH_2Cl_2$ | 8 | 80 |
| 7 | MeOH | 8 | 58 |
| 8 | EtOH | 8 | 64 |

[a] Reaction condition: benzoyl chloride (1 mmol), potassium hexacyanoferrate(II) (0.2 mmol), triphenylphosphine (0.5 mmol), and triethylamine (0.02 mmol) in 10 mL of solvent for 8 h.
[b] The isolated yield.

Base on these promising findings, a series of 2,3-diaryloxirane-2,3-dicarbonitriles were synthesized under the similar conditions (Scheme 1). Aroyl chlorides bearing both electron-donating ($CH_3$) and electron-withdrawing (Cl, F) groups could participate in reactions to afford the desired 2,3-diaryloxirane-2,3-dicarbonitriles in high yield. The substituents on the aryl rings have no obvious effect on the yield of reactions. The heteroaroyl chloride, such as furoyl chloride, was also available for the synthetic reaction. However, the tests for aroyl chlorides bearing nitro, bromo, 2,4-dichloro, and methoxy groups were not succeeded presumably because of strong electronic properties. In addition, some aliphatic acid chlorides such as acetyl chloride, propionyl chloride, and butyryl chloride instead of aroyl chlorides were also tested for the similar reactions for the direct synthesis of 2,3-dialkyloxirane-2,3-dicarbonitriles using potassium hexacyanoferrate(II) as an eco-friendly cyanide source. However it was found that no corresponding products were observed. The promoter, triphenylphosphine, was transformed into triphenylphosphine oxide in the reactions, which could be easily recovered from the reaction system.

A plausible mechanism for the synthesis of 2,3-diaryloxirane-2,3-dicarbonitriles is shown in Scheme 2. Aroyl chlorides reacted with potassium hexacyanoferrate(II) to afford aroyl cyanides first. Then aroyl cyanides were, respectively, attacked by triphenylphosphine and triethylamine to give intermediates **A** and **B**. The similar intermediates were also reported by Shi.[15] Intermediates **B** were nucleophilic substituted by oxygen ions of intermediates **A** to yield intermediates **C** after loss of triethylamine. Intermediates **C** underwent transient states **D**, followed by releasing triphenylphosphine oxide to give the final products, 2,3-diaryloxirane-2,3-dicarbonitriles.

## 3. Conclusion

A direct synthetic method for 2,3-diaryloxirane-2,3-dicarbonitriles from aroyl chlorides using potassium hexacyanoferrate(II) as an eco-friendly cyanide source, triphenylphosphine as a promoter, and triethylamine as a catalyst has developed. This protocol has the features of no use of strong toxic cyanide sources, high yield, and simple work-up procedure.

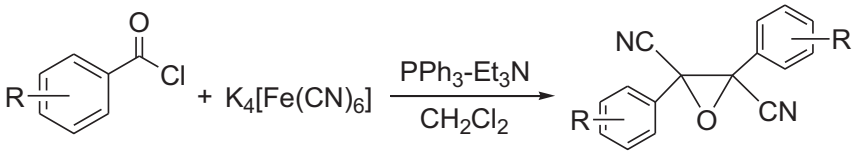
## 4. Experimental

### 4.1. General information

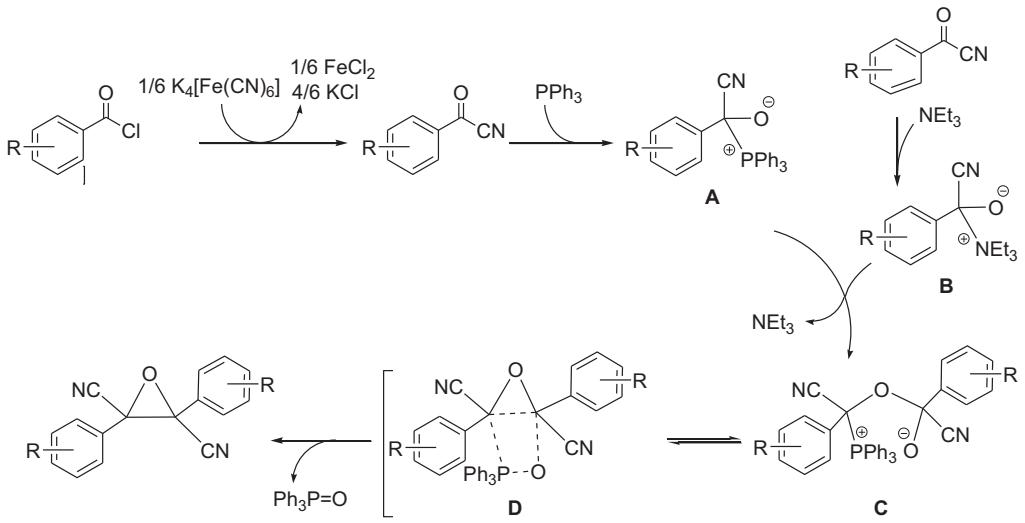
IR spectra were recorded using KBr pellets on an Alpha Centauri FTIR spectrophotometer. $^1H$ NMR and $^{13}C$ NMR spectra on a Mercury-400BB instrument using $CDCl_3$ as solvent and $Me_4Si$ as internal standard. Melting points were observed in an electrothermal melting point apparatus. Potassium hexacyanoferrate(II) was dried at 80 °C under vacuum for 24 h and finely powdered prior to use.

### 4.2. Typical procedure for the synthesis of 2,3-diaryloxirane-2,3-dicarbonitriles

The mixture of $K_4[Fe(CN)_6]$ (0.2 mmol) and aroyl chloride (1 mmol) was heated at 160 °C for 3 h. Then the reaction mixture was cooled to room temperature, and triphenylphosphine (0.5 mmol) and triethylamine (0.02 mmol) in 10 mL of $CH_2Cl_2$ were added. The resulting mixture was stirred at room temperature for appropriate time indicated in Table 3. After completion of the reaction, monitored by TLC, the resulting mixture was evaporated off

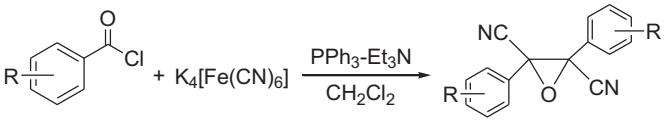


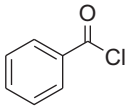
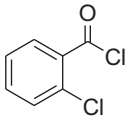
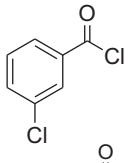
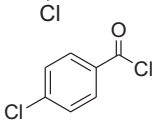
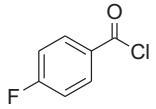
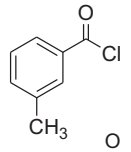
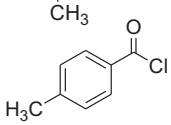
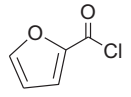

**Scheme 1.** Synthesis of 2,3-diaryloxirane-2,3-dicarbonitriles using $K_4[Fe(CN)_6]$ as cyanide source.




**Scheme 2.** Proposed mechanism for the synthesis of 2,3-diaryloxirane-2,3-dicarbonitriles using $K_4[Fe(CN)_6]$ as a cyanide source.

**Table 3**
Synthesis of 2,3-diaryloxirane-2,3-dicarbonitriles using $K_4[Fe(CN)_6]$ as cyanide source




| Entry | Aroyl chloride | Reaction time (h) | Yield[a] (%) | Mp (°C) |
|---|---|---|---|---|
| 1 |  | 8 | 80 | 112–114 |
| 2 |  | 12 | 75 | 133–135 |
| 3 |  | 10 | 70 | 168–169 |
| 4 |  | 8 | 68 | 193–195 |
| 5 |  | 8 | 76 | 185–186 |
| 6 |  | 10 | 73 | 105–107 |
| 7 |  | 10 | 77 | 136–137 |
| 8 |  | 10 | 65 | 145–146 |

[a] Yields refer to the isolated products.

the solvent, and the residue was subjected to column chromatography to give pure product. The analytical data for products are given below.

*4.2.1. 2,3-Diphenyloxirane-2,3-dicarbonitrile (Table 3, entry 1).* White solid, mp 112–114 °C (known compound);[1] IR (KBr): 3067, 2925, 2232, 1556, 1491, 1447, 771 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta$ 8.11–8.13 (m, 2H), 8.03–8.05 (m, 2H) 7.53–7.56 (m, 6H); $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta$ 161.0, 157.6, 131.7, 131.1, 129.4, 129.1, 126.9, 125.7, 125.7, 125.3, 113.9. Anal. Calcd for $C_{16}H_{10}N_2O$: C, 78.03; H, 4.09; N, 11.38. Found: C, 77.94; H, 4.08; N, 11.35.

*4.2.2. 2,3-Bis(2-chlorophenyl)oxirane-2,3-dicarbonitrile (Table 3, entry 2).* White solid, mp 133–135 °C; IR (KBr): 3070, 2925, 2239, 1532, 1465, 1438, 768 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta$ 8.07–8.10 (m, 1H), 7.75–7.78 (m, 1H), 7.41–7.61 (m, 6H); $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta$ 160.0, 155.9, 133.2, 133.0, 132.4, 132.3, 131.4, 131.2, 131.0, 130.9, 127.2, 127.0, 124.4, 124.2, 113.5, 112.6. Anal. Calcd for $C_{16}H_8Cl_2N_2O$: C, 60.98; H, 2.56; N, 8.89. Found: C, 61.05; H, 2.56; N, 8.87.

*4.2.3. 2,3-Bis(3-chlorophenyl)oxirane-2,3-dicarbonitrile (Table 3, entry 3).* White solid, mp 168–169 °C; IR (KBr): 3070, 2923, 2233, 1556, 1477, 1413, 792 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta$ 8.10–8.11 (m, 1H), 7.95–8.02 (m, 3H), 7.46–7.55 (m, 4H); $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta$ 160.0, 153.1, 135.6, 135.3, 132.0, 131.3, 130.8, 130.5, 126.9, 126.9, 126.5, 125.6, 125.0, 123.8, 113.2, 110.5. Anal. Calcd for $C_{16}H_8Cl_2N_2O$: C, 60.98; H, 2.56; N, 8.89. Found: C, 60.88; H, 2.55; N, 8.91.

*4.2.4. 2,3-Bis(4-chlorophenyl)oxirane-2,3-dicarbonitrile (Table 3, entry 4).* White solid, mp 193–195 °C; IR (KBr): 2963, 2925, 2232, 1604, 1554, 1485, 837 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta$ 8.04 (d, 2H $J$=8.0 Hz), 7.96 (d, 2H $J$=8.0 Hz), 7.50–7.55 (m, 4H); $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta$ 156.7, 138.3, 137.5, 129.8, 129.5, 128.1, 127.0, 124.0, 123.6, 113.8, 107.3. Anal. Calcd for $C_{16}H_8Cl_2N_2O$: C, 60.98; H, 2.56; N, 8.89. Found: C, 60.92; H, 2.57; N, 8.86.

*4.2.5. 2,3-Bis(4-fluorophenyl)oxirane-2,3-dicarbonitrile (Table 3, entry 5).* White solid, mp 185–186 °C; IR (KBr): 3074, 2921, 2229, 1607, 1504, 1414, 839 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta$ 8.09–8.12 (m, 2H), 8.01–8.05 (m, 2H), 7.24–7.28 (m, 4H); $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta$ 166.1, 165.4, 163.6, 162.9, 160.0, 156.8, 129.2, 129.1, 128.0, 127.9, 121.9, 121.5, 116.9, 116.7, 116.6, 116.4, 113.7, 109.7. Anal. Calcd for $C_{16}H_8F_2N_2O$: C, 68.09; H, 2.86; N, 9.93. Found: C, 68.20; H, 2.87; N, 9.95.

*4.2.6. 2,3-Bis(3-tolyl)oxirane-2,3-dicarbonitrile (Table 3, entry 6).* White solid, mp 105–107 °C; IR (KBr): 3056, 2919, 2231, 1593, 1556, 1479, 795 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): 7.89–7.92 (m, 2H), 7.82–7.85 (m, 2H), 7.31–7.45 (m, 4H), 2.47 (s, 3H), 2.46 (s, 3H); $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta$ 161.0, 157.7, 139.2, 139.0, 132.5, 131.9, 129.2, 129.0, 127.3, 126.1, 125.6, 125.2, 124.0, 122.9, 114.0, 109.2, 21.5, 21.4. Anal. Calcd for $C_{18}H_{14}N_2O$: C, 78.81; H, 5.14; N, 10.21. Found: C, 78.93; H, 5.13; N, 10.23.

*4.2.7. 2,3-Bis(4-tolyl)oxirane-2,3-dicarbonitrile (Table 3, entry 7).* White solid, mp 136–137 °C; IR (KBr): 2921, 2852, 2230, 1615, 1500, 816 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): 7.98 (d, 2H, $J$=8.0 Hz), 7.91 (d, 2H $J$=8.0 Hz), 7.31–7.35 (m, 4H), 2.44 (s, 3H), 2.43 (s, 3H); $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta$ 160.9, 157.7, 142.2, 141.6, 130.0, 129.8, 126.8, 125.7, 123.1, 122.7, 114.1, 108.7, 21.6. Anal. Calcd for $C_{18}H_{14}N_2O$: C, 78.81; H, 5.14; N, 10.21. Found: C, 78.75; H, 5.12; N, 10.18.

*4.2.8. 2,3-Di(furan-2-yl)oxirane-2,3-dicarbonitrile (Table 3, entry 8).* White solid, mp 136–137 °C; IR (KBr): 3120, 2924, 2234, 1622, 1539, 1481, 758 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): 7.65 (d, 2H, $J$=12.0 Hz), 7.17 (d, 1H, $J$=4.0 Hz), 7.10 (d, 1H, $J$=4.0 Hz), 6.60–6.63 (m, 2H); $^{13}C$ NMR ($CDCl_3$, 100 MHz): $\delta$ 152.9, 149.2, 145.8, 145.5, 140.9, 140.7, 114.2, 112.8, 112.5, 112.3, 108.3. Anal. Calcd for $C_{12}H_6N_2O_3$: C, 63.72; H, 2.67; N, 12.39. Found: C, 63.66; H, 2.68; N, 12.35.

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## Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2012.08.042.

## References and notes

1. Muller, A. J.; Nishiyama, K.; Griffin, G. W.; Ishikawa, K.; Gibson, D. M. *J. Org. Chem.* **1982**, *47*, 2342.
2. (a) Konovalova, I. V.; Ofitserova, E. K.; Mironov, V. F.; Ofitserov, E. N.; Ostanina, I. L.; Pudovik, A. N. *J. Gen. Chem. USSR (Engl. Transl.)* **1982**, *52*, 2715; (b) Konovalova, I. V.; Burnaeva, L. A.; Khusnutdinova, E. K.; Khafizova, G. S.; Pudovik, A. N. *J. Gen. Chem. USSR (Engl. Transl.)* **1985**, *55*, 2189.
3. Haase, K.; Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 83.
4. (a) Sukata, K. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 1085; (b) Pazdera, P.; Simbera, J.; Dlouhy, M. *Org. Prep. Proced. Int.* **2011**, *43*, 285.
5. Macias-Ruvalcaba, N. A.; Evans, D. H. *J. Org. Chem.* **2007**, *72*, 589.
6. (a) Patrocinio, A. F.; Moran, P. J. S. *J. Braz. Chem. Soc.* **2001**, *12*, 7; (b) Cao, Y. Q.; Du, Y. F.; Chen, B. H.; Li, J. T. *Synth. Commun.* **2004**, *34*, 2951.
7. (a) Wei, Z.; Yang, J. Y.; Meng, B.; Zhang, B.; Jiang, M. Z.; Chen, F. X. *Lett. Org. Chem.* **2009**, *6*, 637; (b) Duplais, C.; Bures, F.; Sapountzis, I.; Korn, T. J.; Cahiez, G.; Knochel, P. *Angew. Chem., Int. Ed.* **2004**, *43*, 2968.
8. (a) Schareina, T.; Zapf, A.; Beller, M. *J. Organomet. Chem.* **2004**, *689*, 4576; (b) Weissman, S. A.; Zewge, D.; Chen, C. *J. Org. Chem.* **2005**, *70*, 1508; (c) Grossman, O.; Gelman, D. *Org. Lett.* **2006**, *8*, 1189; (d) Cheng, Y. N.; Duan, Z.; Yu, L. J.; Li, Z. X.; Zhu, Y.; Wu, Y. J. *Org. Lett.* **2008**, *10*, 901; (e) Jia, X. F.; Yang, D. P.; Wang, W. H.; Luo, F.; Cheng, J. *J. Org. Chem.* **2009**, *74*, 9470; (f) Kim, J.; Chang, S. *J. Am. Chem. Soc.* **2010**, *132*, 10272; (g) Yeung, P. Y.; Tsang, C. P.; Kwong, F. Y. *Tetrahedron Lett.* **2011**, *52*, 7038.
9. Ren, Y. L.; Yan, M. J.; Zhao, S.; Sun, Y. P.; Wang, J. J.; Yin, W. P.; Liu, Z. F. *Tetrahedron Lett.* **2011**, *52*, 5107.
10. Yan, G. B.; Kuang, C. X.; Zhang, Y.; Wang, J. B. *Org. Lett.* **2010**, *12*, 1052.
11. Li, Z.; Shi, S. Y.; Yang, J. Y. *Synlett* **2006**, 2495.
12. Li, Z.; Tian, G. Q.; Ma, Y. H. *Synlett* **2010**, 2164.
13. Li, Z.; Ma, Y. H.; Xu, J.; Shi, J. H.; Cai, H. F. *Tetrahedron Lett.* **2010**, *51*, 3922.
14. (a) Zhao, Z. X.; Li, Z. *Eur. J. Org. Chem.* **2010**, 5460; (b) Zhao, Z. X.; Li, Z. *J. Braz. Chem. Soc.* **2011**, *22*, 148.
15. Zhang, W.; Shi, M. *Tetrahedron* **2006**, *62*, 8715.