Heteroatom Chemistry
Volume 23, Number 3, 2012

Synthesis of 1-Acetoxy-2-aminoakenes via Condensation of Amino with Carbonyl and C=C Acetoxylation

Wei-Bing Liu, Cui Chen, and Qing Zhang

School of Chemistry and Life Science, Guangdong University of Petrochemical Technology, Maoming 525000, People's Republic of China

Received 28 December 2011; revised 17 February 2012

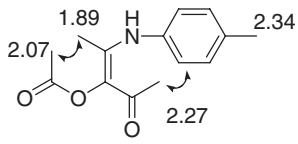
ABSTRACT: *1-Acetoxy-2-aminoakenes were synthesized through an effective synthetic route using acid as the catalyst and (diacetoxyiodo)benzene as the oxidant, which is also a novel strategy for the formation of two C-heteroatom bonds in the same reaction. In addition, it is a practical protocol with high regioselectivity, atom efficiency, and good substrate scope.* © 2012 Wiley Periodicals, Inc. Heteroatom Chem 23:290–294, 2012; View this article online at wileyonlinelibrary.com. DOI 10.1002/hc.21016

INTRODUCTION

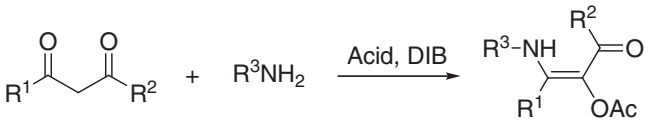
Alkenes are one of the most important classes of organic compounds as they are not only a key structural attribute of many bioactive natural products [1,2], but also an useful and versatile building block that can be used as starting materials for many classes of compounds in organic synthesis [3–7]. Not surprisingly, many synthetic methods have been reported for preparation of general alkenes [8–14]. Nevertheless, there are no simple, general procedures available for the preparation of 1,2-diheteroatom-substituted alkenes [15]; some of them suffer from poor stereoselectivity, low yields, or the use of expensive reagents or transition metal-catalysts, as well as frequently require multistep syntheses or extreme reaction conditions. In connection with our interest in polyvalent iodine reagents [16–18], they have been extensively used in modern organic synthesis in oxidative coupling to form novel C—C, C—O, and C—N bonds due to their low toxicity, easy handling, and high reactivity [19–25]. Recently, we observed a notable outcome, including condensation of primary amines with carbonyl and subsequent diacetoxyiodobenzene (DIB), a mediated C—H bond acetoxylation, representing an example of constructing new 1-acetoxy-2-aminoakenes (Scheme 1).

RESULTS AND DISCUSSION

To achieve the suitable conditions of the above transformation, a series of experiments were carried out (Table 1). As shown in Table 1, this reaction was sensitive to the solvent medium (Table 1, entries 6–9). Among the various solvents examined, the best result was obtained in dichloromethane (Table 1, entries 1–5). The reaction time as well as temperature had an obvious effect on this reaction. The results showed that the desirable reaction temperature was 0° C, and the preferable reaction time was 12 h (Table 1, entries 6–9). The structure of products was confirmed by ^{1}H NMR, ^{13}C NMR, and NOE. The configuration of the 1-acetoxy-2-aminoakenes was further confirmed by NOE studies on compound **6**.

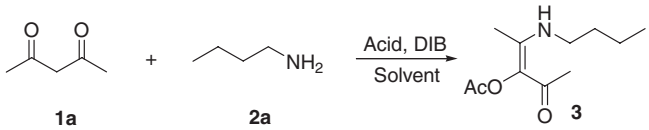


Correspondence to: Wei-Bing Liu; e-mail: lwb409@yahoo.com.cn.
Contract grant sponsor: Guangdong University of Petrochemical Technology of China.
Supporting Information is available in the online issue at wileyonlinelibrary.com.



SCHEME 1 Synthesis of 1,2-diheteroatom-substituted (*E*)-alkenes.

TABLE 1 Optimization of Reaction Conditions[a]



1a **2a**

Entry	*Solvent*	*Temperature (°C)*	*Reactional Time (h)*	*Yield (%)[b]*
1	Toluene	0	12	26
2	1,2-dichloroethane (DCE)	0	12	80
3	CH_2Cl_2	0	12	83
4	Dioxane	0	12	73
5	Acetonitrile	0	12	42
6	CH_2Cl_2	r. t.	12	63
7	CH_2Cl_2	−10	12	78
8	CH_2Cl_2	0	8	71
9	CH_2Cl_2	0	24	84

[a]The reaction was carried out using 0.25 mmol of **1a**, 0.25 mmol of **2a**, 0.20 equiv. of acetic acid, 1.2 equiv. of DIB, 2.0 mL of solvent.
[b]GC yield.

A variety of 1,3-dicarbonyl compounds and amines were subjected to the above optimal reaction conditions (Table 1, entry 3) to probe the reaction scope and generality (Scheme 2). As revealed in Scheme 2, amines, regardless of whether with aliphatic-substituted groups or aromatic-substituted groups, appear quite tolerant for this protocol and make this transformation proceed smoothly with high stereoselectivity and afford the desired product in moderate to excellent yields. For example, the reactions of acetylacetone (**1a**) with *n*-butylamine (**2a**) or aniline (**2c**) both led to 1-acetoxy-2-aminoakenes in good isolated yields (**3, 5**). However, the substituents on the 1,3-dicarbonyl compounds have an obvious effect on this reaction. As revealed in Scheme 2, when $R^1 = R^2$, this transformation would proceed smoothly (**3–6**); whereas when $R^1 \neq R^2$, the reaction would lead to inferior results. For example, when $R^1 = CH^3$, $R^2 =$ Oet, or $R^2 =$ benzene, the reactions would lead to inferior yields (**7:** 72%; **8**: 67%; **9**: 60%; **10**: 65%; **11**: 66% and **12**: 58%).

The plausible mechanism for this transformation, exemplified by the formation of (*E*)-2-(butylamino)-4-oxopent-2-en-3-yl acetate **3**, is summarized in Scheme 3. This reaction is initiated with the formation of enamine **16 [**26, 27], which was followed by the iodine(III) electrophile attack on nitrogen [17, 18] or C=C bond [28] to give intermediate **17** or **19** by losing one molecule of acetic acid. The subsequent N–I bond or C–I bond cleavage along with nucleophilic attack of acetic acid on the C=C bond or C–C bond affords imine **18** by eliminating 1 equiv of iodobenzene and 1 equiv of acetic acid. Finally, the desired product **3** is produced after isomerization of **18** to a more stable conjugated enamine form.

CONCLUSIONS

In summary, we have demonstrated here an effective synthetic route for the synthesis of 1-acetoxy-2-aminoakenes with high stereoselectivity. These compounds are attractive substrates for use in inverse electron demand Diels–Alder, Paterno–Büchi, and enamine reactions, among others. Further investigations into the scope of this catalytic/oxidative procedure and applications to synthesis are currently under way in this laboratory.

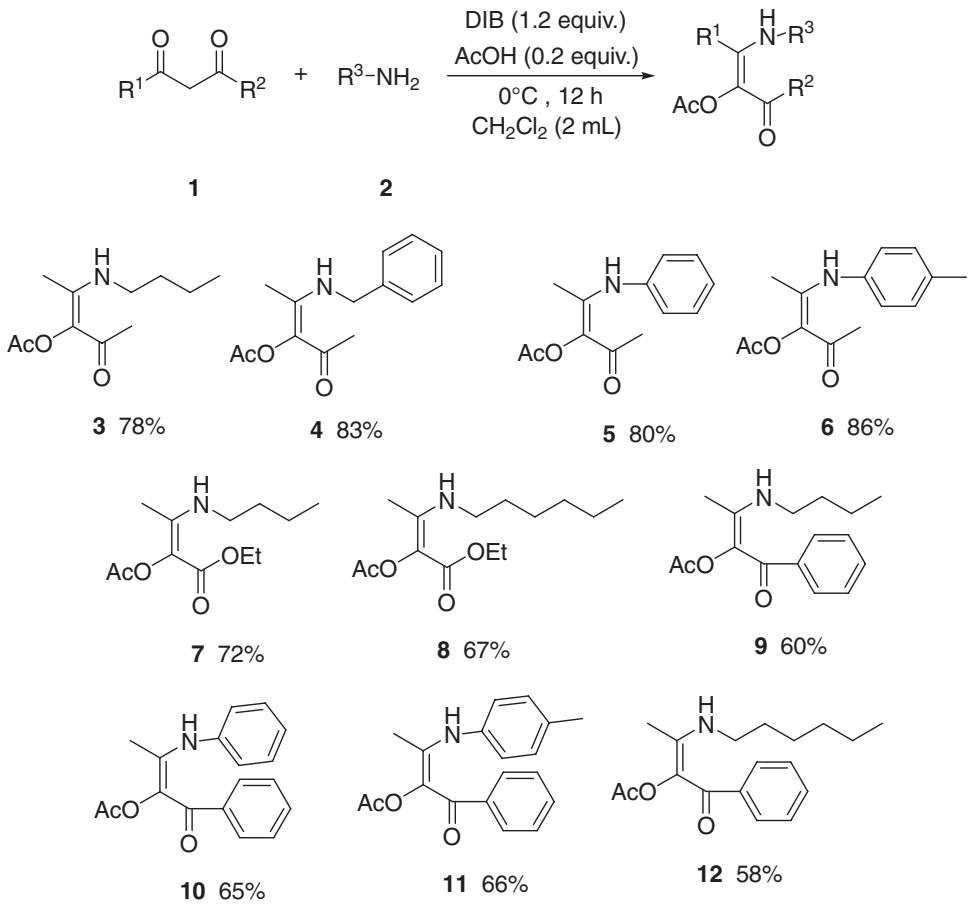
EXPERIMENTAL

General Procedure

All the reactions were carried out at 0°C in a Schlenk tube equipped with a magnetic stir bar. Solvents and all reagents were used as received. ^{1}H NMR spectra were recorded in $CDCl_3$ at 400 MHz, and ^{13}C NMR spectra were recorded in $CDCl_3$ at 100 MHz. GC–MS was obtained using electron ionization (EI). TLC was performed using commercially prepared 100–400 mesh silica gel plates (GF254), and visualization was effected at 254 nm. All the other chemicals were purchased from Aldrich (Guangzhou, Guangdong Province, China).

Typical Procedure for the Synthesis of (E)-2-(Butylamino)-4-oxopent-2-en-3-yl Acetate **3**

A mixture of DIB (386 mg, 1.2 mmol), AcOH (12 mg, 0.2 mmol), dichloromethane (2 mL), acetylacetone (**1a**) (100 mg, 1.0 mmol), and *n*-butylamine (**2a**) (73 mg, 1 mmol) was added successively in a Schlenk tube. After stirring for 12 h at 0°C, the solution was directly subjected to isolation by PTLC (prepared thin-layer chromatography) (GF254) eluted with a 10:3 petroleum ether/ethyl acetate mixture, which furnished (*E*)-2-(butylamino)-4-oxopent-2-en-3-yl acetate **3** (134.9 mg, 78%) as a dark brown viscous oil.



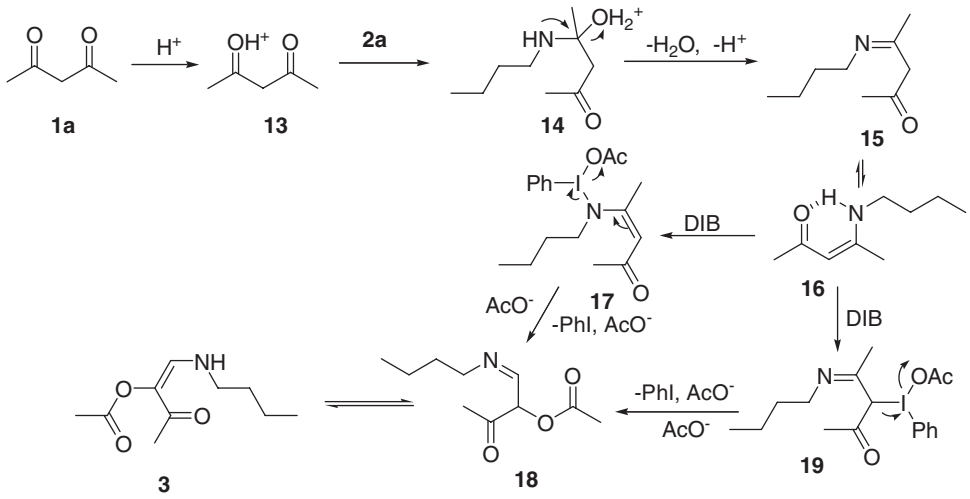
SCHEME 2 Synthesis of 1, 2-diheteroatom-substituted (*E*)-alkenes from 1,3-dicarbonyl compounds and amines. The yields of isolated products are listed.

(E)-2-(Butylamino)-4-oxopent-2-en-3-yl acetate (**3**). Dark brown viscous oil, IR ν_{max} (KBr): 3382, 1752, 1688, 1433, 1208, 1027, 853, 707, 666, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 10.69 (s, 1H), 3.23–3.18 (t, 2H, J = 8.0 Hz), 2.20 (s, 3H), 1.95 (s, 3H), 1.84 (s, 3H), 1.57–1.54 (m, 2H), 1.41–1.35 (m, 2H), 0.93–0.89 (t, 3H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.5, 170.9, 156.6, 123.3, 42.9, 31.9, 24.9, 20.5, 19.9, 13.7, 12.7; GC-MS *m/z* (% rel inten.): 213.10 (M^+, 38.23), 170.99 (100); Anal. Calcd for $C_{11}H_{19}NO_3$: C, 61.95; H, 8.98; N, 6.57; Found: C, 61.82; H, 8.88; N, 6.72.

(E)-2-(Benzylamino)-4-oxopent-2-en-3-yl acetate (**4**). Yellow dark brown viscous oil, IR ν_{max} (KBr): 3396, 1715, 1675, 1600, 1580, 1432, 1215, 1027, 670, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 10.94 (s, 1H), 7.32–7.30 (m, 2H), 7.26–7.22 (m, 3H), 4.45–4.44 (d, 2H, J = 8.0 Hz), 2.21 (s, 3H), 1.99 (s, 3H), 1.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.5, 170.7, 156.3, 137.5, 128.7, 127.4, 126.6, 123.6, 46.8, 25.0, 20.4, 12.7; GC-MS *m/z* (% rel inten.): 246.98 (M^+, 12.98), 90.78 (100); Anal. Calcd for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.66; Found: C, 68.25; H, 6.81; N, 5.82.

(E)-4-Oxo-2-(phenylamino)pent-2-en-3-yl acetate (**5**). Pale yellow crystal, mp: 102–104°C; IR ν_{max} (KBr): 3462, 3310, 1732, 1666, 1610, 1500, 1458, 1220, 1025, 707, 670, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 12.17 (s, 1H), 7.46–7.42 (m, 1H), 7.35–7.33 (m, 2H), 7.12–7.10 (m, 2H), 2.27 (s, 3H), 2.08 (s, 3H), 1.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.73, 170.59, 153.21, 138.02, 129.12, 128.26, 125.80, 125.12, 25.32, 20.54, 14.11; GC-MS *m/z* (% rel inten.): 233.08 (M^+, 20.85), 117.90 (100); Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.94; H, 6.48; N, 6.00; Found: C, 67.12; H, 6.46; N, 6.11.

(E)-2-(p-Tolylamino)-4-oxopent-2-en-3-yl acetate (**6**). Dark brown viscous oil, IR ν_{max} (KBr): 3458, 3330, 1741, 1692, 1588, 1395, 1375, 1230, 1135,



SCHEME 3 Possible reaction mechanism.

1010, 910, 808, 760, 678, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 12.10 (s, 1H), 7.16–7.14 (d, 2H, $J = 8.0$ Hz), 7.00–6.98 (d, 2H, $J = 8.0$ Hz), 2.34 (s, 3H), 2.27 (s, 3H), 2.07 (s, 3H), 1.89 (s, 3H);^{13}C NMR (100 MHz, $CDCl_3$): δ 191.4, 170.6, 153.7, 135.8, 135.3, 129.7, 129.4, 125.2, 124.7, 119.9, 25.2, 20.9, 20.5, 14.0; GC-MS *m/z* (% rel inten.): 247.02 (M^+, 22.88), 131.89 (100); Anal. Calcd for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.66; Found: C, 68.13; H, 6.55; N, 5.74.

*(E)-Ethyl 2-acetoxy-3-(butylamino)but-2-enoate (**7**).* Yellow viscous oil, IR ν_{max} (KBr): 3350, 1695, 1664, 1439, 1375, 1250, 1021, 910, 890, 715, 690, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 10.52 (s, 1H), 4.26–4.22 (m, 2H), 3.80–3.77 (t, 2H, $J = 8.0$ Hz), 2.31 (s, 3H), 2.20 (s, 3H), 1.57–1.54 (m, 2H), 1.29–1.27 (m, 5H), 0.87–0.85 (t, 3H, $J = 8.0$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.45, 164.47, 135.13, 128.12, 55.39, 44.34, 27.18, 26.47, 22.48, 20.82, 20.40, 13.96; GC-MS *m/z* (% rel inten.): 243.29 (M^+, 5.21), 83.88 (100); Anal. Calcd for $C_{12}H_{21}NO_4$: C, 59.24; H, 8.70; N, 5.76; Found: C, 59.45; H, 8.68; N, 5.90.

*(E)-Ethyl 2-acetoxy-3-(hexylamino)but-2-enoate (**8**).* Yellow viscous oil, IR ν_{max} (KBr): 3332, 1705, 1682, 1473, 1399, 1255, 1015, 810, 740, 705, cm^{-1}; 1H NMR (400 MHz, $CDCl_3$): δ 10.82 (s, 1H), 4.28–4.21 (q, 2H, $J = 8.0$ Hz), 3.81–3.79 (t, 2H, $J = 8.0$ Hz), 2.40 (s, 3H), 2.02 (s, 3H), 1.61–1.58 (m, 2H), 1.37–1.33 (m, 2H), 1.31–1.27 (m, 7H), 0.97–0.95 (t, 3H, $J = 8.0$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.44, 164.99, 164.95, 135.14, 128.14, 55.39, 44.08, 32.91, 20.82, 20.03, 14.23, 14.17, 13.67, 10.90; GC-MS *m/z* (% rel inten.): 111.92 (100); Anal. Calcd for $C_{14}H_{25}NO_4$: C, 61.97; H, 9.29; N, 5.16; Found: C, 61.90; H, 9.33; N, 5.22.

*(E)-3-(Butylamino)-1-oxo-1-phenylbut-2-en-2-yl acetate (**9**).* Orange viscous oil, IR ν_{max} (KBr): 3311, 1725, 1685, 1605, 1515, 1472, 1377, 1275, 1015, 850, 705, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 10.55 (s, 1H), 8.09–8.07 (q, 2H, $J = 8.0$ H), 7.56–7.53 (m, 1H), 7.46–7.42 (m, 2H), 3.44–3.39 (t, 2H, $J = 8.0$ H), 2.04 (s, 3H), 1.88 (s, 3H), 1.38–1.34 (m, 2H), 1.25–1.23 (m, 2H), 0.99–0.97 (t, 3H, $J = 8.0$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.70, 170.39, 133.82, 131.84, 130.85, 129.44, 128.73, 128.25, 50.03, 30.95, 20.61, 20.12, 13.75, 13.23; GC-MS *m/z* (% rel inten.): 99.94 (100); Anal. Calcd for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69; N, 5.09; Found: C, 69.88; H, 7.82; N, 5.31.

*(E)-1-Oxo-1-phenyl-3-(phenylamino)but-2-en-2-yl acetate (**10**).* Dark brown viscous oil, IR ν_{max} (KBr): 3415, 1730, 1673, 1580, 1455, 1410, 1371, 1230, 1030, 805, 725, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 12.22 (s, 1H), 8.16–8.15 (q, 2H, $J = 8.0$ H), 7.60–7.57 (m, 1H), 7.46–7.38 (m, 7H), 1.69 (s, 3H), 1.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.57, 170.69, 141.88, 133.99, 130.95, 129.88, 128.54, 128.38, 128.25, 21.80, 13.29; GC-MS *m/z* (% rel inten.): 235.93 (100); Anal. Calcd for $C_{18}H_{17}NO_3$: C, 73.20; H, 5.80; N, 4.74; Found: C, 73.03; H, 5.77; N, 4.79.

*(E)-3-(p-Tolylamino)-1-oxo-1-phenylbut-2-en-2-yl acetate (**11**).* Dark brown viscous oil, IR ν_{max} (KBr): 3430, 1735, 1688, 1615, 1572, 1498, 1422, 1382, 1255, 1015, 908, 850, 773, 695, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 12.09 (s, 1H), 8.14–8.13

(m, 2H), 7.58–7.56 (m, 1H), 7.56–7.55 (m, 2H), 7.47–7.22 (m, 4H), 2.37 (s, 3H), 1.67 (s, 3H), 1.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.59, 170.83, 139.26, 138.63, 133.93, 131.98, 130.93, 130.42, 128.35, 127.94, 119.93, 21.72, 21.11, 13.26; GC-MS *m/z* (% rel inten.): 249.98 (100); Anal. Calcd for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19; N, 4.53; Found: C, 73.72; H, 6.30; N, 4.49.

*(E)-3-(Hexylamino)-1-oxo-1-phenylbut-2-en-2-yl acetate (***12***)*. Orange viscous oil, IR ν_{max} (KBr): 3310, 1712, 1691, 1622, 1512, 1465, 1395, 1270, 1010, 912, 785, 700, cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.13 (s, 1H), 8.07–8.05 (m, 2H), 7.44–7.41 (m, 2H), 3.43–3.42 (m, 1H), 3.31–3.32 (m, 1H), 1.89 (s, 3H), 1.62–1.60 (m, 2H), 1.49 (s, 3H), 1.32–1.33 (m, 6H), 0.90–0.88 (t, 3H, J = 8.0 Hz);^{13}C NMR (100 MHz, $CDCl_3$): δ 195.72, 170.37, 133.80, 131.83, 130.84, 128.24, 127.73, 127.28, 50.29, 31.45, 28.87, 26.57, 22.56, 20.62, 13.96, 13.24; GC-MS *m/z* (% rel inten.): 128.05 (100); Anal. Calcd for $C_{18}H_{25}NO_3$: C, 71.26; H, 8.31; N, 4.62; Found: C, 71.44; H, 8.23; N, 4.79.

REFERENCES

[1] Bradshaw, J. W. S.; Baker, R.; Howse, P. E. Nature 1975, 258, 230.
[2] Garson, M. J. Chem Rev 1993, 93, 1699.
[3] Mandal, S. K.; Paira, M.; Roy, S. C. J Org Chem 2008, 73, 3823.
[4] Mochida, S.; Hirano, K.; Satoh, T.; Miura, M. J Org Chem 2009, 74, 6295.
[5] Zhao, J.; Burgess, K. J Am Chem Soc 2009, 131, 13236.
[6] Paderes, M. C.; Chemler, S. R. Org Lett 2009, 11, 1915.
[7] Ward, A. F.; Wolfe, J. P. Org Lett 2010, 6, 1268–1271.
[8] Connon, S. J.; Blechert, S. Angew Chem, Int Ed 2003, 42, 1900.
[9] Lebel, H.; Guay, D.; Paquet, V.; Huard, K. Org Lett 2004, 6, 3047.
[10] Lebel, H.; Paquet, V. J Am Chem Soc 2004, 126, 11152.
[11] Concellón, J. M.; Rodríguez-Solla, H.; Simal, C.; Huerta, M. Org Lett 2005, 7, 5833.
[12] Fioravanti, S.; Pellacani, L.; Tardella, P. A.; Vergari, M. C. Org Lett 2008, 10, 1449.
[13] Negishi, E. I.; Huang, Z. H.; Wang, G. W.; Mohan, S.; Wang, C.; Hattori, H. Acc Chem Res 2008, 41, 1474.
[14] Arthuis, M.; Pontikis, R.; Florent, J. C. J Org Chem 2009, 74, 2234.
[15] Diaz-Requejo, M. M.; DiSalvo, D.; Brookhart, M. J Am Chem Soc 2003, 125, 2038.
[16] Liu, W. B.; Jiang, H. F.; Huang, L. B. Org Lett 2010, 12, 312.
[17] Liu, W. B.; Chen, C.; Zhang, Q. Org Biomol Chem 2011, 9, 6484.
[18] Liu, W. B.; Chen, C.; Zhang, Q.; Zhu, Z. B. Beilstein J Org Chem 2011, 7, 1436.
[19] Chen, Y.; Ju, T.; Wang, J. W.; Yu, W. Q.; Du, Y. F.; Zhao, K. Synlett 2010, 231.
[20] Zhdankin, V. V.; Stang, P. J. Chem Rev 2002, 102, 2523.
[21] Stang, P. J. J Org Chem 2003, 68, 2997.
[22] Zhdankin, V. V.; Stang, P. J. Chem Rev 2008, 108, 5299.
[23] Dohi, T.; Kita, Y. Chem Commun 2009, 2073.
[24] Uyanik, M.; Ishihara, K. Chem Commun 2009, 2086.
[25] Ghosh, H.; Patel, B. K. Org Biomol Chem 2010, 8, 384.
[26] Enriquez, R. G.; Fernandez, J. M.; Leon, I.; Reynolds, W. F.; Yang, J. P.; Yu, M. Can J Chem 1995, 73, 16.
[27] Mukherjee, S.; Yang, J. W.; Hoffmann, S.; List, B. Chem Rev 2007, 107, 5471.
[28] Chen, Y.; Ju, T.; Wang, J. W.; Yu, W. Q.; Du, Y. F.; Zhao, K. Synlett 2010, 2.