Stereoselective cobalt-catalyzed halofluoroalkylation of alkyne

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Stereoselective additions of highly functionalized reagents to available unsaturated hydrocarbons are an attractive synthetic tool due to their high atom economy, modularity, and rapid generation of complexity. We report efficient cobalt-catalyzed (E)-halofluoroalkylations of alkenes that enable the construction of densely functionalized, stereo-defined fluorinated hydrocarbons. The mild conditions (2 mol% cat., 20 °C, acetone/water, 3 h) tolerate various functional groups, i.e. halides, alcohols, aldehydes, nitriles, esters, and heteroarenes. This reaction is the first example of a highly stereoselective cobalt-catalyzed halo-fluoroalkylation. Unlike related cobalt-catalyzed reductive couplings and Heck-type reactions, it operates via a radical chain mechanism involving terminal halogen atom transfer which obviates the need for a stoichiometric sacrificial reductant.

1 Introduction

Fluorinated hydrocarbons constitute key structural motifs in many bioactive molecules, agrochemicals, and pharmaceuticals due to their high metabolic stability, lipophilicity, and bioavailability compared with the parent compounds. Fluoroalkylation methods of easily accessible precursors have therefore attracted great interest in the past years. While many protocols are substitution processes that require highly pre-functionalized starting materials and produce unwanted by-products, direct additions to unsaturated hydrocarbons exhibit higher modularity and atom-economy and provide ample opportunities of regio- and stereocontrol. The addition of halo-fluoroalkanes to alkenes is an especially attractive tool due to the easy availability of the reagents and the great synthetic versatility of the resultant halo-fluoroalkenes. Many methods operate via an atom transfer radical addition (ATRA) mechanism in the presence of radical initiators (e.g. BEt₃, AIBN, Na₂S₂O₅ or light) that showed narrow substrate scope and poor selectivity. Mechanistically closely related transition metal-mediated halo-fluoroalkylations have been recently reported, but with a narrow focus on iodo-fluoroalkylations and/or moderate stereo-control (Scheme 1). Hu et al. devised an iron-catalyzed addition of perfluoroalkyl iodide to alkynes with moderate to good E/Z-selectivities in the presence of Cs₂CO₃. The radical reaction with alkyl-substituted alkynes required long reaction times at 60 °C and could not convert perfluoroalkyl bromides. Besset et al. postulated a different mechanism for the copper-mediated synthesis of difluoromethyl alkynes from BrCF₂CO₂Et and alkynes. However, significantly lower stereoselectivities were obtained and stoichiometric amounts of copper salt were employed. Very recently, Wang and co-workers reported a copper-catalyzed decarboxylative ATRA reaction between ICF₂CO₂Et and substituted propiolic acids.

Despite the developments of novel iron- and copper-catalyzed procedures, the reactions generally utilize expensive fluoroalkyl iodides as starting materials, high catalyst loadings, long reaction times, and high reaction temperatures. An efficient and robust yet highly stereoselective method that operates at mild conditions and low catalyst loadings and that is applicable to various fluoroalkyl halides would constitute
2 Results and discussion

2.1 Discovery of a cobalt-catalyzed ATRA reaction

We commenced our investigations with the reaction of phenylacetylene (1a) and ethyl bromodifluoroacetate (2a). Variations of reaction conditions, solvents, and catalysts led to an optimized procedure that utilized a three-component catalyst comprising of CoBr₂, dpbbz (1,2-bis(diphenylphosphino)benzene) and zinc in acetonitrile/water at 20 °C to furnish the synthesis of the desired adduct ethyl 4-bromo-2,2-difluoro-4-phenylbut-3-enoate (3a) in 83% yield (87% GC yield, Table 1, entry 1). Significantly lower yields were obtained when replacing dpbbz with other bidentate phosphines or 2,2'-bipyridine (entries 5–8). Other transition metals were inactive (entries 9–12). CoCl₂ and CoCl₂·4H₂O exhibited similar activity (entries 13, 14).

2.2 Substrate scope

The substrate scope of reactions between terminal and internal aryl acetylenes and 2a (Scheme 3). Many substitution patterns were tolerated (ortho, meta, para, electron-withdrawing, electron-donating substituents). The reaction displayed remarkable compatibility with functional groups including aldehydes, halides, nitrites, amides, hydroxyl, pyridines, thiophenes. All products were obtained with perfect regiocontrol and high E/Z diastereoselectivity (>50/1). However, alkyl-substituted terminal alkynes fared poorer (Scheme 4). Reactions of 2a with 1-heptyne...
and 4-phenyl-1-butyne, respectively, afforded mixtures of bromodifluoro-alkylation and hydrodifluoroalkylation products in low yields.

We then examined the cobalt-catalyzed halofluoroalkylation with different fluoroalkyl halides (Scheme 5). Iododifluoroacetate \( \text{CF}_2\text{CO}_2\text{Et} \), perfluoroalkyl iodides such as \( \text{C}_4\text{F}_9\text{I} \), \( \text{C}_8\text{F}_{13}\text{I} \), and the perfluoroalkyl bromide \( \text{C}_8\text{F}_{17}\text{Br} \) were competent electrophiles which afforded the desired adducts in good to excellent yields. The fluoroalkyl bromides gave generally better \( E/Z \) selectivities than the iodides. While this trend is in full agreement with the literature, it can now be harnessed at much milder conditions (room temp., 2 mol% catalyst, 3 h), \( \text{BrCF}_2\text{PO(OEt)}_2 \), \( \text{CF}_3\text{I} \), and \( \text{CF}_2\text{Br}_2 \) afforded slightly lower yields; the reaction with \( \text{CF}_3\text{I} \) exhibited low stereocontrol. Reactions of alkyl-substituted alkynes with fluoroalkyl iodides gave good yields and moderate \( E/Z \) selectivities (3ac-3af). The reaction conditions were also applied to reactions of cycloalkenes with halofluoroacetates (3ag-3ak). A method extension to reactions of simple bromoacetates with alkynes gave the desired adducts 3al-3an.

The synthetic utility of the stereoselective cobalt-catalyzed halofluoroalkylation protocol was demonstrated in a gram-scale setup which delivered pure ethyl \( \text{CF}_2\text{CO}_2\text{Et} \) (2a) in 86% isolated yield (1.32 g) after 3 h. Substitution of the Br substituent in 3a by Sono-gahira and Suzuki cross-coupling reactions, respectively, afforded the fluorinated alkenes in very good yields and with complete retention of stereochemistry (Scheme 6).

### 2.3 Mechanistic studies

Further attention was devoted to the study of the reaction mechanism. In addition to the initial optimization reactions (Table 1), key mechanistic experiments were conducted. The model reaction between \( 1 \) and \( 2a \) was completely inhibited in the presence of 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO). The TEMPO–\( \text{CF}_2\text{CO}_2\text{Et} \) adduct was observed by mass spectrometry (Scheme 7, eqn (1)). The TEMPO–\( \text{CF}_2\text{CO}_2\text{Et} \) adduct was not detected when treating \( 2a \) with equimolar Zn which supports the notion that the SET reduction of the alkyl halide is induced by the cobalt catalyst (Scheme 7, eqn (2)). Upon employment of cyclo-propylacetylene \( (4) \), the vinylcyclopropane product was formed in \( 11\% \) yield while ring-opening to the 7-bromohexa-3,4-dienoate \( (56\%) \) was the major pathway. This is in full agreement with the intermediacy of an internal vinyl radical formed by radical addition of \( \text{EtO}_2\text{CCF}_2^+ \) to the alkyne (Scheme 7, eqn (3)). Identical rates and yields were observed in reactions where \( 1a \) and \( 2a \) were successively added to the catalyst solution. The reverse order of addition \( (2a, \text{then } 1a) \) gave an identical result. Importantly, no product was formed when prior to the addition of \( 1a \) and \( 2a \) – the catalyst suspension (\( \text{CoBr}_2 \), dppbz, Zn) was filtered (to remove residual zinc) or when the supernatant solution was decanted into a new reaction vessel (eqn (4)). These experiments suggest that the initially formed Co(0) species alone cannot catalyze the reaction but requires the presence of zinc, at least for the first turnover of the catalytic mechanism. Zn is employed only in catalytic amounts (5 mol%), \( i.e. \) 2.5 equiv. per Co! The addition of sodium iodide and sodium bromide, respectively, shed light on the nature of the operating halogen transfer. \( 1a \) and \( 2a \) reacted with added NaI.
(1.5 equiv.) to give the iodo adduct 3u as major product (3a : 3u = 1 : 20, Scheme 7, eqn (6)). With NaBr added, the reaction between 1a and 2b gave 3a and 3u in a 1 : 6 ratio (Scheme 7, eqn (7)). Control experiments documented that no EtO₂CCF₂I was converted into EtO₂CCF₂Br using NaBr as additive; only minimal amounts of EtO₂CCF₂Br (<2%) were converted to EtO₂CCF₂I with NaI as additive under the same conditions. A similar outcome was observed when the standard reaction was performed with 50 mol% CoBr₂/dppbz (3a : 3u = 1 : 7, Scheme 7, eqn (8)). These experiments document that the halogen atom X in the product does not originate from the electrophilic R₂X via a direct radical chain transfer but is transferred from the cobalt catalyst. This is a fine but important distinction from previously reported ATRA reactions that all involved halogen transfer from R₂X to the vinyl radical. This has great implications for catalyst design and reaction development as the thermodynamics and kinetics of the halogen atom transfer step are...
no longer depending on the nature of the employed substrates but can be finely tuned through the stereoelectronic properties of the catalyst. We further believe that halogen atom transfer to a vinyl radical intermediate (rather than a vinyl cation) is operative: (i) the addition of water (as a nucleophile) resulted in no product bearing oxo functions; (ii) the presence of methyl acrylate as a radical acceptor led to the formation of the heptene-1,7-dioate via radical insertion of the acrylate (eqn (9)). A cationic intermediate would not add to this Michael acceptor. Catalyst formation and substrate additions were monitored by $^{31}$P NMR and $^1$H NMR spectroscopy (Fig. 1). The reduction of the (NMR silent) CoBr$_2$/dppbz mixture with Zn resulted in a Co(i) species with a $^{31}$P resonance at 75.2 ppm. The $^1$H NMR spectrum of this low-spin Co(i) complex gave signals 7–8 ppm. No changes were observed in $^{31}$P and $^1$H NMR spectra when phenyl acetylene (1a) was added to Co(i) which suggests the absence of significant alkyne-catalyst coordination. On the other hand, complete disappearance of the $^{31}$P (75.2 ppm) and $^1$H (7–8 ppm) signals was observed upon addition of EtO$_2$CCF$_2$Br (2a). This is a direct consequence of the reductive activation of 2a which leads to a paramagnetic Co(n,m) species and the carbon-centered radical. These results are consistent with the UV-vis spectra (Fig. 2). Reduction of Co(n) with Zn (and removal of residual Zn) resulted in an intense absorption of the Co(i) complex at 428 nm (green curve). Addition of 1a to this solution gave no change of the absorption in this region (blue curve), whereas the addition of 2a to Co(i) led to immediate colour change and the appearance of two weak bands at 412 and 451 nm (yellow curve).

The standard reaction between 1a and 2a went to completion within 90 min (with 2 mol% catalyst) and 12 min (4 mol% catalyst), respectively. Analysis of the initial rates (0.5–8 min, 1–4 mol% catalyst) displayed a near-2$^{\text{nd}}$ order behavior of the catalyst concentration. We postulate the following reaction mechanism (Scheme 8). Complexation of dppbz with CoBr$_2$ leads to the formation of [Co$^{\text{II}}$(dppbz)$_2$Br]$^+$ as observed by the soft and inert mass spectrometric technique for sensitive organometallics LIFDI-MS (liquid injection field desorption ionization mass spectrometry). Reduction of the Co(ii) complex with equimolar Zn generates the catalytically active [Co(dpdpbz)$_2$Br]$^+$. Exposure to oxygen/air gives [Co$^{\text{III}}$(dpdpbz)$_2$Br(O$_2$)] (LIFDI-MS). [Co$^{\text{I}}$(dpdpbz)$_2$Br]$^+$ effects the reductive single-electron activation of RFBr to give a [R$_4$Co$^{\text{II}}$(dpdpbz)$_2$Br]$^+$ species (LIFDI-MS) which is presumably a direct result of rapid combination of the intermediate Co(n) complex and free radical RF$^\cdot$. We have demonstrated that in the absence of residual zinc [R$_4$Co$^{\text{II}}$(dpdpbz)$_2$Br]$^+$ is not a catalyst (*vide supra*). Therefore, we propose – in contrast to the light-induced Co-R homolysis$^{10,11}$ – the reduction of [R$_4$Co$^{\text{II}}$(dpdpbz)$_2$Br]$^+$ by Zn in the first catalytic turnover to form the unstable complex [R$_4$Co$^{\text{II}}$(dpdpbz)$_2$Br]. Dissociation of the fluoroalkyl radical RF$^\cdot$ regenerates [Co(dpdpbz)$_2$Br]$^{12a,13}$ which can undergo another reductive activation of RFBr to give [R$_4$Co$^{\text{III}}$(dpdpbz)$_2$Br]$^+$. The catalytic amounts of Zn present in the reaction dictate that another mechanism operates from the 2$^{\text{nd}}$ turnover on, most likely an ATRA reaction involving halogen atom transfer from the cobalt complex [R$_4$Co$^{\text{III}}$(dpdpbz)$_2$Br]$^+$. Accordingly, the addition of RF$^\cdot$ to the alkyne results in the formation of a vinyl radical intermediate which undergoes rapid halogen atom abstraction from [Co$^{\text{III}}$(dpdpbz)$_2$Br]$^+$ to form the catalytically active Co(i) complex and RF$^\cdot$. The high $E$-selectivity of the radical addition is no longer depending on the nature of the employed substrates but can be finely tuned through the stereoelectronic properties of the catalyst. We further believe that halogen atom transfer to a vinyl radical intermediate (rather than a vinyl cation) is operative: (i) the addition of water (as a nucleophile) resulted in no product bearing oxo functions; (ii) the presence of methyl acrylate as a radical acceptor led to the formation of the heptene-1,7-dioate via radical insertion of the acrylate (eqn (9)). A cationic intermediate would not add to this Michael acceptor.

Catalyst formation and substrate additions were monitored by $^{31}$P NMR and $^1$H NMR spectroscopy (Fig. 1). The reduction of the (NMR silent) CoBr$_2$/dppbz mixture with Zn resulted in a Co(i) species with a $^{31}$P resonance at 75.2 ppm. The $^1$H NMR spectrum of this low-spin Co(i) complex gave signals 7–8 ppm. No changes were observed in $^{31}$P and $^1$H NMR spectra when phenyl acetylene (1a) was added to Co(i) which suggests the absence of significant alkyne-catalyst coordination. On the other hand, complete disappearance of the $^{31}$P (75.2 ppm) and $^1$H (7–8 ppm) signals was observed upon addition of EtO$_2$CCF$_2$Br (2a). This is a direct consequence of the reductive activation of 2a which leads to a paramagnetic Co(n,m) species and the carbon-centered radical. These results are consistent with the UV-vis spectra (Fig. 2). Reduction of Co(n) with Zn (and removal of residual Zn) resulted in an intense absorption of the Co(i) complex at 428 nm (green curve). Addition of 1a to this solution gave no change of the absorption in this region (blue curve), whereas the addition of 2a to Co(i) led to immediate colour change and the appearance of two weak bands at 412 and 451 nm (yellow curve).

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a direct consequence of the steric hindrance by the R₆ group in
the vinyl radical. The higher E/Z stereoselectivity of the bro-
m-oallylation over the iodoallylation reactions can be explained
by the shorter Co–Br bond (vs. Co–I) in the key catalytic Co(III)
species which effects an enhanced facial differentiation of the
vinyl radical. The facile operation of this halogen atom transfer
step with the intermediate vinyl radical is the key to the realiza-
tion of an overall process that is catalytic in both metals, Co
and Zn.

3 Conclusions

We have developed a convenient cobalt-catalyzed halo- and
fluoroalkylation that exhibits wide substrate scope including
terminal and internal alkynes, alkenes, and various fluoroalkyl
and alkyl bromides and iodides. The protocol enables the highly
regio-selective and stereoselective synthesis of densely func-
tionalized halogenated (E)-alkenes under very mild reaction
conditions (2 mol% catalyst, 5 mol% Zn, acetone/water, 20 °C, 3 h).
Contrary to literature reports, mechanistic studies document-
ed that the first time that the halogen atom transfer is
a cobalt-mediated process. The R₆Co[III]X complex is the key
catalytic intermediate which generates the free R₆X radical and
mediates the halogen atom transfer to the terminal vinyl
radical. This mechanistic deviation from substrate control to
catalyst control may provide the basis for the development of
related halogen atom transfer reactions through catalyst design.
Further, this ATRA reaction operates without a stoichiometric
reductant for the regeneration of the low-valent Co(i) catalyst.
The high functional group tolerance and mild reaction condi-
tions make this protocol highly attractive in the context of
complex molecule synthesis with potential utility for medicinal
chemistry endeavours.

Conflicts of interest

There are no conflicts to declare.

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Notes and references

1 (a) K. Müller, C. Faeh and F. Diederich, Science, 2007, 317, 1881; (b) W. K. Hagmann, J. Med. Chem., 2008, 51, 4359; (c) D. O’Hagan, Chem. Soc. Rev., 2008, 37, 308; (d) S. Purser, P. R. Moore, S. Swallow and V. Gouerneur, Chem. Soc. Rev., 2008, 37, 320; (e) V. Gouerneur and K. Müller, Fluorine in Pharmaceutical and Medicinal Chemistry: From
Biophysical Aspects to Clinical Applications, Imperial College
Press, London, 2012.
2 Trifluoromethylations: (a) T. Furuya, A. S. Kamlet and T. Ritter, Nature, 2011, 473, 470; (b) O. A. Tomashenko and
3 Difluoroalkylations: (a) K. Fujikawa, Y. Fujikawa, A. Kobayashi and H. Amii, Org. Lett., 2011, 13, 5560; (b) P. S. Fier and J. F. Hartwig, J. Am. Chem. Soc., 2012, 134, 5524; (c) Z. He, T. Luo, M. Hu, Y. Cao and J. Hu, Angew. Chem., Int. Ed., 2012, 51, 3944; (d) Q. Qi, Q. Shen and L. J. Angew. Chem., Soc., 2012, 134, 6548; (e) Z. FENG, C. Chen and X. ZHANG, Chem.-Eur. J., 2012, 18, 1320; (f) Z. FENG, Y.-L. XIAO and X. ZHANG, Angew. Chem., Front., 2014, 1, 11; (g) Y.-L. XIAO and W.-H. GUO, Z.-G. HE, Q. PAN and X. ZHANG, Angew. Chem., Int. Ed., 2015, 54, 9909; (m) S. GE, S. I. ARLOW, M. G. MORMINO and J. F. HARTWIG, J. Am. Chem. Soc., 2014, 136, 14401; (n) Z. FENG, Q.-Q. MIN, H.-Y. ZHAO, J.-W. GU and X. ZHANG, Angew. Chem., Int. Ed., 2015, 54, 1270; (o) C. SHAO, G. SHI, Y. ZHANG, S. PAN and X. GUAN, Org. Lett., 2015, 17, 2652; (p) L. AN, Y.-L. XIAO, Q.-Q. MIN and X. ZHANG, Angew. Chem., Int. Ed., 2015, 54, 9079; (q) Z. LI, A. GARCIA-DOMINGUEZ and C. NEVADO, J. Am. Chem. Soc., 2015, 137, 11610; (r) G. LI, T. WANG, F. FEI, Y.-M. SU, Y. LI, Q. LAN and X.-S. WANG, Angew. Chem., Int. Ed., 2016, 55, 3491; (s) Y.-L. XIAO, Q.-Q. MIN, C. XU, R.-W. XANG and X. ZHANG, Angew. Chem., Int. Ed., 2016, 55, 5837; (t) M. V. IVANOVA, A. BAYLE, T. BESSET, T. POISSON and X. PANNECOUCE, Angew. Chem., Int. Ed., 2015, 54, 13406; (u) X. WANG and A. STUDER, Org. Lett., 2017, 19, 2977. For reviews, see ref. 2e and (v) T. BESSET, T. POISSON and X. PANNECOUCE, Eur. J. Org. Chem., 2015, 2765; (w) M.-C. BELHOMME, T. BESSET, T. POISSON and X. PANNECOUCE, Chem.-Eur. J., 2015, 21, 12836.

4 (a) Y. Takeyama, Y. Ichinose, K. Oshima and K. Utimato, Tetrahedron Lett., 1989, 30, 3159; (b) Y. LI, H. LI and J. HU, Tetrahedron, 2009, 65, 478; (c) X. FANG, X. YANG, X. YANG, S. MAO, Y. WANG, G. CHEN and F. WU, Tetrahedron, 2007, 63, 10684; (d) W. HUANG, L. LV and Y. ZHANG, Chin. J. Chem., 1990, 4, 350; (e) G.-B. RONG and R. KEES, Tetrahedron Lett., 1990, 31, 5615; (f) K. TSUCHII, M. IMURA, N. KAMADA, T. HIRAO and A. OGAWA, J. Org. Chem., 1990, 65, 6658. For selected other methods, see: (g) T. ISHIHARA, M. KUROBOSHI and Y. OKADA, Chem. Lett., 1986, 1895; (h) S. MA and X. LU, Tetrahedron, 1990, 46, 357; (i) M. P. JENNINGS, E. A. CORK and P. V. RAMACHANDRAN, J. Org. Chem., 2000, 65, 8763; (j) D. MOTODA, H. KINOSHITA, H. SHINOKUBO and K. OISHIMA, Adv. Synth. Catal., 2002, 344, 261.

5 T. XU, C. CHEUNG and X. HU, Angew. Chem., Int. Ed., 2014, 53, 4910.

6 M.-C. BELHOMME, D. DRU, H.-Y. XIONG, D. CAHRAD, T. BESSET, T. POISSON and X. PANNECOUCE, Synthesis, 2014, 46, 1859.

7 G. LI, Y.-X. CAO, C.-G. LUO, Y.-M. SU, Y. LI, Q. LAN and X.-S. WANG, Org. Lett., 2016, 18, 4806.

8 (a) B. D. Sherry and A. FÜRSTNER, Acc. Chem. Res., 2008, 41, 1500; (b) E. NAKAMURA and N. YOSHIKAI, J. Org. Chem., 2010, 75, 606; (c) R. JANA, T. P. PATHAK and M. S. SIGMAN, Chem. Rev., 2011, 111, 1417; (d) R. B. BEDFORD and P. B. BRENNER, Top. Organomet. Chem., 2015, 50, 19; (e) I. BAUER and H.-J. KNÖLKER, Chem. Rev., 2015, 115, 3170; (f) A. FÜRSTNER, ACS Cent. Sci., 2016, 2, 778; (g) T. L. MAKO and J. A. BYERS, Inorg. Chem. Front., 2016, 3, 766; (h) A. GUÉRINET and J. COSSY, Top. Curr. Chem., 2016, 374, 49.

9 For selected examples, see: (a) L. NICOLAS, P. ANGIBAUD, I. STANFIELD, P. BONNET, L. MEERPOEL, S. REYMOND and J. COSSY, Angew. Chem., Int. Ed., 2012, 51, 11101; (b) M. I. XIAO, F. LIU, M. WANG, L. WU, B. ZHANG, S. LIU, J. ZHONG, Q. BIAN and P. J. WALSH, J. Am. Chem. Soc., 2014, 136, 17662; (c) J. M. HAMMANN, D. HAS and P. KNOCHEL, Angew. Chem., Int. Ed., 2015, 54, 4478; (d) J. M. HAMMANN, D. HASS, C.-P. TULLMANN, K. KARAGIOSOFF and P. KNOCHEL, Org. Lett., 2016, 18, 4778; (e) M. S. HOFMAYER, J. M. HAMMANN, D. HIANA and P. KNOCHEL, Org. Lett., 2016, 18, 6456, and references therein. For selected reviews, see: (f) H. YORIMITSU and K. OISHIMA, Pure Appl. Chem., 2006, 78, 441; (g) C. GOSMINI, J.-M. BÉGOUIN and A. MONCOMBLE, Chem. Commun., 2008, 3221; (h) G. CAHIEZ and A. MOYEUR, Chem. Rev., 2010, 110, 1435.

10 (a) J. ZHOU and G. C. FU, J. Am. Chem. Soc., 2003, 125, 14726; (b) G. D. JONES, J. L. MARTIN, C. McFARLAND, O. R. ALLEN, R. E. HALL, A. D. HALEY, R. J. BRANSON, P. J. DESROCHERS, P. PULAY and D. A. VICIO, J. Am. Chem. Soc., 2006, 128, 1317; (c) J. TERAO and N. KAMBE, Acc. Chem. Res., 2008, 41, 1545; (d) V. B. PHAPALE and D. J. CÁRDENAS, Chem. Soc. Rev., 2009, 38, 1598; (e) A. Rudolph and M. Lautens, Angew. Chem., Int. Ed., 2009, 48, 2656; (f) X. HU, Chem. Sci., 2011, 2, 1867; (g) S. Z. TASKER, E. A. STANLEY and T. F. JAMISON, Nature, 2014, 509, 299; (h) T. IWASAKI and N. KAMBE, Top. Curr. Chem., 2016, 374, 66.

11 S. TORII, T. INOKUCHI and T. YUKAWA, J. Org. Chem., 1985, 50, 5875; (c) M.-H. MU and Y.-L. QIU, J. Fluorine Chem., 1991, 55, 113; (b) C.-M. MU and Y.-L. QIU, Tetrahedron Lett., 1991, 32, 4001; (c) B. P. BRANCHAUD and W. D. DETLEFSEN, Tetrahedron Lett., 1991, 32, 6273; (c) M.-H. MU and Y.-L. QIU, J. Org. Chem., 1992, 57, 3339; (d) Y. IKEDA, T. NAKAMURA, H. YORIMITSU and K. OISHIMA, J. Am. Chem. Soc., 2002, 124, 6514.
W. Affo, H. Ohmiya, T. Fujioka, Y. Ikeda, T. Nakamura, H. Yorimitsu, K. Oshima, Y. Imamura, T. Mizuta and K. Miyoshi, *J. Am. Chem. Soc.*, 2006, **128**, 8068; (f) P. Shukla, Y.-C. Hsu and C.-H. Cheng, *J. Org. Chem.*, 2006, **71**, 655; (g) M. E. Weiss, L. M. Kreis, A. Lauber and E. M. Carreira, *Angew. Chem., Int. Ed.*, 2011, **50**, 11125; (h) S. Lu, T. Jin, M. Bao and Y. Yamamoto, *J. Am. Chem. Soc.*, 2011, **133**, 12842.

12 (a) A. A. Isse, A. Gennaro and E. Vianello, *J. Electroanal. Chem.*, 1998, **444**, 241; (b) A. J. Moad, L. J. Klein, D. G. Peters, J. A. Karty and J. P. Reilly, *J. Electroanal. Chem.*, 2002, **531**, 163; (c) J. D. Persinger, J. L. Hayes, L. J. Klein, D. G. Peters, J. A. Karty and J. P. Reilly, *J. Electroanal. Chem.*, 2004, **568**, 157; (d) P. Vanalabhpatana, D. G. Peters and J. A. Karty, *J. Electroanal. Chem.*, 2005, **580**, 300; (e) P. C. Gach, J. A. Karty and D. G. Peters, *J. Electroanal. Chem.*, 2008, **612**, 22; (f) L. Pan, H. Shimakoshi, T. Masuko and Y. Hisaeda, *Dalton Trans.*, 2009, **38**, 9898; (g) T. Ueda, N. Inazuma, D. Komatsu, H. Yasuzawa, A. Onda, S.-X. Guo and A. M. Bond, *Dalton Trans.*, 2013, **42**, 11146; (h) M. Giedyk, K. Goliszewska and D. Gryko, *Chem. Soc. Rev.*, 2015, **44**, 3391; (i) M. Giedyk, H. Shimakoshi, K. Goliszewska, D. Gryko and Y. Hisaeda, *Dalton Trans.*, 2016, **45**, 8340; (j) H. Shimakoshi, Z. Luo, T. Inaba and Y. Hisaeda, *Dalton Trans.*, 2016, **45**, 10173.

13 (a) D. N. Ramakrishna, R. Symons and M. Symons, *J. Chem. Soc., Faraday Trans. 1*, 1984, **80**, 423; (b) B. D. Gupta and S. Roy, *Inorg. Chim. Acta*, 1988, **146**, 209.

14 (a) R. Breslow and P. L. Khanna, *J. Am. Chem. Soc.*, 1976, **98**, 1297; (b) H. Eckert, D. Lenoir and I. Ugi, *J. Organomet. Chem.*, 1997, **141**, C23; (c) J. Schaffler and J. Retey, *Angew. Chem., Int. Ed. Engl.*, 1978, **17**, 845; (d) A. I. Scott, J. B. Hansen and S. K. Chung, *J. Chem. Soc., Chem. Commun.*, 1980, 388; (e) B. D. Gupta and S. Roy, *Inorg. Chim. Acta*, 1988, **146**, 209.

15 D. B. Bagal, G. Kachkovskiy, M. Knorn, T. Rawner, B. M. Bhanage and O. Reiser, *Angew. Chem., Int. Ed.*, 2015, **54**, 6999.

16 (a) Y. Yauchi, M. Ide, R. Shiogai, T. Chikugo and T. Iwasawa, *Eur. J. Org. Chem.*, 2015, **938**; (b) K. C. Sproul and W. A. Chalifoux, *Org. Lett.*, 2015, **17**, 3334; (c) X. Wang and A. Studer, *J. Am. Chem. Soc.*, 2016, **138**, 2977; (d) X. Wang and A. Studer, *Org. Lett.*, 2017, **19**, 2977.