This is an *Accepted Manuscript*, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. We will replace this *Accepted Manuscript* with the edited and formatted *Advance Article* as soon as it is available.

You can find more information about *Accepted Manuscripts* in the **Information for Authors**.

Journal Name

REVIEW

Radical Reactions of Borohydrides

Takuji Kawamoto[a] and Ilhyong Ryu*[a]

Borohydrides are an important class of reagents in both organic and inorganic chemistry. Though popular as hydride-transfer reagents for reduction, since earlier work from the 1970s, borohydride reagents have also been known to serve as hydrogen-transfer reagents. In pursuit of greener tin hydride substitutes, recent progress has been made to mediate radical C-C bond forming reactions, including Giese reactions, radical carbonylation and addition to HCHO reactions, with borohydride reagents. This review article focuses on state-of-the-art of borohydride based radical reactions, also covering earlier work, kinetics and some DFT calculations with respect to the hydrogen transfer mechanism.

Introduction

The tremendous development of radical chemistry during the past three decades has led to highly efficient methods for the construction of functionalized organic frameworks.[1] This development could not have been attained without the use of tin hydride reagents that possess impressively broad applicability.[2] Organo halides are among the most useful precursors to access carbon-centred radical species. Tin radicals are capable of abstracting a halogen atom from a wide range of organic halides[3] to generate carbon-centred radicals (substrate radicals), and tin hydride reagents are efficient at delivering hydrogen to the radical species (product radicals) to give the product with concomitant liberation of tin radicals,[4] thus creating a radical chain system.

Alternative reagents available for reductive radical chain reactions [5] include tris(trimethylsilyl)silane (TTMSS), [6] germanium hydrides,[5] thiols [7] and substituted 1,4-cyclohexadienes,[8] just to name a few. Unlike the particular case of TTMSS, hydrogen transfer from simple silanes, such as triethylsilane, to common alkyl radicals is sluggish due to unfavourable polar factors; a nucleophilic alkyl radical is required to abstract an electron-rich hydrogen atom from the hydrosilanes. The low reactivity can be ameliorated by the presence of a catalytic amount of thiol which acts as a polarity-reversal catalyst.[9] Recently, O-H bonds of catecholborane-alcohol (or catechol),[10] triethylborane-water (or alcohol)[11] and titanium-water[12] complexes are recognized as useful hydrogen donors, since the O-H bonds are considerably weakened by Lewis acid-base complexation.

Borohydrides are most generally recognized as reagents for hydride (H⁻) reduction in organic synthesis (Scheme 1). In pursuit of a system which minimized the use of toxic tin hydride in radical reactions of alkyl halides, Corey employed sodium borohydride together with a catalytic amount of tin hydride,[13] while Stork employed sodium cyanoborohydride as a milder reagent instead of sodium borohydride.[14] In these two systems, catalytic in tin, the "lead actor" is tin hydride, which functions as the hydrogen source (H•), while the borohydride reagent is the "supporting actor", which acts to provide a hydride source (H⁻) to convert tin halide byproducts to tin hydrides.
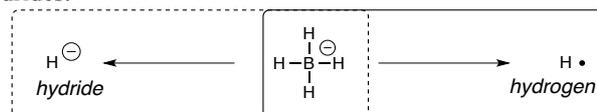
SCHEME 1. TWO FUNCTIONS OF BOROHYDRIDE REAGENTS

However, as we see in the early work of Barltrop (vide infra) published in 1973, sodium borohydride was shown to act as an hydrogen source for the photoreduction of halobenzenes.[15] The progress of radical chemistry based on borohydrides and other tin-free radical mediators has been slow, but with the endeavours of many chemists including us, the chemistry has advanced steadily towards establishing reliable *radical reaction methodology with borohydride reagents*.

It should be noted that work based on the combination of metal catalysts and borohydride reagents have been employed for reductive radical reactions. [16] For example, the $Cp_2TiCl_2/NaBH_4$ system was applied to reductive radical cyclization of aryl halides,[17] and the combination of $Ni(OAc)_2$ with BER (borohydride exchange resin) was applied to the Giese type addition reaction of alkyl halides.[18] More recently $InCl_3$ [19] and $FeCl_2(dppe)$ [20] were used for reductive radical cyclizations of organo halides in the presence of $NaBH_4$. Due to the breadth of metal catalysts that have been used in this chemistry, we have excluded covering these achievements as they would be best reviewed elsewhere.

Accordingly the purpose of this review is to concentrate on giving an overview of the relevance of borohydrides as efficient and effective sources for hydrogen atom transfer by radical chain processes due to matching of the polar factor.[9] Besides borohydrides, concurrent noteworthy progress has taken place with other boron compounds bearing B-H bonds. Catechol borane mediated radical chemistry creates a powerful tin-free radical reactions system.[21] While the potential of NHC-boranes (*N*-heterocyclic carbene-boranes) as radical mediators have been elucidated, and has recently been reviewed by the pioneers of the field.[22]

Kinetic Background of Borohydride Radical Chemistry

Roberts and Giles reported that *tert*-butoxy radical readily abstracts hydrogen from borohydrides and cyanoborohydride to give the corresponding borane radical anions.[23] These species can be detected in solution by ESR spectroscopy (**SCHEME 2**).[24]
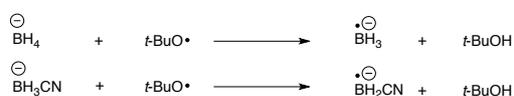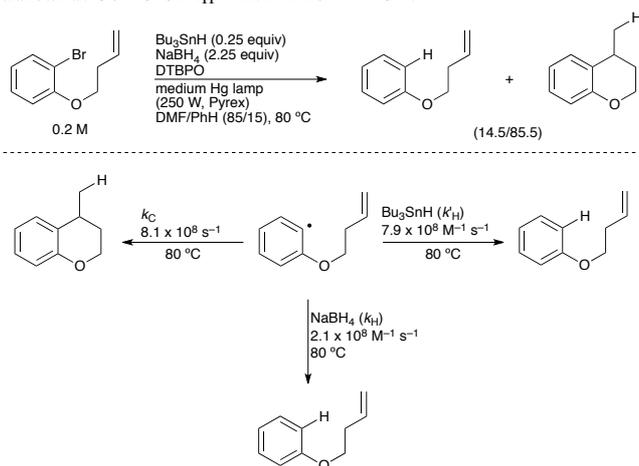
SCHEME 2

The borane radical anion ($BH_3^{\bullet-}$) abstracts halogen atom rapidly from *n*-propyl halides (X = Cl, Br, I) under photoirradiation conditions. In contrast, cyanoborane radical anion ($BH_2CN^{\bullet-}$) fails to react with alkyl chlorides, suggesting that it possess an inferior ability for halogen abstraction. In 2001, Ingold and co-workers determined the absolute rate constants for halogen abstraction by borane radical anion from alkyl halides using laser flash photolysis (LFP).[25] LFP (308 nm) of di-*tert*-butyl peroxide (DTBP) (6%)-benzene solutions in the presence of Bu_4NBH_4 generated the borane radical anion. The decay of this radical was monitored directly in the presence of alkyl halides at different concentrations and the rate constants are summarized in **TABLE 1**. For example, the rate constant for bromine atom abstraction by borane radical anion from cyclohexyl bromide was determined to be 2.0×10^8 M^{-1}s^{-1} at ambient temperature. These measured values are sufficiently rapid that in theory, the radicals generated from alkyl halides could be subsequently employed in synthetic applications.

TABLE 1

| halide	k [M^{-1} s^{-1}]
CCl$_4$	$2.0 \pm 0.3 \times 10^9$
CHCl$_3$	$6.2 \pm 0.3 \times 10^8$
PhCH$_2$Br	$5.3 \pm 0.4 \times 10^8$
t-BuBr	$3.2 \pm 0.2 \times 10^8$
CyBr	$2.0 \pm 0.3 \times 10^8$
n-PrBr	$1.7 \pm 0.2 \times 10^8$
CH$_2$Cl$_2$	$1.1 \pm 0.2 \times 10^8$
PhCH$_2$Cl	$3.0 \pm 0.5 \times 10^7$

Beckwith and co-workers reported the kinetic data for the reaction of aryl radical with borohydride, obtained by applying free-radical clock methodology (**SCHEME 3**).[26] 2-Bromohomoallyloxybenzene was treated with a mixture of Bu_3SnH and $NaBH_4$ in DMF/PhH (85/15) to afford homoallyloxybenzene and 4-methylchroman in a ratio of 14.5/85.5. Using known rate constants for tin hydride mediated aryl radical reduction at 80 ºC of $k_H = 7.9 \times 10^8$ M^{-1}s^{-1} and 6-*exo* cyclization at 80 ºC of $k_c = 8.1 \times 10^8$ s^{-1},[27] gives a calculated rate constant for the reaction of $NaBH_4$ with aryl radical at 80 °C of $k_H = 2.1 \times 10^8$ M^{-1}s^{-1}.

SCHEME 3

We conducted the reaction of pyridine-2-thione-oxycarbonyl (PTOC) ester with Bu_4NBH_3CN to obtain the rate constant for the reaction of a primary alkyl radical with Bu_4NBH_3CN (k_H) (**SCHEME 4**).[28] The reaction gave nonane (6.6%) and 2-nonylthiopyridine (72.9%). When the experiment was carried out without cyanoborohydride the reduced product was obtained in 3.8% yield. Using the rate constant for reaction of nonyl radical with PTOC ester at 25 ºC of $k_T = 1.4 \times 10^6$ M^{-1}s^{-1},[29] one calculates a rate constant for the reaction of Bu_4NBH_3CN with primary alkyl radical at 25 °C of $k_H < 1 \times 10^4$ M^{-1}s^{-1}. This is lower than the corresponding rate constants of tributyltin hydride,[4] tris(trimethylsilyl)silicon hydride,[30]

tributylgermanium hydride,[31] and an NHC−borane such as diMeImd-BH$_3$ (1,3-dimethylimidazol-2-ylidene−borane).[32]
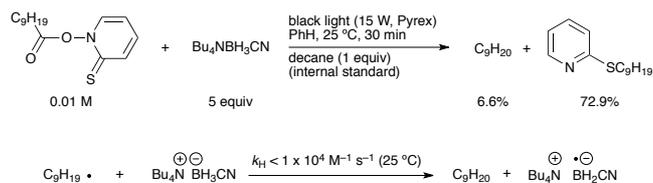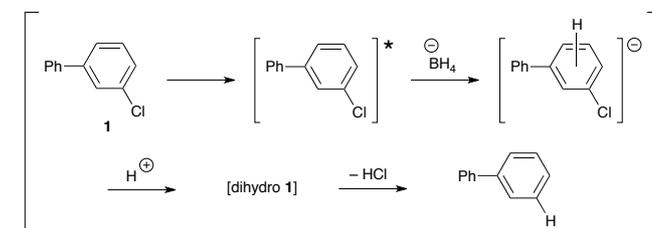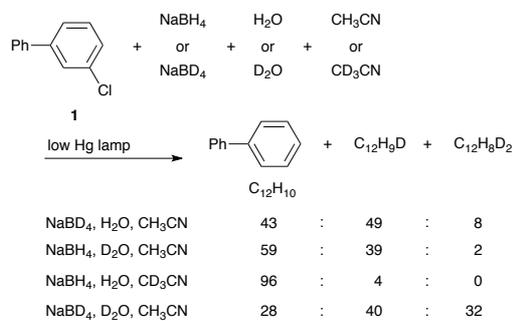

SCHEME 4

Borohydride-Mediated Radical Reduction and Cyclization: Earlier Work

In 1973 Barltrop and Bradbury reported that photoreduction of halobenzenes by sodium borohydride in aqueous acetonitrile solutions (**SCHEME 5**).[15] They proposed a radical chain mechanism for the photoreduction. Phenyl radical, arising from photoirradiation of halobenzene, abstracts hydrogen from borohydride to give benzene and a borane radical anion; this subsequently abstracts a halogen atom from halobenzene to regenerate the phenyl radical. However, non-radical mechanism could not be excluded in the case of chlorobenzene.
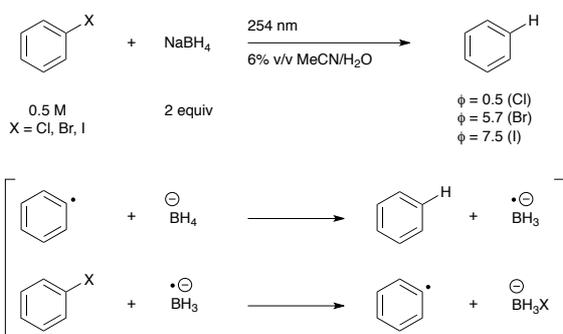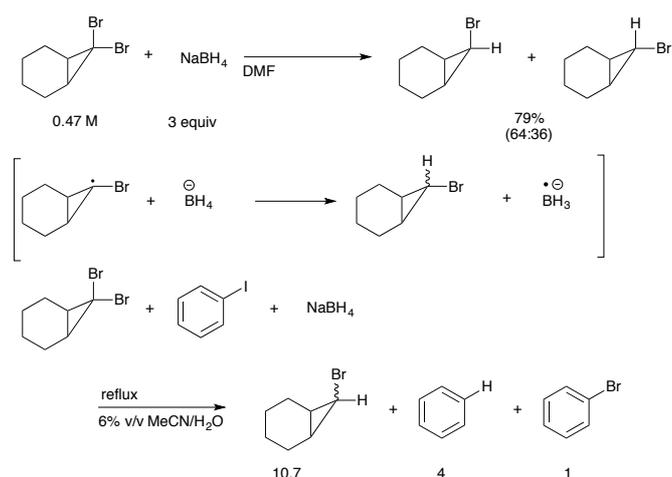

SCHEME 5

In a related study, Ohashi and co-workers reported photoreduction of chloroarenes by sodium borohydride.[33,34] Incorporation of deuterium into biphenyl was observed in the photoreduction of *m*-chlorobiphenyl (**1**) in the presence of deuterated borohydride and solvents (**SCHEME 6**). Since dideuterated product was formed, they proposed that photoreduction of chlorobiphenyl proceeded via consecutive hydride-proton-transfer followed by elimination of hydrogen chloride.


	$C_{12}H_{10}$	$C_{12}H_9D$	$C_{12}H_8D_2$
NaBD$_4$, H$_2$O, CH$_3$CN	43	49	8
NaBH$_4$, D$_2$O, CH$_3$CN	59	39	2
NaBH$_4$, H$_2$O, CD$_3$CN	96	4	0
NaBD$_4$, D$_2$O, CH$_3$CN	28	40	32

SCHEME 6

In 1974, Groves and Ma reported the reduction of 7,7-dibromonorcarane by sodium borohydride under heated conditions (**SCHEME 7**).[35] The reaction gave the singly reduced product, bromonorcarane, as a diastereomeric mixture. They proposed a mechanism in which the bromocyclopropyl radical is formed. Thus, the radical abstracts hydrogen from NaBH$_4$ to give the reduced product and borane radical anion. The borane radical anion abstracts bromine from the dibromocyclopropane to sustain the radical chain. The same reaction in the presence of iodobenzene gave benzene and bromobenzene as byproducts, from which they proposed a common intermediate, phenyl radical. This would arise from iodobenzene via iodine abstraction by the borane radical anion, which then abstracts hydrogen from borohydride or bromine atom from dibromocyclopropane to form either of the byproducts observed in the reaction. No reaction was observed in the absence of molecular oxygen, suggesting the involvement of oxygen in the radical initiation process.
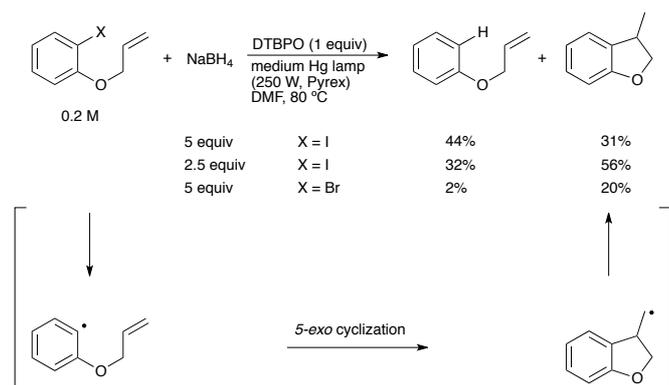

SCHEME 7

In 1986, Beckwith and Abeywickrema reported the reduction of aryl bromides and iodides with sodium borohydride, in which they used DTBP (di(*t*-butyl) peroxide) as a radical initiator under photoirradiation conditions (**TABLE 2**).[26]

TABLE 2
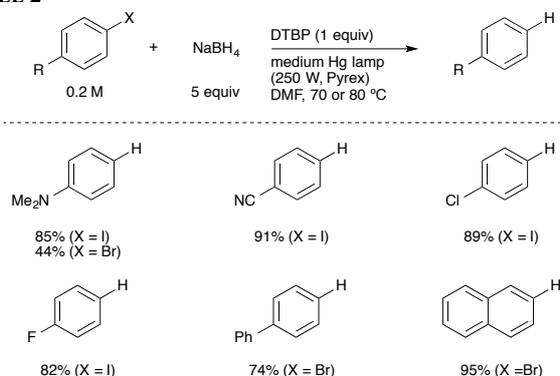
They also demonstrated reductive ring closure reactions of 2-haloallyloxybenzenes, which gave 3-methyl-2,3-dihydrobenzofuran (**SCHEME 8**). The reason for the pronounced direct reduction of the aryl iodides is yet to be elucidated. They determined the rate constant for hydrogenation of aryl radical by sodium borohydride to be 2.1 x 10^8 M^{-1}s^{-1} at 80 °C (vide ante).
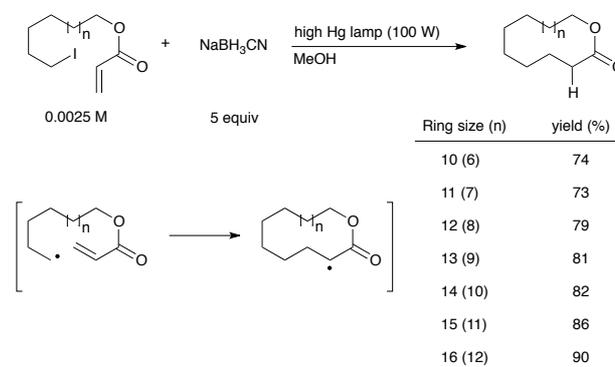

SCHEME 8

In 1990 Fukuzumi and Ishikawa reported that acridine derivatives (l0-methyl-9,10-dihydroacridine, AcrH$_2$) catalyzed dechlorination of *p*-chlorobiphenyl with NaBH$_4$ under photoirradiation conditions (**SCHEME 9**).[36] They proposed that biphenyl radical, generating from the single electron transfer by ^{1}AcrH$_2$*, abstracts hydrogen from AcrH$_2$$^{•+}$ to give dechlorinated product (biphenyl) and 10-mcthylacridinium ion (AcrH$^+$). The resulting AcrH$^+$ was reduced by NaBH$_4$ to regenerate AcrH$_2$. Boisvert and Giasson reported reductive radical cyclization reaction of 2-haloallyloxybenzene by this system.[37]
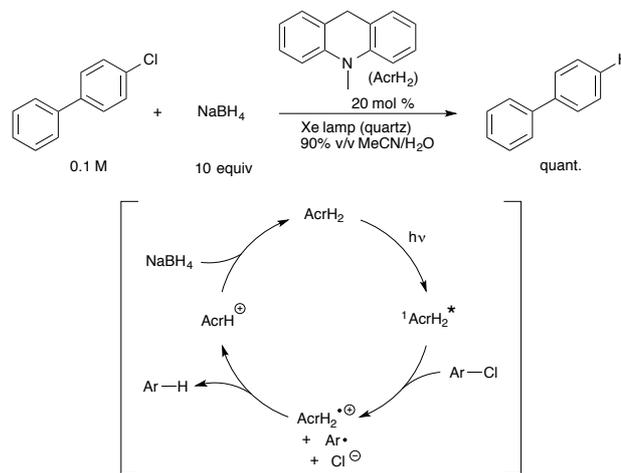
SCHEME 9

In 1994, Kurata and co-workers reported that macrocyclization of iodoalkyl acrylates proceeds in the presence of NaBH$_4$, KBH$_4$ or NaBH$_3$CN under photoirradiation conditions.[38] The combination of NaBH$_3$CN and MeOH was found to be the best, which gave good yields of 10 to 16 membered ring lactones (**TABLE 3**). The reaction also took place under thermal conditions using AIBN (2,2'-azobis(2-methylpropionitrile), albeit in lower yield. A radical chain mechanism involving cyanoborane radical anion was suggested for this reaction.

TABLE 3

Ring size (n)	yield (%)
10 (6)	74
11 (7)	73
12 (8)	79
13 (9)	81
14 (10)	82
15 (11)	86
16 (12)	90

In 2002, Praly and co-workers reported that the photoreduction of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide by NaBH$_3$CN gave 1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-arabino-hexopyranose in high yield (**SCHEME 10**)[39] via a Surzur-Tanner rearrangement.[40] The addition of 10 mol% thiophenol gave the desired debromination product and avoided any byproducts arising from the rearrangement. Thiophenol is likely to act as a polarity-reversal catalyst[9] to facilitate a rapid H-transfer process to the initially formed α-alkoxy radical.
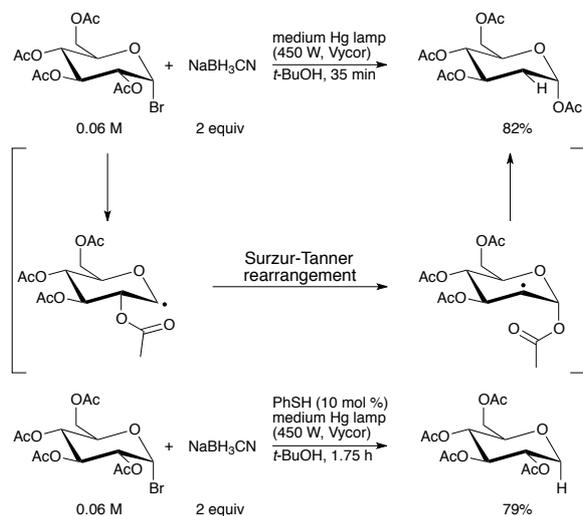
SCHEME 10

In 2005, Liu, Yu and co-workers accomplished a simple photochemical approach to reductive radical cyclization using NaBH$_4$ or NaBH$_3$CN (**TABLE 4**).[41] In the case of substrates bearing an electron-deficient C-C double bond, they preferred NaBH$_3$CN instead of NaBH$_4$ to prevent the direct reduction of the double bond.

TABLE 4
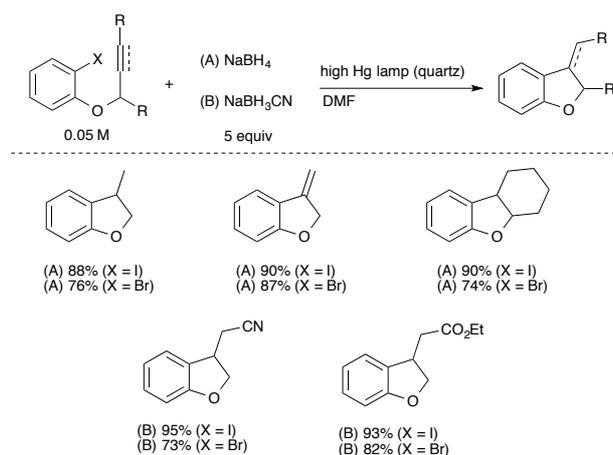
Borohydride-Mediated Radical Addition Reactions

Stimulated by Kurata's macrocyclization using NaBH$_3$CN, we studied Giese type reductive radical addition reactions of alkyl iodides with electron deficient olefins.[42,43] We found that NaBH$_3$CN is a good reagent because it has a relatively slow reducing ability of iodoalkanes, compared with NaBH$_4$.[44] Primary, secondary and tertiary alkyl iodides all worked well in the Giese type addition reaction with ethyl a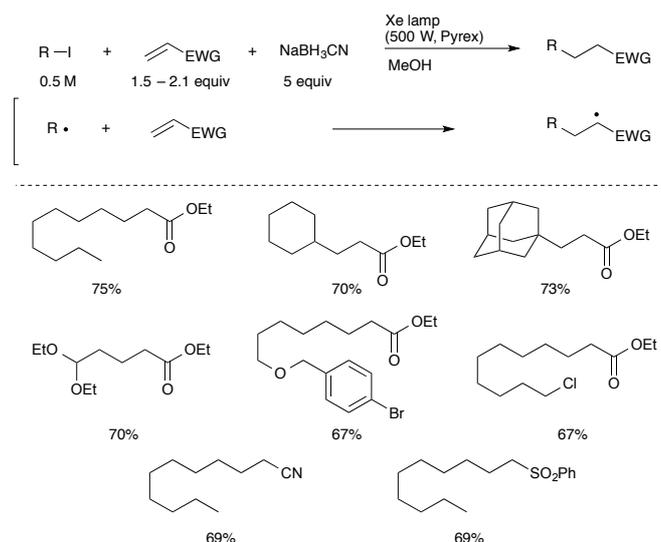crylate, acrylonitrile, and vinyl sulfone (**TABLE 5**). Alkyl bromides and chlorides did not react under the employed conditions but this in turn ensured chemoselective transformations of the substrates bearing both iodine and bromine or chlorine atoms.

TABLE 5

When the NaBH$_3$CN methodology was applied to radical addition reactions to α,β-unsaturated ketones, the undesirable reduction of enones took place to hamper the desired radical addition pathway. We found that the use of an even milder reagent, tetrabutylammonium cyanoborohydride, Bu$_4$NBH$_3$CN, circumvented this problem (**TABLE 6**).

TABLE 6
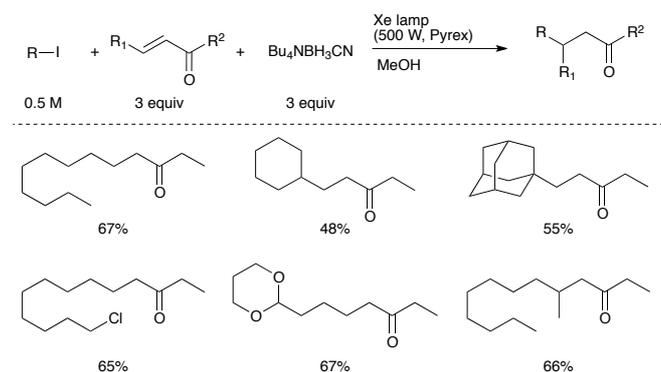
To gain insight into the reaction mechanism for the hydrogen transfer step, we carried out theoretical calculations of cyanoborohydride anion with both α-ester radical and ethyl radical for the comparison. All calculations were performed at the BHandHLYP/6-311+G** level.[44c] After complexation with cyanoborohydride anion, hydrogen abstraction of the α-ester radical (CH$_3$OCOCH$_2$•) from cyanoborohydride is quite smooth, with a calculated activation energy of 29.1 kJ mol^{-1} (Figure 1). On the other hand, the activation energy for hydrogen abstraction of ethyl radical from cyanoborohydride was estimated to be double of this value, at 60.7 kJ mol^{-1} (Figure 2). This is rationalized by the polar effect of the nucleophilic cyanoborohydride anion that would react with the electrophilic α-ester radical more readily. It is known that the resulting cyanoborane radical anion exhibits nucleophilic character.[24]

Figure 1

Figure 2

Employing Bu_4NBH_3CN under aerobic, photoirradiation conditions, it was possible to develop cyanoborohydride promoted radical arylation reactions of benzene with aryl iodides (**TABLE 7**).[45] High functional group tolerance was observed for this arylation reaction.[46]

TABLE 7

Borohydride-Mediated Radical Carbonylation Reactions

Radical carbonylation reactions using carbon monoxide (CO) provide useful methods for the synthesis of a variety of carbonyl compounds.[47] Borohydride-mediated carbonylative three-component coupling reaction of alkyl iodides, CO, and electron-deficient olefins worked well to give unsymmetrical ketones (**TABLE 8**).[44a,c]

TABLE 8

In the absence of electron-deficient olefins, the hydroxymethylation reaction of alkyl iodides with CO took place, for which Bu_4NBH_4 gave better results than Bu_4NBH_3CN. Unlike in the case of tin hydride mediated hydroxymethylation reaction, which required pressurized conditions,[48] this reaction proceeds well even under atmospheric pressure of CO (**TABLE 9**).[49] This is due to a lower ability of borohydride anions for H-donation which prevents the parent alkyl radicals from premature quenching.

TABLE 9

One possible rationale for the hydroxymethylation is that formation of the aldehyde intermediate occurs via hydrogen abstraction of borohydride by the corresponding acyl radical. This intermediate subsequently undergoes hydride reduction to give the hydroxymethylated product. Interestingly, DFT calculations proposed a different mechanism (Figure 3).[50] In this case, the acyl radical undergoes hydride transfer from borohydride to form ketyl radical anion. Single electron transfer from the ketyl radical anion to alkyl iodide affords a borane aldehyde adduct along with the alkyl radical and iodide anion, creating the radical chain. The resulting BH_3-complexed aldehyde undergoes hydroboration to give the hydroxymethylation product. The mechanism based on hydride transfer fits well with our previous observations that acyl radicals exhibit electrophilic nature towards nitrogen of imines[51] and amines[52] and oxygen of aldehydes.[53,54]
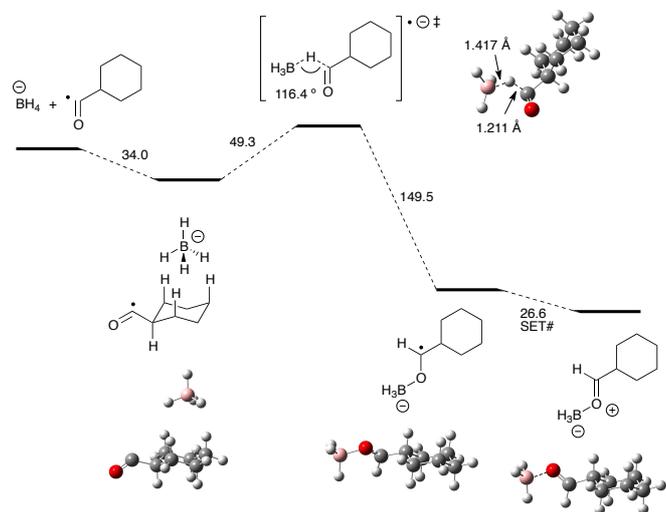

SET to iodocyclohexane.
Energies (in kJ/mol) were calculated on theB3LYP/6-311+G** (for C,H,B,O) and LanL2DZdp (for I).

Figure 3

Limitation of the Bu_4NBH_4-based hydroxymethylation approach, in comparison with tin hydride based approaches,[48] lies in the poorer results of *primary* alkyl iodides and aryl iodides, for which direct reduction competed considerably. In collaboration with the Curran group, we examined the hydroxymethylation reaction of *primary* alkyl and aryl iodides with CO using NHC-boranes[22] such as 1,3-dimethylimidazol-2-ylideneborane, and these reactions proved to work well.[55] Some of the results of hydroxymethylation of alkyl iodides are shown in **TABLE 10**, all were obtained under atmospheric pressure of CO. On the other hand, hydroxymethylation of aryl iodides requires high CO pressure conditions to compete with premature quenching of aryl radicals by NHC-borane. It should be noted that the reaction took place chemoselectively at the aryl-iodine bonds but not at either the aryl-bromine and aryl-chlorine bonds. This allows us to prepare benzylic alcohols bearing a bromine or chlorine moiety on the aromatic rings, which can be further functionalized.

TABLE 10
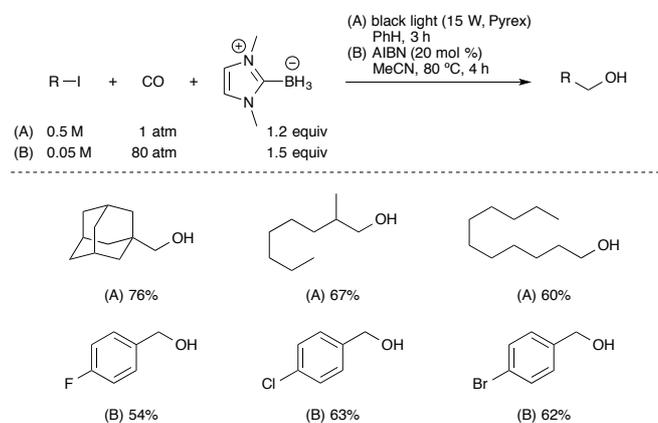
Borohydride-Mediated Radical Reactions of HCHO

Radical addition reactions to formaldehyde (HCHO) was originally investigated in 1960s and 1970s,[56,57] however, the introduction of tin hydride-based radical reactions proved difficult, since hydrogen abstraction by alkyl radicals from tin hydride is faster than the formaldehyde trapping. We developed a hydroxymethylation method of alkyl iodides by radical addition onto HCHO in the presence of Bu_4NBH_3CN as the radical mediator (**TABLE 11**).[58] In this reaction alkoxy radicals undergo hydrogen abstraction from cyanoborohydride anions to give the product and cyanoborane radical anion ($BH_2CN^{\bullet-}$). The anion abstracts an iodine atom from alkyl iodide to generate the alkyl radical and sustain the radical chain. When homoallyl bromide was treated with paraformaldehyde $(HCHO)_n$, the resulting alkoxy radical underwent *5-exo*-cyclization to form the corresponding THF-derivative (**SCHEME 11**).

TABLE 11

(A) 85% (X = I)   (B) 77% (X = I)   (C) 57% (X = Br)   (C) 41% (X = Br)

16%
(dr = 93/7)   7%   14%
(dr = 85/15)
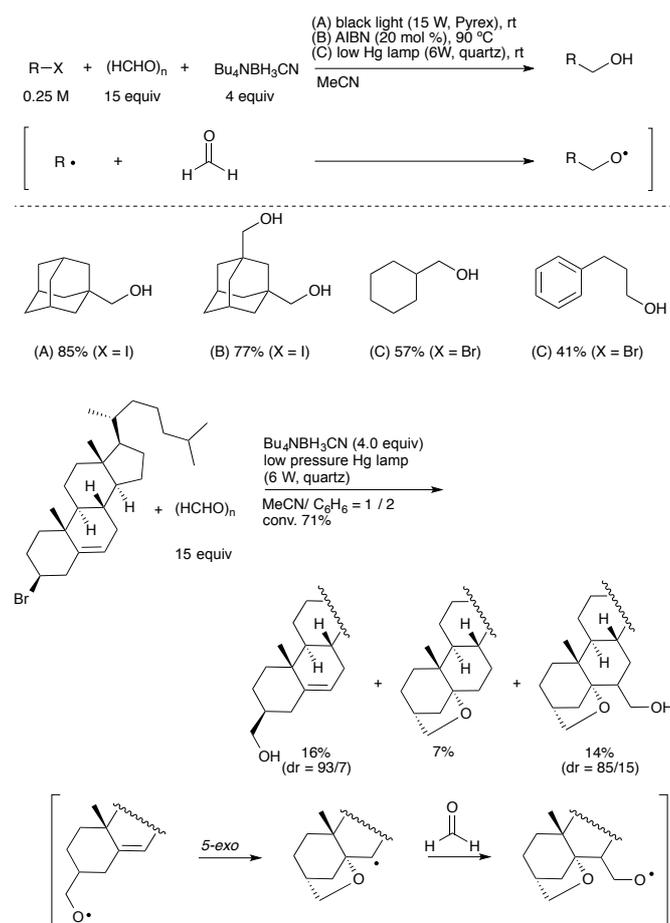
SCHEME 11

Conclusions

In contrast to the long recognition of borohydride reagents as hydride donors, the utility of borohydride reagents as hydrogen donors in radical reactions has been somewhat unclear until recently. Initial work mainly dealt with photoreduction of aromatic halides with NaBH$_4$, in which the radical chain mechanism has been proposed for the reduction of aryl bromides and iodides, whereas non-radical mechanism has been proposed for the reduction of aryl chlorides. Recent work has revealed that radical reactions of alkyl iodides (in some cases bromides) are possible by the use of milder borohydride reagents, such as NaBH$_3$CN and Bu$_4$NBH$_3$CN, whose hydride character is moderately suppressed to ensure efficient radical reactions occur prior to reduction. Rate constants of halogen abstraction by borane radical anions are nearly comparable with tributyltin radicals, whereas hydrogen transfer from borohydrides to carbon-centered radicals differs depending on their structures. In general the hydrogen abstraction of alkyl radicals from borohydrides is sluggish, but the hydrogen abstraction of aryl and electrophilic radicals occurs smoothly, which may be rationalized by the polarity matching with electron-rich borohydride anions. In designing radical C-C bond forming reactions employing borohydride reagents, this slow reaction is a great advantage for the target reaction as it minimizes undesired quenching of the key carbon-centered

radicals. This characteristic has been well exploited and thus borohydride mediated radical reactions including, Giese reactions with nearly equimolar amount of electron-deficient alkenes, radical carbonylation reactions using atmospheric pressure of CO, and radical hydroxymethylation reactions with HCHO have all been achieved. Borohydrides are commercially available, easy to handle reagents. As is evident from this review, borohydrides can now be considered as versatile reagents for radical reactions. We hope that this review will stimulate continued progress of borohydride-mediated radical reactions.

Notes and references

[a] Department of Chemistry, Graduate School of Science, Osaka Prefecture University, Sakai, Osaka 599-8531, Japan.

[1] (a) *Radicals in Organic Synthesis*, ed. P. Renaud and M. P. Sibi, Wiley-VCH, Weinheim, 2001; (b) *Encyclopedia of Radicals in Chemistry, Biology and Materials*, ed. C. Chatgilialoglu and A. Studer, Wiley, Chichester, U.K., 2012.

[2] (a) W. P. Neumann, *Synthesis*, 1987, 665-683; (b) *Tributylstannane. e-Encyclopedia of Reagents for Organic Synthesis,* Wiley, 2004; (c) H. Jasch and M. R. Heinrich, Tin Hydrides and Functional Group Transformations, in *Encyclopedia of Radicals in Chemistry, Biology, and Materials,* ed. C. Chatgilialoglu and A. Studer, Wiley, Chichester, U.K., 2012, vol. 2, pp. 1059-1093.

[3] (a) A. L. J. Beckwith and P. E. Pigou, *Aust. J. Chem.*, 1986, **39**, 77-87; (b) D. P. Curran, C. P. Jasperse and M. J. Totleben, *J. Org. Chem.*, 1991, **56**, 7169-7172.

[4] C. Chatgilialoglu, K. U. Ingold and J. C. Scaiano, *J. Am. Chem. Soc.,* 1981, **103**, 7739-7742.

[5] For a review on tin hydride substitutes in reductive radical chain reactions, see: A. Studer and S. Amrein, *Synthesis*, 2002, 835-849.

[6] For a review on tris(trimethylsilyl)silane in radical reactions, see: C. Chatgilialoglu, *Chem. Eur. J.*, 2008, **14**, 2310-2320.

[7] F. Dénès, M. Pichowicz, G. Povie and P. Renaud, *Chem. Rev.*, 2014, **114**, 2587-2693.

[8] (a) A. Studer and S. Amrein, *Angew. Chem. Int. Ed.*, 2000, **39**, 3080-3082; (b) S. Amrein, A. Timmermann and A. Studer, *Org. Lett.*, 2001, **3**, 2357-2360; (c) S. Amrein and A. Studer, *Chem. Commun.*, 2002, 1592-1593; (d) A. Studer, S. Amrein, F. Schleth, T. Schulte and J. C. Walton, *J. Am. Chem. Soc.*, 2003, **125**, 5726-5733.

ARTICLE

[9] For a review on polarity-reversal catalysts, see: (*a*) B. P. Roberts, *Chem. Soc. Rev.*, 1999, **28**, 25-35; For recent examples on polarity-reversal catalyst in radical reductions with NHC-borane, see: (*b*) X. Pan, E. Lacôte, J. Lalevée and D. P. Curran, *J. Am. Chem. Soc.*, 2012, **134**, 5669-5674. (*c*) X. Pan, J. Lalevée, E. Lacôte and D. P. Curran, *Adv. Synth. Catal.*, 2013, **355**, 3522-3526.

[10] (*a*) D. Pozzi, E. M. Scanlan and P. Renaud, *J. Am. Chem. Soc.*, 2005, **127**, 14204-14205; (*b*) G. Povie, G. Villa, L. Ford, D. Pozzi, C. H. Schiesser and P. Renaud, *Chem. Commun.*, 2010, **46**, 803-805; (*c*) G. Villa, G. Povie and P. Renaud, *J. Am. Chem. Soc.*, 2011, **133**, 5913-5920.

[11] (*a*) D. A. Spiegel, K. B. Wiberg, L. N. Schacherer, M. R. Medeiros and J. L. Wood, *J. Am. Chem. Soc.*, 2005, **127**, 12513-12515; (*b*) M. R. Medeiros, L. N. Schacherer, D. A. Spiegel and J. L. Wood, *Org. Lett.*, 2007, **9**, 4427-4429; (*c*) J. Jin and M. Newcomb, *J. Org. Chem.*, 2007, **72**, 5098-5103; (*d*) J. Jin and M. Newcomb, *J. Org. Chem.*, 2008, **73**, 4740-4742; (*e*) G. Povie, M. Marzorati, P. Bigler and P. Renaud, *J. Org. Chem.*, 2013, **78**, 1553-1558.

[12] (*a*) J. M. Cuerva, A. G. Campaña, J. Justicia, A. Rosales, J. L. Oller-López, R. Robles, D. J. Cárdenas, E. Buñuel and J. E. Oltra, *Angew. Chem. Int. Ed.*, 2006, **45**, 5522-5526; (*b*) J. Jin and M. Newcomb, *J. Org. Chem.*, 2008, **73**, 7901-7905.

[13] E. J. Corey and J. W. Suggs, *J. Org. Chem.*, 1975, **40**, 2554-2555.

[14] G. Stork and N. H. Baine, *J. Am. Chem. Soc.*, 1982, **104**, 2321-2323.

[15] J. A. Barltrop and D. Bradbury, *J. Am. Chem. Soc.*, 1973, **95**, 5085-5086.

[16] (*a*) B. Meunier, *J. Organomet. Chem.*, 1981, **204**, 345-346; (*b*) S.-T. Lin and J. A. Roth, *J. Org. Chem.*, 1979, **44**, 309-310.

[17] (*a*) Y. Liu and J. Schwartz, *J. Org. Chem.*, 1994, **59**, 940-942; (*b*) Y. Liu and J. Schwartz, *Tetrahedron*, 1995, **51**, 4471-4482.

[18] (*a*) N. M. Yoon, J. Choi and H. J. Lee, *Bull. Korean. Chem. Soc.*, 1993, **14**, 543-545; (*b*) N. M. Yoon, H. J. Lee, J. H. Ahn and J. Choi, *J. Org. Chem.*, 1994, **59**, 4687-4688; (*c*) T. B. Sim, J. Choi, M. J. Joung and N. M. Yoon, *J. Org. Chem.*, 1997, **62**, 2357-2361.

[19] K. Inoue, A. Sawada, I. Shibata and A. Baba, *J. Am. Chem. Soc.*, 2002, **124**, 906-907.

[20] A. Ekomié, G. Lefèvre, L. Fensterbank, E. Lacôte, M. Malacria, C. Ollivier and A. Jutand, *Angew. Chem. Int. Ed.*, 2012, **51**, 6942-6946.

[21] For reviews on catechol borane mediated radical reactions, see: (*a*) A.-P. Schaffner and P. Renaud, *Eur. J. Org. Chem.*, 2004, 2291-2298; (*b*) P. Renaud, A. Beauseigneur, A. Brecht-Forster, B. Becattini, V. Darmency, S. Kandhasamy, F. Montermini, C. Ollivier, P. Panchaud, D. Pozzi, E. M. Scanlan, A.-P. Schaffner and V. Weber, *Pure Appl. Chem.*, 2007, **79**, 223-233.

[22] For a review on NHC-borane, see: D. P. Curran, A. Solovyev, M. Makhlouf Brahmi, L. Fensterbank, M. Malacria and E. Lacôte, *Angew. Chem. Int. Ed.*, 2011, **50**, 10294-10317.

[23] For an example on generation of borane radical anion through γ–irradiation of KBH$_4$, see: M. C. R. Symons and H. W. Wardale, *Chem. Commun.*, 1967, 758.

[24] J. R. M. Giles and B. P. Roberts, *J. Chem. Soc., Perkin Trans. 2*, 1983, 743-755.

[25] B. Sheeller and K. U. Ingold, *J. Chem. Soc., Perkin Trans. 2*, 2001, 480-486.

[26] A. N. Abeywickrema and A. L. J. Beckwith, *Tetrahedron Lett.*, 1986, **27**, 109-112.

[27] L. J. Johnston, J. Lusztyk, D. D. M. Wayner, A. N. Abeywickreyma, A. L. J. Beckwith, J. C. Scaiano and K. U. Ingold, *J. Am. Chem. Soc.*, 1985, **107**, 4594-4596.

[28] T. Kawamoto, S. Uehara, H. Hirao, T. Fukuyama, H. Matsubara and I. Ryu, *J. Org. Chem.*, 2014, **79**, 3999-4007.

[29] (*a*) M. Newcomb and J. Kaplan, *Tetrahedron Lett.*, 1987, **28**, 1615-1618; (*b*) M. Newcomb, *Tetrahedron,* 1993, **49**, 1151-1176.

[30] C. Chatgilialoglu, J. Dickhaut and B. Giese, *J. Org. Chem.*, 1991, **56**, 6399-6403.

[31] J. Lusztyk, B. Maillard, D. A. Lindsay and K. U. Ingold, *J. Am. Chem. Soc.*, 1983, **105**, 3578-3580.

[32] A. Solovyev, S.-H. Ueng, J. Monot, L. Fensterbank, M. Malacria, E. Laccôte and D. P. Curran, *Org. Lett.*, 2010, **12**, 2998−3001.

[33] K. Tsujimoto, S. Tasaka and M. Ohashi, *J. Chem. Soc., Chem. Commun.*, 1975, 758-759.

[34] Also see the related dechlorination reactions via hydride-proton transfer: (*a*) G. A. Epling and E. Florio, *Tetrahedron Lett.*, 1986, **27**, 675-678; (*b*) G. A. Epling and E. Florio, *J. Chem. Soc., Chem. Commun.*, 1986, 185.

[35] J. T. Groves and K. W. Ma, *J. Am. Chem. Soc.*, 1974, **96**, 6527-6529.

[36] (*a*) M. Ishikawa and S. Fukuzumi, *Chem. Lett.*, 1990, 963-966; (*b*) M. Ishikawa and S. Fukuzumi, *J. Am. Chem. Soc.*, 1990, **112**, 8864-8870.

[37] G. Boisvert and R. Giasson, *Tetrahedron Lett.*, 1992, **33**, 6587-6590.

[38] (*a*) M. Abe, T. Hayashikoshi and T. Kurata, *Chem. Lett.*, 1994, **23**, 1789-1792; (*b*) T. Kurata and R. Kinoshita, *J. Oleo Sci.,* 2001, **50**, 759-762.

[39] (*a*) J.-P. Praly, A. S. Ardakani, I. Bruyère, C. Marie-Luce and B. B. Qin, *Carbohydr. Res.*, 2002, **337**, 1623-1632; (*b*) I. Bruyère, Z. Tóth, H. Benyahia, J. L. Xue and J.-P. Praly, *Tetrahedron*, 2013, **69**, 9656-9662.

[40] (*a*) J. M. Surzur and P. Teissier, *C. R. Acad. Sci. Fr. Ser. C,* 1967, **264**, 1981-1984; (*b*) D. D. Tanner and F. C. P. Law, *J. Am. Chem. Soc.,* 1969, **91**, 7535-7537.

[41] Q. Liu, B. Han, W. Zhang, L. Yang, Z.-L. Liu and W. Yu, *Synlett*, 2005, 2248-2250.

[42] For examples on tributyltin hydride mediated reductive radical addition reactions, see: (*a*) S. D. Burke, W. F. Fobare and D. M. Armistead, *J. Org. Chem.*, 1982, **47**, 3348-3350; (*b*) B. Giese and J. Dupuis, *Angew. Chem. Int. Ed.*, 1983, **22**, 622-623.

[43] Also see Bu$_3$PBH$_2$Ph mediated reductive radical addition reaction: J. A. Baban and B. P. Roberts, *J. Chem. Soc., Perkin Trans. 2*, **1988**, 1195.-1200

[44] (*a*) I. Ryu, S. Uehara, H. Hirao and T. Fukuyama, *Org. Lett.*, 2008, **10**, 1005-1008; (*b*) T. Fukuyama, T. Kawamoto, M. Kobayashi and I. Ryu, *Beilstein J. Org. Chem.*, 2013, **9**, 1791-1796.

[45] T. Kawamoto, A. Sato and I. Ryu, *Org. Lett.*, 2014, **16**, 2111-2113.

[46] For reviews on radical arylation of benzene, see: (*a*) E. Shirakawa and T. Hayashi, *Chem. Lett.*, 2012, **41**, 130-134; (*b*) S. E. Vaillard

and A. Studer, Radical Arylations, in *Encyclopedia of Radicals in Chemistry, Biology and Materials*, ed. C. Chatgilialoglu and A. Studer, Wiley, Chichester, U.K., 2012, vol. 2, pp. 529-560; (*c*) T. L. Chan, Y. Wu, P. Y. Choy, and F. Y. Kwong, *Chem. Eur. J.*, 2013, **19**, 15802-15814; (*d*) H. Bonin, M. Sauthier and F.-X. Felpin, *Adv. Synth. Catal.*, 2014, **356**, 645-671; (*e*) V. P. Mehta and B. Punji, *RSC Adv.*, 2013, **3**, 11957-11986.

[47] For reviews on radical carbonylation, see: (*a*) I. Ryu and N. Sonoda, *Angew. Chem. Int. Ed.*, 1996, **35**, 1050-1066; (*b*) I. Ryu, N. Sonoda and D. P. Curran, *Chem. Rev.*, 1996, **96**, 177-194; (*c*) I. Ryu, *Chem. Soc. Rev.*, 2001, **30**, 16-25; (*d*) S. Sumino, A. Fusano, T. Fukuyama and I. Ryu, *Acc. Chem. Res.,* 2014, **47**, 1563–1574; (*e*) A. Fusano and I. Ryu, Free-Radical-Mediated Multicomponent Reactions Involving Carbon Monoxide, in *Science of Synthesis: Multicomponent Reactions 2*; ed. T. J. J. Müller, Georg Thieme Verlag KG, Germany, 2014.

[48] (*a*) I. Ryu, T. Niguma, S. Minakata, M. Komatsu, S. Hadida and D. P. Curran, *Tetrahedron Lett.*, 1997, **38**, 7883-7886; (*b*) H. Matsubara, S. Yasuda, H. Sugiyama, I. Ryu, Y. Fujii and K. Kita, *Tetrahedron,* 2002, **58**, 4071-4076.

[49] (*a*) S. Kobayashi, T. Kawamoto, S. Uehara, T. Fukuyama and I. Ryu, *Org. Lett.*, 2010, **12**, 1548-1551; (*b*) S. Kobayashi, T. Kinoshita, T. Kawamoto, M. Wada, H. Kuroda, A. Masuyama and I. Ryu, *J. Org. Chem.*, 2011, **76**, 7096-7103.

[50] T. Kawamoto, H. Matsubara and I. Ryu, *Chem. Lett.,* 2014, **43**, 1140-1142.

[51] (*a*) I. Ryu, K. Matsu, S. Minakata and M. Komatsu, *J. Am. Chem. Soc.*, 1998, **120**, 5838-5839; (*b*) I. Ryu, H. Miyazato, H. Kuriyama, K. Matsu, M. Tojino, T. Fukuyama, S. Minakata and M. Komatsu, *J. Am. Chem. Soc.*, 2003, **125**, 5632-5633; (*c*) M. Tojino, N. Otsuka, T. Fukuyama, H. Matsubara, C. H. Schiesser, H. Kuriyama, H. Miyazato, S. Minakata, M. Komatsu and I. Ryu, *Org. Biomol. Chem.*, 2003, **1**, 4262-4267; (*d*) M. Tojino, N. Otsuka, T. Fukuyama, H. Matsubara and I. Ryu, *J. Am. Chem. Soc.*, 2006, **128**, 7712-7713; (*e*) T. Fukuyama, N. Nakashima, T. Okada and I. Ryu, *J. Am. Chem. Soc.*, 2013, **135**, 1006-1008.

[52] (*a*) M. Tojino, Y. Uenoyama, T. Fukuyama and I. Ryu, *Chem. Commun.*, 2004, 2482-2483; (*b*) Y. Uenoyama, T. Fukuyama, O. Nobuta, H. Matsubara and I. Ryu, *Angew. Chem. Int. Ed.*, 2005, **44**, 1075-1078; (*c*) H. Matsubara, I. Ryu and C. H. Schiesser, *J. Org. Chem.*, 2005, **70**, 3610-3617; (*d*) Y. Uenoyama, T. Fukuyama and I. Ryu, *Org. Lett.*, 2007, **9**, 935-937; (*e*) I. Ryu, T. Fukuyama, M. Tojino, Y. Uenoyama, Y. Yonamine, N. Terasoma and H. Matsubara, *Org. Biomol. Chem.*, 2011, **9**, 3780-3786.

[53] I. Ryu, T. Fukuyama, O. Nobuta and Y. Uenoyama, *Bull. Korean Chem. Soc.*, 2010, **31**, 545-546.

[54] For a recent example on alkoxycarbonylation reaction of aryl iodides, in which *tert*-butoxy anion reacts with acyl radicals to give radical anion intermediates, see: (a) H. Zhang, R. Shi, A. Ding, L. Lu, B. Chen, and A. Lei, *Angew. Chem. Int. Ed.*, 2012, **51**, 12542-12545; (*b*) For original work on alkoxycarbonylation of alkyl iodides under photoirradiation conditions, see: (b) K. Nagahara, I. Ryu, M. Komatsu and N. Sonoda, *J. Am. Chem. Soc.*, 1997, **119**, 5465-5466

[55] T. Kawamoto, T. Okada, D. P. Curran and I. Ryu, *Org. Lett.*, 2013, **15**, 2144-2147.

[56] (*a*) G. Fuller and F. F. Rust, *J. Am. Chem. Soc.,* 1958, **80**, 6148-6149; (*b*) N. Miyaura, M. Itoh, A. Suzuki, H. C. Brown, M. M. Midland and P. Jacob, III *J. Am. Chem. Soc.*, 1972, **94**, 6549-6550.

[57] For a review, see T. Kawamoto and I. Ryu, *Chimia*, 2012, **66**, 372-376.

[58] T. Kawamoto, T. Fukuyama and I. Ryu, *J. Am. Chem. Soc.*, 2012, **134**, 875-877.