Boracene-Based Alkylborate Enabling Ni/Ir Hybrid Catalysis

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Boracene-Based Alkylborate Enabling Ni/Ir Hybrid Catalysis†

Yukiya Sato,[a] Yusuke Miyamoto,[a] Yuto Sumida,*[a] Takamitsu Hosoya[b,c] and Hirohisa Ohmiya*[a,d]

The boracene-based alkylborate enabled visible light-mediated metallaphotoredox catalysis. The directly excited borate was easily oxidatively quenched by the excited Ir photoredox catalyst. The Ni/Ir hybrid catalysis afforded the products under significantly low irradiance.

The momentum of photoredox chemistry,[1] which has developed exponentially over the past more than a decade, has not still to stop. The metallaphotoredox catalysis arisen from the merger of transition metal catalysis and photoredox catalysis has realized numerous elusive bond formations.[2] With the development of transformations driven by metallaphotoredox catalysis, various precursors have been developed to produce radicals based on single electron transfer (SET) oxidation or reduction (Figure 1A). In this context, we previously reported rationally designed alkylborate prepared from the boron-doped π-extended molecule, boracene,[3] enabling generation alkyl radical via direct excitation[4] (Figure 1B). The strategy based on direct excitation of the substrate has emerged as a new tributary in this field, and the possibility to unlock unconventional reactivity.[5] The boracene-based alkyl borate acts as a strong reductant and efficient radical donor under visible light irradiation. The application of this direct excitable molecule to metallaphotoredox catalysis would develop a high-energetically effective system (Figure 1C). The photo-inducible borate can also provide a strong single electron donor, and thus, an expeditious SET event with photoredox catalyst would generate alkyl radical and apply to diverse transformations. Alternatively, energy transfer (ET) also possibly occurs from excited photoredox catalyst to the borate to form the excited state,[6] which results in the homolytic cleavage to generate

alkyl radicals. Both pathways can be energetically beneficial because of the relatively high redox potential (0.78 V vs. SCE).[4]

A. Metallaphotoredox Catalysis
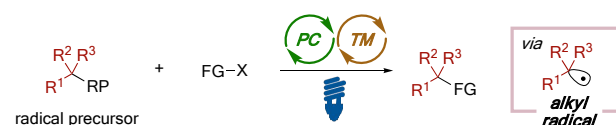
B. Alkyl Radical from Direct Excitation (our previous work)
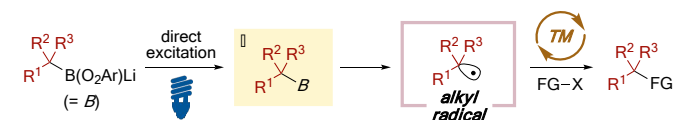
C. Metallaphotoredox with Direct Excitable Precursor (**this work**)

Figure 1. Metallaphotoredox catalysis and direct excitation of boracene-based alkylborate.

Accordingly, we started to develop a Ni/Ir hybrid catalysis[7,8] associated with the direct excitation of the boracene-based alkylborate. As previously reported, the nickel-catalyzed alkylation of 4-bromobiphenyl (**3a**) using the *t*-butyl borate **2a** derived from boracene **1** under photo-irradiation for 14 h gave the corresponding product in 76% yield (Table 1, entry 1).[4] In contrast, the addition of Ir photoredox catalyst to the conditions dramatically enhanced the cross-coupling (entry 2). Addition of catalytic amount of [Ir(ppy)$_2$dtbpy]PF$_6$[9] (**PC1**) afforded the shorter reaction time, higher product yield, even under significantly lower irradiance. In the Ni/Ir hybrid catalysis using the borate **2a**, we used Micro Photochemical Reactor, which has weak spectral irradiances compared to the most commonly-used light source, Kessil Lamp. According to the measurement of each spectral irradiances, we found that Kessil Lamp (measured with 1% transmittance neutral-density filter) showed more than 700 times higher irradiance at 440 nm[10] than Micro Photochemical Reactor (Figure 2). The Ni-catalyzed cross-coupling with the direct excitation method

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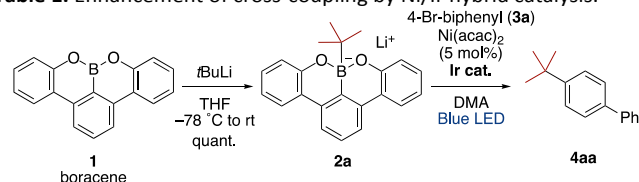d. *JST, PRESTO, 4-1-8 Honcho, Kawaguchi, Saitama, 332-0012, Japan.*

using Micro Photochemical Reactor provided only 22% yield even after 120 hours (entry 3). Thus, Ni/Ir hybrid catalysis with the boracene-based borate improved the rate and efficiency of the *tertiary* alkylation of aryl halide.

Table 1. Enhancement of cross-coupling by Ni/Ir hybrid catalysis.

entry	Ir catalyst	time (h)	Yield of **4aa** (%)
1	none	14	76[b]
2	[Ir(ppy)$_2$dtbpy]PF$_6$ (**PC1**)[a]	1	**89**[c]
3	none	120	22[c,d]

[a] 1 mol% of Ir catalyst was used. ppy = 2-phenylpyridine. dtbpy = 4,4'-Di-tert-butyl-2,2'-dipyridyl. [b] Kessil lamp was used as a light source. [c] Micro Photochemical Reactor was used as a light source. [d] ^{1}H NMR yield.
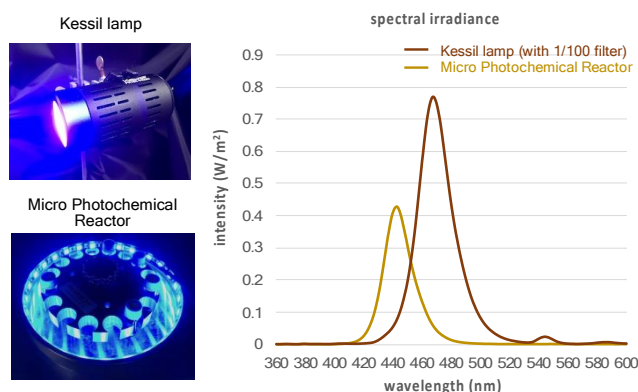

Figure 2. Spectral irradiance of each light source.

With the hybrid catalysis of Ni(acac)$_2$ and [Ir(ppy)$_2$dtbpy]PF$_6$, we compared the efficiency and versatility with the direct excitation method using the selected examples (Figure 3, top). 4'-Bromoacetophenone, which gave meager yield in the direct excitation, afforded the cross-coupling product **4ab** almost quantitatively.[11] Additionally, the cross-coupling by the direct excitation with Ni(acac)$_2$ as a catalyst proceeded with the generation of a significant amount of isobutylated arenes in some cases. Such the undesired isomerization was confined with the reaction using the Ir catalyst. As well as the direct excitation method, the cross-coupling of the electron-rich bromoarene was permitted and give a higher yield of the product **4ac**, which was difficult to achieved by the reported conditions.[8b] Interestingly, while the cross-coupling of *tertiary*-alkyl borate with heteroarene was unavailable without Ir catalyst, a good yield of **4ae** was obtained from 3-bromoquinoline (**3e**) with Ni/Ir co-catalytic conditions. Unfortunately, no cross-coupling product was produced in the case of 3-bromobenzothiophene under both catalytic systems. Although the Ni/Ir catalyzed reaction of 9-bromophenanthrene

afforded the product **4ag** in moderate yield with the generation of phenanthrene in 21% yield via protodebromination, the formation of phenanthrene was major pathway with the direct excitation method. Similarly, the cross-coupling using *secondary* and *primary*-alkylborate were also accelerated under the Ni/Ir hybrid catalysis. The higher yields of the corresponding products were obtained in each case (Figure 3, middle).
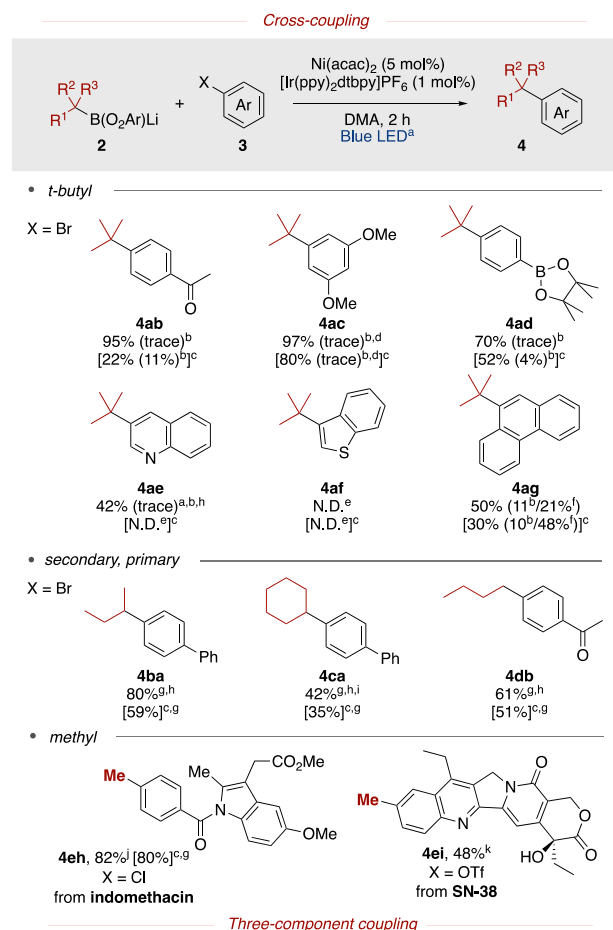

Figure 3. Effects on Ni/Ir hybrid catalysis [a] Micro Photochemical Reactor was used as a light source. [b] Number in parenthesis is an NMR yield of isobutylated arene. [c] A reaction was performed in the absence of Ir catalyst with Kessil Lamp for 14 h in brackets. [d] Bis(2,2,6,6-tetramethyl-3,5-heptanedionato)nickel(II) was used instead of Ni(acac)$_2$. [e] N.D. = not detected. [f] Number in parenthesis is NMR yield of phenanthrene. [g] NiBr$_2$·diglyme (5 mol%) and dtbpy (6 mol%) in THF

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were used as catalytic conditions. [h] Stirred for 4 h. [i] The borate was prepared from cyclohexylmagnesium bromide. [j] The reaction was performed using NiBr$_2$·diglyme (10 mol%) and dtbpy (12 mol%) in THF for 48 h. [k] The reaction was performed using NiBr$_2$·diglyme (10 mol%) and dtbpy (12 mol%) in THF for 8 h. The average NMR yield of two experiments.

Given that methylation of aryl halide was sluggish via methyl radical from the direct excitation of methylborate,[4] the enhancement by Ni/Ir hybrid catalysis would provide a more versatile methylation.[12] The methylation of pharmaceuticals can be achieved, as demonstrating the synthesis of indomethacin **4eh** and camptothecin derivatives **4ei**.[13]

Subsequently, the tendency of three-component *vicinal* alkylarylation[14] of alkene was also investigated under Ni/Ir hybrid catalysis, comparing the direct excitation (Figure 3, bottom). However, the addition of the Ir catalyst has not shown a positive effect on the three-component coupling. The *vicinal* alkylarylation of vinyl pivalate that was smoothly progressed using the direct excitation method gave no product **6aaa** of three-component coupling and, instead, the cross-coupling product **4aa** from **2a** and **3a** was only observed in 31% yield. The *vicinal* alkylarylated products **6aba** and **6bba** were obtained from the reaction using an electron-deficient olefin, *t*-butyl acrylate. Although the Ni/Ir catalyzed reaction proceeded under the lower photo irradiances and shorter reaction time than the direct excitation conditions, the product yields depended on the substrates.

Table 2. Evaluation of Ir photoredox catalyst.
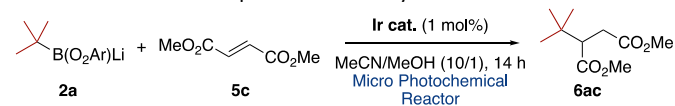
entry	Ir catalyst	ET (kcal/mol)[a]	$E_{1/2}^{III*/II}$ (V)[b]	Yield of **6ac** (%)[c,d]
1	**PC2**	59	+1.32	98
2	**PC3**	61	+1.21	82
3	**PC1**	49	+0.66	73
4	**PC4**	58	+0.31	48

[a] Triplet energies were calculated from the reported emission maximum peaks. [b] The reported values. [c] NMR yields. [d] The average yield of three times experiments.
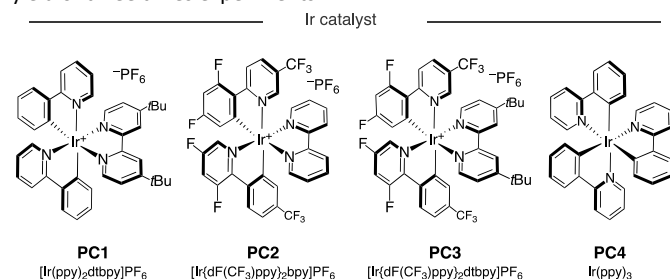
Ir catalyst

Considering the possibility of ET or SET from the excited Ir catalyst to the Ni complexes, the simple alkyl radical reaction with electron-deficient olefin, the Giese addition[15] is suitable to evaluate the enhancement ability of Ir photoredox catalyst

for radical generation. Thus, the Giese addition of *t*-butyl borate **2a** with dimethyl fumarate (**5c**) was conducted in the presence of various Ir catalysts. Among the Ir catalysts tried, [Ir{dF(CF$_3$)ppy}$_2$bpy]PF$_6$ (**PC2**) showed the highest reactivity to afford the *t*-butyl adduct in almost quantitative yield (Table 2, entry 1). Overviewing the triplet energies or electron transfer ability of **PC1–4**, as shown in Table 2,[16] the product yield was correlated with the oxidation potential of the Ir catalyst. While the rapid SET process affected the reaction efficiency, Ir catalyst **PC4**, the weaker oxidant at excited state (+0.31 V), performed lower catalytic activity despite the highest triplet energy (entry 4). This result suggests that the radical generation derived from highly efficient SET oxidation of the borate, not by energy transfer (ET) from the excited Ir photoredox catalyst. The lifetime of the excited state is exceedingly short in general. Thus, the SET oxidation likely occurs between the excited Ir catalyst and the ground state of the borate. However, considering the reduction potential of the borate (0.78 V in MeCN vs. SCE), the SET oxidation with **PC3** and **PC4** are difficult to progress with the ground state of the borate. Therefore, the pathway via SET oxidation with the excited borate can not be ruled out.

To gain a further assessment of Ir catalysts, we conducted Stern–Volmer quenching studies (Figure 4). Although the concentration-dependent of the borate **2a** can quench the fluorescence of the four Ir catalysts **PC1–4** in either case, non-linear Stern–Volmer plot was obtained,[17] and the efficiency varied from the Ir catalysts. The order of the quenching efficiency showed good agreement with the result of Giese addition experiments. The reason for the non-linearity of the Stern–Volmer plots is unclear at present. The formation of a non-fluorescent complex between photocatalyst and the borate in the ground state would be possible. Additionally, since the borate also showed weak fluorescence, the quenching study with Ni(acac)$_2$, which is the catalyst of cross-coupling, was conducted. Changing the Ni complex concentration, we observed the concentration of Ni(acac)$_2$ dependent quenching of the fluorescent of the borate **2a**. This result revealed that the SET process could occur between the excited state of **2a** with Ir catalysts and Ni(acac)$_2$.[18]
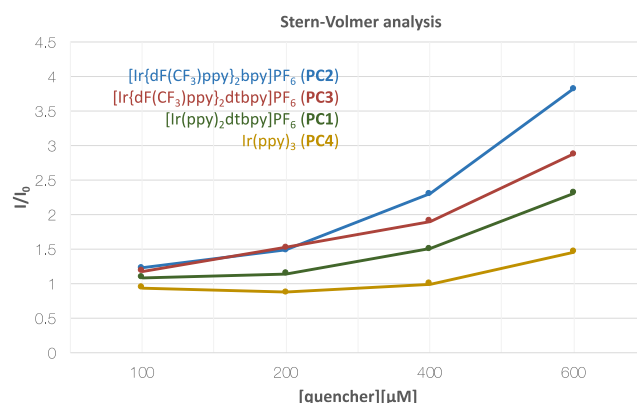

Figure 4. Stern–Volmer analysis of Ir catalysts.

Conclusions

In summary, we have developed a Ni/Ir metallaphotoredox catalysis using the boracene-based alkylborate, oxidatively quenchable alkyl radical precursor. The hybrid catalysis enabled the cross-coupling with shorter reaction time, higher product yield, even under significantly lower irradiances. According to the reaction analyses, the Ir photoredox catalyst would enhance the radical generation step with borate.
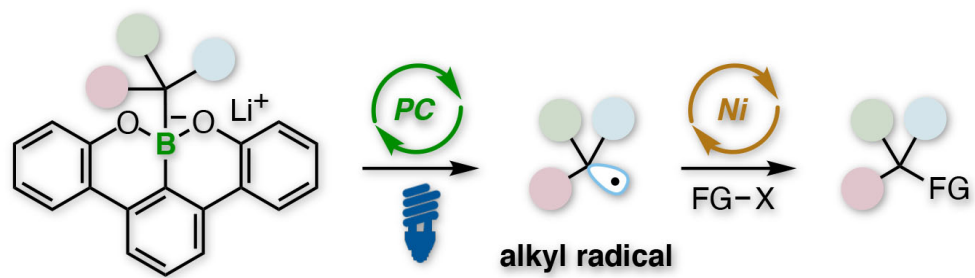
Conflicts of interest

There are no conflicts to declare.

Acknowledgement

Notes and references

1   (a) L. Buzzetti, G. E. M. Crisenza and P. Melchiorre, *Angew. Chem. Int. Ed.*, 2019, **58**, 3730-3747. (b) C. Stephenson, T. Yoon, D. W. C. MacMillan, *Visible Light Photocatalysis in Organic Chemistry*, 1st ed. Weinheim, Wiley-VCH, 2018. (c) M. H. Shaw, J. Twilton and D. W. C. MacMillan, *J. Org. Chem.*, 2016, **81**, 6898-6926.

2   Selected reviews: (a) A. Lipp, S. O. Badir and G. Molander, *Angew. Chem. Int. Ed.*, DOI: 10.1002/anie.202007668. (b) M. De Abreu, P. Belmont and E. Brachet, *Eur. J. Org. Chem.*, 2020, **2020**, 1327-1378. (c) J. Twilton, C. Le, P. Zhang, M. H. Shaw, R. W. Evans and D. W. C. MacMillan, *Nat. Rev. Chem.*, 2017, **1**, 0052.

3   (a) M. Numano, N. Nagami, S. Nakatsuka, T. Katayama, K. Nakajima, S. Tatsumi, N. Yasuda and T. Hatakeyama, *Chem. Eur. J.*, 2016, **22**, 11574-11577. (b) Y. Sumida, R. Harada, T. Kato-Sumida, K. Johmoto, H. Uekusa and T. Hosoya, *Org. Lett.*, 2014, **16**, 6240-6243.

4   Y. Sato, K. Nakamura, Y. Sumida, D. Hashizume, T. Hosoya and H. Ohmiya, *J. Am. Chem. Soc.*, 2020, **142**, 9938-9943.

5   (a) Y. Wei, Q.-Q. Zhou, F. Tan, L.-Q. Lu and W.-J. Xiao, *Synthesis*, 2019, **51**, 3021-3054. (b) K. Zhang, L. Q. Lu, Y. Jia, Y. Wang, F. D. Lu, F. Pan and W. J. Xiao, *Angew. Chem. Int. Ed.*, 2019, **58**, 13375-13379. (c) T. van Leeuwen, L. Buzzetti, L. A. Perego and P. Melchiorre, *Angew. Chem. Int. Ed.*, 2019, **58**, 4953-4957. (d) E. Gandolfo, X. Tang, S. Raha Roy and P. Melchiorre, *Angew. Chem. Int. Ed.*, 2019, **58**, 16854-16858. (e) X. Chen, F. Ye, X. Luo, X. Liu, J. Zhao, S. Wang, Q. Zhou, G. Chen and P. Wang, *J. Am. Chem. Soc.*, 2019, **141**, 18230-18237. (f) L. Buzzetti, A. Prieto, S. R. Roy and P. Melchiorre, *Angew. Chem. Int. Ed.*, 2017, **56**, 15039-15043.

6   (a) F. Strieth-Kalthoff, M. J. James, M. Teders, L. Pitzer and F. Glorius, *Chem. Soc. Rev.*, 2018, **47**, 7190-7202. (b) E. R. Welin, C. Le, D. M. Arias-Rotondo, J. K. McCusker and D. W. C. MacMillan, *Science*, 2017, **355**, 380-385.

7   Selected reviews for Ni/Ir metallaphotoredox catalysis: (a) S. O. Badir and G. A. Molander, *Chem*, 2020, **6**, 1327-1339. (b)

J. A. Milligan, J. P. Phelan, S. O. Badir and G. A. Molander, *Angew. Chem. Int. Ed.*, 2019, **58**, 6152-6163. (c) J. K. Matsui, S. B. Lang, D. R. Heitz and G. A. Molander, *ACS Catal.*, 2017, **7**, 2563-2575.

8   (a) M. Yuan, Z. Song, S. O. Badir, G. A. Molander and O. Gutierrez, *J. Am. Chem. Soc.*, 2020, **142**, 7225-7234. (b) D. N. Primer and G. A. Molander, *J. Am. Chem. Soc.*, 2017, **139**, 9847-9850. (c) R. Alam and G. A. Molander, *J. Org. Chem.*, 2017, **82**, 13728-13734. (d) R. Karimi-Nami, J. C. Tellis and G. A. Molander, *Org. Lett.*, 2016, **18**, 2572-2575. (e) D. R. Heitz, J. C. Tellis and G. A. Molander, *J. Am. Chem. Soc.*, 2016, **138**, 12715-12718. (f) Y. Yamashita, J. C. Tellis and G. A. Molander, *Proc. Natl. Acad. Sci. U. S. A.*, 2015, **112**, 12026-12029. (g) D. N. Primer, I. Karakaya, J. C. Tellis and G. A. Molander, *J. Am. Chem. Soc.*, 2015, **137**, 2195-2198. (h) J. C. Tellis, D. N. Primer and G. A. Molander, *Science*, 2014, **345**, 433-436.

9   See Supporting Information for detailed optimization of reaction conditions.

10 We confirmed that the reaction proceeded with comparable efficiency using longpass filter, Cut-Off Wavelength: 430 nm.

11 We also compared the efficiency of the cross-coupling with *t*BuBF₃K. See Supporting Information in details.

12 (a) S. K. Kariofillis, B. J. Shields, M. A. Tekle-Smith, M. J. Zacuto and A. G. Doyle, *J. Am. Chem. Soc.*, 2020, **142**, 7683-7689. (b) A. M. Haydl and J. F. Hartwig, *Org. Lett.*, 2019, **21**, 1337-1341.

13 T. Yaegashi, S. Sawada, H. Nagata, T. Furuta, T. Yokokura and T. Miyasaka, *Chem. Pharm. Bull.*, 1994, **42**, 2518-2525.

14 (a) S.-Z. Sun, Y. Duan, R. S. Mega, R. J. Somerville and R. Martin, *Angew. Chem. Int. Ed.*, 2020, **59**, 4370-4374. (b) M. W. Campbell, J. S. Compton, C. B. Kelly and G. A. Molander, *J. Am. Chem. Soc.*, 2019, **141**, 20069-20078. (c) A. Garcia-Dominguez, R. Mondal and C. Nevado, *Angew. Chem. Int. Ed.*, 2019, **58**, 12286-12290.

15 B. Giese, *Angew. Chem. Int. Ed. Engl.*, 1983, **22**, 753-764.

16 (a) C. B. Kelly, N. R. Patel, D. N. Primer, M. Jouffroy, J. C. Tellis and G. A. Molander, *Nat. Protoc.*, 2017, **12**, 472-492. (b) Z. Lu and T. P. Yoon, *Angew. Chem. Int. Ed.*, 2012, **51**, 10329-10332. (c) M. S. Lowry, J. I. Goldsmith, J. D. Slinker, R. Rohl, R. A. Pascal, G. G. Malliaras and S. Bernhard, *Chem. Mater.*, 2005, **17**, 5712-5719.

17 H. Zeng and G. Durocher, *J. Lumin.*, 1995, **63**, 75-84.

18 See Supporting Information.

The boracene-based alkylborate enabled visible light-mediated Ni/Ir metallaphotoredox catalysis.

116x35mm (300 x 300 DPI)