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Visible Light-Induced Radical Carbo-Cyclization/*gem*-Diborylation Through Triplet Energy Transfer between a Gold Catalysts and Aryl Iodides

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ABSTRACT: Geminal diboronates have attracted significant attention because of their unique structures and reactivity. However, benzofuran-, indole- and benzothiophene-based benzylic *gem*-diboronates, building blocks for biologically relevant compounds, are unknown. A promising protocol using visible light and aryl iodides for constructing valuable building blocks, including benzofuran-, indole- and benzothiophene-based benzylic *gem*-diboronates, via radical carbo-cyclization/*gem*-diborylation of alkynes with a high functional group tolerance is presented. The utility of these *gem*-diboronates has been demonstrated by a ten gram scale conversion, by versatile transformations, by including the synthesis of approved drug scaffolds and two approved drugs, and even by polymer synthesis. The mechanistic investigation indicates that the merging of the dinuclear gold catalyst (photoexcitation by 315-400 nm UVA light) with Na_2CO_3 is directly responsible for photosensitization of aryl iodides (photoexcitation by 254 nm UV light) with blue LEDs light (410-490 nm, λ_{max} = 465 nm) through an energy transfer (EnT) process, followed by homolytic cleavage of the C-I bond in the aryl iodide substrates.

INTRODUCTION

Contemporary organic chemistry is a particularly interdisciplinary science, it also is of importance for biology, physics and materials science. This inspired us not only to pursue merely molecular transformations but also constructing valuable structures for drug discovery and materials synthesis. Recently, geminal diboronates[1] have attracted significant attention as important building blocks. Due to the empty *p*-orbital at the boron atoms, the *gem*-C-B bonds are activated and *α*-carbanionic intermediates are stabilized. It has been successfully applied in cross-coupling reactions,[2] two-fold functional groups conversion and even asymmetric transformations.[3] So far, several novel methods have been developed to access geminal diboronates, even benzylic diboronates.[4] However, benzofuran-, indole- and benzothiophene-based benzylic *gem*-diboronates, building blocks for biologically relevant compounds, are unknown. The most ideal and efficient strategy for the construction of these biologically relevant building blocks would be carbo-cyclization/borylation. However, only cyclized vinylboronic esters were obtained, either by using stoichiometric amount of *n*-BuLi, followed by carbo-cyclization of a alkynylchloride[5] or through carbo-borylation of arylzinc reagents by cobalt and chromium catalysts under harsh conditions (Fig. 1, A).[6]

Since light-induced radical carbo-cyclization[7] is among the most powerful and versatile methods for the constructing mono- and polycyclic systems with the advantage of high functional group tolerance, mild reaction conditions, a high level of regio- and stereoselectivity, we assumed that this could be an ideal protocol. Aryl halides, widely commercial available building blocks, have been successfully used in photochemistry.[8] It is well recognized that aryl radical could be produced either by direct photoexcitation (irradiation with UV light) (Fig. 1, B) or by single electron transfer (SET) process in presence of photocatalysts. However, another possibility, an energy transfer (EnT)[9] mediated by visible light, has remain relatively undeveloped: upon excitation by visible light, the excited state of photosensitizer can subsequently transfer its excited state energy to the ground state of aryl halides, leading to the triplet state of the aryl halides. The reactive triplet state of organic compounds would be efficiently and selectively accessed by EnT process (visible light) while overcoming the issues (selectivity, applicability, functional groups tolerance *etc.*) of direct photoexcitation (UV light) and providing opportunities for inventing new reactions.

Among many research groups in the field of photochemistry,[10] our group has dedicated considerable efforts to the development of novel methodologies relying on light-driven processes,[11] especially to photochemistry involving dinuclear bis(diphosphine) complex [Au₂(*μ*-dppm)₂]Cl₂ (dppm = bis(diphenylphosphino)methane), a bench stable complex possessing unique photophysical properties as a long-lived excited state (around 850 ns in MeCN) and a distinctive inner-sphere oxidation quenching (exciplex) pathway.[12] Generally, the ground state of [Au₂(*μ*-dppm)₂]Cl₂ inherently relays on an UVA light source for its photoexcitation (Fig. 1, C), only single electron transfer (SET) process between the photoexcited state of the [Au₂(*μ*-dppm)₂]Cl₂ and aryl/alkyl halides has been reported. Until recently, our group has explored a highly efficient C-C coupling by desulfurizing gold-catalyzed radical reaction[13] which shows the possibility

of using blue LEDs' light as light source for new reactions. The red shift of the absorption wavelength originates from the combination of [Au$_2$(μ-dppm)$_2$]Cl$_2$ and ligand (Ph$_3$P or mercaptan). *Inspired by this work, we were wondering whether new gold complexes, formed in situ, would bring us new physical properties and chemical reactivity by counter anion exchange,[14] coordination[15] or aggregation.[16]*

RESULTS AND DISCUSSION

Herein, benzofuran-, indole- and benzothiophene-based benzylic *gem*-diboronates building blocks, have selectively been obtained via a visible light-induced carbo-cyclization/*gem*-diborylation protocol, catalyzed by dinuclear-gold(I) complexes in the presence of half an equivalent of sodium carbonate (Fig. 1, D). The necessary triplet state of aryl iodides was accessed by an energy transfer process rather than the widely developed single electron transfer pathway.
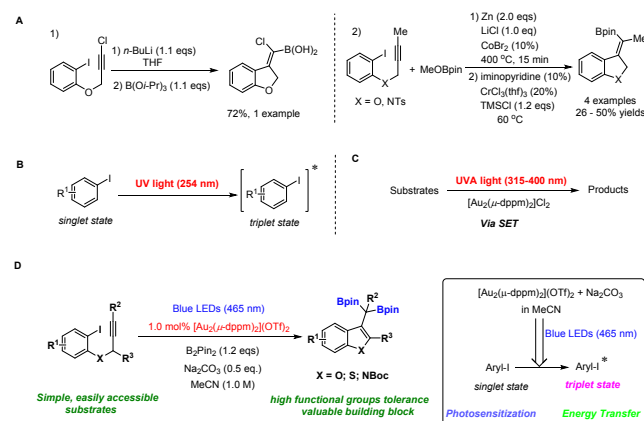
Figure 1. Previous studies and this work; **A**: Previous contributions on carbo-cyclization/borylation of alkynes; **B**: Direct photoexcitation for reactive triplet state of aryl iodides. **C**: Previous reports on the light source for dinuclear gold as photocatalyst: UVA (inherently) and mechanistic pathway (single electron transfer); **D**: This work.

The carbo-cyclization/*gem*-diborylation product **3aa** was accessible in 90% isolated yield from **1aa** (1.0 eq.) and B$_2$Pin$_2$ (1.2 eqs) in the presence of [Au$_2$(μ-dppm)$_2$](OTf)$_2$ (1.0 mol%) and Na$_2$CO$_3$ (0.5 eq.) in MeCN (1.0 M) by the simple exposure to blue LED light for 15 h (Scheme 1, entry 1). Our control experiments indicate that Na$_2$CO$_3$, blue LED light and [Au$_2$(μ-dppm)$_2$](OTf)$_2$ are all critical for the reaction (entries 2-4). In the absence of [Au$_2$(μ-dppm)$_2$](OTf)$_2$, no desired product was formed by merely adding each of the components of catalyst (entries 5-6). The possibility of a thermal reaction has been excluded by operating the standard reaction at 50 °C in the absence of light (entry 7). No conversion was observed with the mononuclear gold catalyst Ph$_3$PAuCl (entry 9). Other widely used photosensitizers resulted in no conversion (entries 10-12). This reaction also proceeded well under CFL (compact fluorescent lamp) light (entry 13). Only 52% yield of the desired product was obtained under UVA light irradiation (entry 14).

Scheme 1. Control experiments

Entry	Variation	Yield [%]	Conversion [%]
1	no variation	90	100
2	no base	0	0
3	no light	0	0
4	no Au$_2$(μ-dppm)$_2$(OTf)$_2$	0	0
5	NaOTf (10 mol%)	0	0
6	dppm (10 mol%)	0	0
7	no light, heated at 50 °C	0	0
8	Au$_2$(μ-dppm)$_2$Cl$_2$	70	89
9	Ph$_3$PAuCl	0	0
10	[Ir(ppy)$_2$(dtbbpy)]PF$_6$	0	0
11	[Ru(bpy)$_3$](PF$_6$)$_2$	0	0
12	Mes-Acr-Me$^+$BF$^-$	0	0
13	CFL light	78	100
14	UVA (λ_{max} = 365 nm)	52	85

Reactions were run with 0.2 mmol scale, % yields and % conversions were calculated based on ^{1}H NMR spectroscopy using 1,3,5-trimethoxybenzene (0.1 mmol) as an internal standard.

With the optimal condition in hand, we next determined the scope of this chemoselective and stereoselective cascade cyclization/*gem*-diborylation protocol. As shown in Scheme 2, either terminal alkynes (**3aa**, 90% yield) or mono/bis-alkyl-substituted alkynes (**3ab-3ae**, 60-88% yields) all react very well. Furthermore, a diverse array of both electron-withdrawing and electron-donating substituents on the phenyl groups (acyl, carboxylic acid esters, methoxy, *tert*-butyl, trifluoromethyl) gave the corresponding cyclization/*gem*-diborylation products (**3af-3ak**) in good yields (59-85%). Interestingly, other halogens (fluorine, chlorine, bromine) were also tolerated and the products (**3al-3ao**) can be isolated in excellent yields (75-88%). The reaction is also worked well for an amide substituent (**3ap**, 70%). For R^2 being a phenyl group, carbo-cyclization/iodination product **3aq** is the major product which could be caused by steric hindrance or electronic effects. After constructing complex benzofurans, we continued to expand this protocol to the synthesis of benzothiophenes. As expected, terminal and non-terminal alkynes provide cyclization/*gem*-diborylation products (**3ar-3at**) in 67%-87% yield. Also indoles could be converted, both terminal and alkyl-substituted alkyne substrates were successfully converted to the corresponding cyclization/*gem*-diborylation products (**3au** and **3av**) in good yields (80% and 75%). Scaffolds related to the approved drug Almotriptan, **3aw** and **3ax**, were obtained by this protocol in 77% and 82% yield.

Scheme 2. Scope of cascade *gem*-bis(borylations)
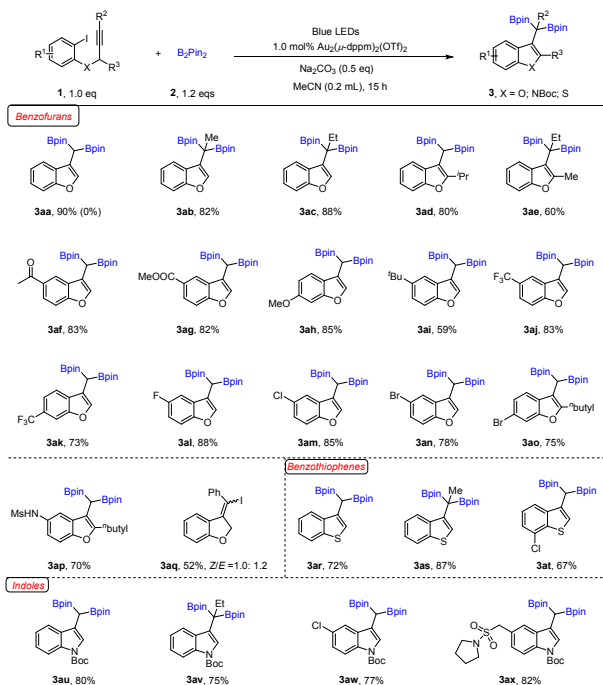
Reactions were run in 0.2 mmol scale, isolated yields.

Next, the synthetic utility of the products were also investigated. As shown in Figure 2A, both a one gram and a ten gram scale reaction with the easily accessible substrate **1aa**, using either 1.0 mol% of [Au$_2$(μ-dppm)$_2$](OTf)$_2$ (89% yield) or 0.1 mol% of [Au$_2$(μ-dppm)$_2$](OTf)$_2$ (65% yield). The X-ray structure of **3aa** is shown in Figure 2B; it is worth to mention that this compound remain intact after storing in the fridge at –20 °C in 5 g scale for ten months. Furthermore, versatile transformations of **3aa** were also explored (Fig. 2C). **3aa** was successfully converted to compounds **4** or **5** by deborylation and protonation.[3f] Compounds **6** and **7** were generated by nucleophilic substitution of the carbanion intermediate in the presence of bases.[3f] **3aa** was oxidized to benzyl alcohol **8** or aldehyde **9** by different oxidants. In addition, **3aa** can undergo a metal-catalyzed cross-coupling reaction to result compounds **10** with a palladium catalyst.[2] The 1,2-addition to carbonyl compounds afforded secondary alcohols **11**[2f] or **12**[2g] in the presence of LiTMP or AgOAc.

Finally, we successfully applied this *gem*-diboronate building block in the synthesis of the approved drugs Sertaconazole **15** and Dronedarone **18** and also utilized in the synthesis of the polymer **19**. Our synthetic building block **3at** undergo oxidation, chlorination of the hetero-benzylic alcohol and nucleophilic substitution in the presence of a base, to afford the approved drug **15** in good yields (Fig. 2D). The approved drug **18** could be accessed from *gem*-diboronates **3ap** by oxidation to the aldehyde **16** and a subsequent 1,2-carbonyl addition to afford secondary alcohol **17** and a final PCC oxidation. Polymer **19** has been successfully synthesized by a cross-coupling reaction with the number-average weight (M_n) being 2155 g mol^{-1} and the polydispersity (Đ) being 1.7.
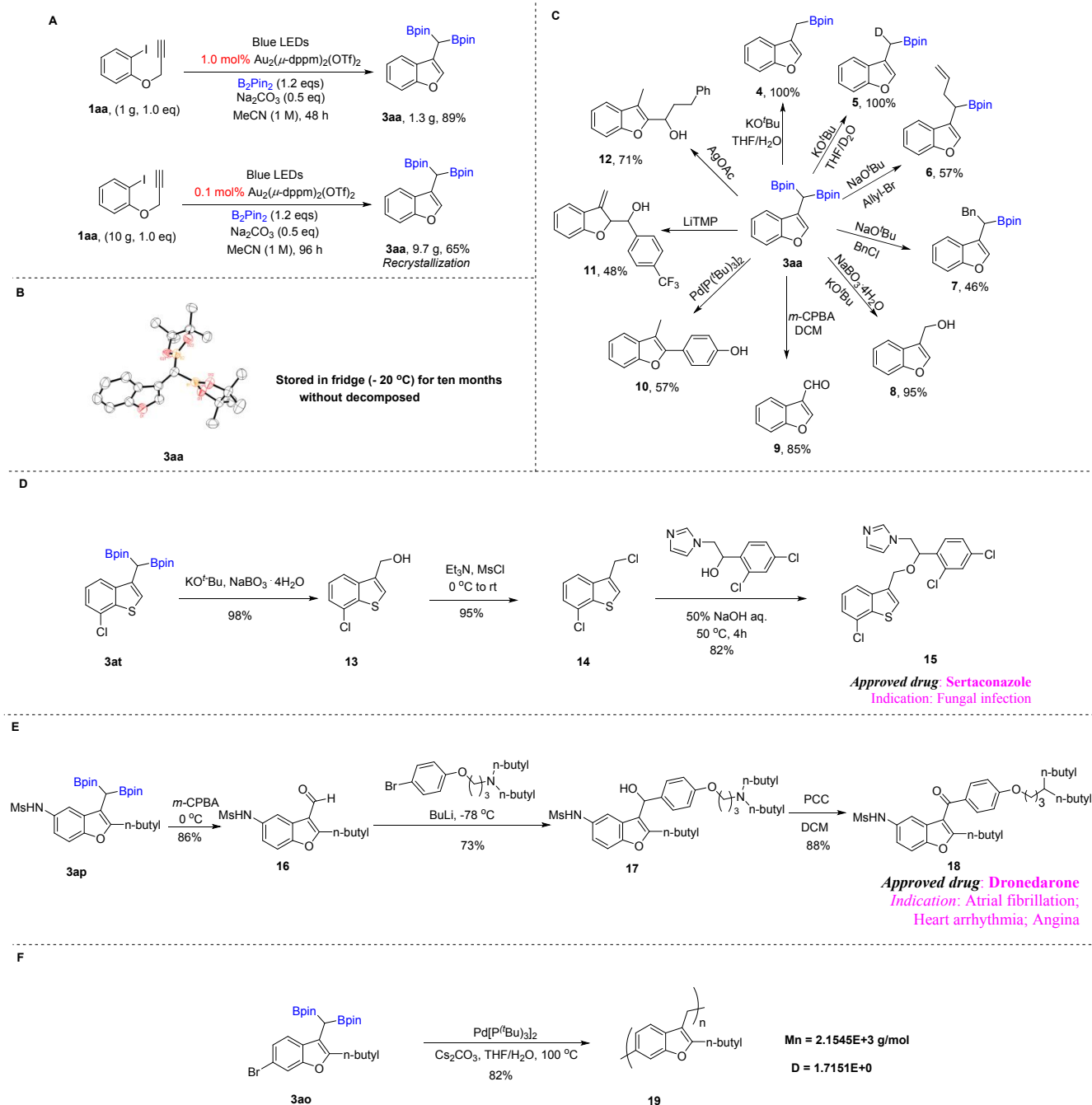
Figure 2. Applications. **A**: Gram scale synthesis; **B**: X-ray structure of **3aa**; **C**: Versatile transformations; **D**: Synthesis of approved drug **Sertaconazole**; **E**: Synthesis of approved drug **Dronedaron**; **F**: Polymer synthesis.

After exploration of the reaction scope and demonstrating the synthetic value of the products, we turned to mechanistic studies. First, we tried to explore the nature of the real photocatalysts in this transformation. Both $[Au_2(\mu\text{-}dppm)_2](OTf)_2$ and aryl iodides show no absorption in the blue LEDs' emission wavelength (410-490 nm, λ_{max} = 465 nm). According to our ^{31}P NMR detection, a new gold complex was formed by the combination of $[Au_2(\mu\text{-}dppm)_2](OTf)_2$ and Na_2CO_3 (Figure 3). This newly formed gold complex shows a red shift of the absorption wavelength, overlapping with the emission wavelength of the blue LEDs light. This newly formed gold complex shows similar UV-vis absorption wavelengths and ^{31}P NMR characteristic peaks including chemical shifts and signal multiplicities compare with the signals detected in the reaction mixture. At this moment, we propose that this new gold complexes could be resulted from an aggregation of $[Au_2(\mu\text{-}dppm)_2](OTf)_2$ in the presence of Na_2CO_3. A triplet and a multiple peaks are observed in the ^{31}P NMR rather than a singlet peak, and the $[Au_2(\mu\text{-}dppm)_2](OTf)_2$ catalyst can be recovered from this newly formed gold complex after evaporating the CD_3CN and dissolving in $CDCl_3$ (as detected by ^{31}P NMR, see SI).

(A₁)   (A₂)
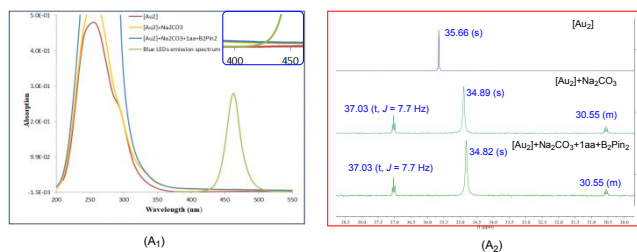
Figure 3. The nature of the real photocatalysts or photosensitizers. (A$_1$) All of samples are measured in MeCN with 0.01 mM concentration. See details in SI; (A$_2$) ^{31}P NMR spectra are measured in CD$_3$CN.

The reaction has been operated in the presence of radical inhibitors (Scheme 3A), no desired product was formed in the presence of TEMPO and a decreased yield (53%) was observed with 1,9-dihydroanthracene (DHA), which suggested a radical pathway. Besides, in the absence of B$_2$Pin$_2$, aryl iodides **1aa** has been converted to vinyl iodide **20** in 92% yield (Scheme 3B) which indicates that B$_2$Pin$_2$ does not play any role for the formation of aryl radical from aryl iodides. Taking UV−vis absorption, ^{31}P NMR peaks and our control experiments into account, we propose the merging of [Au$_2$(μ-dppm)$_2$](OTf)$_2$ with Na$_2$CO$_3$ is directly responsible for the initiation of this photoreaction under blue LEDs light irradiation. Attempts to isolate this species failed, suggesting the complex maybe only exist in solution. More interestingly, in the presence or absence of B$_2$Pin$_2$, only carbo-cyclization/iodination product **22** has been formed in the case of aryl iodide **21**. Even through the presence of B$_2$Pin$_2$ could slight increase the efficiency of this transformation, no detectable borylation product **23** was formed, which obviously is inconsistent with previous reports[17] for an SET process. Besides, , aryl radical should also be produced from aryl bromides if SET process is really proceeded in our reaction because the inner-sphere oxidation quenching (exciplex) pathway have no limitation of redox potentials,[11,12] however aryl bromide results in no conversion. And the possibility by going through atom transfer radical cyclization (ATRC) process could also be ruled out because of the bond dissociation energy,[7b,18] an alkyl radical cannot abstract an iodine atom from an aryl iodide. And also our quantum yield results (Φ= 35% for cyclization/*gem*-diborylation; Φ = 34% for carbo cyclization/iodination, see SI) indicate that this transformation is not radical chain process dominated.

Scheme 3. Radical trapping experiments and ruling out the possibility of involving SET or ATRC radical chain processes
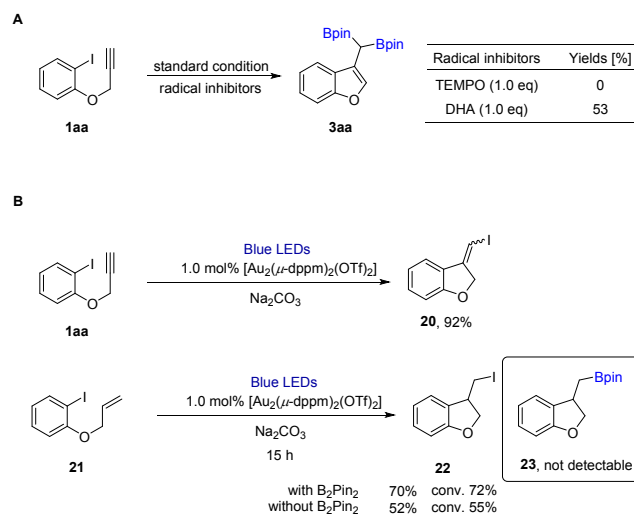
In addition of going through photoredox catalysis and photoinitiation, we now considered the possibility to EnT process. The direct excitation experiment with UV light (254 nm), which are often used to indicate if excited (triplet) state intermediates are indeed present in the reaction mechanism,[9,19] shown the possibility of an EnT process. As shown in Scheme 4A, direct photoexcitation of aryl iodide **21** under UV light irradiation in the absence of gold catalyst also gave only carbo-iodination product **22**, but less efficiently. And also direct photoexcitation of aryl iodide **1aa** generated the desired cyclization/*gem*-diborylation product **3aa** in 30% yield after extending the reaction time to 72 h (Scheme 4B). It is well known that the ground state of aryl iodides could be converted to the photoexcited triplet state by UV light,[7,8] exothermically homolytic cleavage of aryl C-I bond affords aryl free radical and iodo free radical, resulting cyclization iodination products.
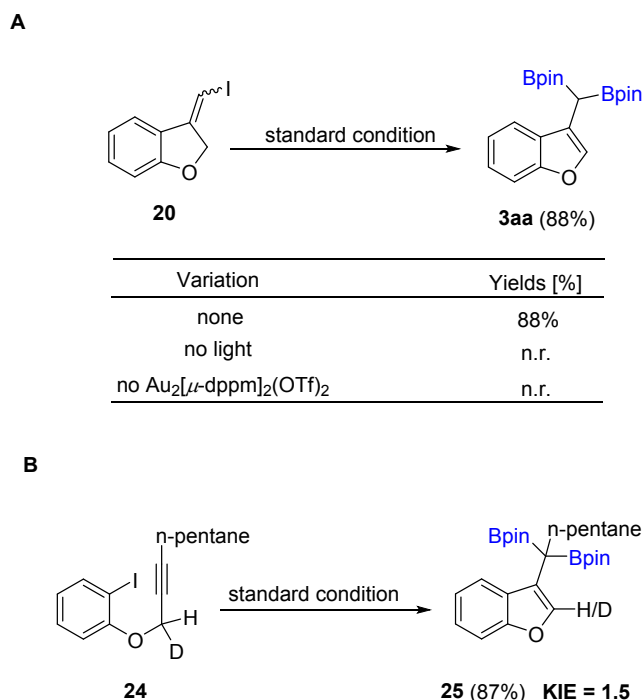
Scheme 4. Direct excitation experiments
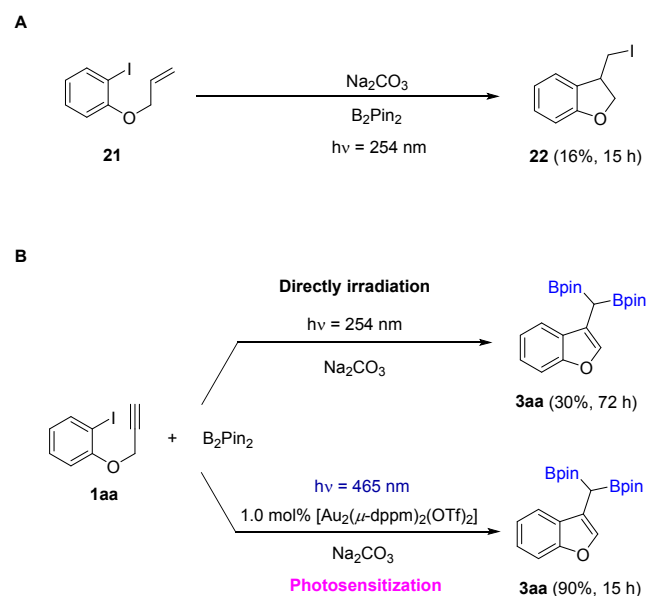
Furthermore, vinyl iodide has been converted to the desired product by our standard condition (Scheme 5A), without light or gold catalysts result no conversion which indicates that

further photoexcitation of vinyl iodide is involved and the dehydroborylation step occurred after the cyclization step. The KIE value observed in Scheme 5B, indicate that dehydrogenation is not involved in rate-determination step (the degree of deuteration of **24** is more than 99%).

Scheme 5. Cyclization/gem-diborylation of vinyl iodide and kinetic isotopic effect measurement

Figure 4. Proposed mechanism

CONCLUSIONS

In conclusion, this protocol presents a significant advance in the field of carbo-cyclization/borylation of alkynes through energy transfer pathway under visible light irradiation. The synthetically useful protocol provides a variety of *gem*-diboronates, which not only can act as highly functionalized substrates for methodology research, but also as useful building blocks which simplify the synthesis of relevant approved drugs and accelerate the process of discovering new drugs or polymers.

ASSOCIATED CONTENT

The supporting information is available free of charge via the Internet at http://pubs.acs.org.
Experimental procedures and compound characterization (PDF)
Accession Code
CCDC 1991449 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via https://www.ccdc.cam.ac.uk/structures/.

Taking all these results together, a possible mechanism cycle have been proposed (Fig. 4). The combination of $[Au_2(\mu\text{-}dppm)_2](OTf)_2$ with Na_2CO_3 in acetonitrile provides a new gold complex. After photoexcitation, the aryl iodide leads to photoexcited triplet state through energy-transfer process (EnT) with newly formed gold complex (Fig. 4A), followed by homolytic cleavage aryl-I bond and resulting aryl free radical and iodo free radical. The resulting aryl radical **27** goes through 5-*exo*-cyclization with high regio-selectivity affording vinyl radical **28 (**Fig. 4B**)**, followed by radical-radical combination leading to vinyl iodide **20**, which can be converted to vinyl radical **28** again by further photosensitization (Fig.4C)**.** The vinyl radical **28** could be trapped by the ate-complex **29** resulting to vinyl boronate **30** and **31**.[20] Then the desired produce can be accessed by electrophilic borylation of vinyl boronate **29** with Bpin-I or Bpin-OCO$_2$Na, resulting the stabilized benzyl cation **32**, followed by rapidly β-H elimination. The intermediate vinyl iodide **20** has been detected during the reaction and also been isolated. The intermediate vinyl boronate **30** is very unstable and we have failed to isolate it, however around 8% yield of compound **4** has been isolated after quenching the reaction mixture.[21]
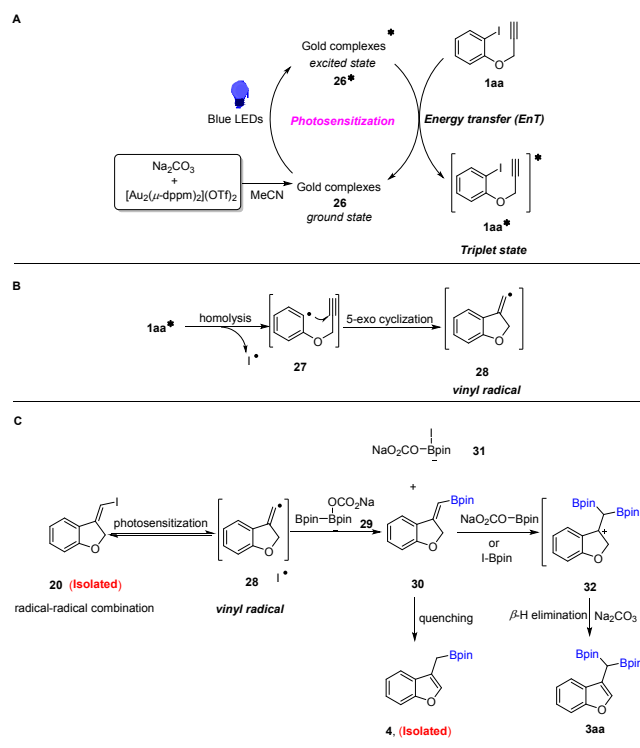
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Author Contributions

All authors have given approval to the final version of the manuscript. / ‡These authors contributed equally.

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REFERENCES

(1) Recent reviews on *gem*-diboronates, see: (a) Nallagonda, R.; Padala, K.; Masarwa, A. *gem*-Diborylalkanes: recent advances in their preparation, transformation and application. *Org. Biomol. Chem.* **2018**, *16*, 1050. (b) Wu, C.; Wang, J. Geminal bis(boron) compounds: Their preparation and synthetic applications. *Tetrahedron Lett.* **2018**, *59*, 2128. (c) Miralles, N.; Maza, R. J.; Fernández, E. Synthesis and reactivity of 1,1-diborylalkanes towards C–C bond formation and related mechanisms. *Adv. Synth. Catal.* **2018**, *360*, 1306.

(2) Selected articles for cross-coupling reactions, see: (a) Endo, K.; Ohkubo, T.; Hirokami, M.; Shibata, T. Chemoselective and regiospecific suzuki coupling on a multisubstituted sp³-carbon in 1,1-diborylalkanes at room temperature. *J. Am. Chem. Soc.* **2010**, *132*, 11033. (b) Endo, K.; Ohkubo, T.; Shibata, T. Chemoselective suzuki coupling of diborylmethane for facile synthesis of benzylboronates. *Org. Lett.* **2011**, *13*, 3368; (c) Endo, K.; Ohkubo, T.; Ishioka, T.; Shibata, T. Cross coupling between sp³-carbon and sp³-carbon using a diborylmethane derivative at room temperature. *J. Org. Chem.* **2012**, *77*, 4826. (d) Cho, S. H.; Hartwig, J. F. Iridium-catalyzed diborylation of benzylic C–H bonds directed by a hydrosilyl group: synthesis of 1,1-benzyldiboronate esters. *Chem. Sci.* **2014**, *5*, 694. (e) Li, H.; Zhang, Z.; Shangguan, X.; Huang, S.; Chen, J.; Zhang, Y.; Wang, J. Palladium(0)‐catalyzed cross‐coupling of 1,1‐diboronates with vinyl bromides and 1,1‐dibromoalkenes. *Angew. Chem. Int. Ed.* **2014**, *53*, 11921. (f) Endo, K.; Hirokami, M.; Shibata, T. Stereoselective synthesis of tetrasubstituted alkenylboronates via 1,1-organodiboronates. *J. Org. Chem.* **2010**, *75*, 3469. (g) Joannou, M. V.; Moyer, B. S.; Goldfogel, M. J.; Meek, S. J. Silver(I)-catalyzed diastereoselective synthesis of anti-1,2 hydroxyboronates. *Angew. Chem. Int. Ed.* **2015**, *54*, 14141.

(3) For selected articles for functional-groups conversion and asymmetric synthesis, see: (a) Potter, B.; Edelstein, E. K.; Morken J. P. Modular, Catalytic enantioselective construction of quaternary carbon stereocenters by sequential cross-coupling reactions. *Org. Lett.* **2016**, *18*, 3286. (b) Shimizu, M.; Schelper, M.; Nagao, I.; Shimono, K.; Kurahashi, T.; Hiyama, T. Synthesis and applications of 1,1-diborylated cyclopropanes: facile route to 1,2-Diboryl-3-methylenecyclopentenes. *Chem. Lett.* **2006**, *35*, 1222. (c) Lee, Y.; Baek, S.-y.; Park, J.; Kim, S.-T.; Tussupbayev, S.; Kim, J.; Baik, M.-H.; Cho, S. H. Chemoselective coupling of 1,1-Bis[(pinacolato)boryl]alkanes for the transition-metal-free borylation of aryl and vinyl Halides: a combined experimental and theoretical investigation. *J. Am. Chem. Soc.* **2017**, *139*, 976. (d) Potter, B.; Szymaniak, A. A.; Edelstein, E. K.; Morken, J. P. Nonracemic allylic boronates through enantiotopic-group-selective cross-coupling of geminal bis(boronates) and vinyl halides. *J. Am. Chem. Soc.* **2014**, *136*, 17918. (e) Liu, X.; Deaton, T. M.; Haeffner, F.; Morken, J. P. A boron alkylidene–alkene cycloaddition reaction: application to the synthesis of aphanamal. *Angew. Chem. Int. Ed.* **2017**, *56*, 11485. (f) Hong, K.; Liu, X.; Morken, J. P. Simple access to elusive *α*-boryl carbanions and their alkylation: an umpolung construction for organic synthesis. *J. Am. Chem. Soc.* **2014**, *136*, 10581.

(4) Selected methods for preparing *gem*-diboronates: (a) Matteson, D. S.; Moody, R. J. Deprotonation of 1,1-diboronic esters and reactions of the carbanions with alkyl halides and carbonyl compounds. *Organometallics* **1982**, *1*, 20. (b) Endo, K.; Hirokami, M.; Shibata, T. Synthesis of 1,1-organodiboronates via Rh(I)Cl-catalyzed sequential regioselective hydroboration of 1-alkynes. *Synlett* **2009**, 1331; (c) Ito, H.; Kubota, K. Copper(I)-catalyzed boryl substitution of unactivated alkyl halides. *Org. Lett.* **2012**, *14*, 890. (d) Li, H.; Wang, L.; Zhang, Y.; Wang, J. Transition‐metal‐free synthesis of pinacol alkylboronates from tosylhydrazones. *Angew. Chem., Int. Ed.* **2012**, *51*, 2943. (e) Li, H.; Shangguan, X.; Zhang, Z.; Huang, S.; Zhang, Y.; Wang, J. Formal carbon insertion of N-tosylhydrazone into B–B and B–Si bonds: *gem*-diborylation and *gem*-silylborylation of sp³ carbon. *Org. Lett.* **2014**, *16*, 448. (f) Hong, K.; Liu, X.; Morken, J. P. Simple access to elusive *α*-boryl carbanions and their alkylation: an umpolung construction for organic synthesis. *J. Am. Chem. Soc.* **2014**, *136*, 10581. (g) Wommack, A. J.; Kingsbury, J. S. On the scope of the Pt-catalyzed Srebnik diborylation of diazoalkanes. An efficient approach to chiral tertiary boronic esters and alcohols via B-stabilized carbanions. *Tetrahedron Lett.* **2014**, *55*, 3163. (h) Palmer, W. N.; Obligacion, J. V.; Pappas, I.; Chirik, P. J. Cobalt-catalyzed benzylic borylation: enabling polyborylation and functionalization of remote, unactivated C(sp³)–H bonds. *J. Am. Chem. Soc.* **2016**, *138*, 766. (i) Palmer, W. N.; Zarate, C. P.; Chirik, J. Benzyltriboronates: building blocks for diastereoselective carbon–carbon bond formation. *J. Am. Chem. Soc.* **2017**, *139*, 2589.

(5) Lhermet, R.; Ahmad, M.; Fressign, C.; Silvi, B.; Durandetti, M.; Maddaluno, J. Carbolithiation of chloro‐substituted alkynes: a new access to vinyl carbenoids. *Chem. Eur. J.* **2014**, *20*, 10249.

(6) Komeyama, K.; Kiguchi, S.; Takaki, K. The drastic effect of cobalt and chromium catalysts in the borylation of arylzinc reagents. *Chem. Commun.* **2016**, *52*, 7009.

(7) (a) Suzuki, Y.; Okita, Y.; Morita, T.; Yoshimi, Y. An approach to the synthesis of naphtho[b]furans from allyl bromonaphthyl ethers employing sequential photoinduced radical cyclization and dehydrohalogenation reactions. *Tetrahedron Lett.* **2014**, *55*, 3355. (b) Hartmann, M.; Studer, A. Cyclizing radical carboiodination, carbotelluration, and carboaminoxylation of aryl amines. *Angew. Chem. Int. Ed.* **2014**, *53*, 8180. (c) Bhandal, H.; Patel, V. F.; Pattenden, G.; Russell, J. J. Cobalt-mediated radical reactions in organic synthesis. Oxidative cyclisations of aryl and alkyl halides leading to functionalised reduced heterocycles and butyrolactones. *J. Chem. Soc. Perkin Trans.* **1990**, *1*, 2691. (d) Koziakov, D., Majek, M.; von Wangelin, A. J. Metal-free radical thiolations mediated by very weak bases. *Org. Biomol. Chem.* **2016**, *14*, 11347. (e) Beckwith, A. L. Regio-selectivity and stereo-selectivity in radical reactions. *Tetrahedron*, **1981**, *37*, 3073; (f) Giese, B.; Kopping, B.; Göbel, T.; Dickhaut, J.; Thoma, G.; Kulicke, K. J.; Trach, F. Radical cyclization reactions. *Organic Reactions*, **1996**.

(8) Qiu, G.; Lib, Y.; Wu, J. Recent developments for the photoinduced Ar–X bond dissociation reaction. *Org. Chem. Front.* **2016**, *3*, 1011.

(9) (a) Strieth-Kalthoff, F.; James, M. J.; Teders, M.; Pitzer, L.; Glorius, F. Energy transfer catalysis mediated by visible light: principles, applications, directions. *Chemical Society Reviews*, **2018**, *47*, 7190. (b) Pagire, S. K.; Föll, T.; Reiser, O. Shining visible light on vinyl halides: expanding the horizons of photocatalysis. *Acc. Chem. Res.* **2020**, *53*, 782.

(10) (a) Skubi, K. L.; Blum, T. R.; Yoon, T. P. Dual catalysis strategies in photochemical synthesis. *Chem. Rev.* **2016**, *116*, 10035. (b) Romero, N. A.; Nicewicz, D. A. Organic photoredox catalysis. *Chem. Rev.* **2016**, *116*, 10075. (c) Shaw, M. H.; Twilton, J.; MacMillan, D. W. C. Photoredox catalysis in organic chemistry. *J. Org. Chem.* **2016**, *81*, 6898. (d) Hopkinson, M. N.; Tlahuext-Aca, A.; Glorius, F. Merging visible light photoredox and gold catalysis. *Acc. Chem. Res.* **2016**, *49*, 2261. (d) Twilton, J.; Le, C. C.; Zhang, P.; Shaw, M. H.; Evans, R. W.; MacMillan, D. W. C. The merger of transition metal and photocatalysis. *Nat. Rev. Chem.* **2017**, *1*, 52. (e) Xie, J.; Jin, H. M.; Hashmi, A. S. K. The recent achievements of redox-neutral radical C–C cross-coupling enabled by visible-light. *Chem. Soc. Rev.* **2017**, *46*, 5193. (f) Xu, W.; Ma, J.; Yuan, X.; Dai, J.; Xie, J.; Zhu, C. Synergistic catalysis for the umpolung trifluoromethylthiolation of tertiary ethers. *Angew. Chem. Int. Ed.* **2018**, *57*, 10357. (g) Li, W.; Xu, W.; Xie, J.; Yu, S.; Zhu, C. Distal radical migration strategy: an emerging synthetic means. *Chem. Soc. Rev.* **2018**, *47*, 654.

(11) For selected articles in recent years in the field of photochemistry: (a) Xie, J.; Rudolph, M.; Rominger, F.; Hashmi, A. S. K. Photoredox‐controlled mono‐ and di‐multifluoroarylation of C(sp³)−H bonds with aryl fluorides. *Angew. Chem., Int. Ed.* **2017**,

56, 7266; (b) Xie, J.; Sekine, K.; Witzel, S.; Krämer, P.; Rudolph, M.; Rominger, F.; Hashmi, A. S. K. Light‐induced gold‐catalyzed Hiyama arylation: a coupling access to biarylboronates. *Angew. Chem., Int. Ed.* **2018**, *57*, 16648. (c) Zhang, L.; Si, X.; Yang, Y.; Zimmer, M.; Witzel, S.; Sekine, K.; Rudolph, M.; Hashmi, A. S. K. The Combination of benzaldehyde and nickel‐catalyzed photoredox C(sp³)−H alkylation/arylation. *Angew. Chem., Int. Ed.* **2019**, *58*, 1823. (d) Si, X.; Zhang, L.; Hashmi, A. S. K. Benzaldehyde- and nickel-Catalyzed photoredox C(sp³)–H alkylation/arylation with amides and thioethers. *Org. Lett.* **2019**, *21*, 6329.

(12) (a) Ma, C.; Chan, C. T. L.; To, W. P.; Kwok, W. M.; Che, C. M. Deciphering photoluminescence dynamics and reactivity of the luminescent metal‐metal‐bonded excited state of a binuclear gold(I) phosphine complex containing open coordination sites. *Chem. Eur. J.* **2015**, *21*, 13888. (b) McCallum, T.; Rohe, S.; Barriault, L. Thieme chemistry journals awardees – where are they now? what's golden: recent advances in organic transformations using photoredox gold catalysis. *Synlett* **2017**, *28*, 289; (c) Zidan, M.; Rohe, S.; McCallum, T.; Barriault, L. Recent advances in mono and binuclear gold photoredox catalysis. *Catal. Sci. Technol.* **2018**, *8*, 6019.

(13) Zhang, L.; Si, X.; Yang, Y.; Witzel, S.; Sekine, K.; Rudolph, M.; Rominger, F.; Hashmi, A. S. K. Reductive C–C coupling by desulfurizing gold-catalyzed photoreactions. *ACS Catal.* **2019,** *9*, 6118.

(14) Farney, E. P.; Chapman, S. J.; Swords, W. B.; Torelli, M. D.; Hamers, R. J.; Yoon, T. P. Discovery and elucidation of counteranion dependence in photoredox catalysis. *J. Am. Chem. Soc.* **2019***, 141*, 6385.

(15) (a) King, C.; Khan, M. N.; Staples, R. J.; Fackler Jr, J. P. Luminescent mononuclear gold(I) phosphines. *Inorg. Chem.* **1992**, *31*, 3236. (b) Sinha, P.; Wilson, A. K.; Omary, M. A. Beyond a T-shape. *J. Am. Chem. Soc.* **2005**, *127*, 12488. (c) Gimeno, M. C.; Laguna, A. Three- and four-coordinate gold(I) complexes. *Chem. Rev.* **1997**, *97*, 511.

(16) (a) Zakaria, H. M.; Shah, A.; Konieczny, M.; Hoffmann, J. A.; Nijdam, A. J.; Reeves, M. E. Small molecule- and amino acid-induced aggregation of gold nanoparticles. *Langmuir*, **2013**, *29*, 7661. (b) Amendola, V.; Meneghetti, M. Size evaluation of gold nanoparticles by UV−vis spectroscopy. *J. Phys. Chem. C* **2009**, *113*, 4277. (c) Haiss, W.; Thanh, N. T. K.; Aveyard, J.; Fernig, D. G. Determination of size and concentration of gold nanoparticles from UV−Vis spectra. *Anal. Chem.* **2007**, *79*, 4215. (d) Murphy, C. J.; Sau, T. K.; Gole, A. M.; Orendorff, C. J.; Gao, J.; Gou, L.; Hunyadi, S. E.; Li, T. Anisotropic metal nanoparticles: synthesis, assembly, and optical applications. *J. Phys. Chem. B* **2005**, *109*, 13857. (e) Link, S.; El-Sayed, M. A. Shape and size dependence of radiative, non-radiative and photothermal properties of gold nanocrystals. *Int. Rev. Phys. Chem.* **2000**, *19*, 409. (f) Kreibig, U.; Vollmer, M. Optical properties of metal clusters. Springer Science & Business Media. **2013**, *25*.

(17) Nitelet, A.; Thevenet, D.; Schiavi, B.; Hardouin, C.; Fournier, J.; Tamion, R.; Pannecoucke, X.; Jubault, P.; Poisson, T. Copper-photocatalyzed borylation of organic halides under batch and continuous-flow conditions. *Chem. Eur. J.* **2019**, *25*, 3262.
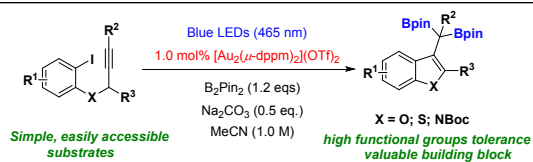
(18) Li, C. in Encyclopedia of Radicals in Chemistry, Biology and Materials, Vol. 2 (Eds.: C. Chatgilialoglu, A. Studer), Wiley, Chichester **2012**, *943*.

(19) (a) Welin, E. R.; Le, C.; Arias-Rotondo, D. M.; McCusker, J. K.; MacMillan, D. W. Photosensitized, energy transfer-mediated organometallic catalysis through electronically excited nickel(II). *Science*, **2017**, *355*, 380. (b) Hurtley, A. E.; Lu, Z.; Yoon, T. P. [2+2] Cycloaddition of 1,3‐dienes by visible light photocatalysis. *Angew. Chem., Int. Ed.* **2014**, *53*, 8991.

(20) Friese, F. W.; Studer, A. New avenues for C–B bond formation via radical intermediates. *Chem. Sci.* **2019**, *10*, 8503.

(21) Our control experiment by reacting product **3aa** in our standard condition in the absence of light gave no **4**, which indicated

that **4** does not result from **3aa** and intermediate **29** may be involved during the reaction.

Blue LEDs (465 nm)

1.0 mol% [Au$_2$(μ-dppm)$_2$](OTf)$_2$

B$_2$Pin$_2$ (1.2 eqs)

Na$_2$CO$_3$ (0.5 eq.)

MeCN (1.0 M)

Simple, easily accessible substrates

X = O; S; NBoc

high functional groups tolerance valuable building block

Scope: 24 examples, 60-90% yields

Application:

Mechanistic studies: energy transfer

10 grams synthesis
9 transformations
2 approved drugs
1 polymer