
REVIEWER REPORT

EVALUATION:

Reviewer's Responses to Questions

1. Please rate the importance of the reported results

Reviewer #1: Important

Reviewer #2: Highly important (top 20%)

Reviewer #3: Highly important (top 20%)

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2. Please rate the citation of previous publications

Reviewer #1: Insufficient

Reviewer #2: Appropriate

Reviewer #3: Appropriate

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3. Please rate the length of the manuscript

Reviewer #1: Concise

Reviewer #2: Concise

Reviewer #3: Concise

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4. Please rate the verification of hypotheses and conclusions by the presented data

Reviewer #1: Major inconsistencies

Reviewer #2: Fully consistent

Reviewer #3: Major inconsistencies

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5. Please indicate which other journal you consider more appropriate

Reviewer #1: (No Response)

Reviewer #2: (No Response)

Reviewer #3:
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COMMENTS TO AUTHOR:

Reviewer 1: This manuscript from Liu, Wu and co-workers reports the use of BBr3/Hunig's base combinations for the hydroboration of alkenes and alkynes. The selective hydroboration of terminal alkenes and alkynes is a solved challenge (and the methodology reported herein looks to have less FG tolerance compared to other systems), so that section is not of ACIE quality. Thus the most notable sections are the regioselective hydroboration of internal alkenes and the proposed radical FLP mechanism. Regarding the former, the introduction is not quite correct, there are reports for selective metal catalysed hydroboration of internal alkenes using Rh and Ni complexes (see: Tetrahedron Letters, Vol. 37, No. 19, pp. 3283-3286, 1996 for example). While BBr3 is preferable to Rh/Ni based catalysts from certain perspectives, the scope with BBr3 is always going to be restricted due to the significant Lewis acidity of this reagent. Linked to this, for internal alkenes the functional group
tolerance should be demonstrated to some extent using BBr3/amine, e.g. with groups like CF3, SMe. Often in reactions with BX3 the tolerance of functional groups is a question of the relative rate of reaction of BX3 with the pi system versus with the functional group, thus similar functional group tolerance for terminal versus internal substrates cannot be assumed.

This leaves the final point the unusual proposed mechanism, this in my

opinion is not proven, with the control reactions far from conclusive. Firstly, the addition of oxo-based radicals to BBr3 is inconclusive as the strongly oxophilic BBr3 reacts with these radicals to give diamagnetic species (as per: Eur. J. Inorg. Chem. 2013, 3817-3820 which has to be referenced in this study as they explain why no radical is seen with BBr3 + TEMPO). The DHA chemistry may indicate radicals, but other possibilities can be put forward - what is seen in this reaction? Is ethylbenzene formed? Or is starting material left unchanged? (BBr3 interaction with the alkene can form a carbocationic type species which could abstract hydride from DHA forming a strong Bronsted acid which then does protodeboronation leading to ethylbenzenes). The use of cyclopropane ring opening as confirmation of radicals also has to be interpreted with care as BBr3 is known to open cyclopropanes with no radicals
involved (see: Angew. Chem. Int. Ed. 2018, 57, 16861). Indeed if radicals were involved it maybe expected to see some bromine incorporation into some of the products (see: Chem. Sci., 2020,11, 9426, unless E2 elimination proceeds and the alkene is reformed - are any brominated minor products observed?). Thus I am not convinced by a radical "FLP" mechanism (the HOMO and LUMO energies of the FLP components. BBr3 and NR3 are completely wrong for electron transfer). The recent work of Slootweg et al. on radical FLPs (cited in this work) indicates radical FLP chemistry is often photon mediated, so is there any change in conversion when the reactions are performed in the dark. If not then this is a closed shell mechanism in my opinion. For example, boron and carbon Lewis acids are well documented to abstract hydride from amines like Hunigs base (see ref 17 for a review), thus one other possible mechanism is interaction of BBr3 with the pi system which makes a carbon electrophile
that abstracts hydride from the amine to form an iminium cation. Looking at the SI, the 11B spectra of BBr3 + Hunigs base is v. interesting, can the 11B{1H} be run, are there any B-H species in there (there looks to be some multiplicity in some of those boron resonances indicating B-H species)? The presence of B-H species in Fig S8 is even clearer - thus a Matteson type hydroboration with HBBr2 is still possible, with isomerization precluded by the base sequestering any Brønsted acid impurities that are often responsible for isomerisation of alkenes. Thus with this mechanistic uncertainty, plus the limited functional group tolerance this paper is not suited for publication in ACIE.

Minor comments

In scheme 3 there is a change between reporting the yield with respect to the alkene, and then reporting the yield with respect to BBr3. This is confusing, also why is excess alkene required for five of those substrates? For 2ck to 2cn you state regioselective hydroboration, but 2 of the substrates are not

regioselective (assuming the 75:25 in parenthesis refers to selectivity), thus terminology should be altered.

Reviewer 2: The paper by Wu describes hydroboration of alkenes with BX3 as the boration reagent in the presence of iPr2NEt. The major advance here is the exclusive installation of a boron group at the original double-bond position of internal alkenes. This hydroboration of internal alkynes with transition-metal catalysts would be difficult due to the double-bond isomerization. Studies on the mechanism as well as detailed DFT calculations suggested a reaction pathway that operate through FLP-type single-electron transfer mechanism. This is interesting and useful. Therefore, I believe that minor revisions are necessary before publishing in ACIE is recommended.
1) The transformation presented affords the products in only moderate yields. I am sure the authors tried to improve the yields, but an explanation for the low yields is required. Moreover, an explanation on any other side product formation will be helpful.
2) The alkynes mainly limited to simple hydrocarbons. The authors should show the alkenes with functional groups such carbonyls or amines.

Reviewer 3: The manuscript by Li et al. reports the application of halo boranes in combination of Huenig's base to trigger the hydroboration of alkenes. After quenching with diols or diamines, the corresponding boronates are obtained in good to excellent yields. This reactivity is unique and certainly worth for publication in Angew. Chem.
The authors spend some time on the demonstration of the substrate scope and also on mechanistic studies, which provide mostly a coherent picture. However, there are some issues, which need to be adressed.
1) Substrate scope: the exploration of the substrate scope should not only be a mere accumulation of molecules but it should show the limits of the method. I cannot understand why the authors wast their time with making 50 examples of which only 6 bear a functinal group (1 indole, 3 thioether, 2 aliphatic bromides). The authors disclose only 3 functional groups! What about ester, nitro, amines, imines, aldehydes, ketones ...? If the reaction only works for unfunctionalized olefins (as the authors show 6 out of 50 functionalized examples, 12%), this needs to be addressed. Furthermore, the authors then need to revise the introductory part, in which they citicizes the lack of functional group tolerance of other methods.
2) Hammett plot, data in Supporting Info: As evidenced form the SI, the authors deterined the rate of the reaction by using two point: the starting point, 0% product and after 1h. Firstly, to deduce rate constants form a two-

point plot is scientifically unacceptable. Secondly, each rate measurement should be reproduced at least three times. This would also allow a minimum of error treatment. Otherwise the data and the Hammett-plot in the manuscript is bare of any meaning.

Alfter these issues have been addressed, the manuscript may be reconsidered by Angew. Chem. for publication.