

REVIEWER REPORTS

EVALUATION:

Reviewer's Responses to Questions

1. Please rate the importance of the reported results

Reviewer #1: Important

Reviewer #2: Important

2. Please rate the citation of previous publications

Reviewer #1: Appropriate

Reviewer #2: Appropriate

3. Please rate the length of the manuscript

Reviewer #1: Concise

Reviewer #2: Concise

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

Reviewer #1: Minor inconsistencies

Reviewer #2: Fully consistent

5. Please indicate which other journal you consider more appropriate

Reviewer #1:

- Chemistry—A European Journal

Reviewer #2:

- Chemistry—A European Journal

6. Please indicate whether you have included attachments

Reviewer #1:

- No

Reviewer #2:

- No
-

7. Please rate the quality of the Supporting Information

Reviewer #1: Insufficient or incomplete

Reviewer #2: Satisfactory

COMMENTS TO AUTHOR:

Reviewer 1: Liu, Wu, Stephan and co-workers report the stoichiometric reactions of alkoxyphosphorane and N-silyl compounds in the presence of $B(C_6F_5)_3$, yielding alkylation products. Since phosphonium is a proposed intermediate and phosphine oxide is generated as the byproduct, the authors manifest this reaction resembles the Mitsunobu reaction.

The initial finding is the formation of zwitterionic species (3a/3b) via the cleavage of the ring P-O bond rather than the exocyclic P-OR bond, to give the phosphonium with an alkoxy group. Although this conversion is nice, it might not be very challenging given Ramirez studied the open dipolar form of phosphorane. Compounds 2a/2b are neither experimentally observed nor computationally explored, and the description in Scheme 1 as if they are in equilibrium is not proper.

Based on the mechanistic study (Fig 4), (3a) is a just resting state and the actual FLP parts to activate the Si-C bond consist of the O atom of (1a) and the B in $B(C_6F_5)_3$. Nevertheless, the sentence like '(Figure S67). This arrangement is an umpolung of the unquenched HOMO and LUMO orbitals seen in classic FLPs and suggested that these salts might also exhibit unique reactivity.' is very confusing. Or for the formation of (7, 8, Cl-Et, H-Et), the nucleophiles directly attack the phosphonium part in (3a)?

The Mitsunobu reaction is already established, the steric control; inversion of the carbon center in secondary alcohol is well studied, the catalytic versions are known, and a variety of nucleophiles are available. Contrary, the scope of the alkyl groups (Et, Bn) as well as nucleophiles are limited in this study, those ethylation products are gained in low to moderate yields, not really attractive in the synthetic community. I could not find the critical advantage of the present reaction, why are they needed to prepare by this method starting from the specific phosphorane?

Overall, although the basic mechanistic aspect is interesting, the impact and significance do not meet to merit publication on a first-rank platform, but it

would be suitable for a more specialised journal.

Additionally, the manuscript is not carefully prepared, it contains several errors, that should be fixed.

- ref 13, the author is only 'F. Ramirez'. Page-2, left line 4, Ramirez "et al." should be removed.
- Page 2, right line 54-57, '6 was isolated ~ Figure 3b', but Fig 3b shows (7).
- the caption of scheme 2, those are not only N-silyl compounds.
- remove a period "." before Scheme 1.
- Fig S22, the phase is not adjusted appropriately.
- Fig S24, the ¹³C peaks are too small.
- FigS32, what is the broad peak around 0 ppm?

Reviewer 2: Liu, Wu, Stephan and co-workers report a novel P/B frustrated Lewis pair (FLP) that enables the alkylation of N-heterocyclic carbenes (NHC) and silyl-based nucleophiles under formation of C-C, C-N, C-H and C-Cl bonds. Key to success is the combination of the boron Lewis acid B(C₆F₅)₃ with a P(V) alkoxyphosphorane bearing a perchlorinated catecholate ligand. DFT calculations revealed that a FLP activation mechanism is operative, forming an alkoxyphosphonium intermediate which acts as the alkylating agent akin to the Mitsunobu reaction.

Overall, this is a solid piece of work. The experimental work has been carried out carefully and the free energy profile of the reaction of the P/B-based FLP with trimethylsilyl cyanide (TMSCN) was calculated. The results are adequately documented in the Supporting Information. The molecular structures of all (!) compounds including zwitterions 3 and coupling products 4-10 were confirmed by X-ray diffraction analysis. This is clearly the strong part of this study. However, I do not think that the present work is suitable for publication in *Angewandte Chemie*. My concern is in a strict sense the usefulness/application and impact of this stoichiometric methodology. Moreover, the mechanism is solely based on computations, and no control experiments have been performed (see below). At the current stage, the study would be more suitable for publication in *Chemistry—A European Journal*.

Further comments and questions:

- 1) The authors state that the alkoxyphosphorane 1 alone does not react with TMSCN and that the addition of the Lewis acid B(C₆F₅)₃ is required. Did the authors also try other Lewis acids than B(C₆F₅)₃ (e.g., BF₃)?
- 2) Is perchlorination of the catechol ligand crucial for the alkylation reaction?
- 3) Have the authors tried a catalytic reaction by the addition of stoichiometric amounts of a methylating agent such as EtOTf? The authors themselves have indicated in Scheme 1 that "remethylation" of the phosphine oxide is feasible, but an explanation is missing.

4) According to the DFT calculations, the transfer of the alkyl group proceeds via a SN2 mechanism (see TS3). The stereochemistry could be verified experimentally.

Minor points:

- 1) Page 1, left column, line 43: Please replace "amides" by "N,N-bis-sulfonamides".
- 2) Page 1, left column, line 53: Please specify what is meant by "hydrosilylation of C-F bonds". I assume that it is hydrodefluorination with hydrosilanes?
- 3) Page 2, left column, line 8: "Ph₂P(OEt)(O₂C₆Cl₄) 1a was prepared in a fashion similar to that of previous reported for (C₆Cl₄O₂)P(OEt)₃[14] (Figure 2a)." It would be helpful to the reader if the authors could include the synthesis of 1a in Scheme 1.
- 4) Title of Scheme 1: Please replace "N-silyl compounds" by "NHC".
- 5) It would be helpful to the reader if the yields given in the Supporting Information are also provided in Schemes 1 and 2.