

Recommendation: Publish in JACS after minor revisions.

Comments:

This is a very interesting paper describing for the first time (to the best of my knowledge) the involvement of a cyclic (alkyl)(amino)carbene as a H shuttle.

This process is reminiscent of the observation that a CAAC-Cu-H rearranges by migration of the hydride to the carbene center (Chem. Asian J. 2011, 6, 402-405).

The scope of the reaction seems quite broad and specific to the nitro group, and consequently should attract a lot of attention from the synthetic community.

The work has been done very carefully, but English editing is absolutely necessary. Many sentences are awkward.

Additional Questions:

Significance: Highest (top 5%, suitable for JACS)

Novelty: Highest (top 5%, suitable for JACS)

Broad interest: Highest (top 5%, suitable for JACS)

Scholarly presentation: Moderate (not suitable for JACS)

Are the conclusions adequately supported by the data?: Yes

Are the literature references appropriate and correct?: Yes

Do the contents justify the length of this manuscript?: Yes

Recommendation: Publish in JACS after minor revisions.

Comments:

This manuscript by Zeng and coworkers reports a deoxy-hydroboration to generate anilines and alkyl amines. While this reaction is known under harsh conditions, Zeng and coworkers demonstrate that their catalyst works under very mild conditions.

Insights into the mechanism are also provided through kinetic and Hammett studies as well as *in silico* insights. The ligand used for the transformation is a bidentate ligand containing both CAAC and imino donors. The authors conclude that the unique donor properties of the ligand are somewhat responsible for the mild conditions by which this transformation proceeds. An extensive substrate scope is provided and displays excellent functional group tolerance, even tolerating commonly hydroborated or reduced functionalities such as alkynes and amides. A number of biologically relevant molecules are also synthesized in excellent yield, demonstrating the utility of the transformation.

One of my few critiques of this paper is the claims about the importance of the ligand. In the initial optimization table, NHCs, bisimino, and other CAAC ligands work comparably, certainly with optimizable yields (e.g. 78%). While the computational studies provide details into how the CAAC ligand could be enhancing the reactivity of the complexes, I think that insight into the ligand as a whole – the fact it is a CAAC, it is bidentate, etc must be considered. Perhaps additional studies on the impact of the poorer, albeit still good, donor properties of NHCs could enhance their argument and support their conclusions.

An additional study could be performed with different H–B reagents, such as H–Bcat, H–Bneo, etc to more carefully examine the impact of the hydricity of those bonds on the high reactivity.

One other small comment is that TS2 undergoes sigma bond metathesis. Citations about SBM at zero valent metals would be helpful to back up this claim. Many in the field would consider this mechanism to only proceed at electrophilic higher oxidation states (although I think the community is expanding its definition).

Overall, this paper is nearly flawless and would be of broad interest to the readership of JACS.

Additional Questions:

Significance: High (suitable for JACS)

Novelty: High (suitable for JACS)

Broad interest: High (suitable for JACS)

Scholarly presentation: Highest (top 5%, suitable for JACS)

Are the conclusions adequately supported by the data?: Yes

Are the literature references appropriate and correct?: Yes

Do the contents justify the length of this manuscript?: Yes

Recommendation: Publish elsewhere.

Comments:

Zeng and co-workers reported the reduction of nitro compounds to amines using HBpin catalyzed by Cr-homogeneous catalyst. Interestingly, the molecularly defined cyclic(alkyl)(amino)carbene ligated chromium complex has been prepared and its applicability for the Hydroboration of nitro compounds is demonstrated. In addition to the synthesis, the mechanistic investigations including DFT studies have been made.

Now the point, is it really requires so sophisticated homogeneous catalyst based on chromium for a simple and well-established reaction?

Next, why one wants to use HBpin as the reducing agent for a simple nitro reduction? There are number of Fe, Co, Ni catalysts are known to catalyze hydrogenation of nitro compounds including reduction with stoichiometric reductants.

Moreover, heterogeneous catalysts based on Fe, Co, Ni are well established for the both reduction and hydrogenation of nitro compounds. It's a general fact that heterogeneous catalysts are preferable over homogeneous complexes.

In general, the reduction using hydrogen (hydrogenation) is interesting but not with HBpin or silanes, which obviously produce large amounts of wastes. On standpoint of sustainable synthesis, HBpin is not a suitable reducing agent and that to a simple nitro reduction. Hydrogenation of nitro compounds is still interesting, but not the reduction with stoichiometric reducing agents.

Talking about chromium, how chromium is beneficial compared to Fe or Co or Mn or Ni?. Obviously, Cr is not advantageous over Fe or Co or Mn or Ni as catalyst. The homogeneous system, which require sophisticated/synthetically required special carbene ligands is not so demanding for nitro reduction.

Of-course, the design of Cr catalysts is interesting for more challenging reactions, but not for nitro reduction, for this reaction several catalysts are known, which for better and advantageous

than Cr. This work is not scientifically sounding with respect to both catalyst and synthetic applications.

Hence, this manuscript is not up to the level to publish in JACS or even ACS catalysis. It can be considered to publish in Journal of Organic Chemistry.

Additional Questions:

Significance: Lowest (not suitable for JACS)

Novelty: Lowest (not suitable for JACS)

Broad interest: Lowest (not suitable for JACS)

Scholarly presentation: Moderate (not suitable for JACS)

Are the conclusions adequately supported by the data?: Yes

Are the literature references appropriate and correct?: Yes

Do the contents justify the length of this manuscript?: Yes

Recommendation: Too preliminary for publication.

Comments:

Well, the catalytic conversion looks pretty interesting, particularly the selectivity for NO₂ versus a number of other functionalities.

The selectivity is confusing in some cases because HBpin and acids should react to form borates, which I suspect are being hydrolyzed back to acid form during workup. The authors should clarify that more HBpin is needed for those cases. In general, the stoichiometry is not specified for the HBpin reactant, and that also confuses the chemistry.

The identification of this Cr catalyst appears to be a significant advance.

It would be helpful for the authors to benchmark the selectivity in this system against typical nitro hydrogenation catalysts, which are pretty effective and well established.

The quality of the mechanistic work, in contrast, is extremely poor. The data shown in Figure 2(c) shows that there is an induction period, and then the authors use initial rates to examine the order in reactants. They are clearly not measuring anything corresponding to the active catalyst with initial rates, instead their results analyze an induction period.

In case there is further confusion about the quality of these data, the method described in the SI indicates they are only using single time-point yields to determine initial rates. This approach is extremely error prone, to the point of being a useless method (to study the wrong portion of the reaction!).

I don't see any meaningful value in the computational work either. No justification is given for reduction to Cr(0). The justification for a Cr-nitroso intermediate is that nitroso compounds may be reduced under catalytic conditions, which reduce nitro compounds; while a useful experiment, seems hardly compelling for assigning the structure of a Cr compound.

I also, generally, find it bizarre that a Cr(OH)₂-CAAC would not transfer a H to the carbene, but a Cr-H migrates? The only evidence for the claim of non-innocent behavior appears to be the calculation. The authors talk about reversing the polarity of the B-H bond, but that idea is poorly flushed out during calculation discussion.

In the context of the above questions (and many more), the scheme in Figure 3 is not informative. For example, the difference between TS1 and IN4 seems to be dotted vs solid lines?

To summarize, the authors have clearly made an advance, discovering and studying the substrates that can undergo nitro reduction by Cr catalysis. The second half of their paper is of

poor quality, and should not be published anywhere until the methods are improved and the calculations are grounded in reality.

Also, the precatalyst (2a), as drawn in Figure 1, looks like Cr(IV) due to an error that propagates in the paper.

Additional Questions:

Significance: High (suitable for JACS)

Novelty: High (suitable for JACS)

Broad interest: High (suitable for JACS)

Scholarly presentation: Lowest (not suitable for JACS)

Are the conclusions adequately supported by the data?: No

Are the literature references appropriate and correct?: Yes

Do the contents justify the length of this manuscript?: No

After Rebuttal:

Reviewer: 1

Recommendation: Publish in JACS after minor revisions.

Comments:

I was asked to act as an adjudicative referee. In order not to have the author wait much longer, I looked into it right away.

In this manuscript, Zeng and coworkers report on a deoxygenative hydroboration of nitro groups using a CAAC-Cr catalyst. The authors demonstrate the utility of their process with a broad substrate scope and various mechanistic experiment including DFT calculations. From a synthetic point of view, the use of HBpin as a reductant is not ideal, especially when looking at atom economy and costs. However, the mild conditions of this protocol, the overall high TON combined with the chemoselectivity / tolerance for otherwise reactive functional groups (e.g. halides and alkynes) make this reaction very interesting. Additionally, the employed CAAC-Cr

catalyst is intriguing and might facilitate other novel reactions. This is particularly noteworthy, having in mind the recent interest in Cr catalysis for cross-coupling, C-H activation, hydrogenation and photoredox catalysis, respectively. The mechanistic studies were carefully revised in the current manuscript and support the proposed polarity reversal of the hydride.

Concerning the mechanistic studies that Reviewer 4 criticized. These were carefully revised in the current manuscript. The authors now demonstrate that the induction period does not occur if a preformed Cr catalyst is employed. The oxidation state of the active species was identified as ± 0 using XPS analysis. Using the preformed Cr(0) catalyst, the kinetic profiles were measured (6 time-point determination compared to 1 time-point in the previous manuscript) and support a mechanism, in which both the Cr catalyst and HBpin is involved in the rate-determining step. Additionally, an Eyring plot was added to the manuscript to support the proposed mechanism. The experimentally determined activation barrier of 29.3 kcal/mol is in good agreement with the calculated activation barrier of 31.9 kcal/mol. Overall, the revised mechanistic studies support the proposed mechanism.

Before publication, I have a minor concern about the preparation of catalyst 2a. The authors state in the manuscript: "The reaction mixture was again cooled to $-78\text{ }^{\circ}\text{C}$ and a solution of CrCl_3 (79 mg, 0.5 mmol) in THF (4 mL) was added slowly." I find it odd that the authors use CrCl_3 here, since it is not soluble in THF or at least not to the extent (amount) indicated, which is the reason you typically employ $\text{CrCl}_3(\text{THF})_3$ for such processes. Can the authors comment on that? Additionally, the first use of chromium in dual photoredox catalysis should be cited among the other papers of reference 34 (JACS 2018, 140, 12705). Also, there is a small mistake in the Associated Content. The authors state that the OPTeP drawing of (CAAC)Rh complex 2a can be found in the Supporting Information. This should be corrected to CAAC-Cr complex 2a. Apart from that I don't really have any major negative feedback to this manuscript, therefore I support publication in J. Am. Chem. Soc.

Additional Questions:

Significance: High (suitable for JACS)

Novelty: High (suitable for JACS)

Broad interest: High (suitable for JACS)

Scholarly presentation: High (suitable for JACS)

Are the conclusions adequately supported by the data?: Yes

Are the literature references appropriate and correct?: Yes

Do the contents justify the length of this manuscript?: Yes

Reviewer: 2

Recommendation: Publish in JACS after minor revisions.

Comments:

This is an interesting and useful paper on the reduction of NO₂ to NH₂ via Cr-mediated hydroboration. The authors do a great job framing the importance of the problem and describing the synthesis of the catalyst, its characterization, its utility in a broad scope of substrates (>70) and applying the protocol to the synthesis of 7 drugs or drug precursors. The mechanism is probed experimentally and computationally in expert fashion. The paper is thorough complete and extremely well done. It is most impressive. The work is clearly important as it described an important transformation that will be of utility to a broad cross section of the chemistry community. I strongly recommend publication following attention to the minor point below.

1. TONs up to 1,806,900. This implies 5 significant figures. I am not sure that is correct perhaps 1.8×10^6 is more appropriate.

Additional Questions:

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Broad interest: Highest (top 5%, suitable for JACS)

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