Addressing the Reproducibility of Photocatalytic Carbon Dioxide Reduction

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Reproducibility of photocatalytic reactions, especially when conducted on small scale for improved turnover numbers with *in situ* formed catalysts can prove challenging. Herein, we showcase the problematic reproducibility on the example of attractive photocatalytic CO₂ reduction utilizing [FeFe] hydrogenase mimics. These Fe complexes, well-known for their application in proton reduction reactions, were combined with a heteroleptic Cu photosensitizer and produced CO/H₂/HCO₂H mixtures of variable constitution. However, the reactions indicated a poor reproducibility, even when conducted with well-defined complexes. Based on our experience, we make suggestions for scientists working in the field of photocatalysis on how to address and report the reproducibility of novel photocatalytic reaction protocols. In addition, we would like to highlight the importance of studying reproducibility of novel reaction protocols, especially in the fields of photocatalytic water splitting and CO₂ reduction, where TONs are widely used as the comparable measure for catalytic activity.

**Introduction**

Photocatalysis is arguably one of the most active fields in nowadays catalysis research.[1–3] Hence, numerous researchers all over the world investigate photocatalytic water splitting[4] or reduction of CO₂ to potential energy carriers.[5] In addition, photocatalysis is intensely applied for producing more value added compounds, such as fine chemicals or life science molecules.[6] The strong interest in this technology can readily be explained by the intrinsic advantage offered by direct utilization of sunlight as an abundant and sustainable energy source. Not surprisingly, the number of publications in these fields has skyrocketed over the last decade, outlined by a more than 10-fold increase in publication numbers in the field of photocatalytic CO₂ reduction (Figure 1). With respect to the major challenges mankind has to face in the upcoming decades, which are probably the man-made climate change as a result of extensive usage of fossil fuels and an increasing demand in energy and food eventuating from the on-going demographic growth,[7] the enhanced interest in those research areas are justified. The ambition of scientists to compete with or even outperform previously reported methods and to aim for new record results for those transformations is certainly the foundation for future improvement. However, the stride towards better catalyst performance can just as well become ambivalent when pursued at all costs. This becomes obvious by the recent trend of lowering catalyst loadings to achieve higher turnover numbers (TONs) which are then reported as the prime measure of catalyst activity. In the case of synthetic applications, product yield and substrate conversion are direct indicators of the applicability of those lowered catalyst loadings and a reduced amount of catalyst giving similar yields is undoubtedly preferred. In contrast, photocatalytic CO₂ reduction reactions or water splitting processes are usually far from reaching full conversion under batch reaction conditions.

![Figure 1. Number of publications in the area of photocatalytic CO₂ reduction, (compiled using SciFinder searching for “Photocatalysis CO₂ reduction” on August 12, 2019).](https://doi.org/10.1002/cctc.201901686)
Hence, lower catalyst loadings, albeit feigning higher catalytic activity, diminish the applicability of these systems, since intricate upscaling of those reactions is most often not performed.

In addition, the impact of impurities on the catalyst performance becomes more pronounced at lower catalyst concentrations, potentially resulting in poor reproducibility for the described reactions. Combined with elaborate reaction setups used for photocatalytic CO₂ reduction reactions and the crucial influence of the light source (position and constant radiant flux)³⁹,⁴⁰ reproducibility of reported systems and further improvement of literature-known CO₂ reduction protocols can prove challenging. Interestingly, the reproducibility of photocatalytic CO₂ reduction reactions is seldom addressed and often no information on the number of reaction runs utilized for the calculation of the TONs is given.

Herein, we showcase the importance of these factors on the example of photocatalytic CO₂ reduction using [FeFe] hydrogenase mimics. Based on this example, we would like to encourage researchers in the field of photocatalysis to pay special attention to the reproducibility of novel reaction protocols.

Results and Discussion

Recently, Wang and co-workers reported the electrocatalytic CO₂ reduction to CO, hydrogen and formate utilizing [FeFe] hydrogenase mimics [Fe₆(μ₆-bdt)(CO)₄] (1, bdt = benzene-1,2-dithiolate) and [Fe₆(μ₆-edt)(CO)₄] (edt = ethane-1,2-dithiolate). In parallel to their study, we investigated the photocatalytic CO₂ reduction using complex 1 and similar hydrogenase mimics. We started our investigations based on 1 in combination with a heteroleptic copper photosensitizer (CuPS) 2 previously utilized for photocatalytic CO₂ reduction in our group. CuPS 2 can be readily formed in situ from [Cu(MeCN)₄]PF₆, bathocuproine and xanthophos in a 1:1:3 ratio. At a wavelength of 415 nm and a radiant flux of 1.00 W, we were pleased to find simultaneous CO₂ reduction with a total TON for CO, HCO₃⁻ and proton reduction with a TON of 614 (average of 7 reactions, detailed results are presented in Table S1). While at first a comparably high catalytic activity of 880 TON was the main result from a more complex equilibrium that includes the [FeFe] hydrogenase mimic itself.

For optimizing this equilibrium, we investigated the influence of the [Cu(CH₃CN)₄]PF₆/bathocuproine/xanthophos ratio on the overall catalytic activity of the catalyst system (Table S2). The optimum composition was found to be a 1/2/5 Cu/HCO₃⁻/H ratio with a total TON of 756 at a CO/H₂/HCO₃⁻ ratio of 1.7/1.1/1 (average of 5 reactions). However, we witnessed a diminished reproducibility under these conditions, which became even more obvious when optimizing the illumination conditions by switching to a broader 400–500 nm irradiation at an increased radiant flux of 1.50 W (Table S3). While at first a comparably high catalytic activity of 880 TON with a CO/H₂/HCO₃⁻ ratio of 2/1/1 (average over 3 reactions) was obtained and the reproducibility for CO was within 10% range (TON(CO): 445, 417, 466), this reproducibility dramatically decreased after repeating the same reaction six months later (all results are presented in Table S4). After changing all the employed reagents and the solvent, we were unable to identify the cause of the poor reproducibility observed for this reaction (Figure 2). Notably, a five-fold increase in the utilized catalyst amount did not facilitate complete reproducibility, with an almost 200% difference in TON(CO) for reactions conducted within a timeframe of one month (Table S5).

To evaluate, whether this poor reproducibility occurs only in the single case of [Fe₆(μ₆-bdt)(CO)₄] (1), we also evaluated the photocatalytic CO₂ reduction using [Fe₆(μ₆-pbd)(CO)₄] (3), [Fe₆(μ₆-Cl-bdt)(CO)₄] (4), and simple [Fe₆(CO)₄] (5). In all cases, moderate to poor reproducibility was observed with respect to CO, HCO₃⁻ and H₂ formation under the previously optimized conditions, even though general trends in the product mixture composition were observable (Figure 3, for detailed results see Table S6).

As mentioned earlier, Cu complexes, such as 2, exist in an equilibrium with the homoleptic [Cu(N’N)₂]⁺ complex in solution. This equilibrium is depending on the solvent, the illumination conditions and the amount of ancillary ligands present in the reaction mixture. Since no excess bisphosphine ligand is present in the well-defined 2, enhanced formation of the [Cu(N’N)₂]⁺ complex could occur in this case. Even though this might account for the decreased catalytic activity with respect to CO formation of the well-defined CuPS 2, the plain difference compared to the in situ CuPS could also result from a more complex equilibrium that includes the [FeFe] hydrogenase mimic itself.

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As mentioned earlier, Cu complexes, such as 2, exist in an equilibrium with the homoleptic [Cu(N’N)₂]⁺ complex. Since CO replacement by bidentate N or P donor ligands is
well-known for [FeFe] hydrogenase mimics, we supposed that a reaction of the Fe carbonyl complexes employed as catalysts with the in situ CuPS might occur under our reaction conditions. This would further complicate the equilibria within the mixture and might eventually cause the poor reproducibility observed.

Thus, we reacted 1 with an equimolar amount of either bathocuproine or xantphos in toluene under illumination (415 nm, 1.00 W). To our delight, this resulted in the formation of novel diiron complexes 6 and 7 in mediocre to good yield (64 % for 6; 76 % for 7) (Scheme 2).

Crystals suitable for X-ray crystallographic analysis were obtained from CH$_2$Cl$_2$/hexane and enabled indisputable elucidation of their solid state structures (Figures 4 & 5). In both cases, the dithiolate bridge remained unaltered and one molecule of the bidentate ligand is coordinated in a chelating fashion to one of the two Fe centers. This is in accordance with previously reported compounds of this type.[13a–j]

Our result also emphasized the universality of the synthesis of chelated diiron dithiolate complexes via irradiation of the hexacarbonyl precursor and the bidentate ligand.[13a,b] Interestingly, we were able to perform this reaction without the explicit utilization of UV light (maximum at 415 nm), which indicates that CO dissociation for the [Fe$_2$(μ-bdtl)(CO)$_6$] can indeed be achieved using visible light i.e. our reaction conditions.[14]

Having isolated these new complexes, we evaluated their activity in the photocatalytic CO$_2$ reduction. We hoped that these isolated complexes in combination with either the in situ or the well-defined CuPS 2 might give entirely reproducible results. Combining complex 6 with the isolated CuPS 2 gave a low TON for CO of 10, a TON of 159 for HCO$_2$H, and a TON for H$_2$ of 340 (average of two runs, Figure 6a), detailed results are

Figure 2. Single experiment results for the photocatalytic CO$_2$ reduction conducted with in situ formed CuPS 2 and Fe catalyst 1 underscoring the poor reproducibility.

Figure 3. Reproducibility of the photocatalytic CO$_2$ reduction utilizing in situ generated CuPS 2 and various dinuclear Fe complexes. a) [Fe$_2$(μ-pbdtl)(CO)$_6$] (3). b) [Fe$_2$(μ-Cl-bdtl)(CO)$_6$] (4). c) [Fe$_2$(CO)$_6$] (5).

Scheme 2. Synthesis of the new [FeFe] complexes 6 and 7 via photolytic CO replacement by xantphos and bathocuproine.
given in Table S8 & S9), which seemed fairly reproducible. However, the combination of 6 with the \textit{in situ} formed CuPS resulted once again in poor reproducibility (Figure 6, b)). Similar observations were made for the combination of 7 and the \textit{in situ} generated or the isolated CuPS \textit{2} (Figure 6c) & d)).

Again, this outlines that the observed reproducibility is not a result of the employed pre-catalyst. Interestingly, 7 appeared to yield higher TONs for CO\textsubscript{2} conversion compared to 6. This might indicate a privileged role of 7 in the formation of an active CO\textsubscript{2} reduction catalyst, which would be similar to the effect of 2,2’-bipyridine in the photocatalytic CO\textsubscript{2} reduction using [Fe\textsubscript{3}(CO)\textsubscript{12}].\cite{15} However, the poor reproducibility prohibits a conclusive statement based exclusively on these experimental results.

**Conclusions**

In summary, we demonstrated the importance of assessing the reproducibility of a novel catalytic system for photocatalytic reduction of carbon dioxide. Here, significant reproducibility issues arose, arguably due to one of the following factors: 1. specific problems of photocatalysis (i.e. light source, transmission), 2. dynamic catalyst systems (ligand exchange), and 3. gas-liquid reaction system. If one of these or related problems exist, reproducibility issues become especially important. The results obtained for our photocatalytic CO\textsubscript{2} and proton reduction system based on [FeFe] hydrogenase mimics and a CuPS clearly indicate the unreliability of single experiments. In this specific case it might be partially due to a complex equilibrium between the CuPS and the [FeFe] complexes, suggested by the isolation of two new dinuclear Fe complexes formed via photolytic CO dissociation. However, utilization of the isolated complexes in combination with a well-defined CuPS still resulted in low reproducibility. Therefore, an important lesson from this study is that application of isolated
complexes or well-structured nanomaterials does not guarantee reproducibility. Nevertheless, reproducibility constitutes the fundamental base for any research, especially for cutting-edge transformations, such as CO₂ reduction or water oxidation, which mostly rely on the catalytic activity reported in terms of turnover frequencies or TONs and not product yield/conversion as their quality index. In addition, the exact number of conducted reactions and the deviance of those single experiments are seldom stated for novel catalytic transformations.

Hence, we would like to make the following recommendations for scientists working in such fields as catalyst and/or method development:

1. The number of independent experiments should always be stated when reporting a novel catalytic transformation or a new catalyst system. This is especially the case for results obtained from single experiments.

2. Ideally, a minimum of two independent reactions (i.e. not the same stock solutions) on different dates should be performed.

3. Reduction of the catalyst concentration to obtain higher TONs should only be conducted when reproducibility at the reduced catalyst concentrations is still granted. This should be proven by reporting results of single experiments at those reduced concentrations. Ideally, reproducibility should be verified utilizing a minimum of two significantly different catalyst loadings. We believe that by taking care of the crucial purity of reagents and solvents and following these simple guidelines, a higher standard for entirely reproducible catalytic systems in the fields of water splitting and CO₂ reduction can be achieved. An increased proportion of reproducible results in those fields will not only facilitate improvement of catalysis systems, but also simplify the establishment of catalytic benchmarks.

**Experimental Section**

Experimental procedures, chromatograms and spectra are provided free of charge in the electronic supporting information. Deposition number CCDC 1855538 (6) and CCDC 1855539 (7) contain the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service www.ccdc.cam.ac.uk/structures.

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**Conflict of Interest**

The authors declare no conflict of interest.

**Keywords**

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