Editorial comments:  
Changes to be made by the Author(s):

1. Please take this opportunity to thoroughly proofread the manuscript to ensure that there are no spelling or grammar issues. The JoVE editor will not copy-edit your manuscript and any errors in the submitted revision may be present in the published version.

The manuscript was thoroughly read-proofed.

2. Please ensure that the references appear as the following: [Lastname, F.I., LastName, F.I., LastName, F.I. Article Title. Source. Volume (Issue), FirstPage – LastPage, doi: DOI (YEAR).] For more than 6 authors, list only the first author then et al.

Done.

3. Please abbreviate all journal titles.

Done

4. Please include volume, issue numbers, and DOIs for all references.

Done.

5. Please define all abbreviations before use.

Done.

6. Figure 8: Please use correct subscripts in the chemical nomenclature.

Figure 8 was reviewed. It was not clear what “correct subsrcipts in the chemical nomenclature” was referred to. As a consequence, no changes were made.

7. Please remove the references from the Abstract.

Done.

8. Please number all references individually.

Done.

9. Please remove the brackets around the superscripted reference numbers.

Done.

10. Please remove the embedded figure(s) from the manuscript. All figures should be uploaded separately to your Editorial Manager account. Each figure must be accompanied by a title and a description after the Representative Results of the manuscript text.

The figures will be downloaded individually.

11. Please ensure that all text in the protocol section is written in the imperative tense as if telling someone how to do the technique (e.g., “Do this,” “Ensure that,” etc.). The actions should be described in the imperative tense in complete sentences wherever possible. Avoid usage of phrases such as “could be,” “should be,” and “would be” throughout the Protocol. Any text that cannot be written in the imperative tense may be added as a “Note.” However, notes should be concise and used sparingly. Please include all safety procedures and use of hoods, etc.

Done.

12. The Protocol should contain only action items that direct the reader to do something. Please move the discussion about the protocol to the Discussion.

Done.

13. Please quantitate all volumes used throughout and avoid vague language: appreciable, etc.

Done.

14. 3.2: What is an addition, the same as the reaction volume?

This was clarified as the protocol was reviewed.

15. 5.1.1: How are the solutions prepped?

The information was provided.

16. Please ensure that all Greek characters are in the same font as the rest of the manuscript (Calibri).

Done.

17. As we are a methods journal, please revise the Discussion to explicitly cover the following in detail in 3-6 paragraphs with citations:  
a) Critical steps within the protocol  
b) Any modifications and troubleshooting of the technique  
c) Any limitations of the technique  
d) The significance with respect to existing methods  
e) Any future applications of the technique  
  
  
The following was added in the discussion:

Limitation and considerations:

The formation of solids (i.e. precipitates) during the reaction is an important parameter when considering flow processes. In those instances, one must consider (i) modifying the protocol in batch-mode to maintain homogeneity throughout the reaction (i.e. changing reagents, solvent, temperature etc..) or (ii) design the reactor to allow for the processing of slurries. The latest option may be viable with optimization and tailored reactor design. In practice, the two most limiting factors for flow processes are (i) viscous solutions: the ability to pump viscous liquids and the resulting pressure drop are often prohibitive and (ii) using heterogeneous (solid/liquid) feeding streams. It is difficult to consistently and effectively pump fine suspensions (for example in the cases of heterogeneous catalyst). In addition, accumulation of particles in the reactor can lead to blockage, and ultimately failure.

Overall, flow chemistry has been demonstrated to be superior (to batch processes) for synthetic transformations that (i) require precise temperature control (i.e. avoid hot spot, competitive reaction etc..), (ii) involve the formation of highly reactive or unstable intermediates, (iii) require enhanced mixing with multi-liquid phases for example.

Reviewers' comments:  
**Reviewer #1:**  
*Manuscript Summary:*  
Generally well thought out and well written manuscript. Particularly good discussion of continuous flow reactions in general, the specific reaction discussed, and the equipment used.  
  
*Major Concerns:*  
-There were three names given to p-nitrobenzoic acid in various places in the manuscript (paranitrobenzoic acid, p-NO2 benzoic acid, and p-nitrobenzoic acid). I suggest using only the p-nitrobenzoic acid consistently.

p-nitrobenzoic acid was consistently used as suggested.

-At line 175 begins the protocol for the synthesis of DDM, the term DDM is not previously defined. For clarity I suggest that the first time diphenyldiazomethane is mentioned, it should be "diphenyldiazolmethane (DDM)". the same is true for DCM, introduced at line 186.

All abbreviations were defined the first time they are used.

-In this same section, line 180 states "10 g (.7205 equivalents)" of anhydrous KH2PO4. This is clearly mixing significant figures (should it be 10.00 g or .72 equivalents). The same problem occurs at line 186.

Significant figures were reviewed throughout the manuscript for consistency.

*Minor Concerns:*  
-Numerous typos and difficulties with English language conventions.

Manuscript was read-proofed carefully to address those.   
  
*Additional Comments to Authors:*  
N/A  
  
  
**Reviewer #2:**  
*Manuscript Summary:*  
The contribute by Pollet and co-workers would provide a blueprint to transfer a chemical processes from batch to flow mode. The manuscript is well written and could be accepted for publication in Jove after the small changes reported below.  
  
*Major Concerns:*  
No major concerns.  
  
*Minor Concerns:*  
A picture of the complete flow system need to be included.

A picture was included with the schematic of the reactor.

References: The following very recent reviews on flow chemistry must be included:  
Chem. Rev. 2017, DOI: 10.1021/acs.chemrev.7b00183;

Added.

Beilstein J. Org. Chem. 2017, 13, 520.

Our institution does not have direct access to this journal. The reference was not added as we could not read the article.

J. Flow Chem. 2016, 6, 136.

Added.

Current Opinion in Green and Sustainable Chemistry 2017, doi: 10.1016/j.cogsc.2017.06.003.

Added.  
  
*Additional Comments to Authors:*  
N/A