This paper (*J. Org. Chem.* **2022**, *87*, 9969) examines the catalytic hydrodefluorination of aryl amides. Additional resources are included to provide context for the importance of hydrodefluorination.

1. Thinking back to your introductory chemistry classes, what topics do you recall where it seemed like with the exception fluoride, all of the rest of the halides behave in a particular way?
2. Read the introduction to the *J. Org. Chem.* paper, the article from C&EN, and sections 2, 3, 5 and 6 in the linked chapter (*Organofluorine Compounds in Biology and Medicine* **2015**, 1-27 [https://doi.org/10.1016/B978-0-444-53748-5.00001-0](https://doi-org.ezproxy.lafayette.edu/10.1016/B978-0-444-53748-5.00001-0)) on organofluorine compounds. In your own words, briefly summarize why should we care about hydrodefluorination.
3. Table 1 in the *J. Org. Chem.* paper is a summary of a previous study by the authors. Citing specific combinations of entries, what conclusions can be drawn from this table? Be sure to examine each variable that is changed in the table. An initial example examining the role of the solvent is included below.
4. Of the nickel precatalysts shown in Table 1, the most effective is significantly different from the other nickel compounds examined. To fully appreciate this, you should use the CBC method to classify the nickel precatalysts and provide the valence on nickel.
5. The most effective ligand in this study appears to be dtbpy. What is dtbpy?
6. Would you expect dtbpy to be more or less electron-donating than bpy? Why?
7. Would you expect compounds containing bpy to be more or less soluble in organic solvents than corresponding compounds with dtbpy? Why?
8. The most effective solvent in this study is DMA. What is DMA? Is DMA polar or non-polar? Is it protic or aprotic? What is the boiling point of DMA?
9. The reaction scheme at the start of Table 2 presents the experimental conditions used in this study. Based on the information provided, how many millimoles of each substance (excluding the solvent) are present in the typical reaction?
10. Table 2 presents new results examining the effect of the base and the hydride. Summarize what conclusions you can draw from this data being sure to cite combinations of entries to support your conclusions.
11. Of the conclusions in the previous question, are there any that are debatable, especially in the context of atom economy? Which and why?
12. Figure 2 presents several different substrates that were studied in this reaction. What general trend do you observe in comparing the reactivity of 1a-1j?
13. Rationalize the results of 1a, 1k and 1l to the C-X bond strengths discussed in question 2.
14. The authors studies several polyfluorinated substrates as presented in Figure 3. What conclusions can be drawn from this figure?
15. Figure 4 presents several different substrates in which the group on the amide nitrogen is changed. What general conclusions can be drawn from this figure?
16. A mechanism is proposed in Scheme 1. Starting in the upper right corner, provide names or descriptions for the different steps presented below. Provide support for your assignment. The compound labeled as A presumably forms *in situ* when the dtbpy and Ni(COD)2 are combined. It is possible that an additional ligand, perhaps COD or a solvent molecule, remains on the nickel at this point.

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| **Step** | **Description** | **Reaction type and support** |
| 1 | Reaction of 1a |  |
| 2 | A to B |  |
| 3 | B to C |  |
| 4 | C to D |  |
| 5 | D to E |  |
| 6 | E to A |  |
| 7 | Formation of 2a |  |

1. Does this proposed mechanism provide any potential insight into why the Ni(COD)2 was the most efficient nickel catalyst in this study?