Jin-Quan Yu’s group at Scripps published (JACS **2011**, *133*, 18183–18193) a fascinating study of C–H functionalization at Pd(II) centers supported by protected amino acids. Begin by reading the attached paper, then answer the following questions using the information in the paper and appropriate references.

1. A generic reaction like the ones reported in the paper is drawn below. What is the role of each reagent listed below?



*Reagents in question:* Pd(OAc)2 (catalytic)
Ac-Ile-OH (catalytic)
BQ (catalytic)
Ag2CO3 (stoichiometric)
Ph–BF3K (stoichiometric)
KHCO3 (superstoichiometric)

1. Most cross-coupling reactions that form C–C bonds do not require oxidant. Why is an oxidant required here?
2. All of the substrates examined have a phenylacetic acid group. What is the role of the carboxylic acid (if any) in the reported transformation?
3. Phosphines have been extensively developed as ligands for traditional cross-coupling reactions, but they have not found use in oxidative cross couplings. Why are phosphines not useful in reactions like the one reported here?
4. What are the structures of Ac-Ile-OH and Boc-Val-OH (the two ligand precursors used here)? Draw structures of each of these ligands bonded in the expected manner to Pd(II).
5. The authors note that isoleucine derivatives with Me or H attached at nitrogen shut down the reaction; why is an electron-withdrawing protecting group required?
6. What is the role of silver carbonate in this reaction? Why is Ag(I) better at facilitating catalytic turnover than oxygen? Think about the possible interactions of Ag(I) with Pd(II) [it may help to check out reference 25].
7. The authors claim that Ph–BF3K must be transformed into an active boronic acid or boronate ester prior to Ph− transfer to palladium. Ph–BF3− is already anionic, so why must it be activated prior to Ph− transmetallation? Think about the relative electronics of Ph–BF3− and Ph–B(OH)3−.
8. It was found that optimal yields were obtained for the reported reactions when 2 equiv of Ag2CO3 and 3 equiv of arylboron reagent were used. Why is an excess of these reagents required in order to consume all of the starting phenylacetic acid?
9. The data presented in Table 9 are particularly noteworthy in terms of the authors’ interpretation about mechanism of C–H activation in the amino-acid-supported systems versus the systems with no added ligand. How do the results from Table 9 support a change in mechanism of C–H activation upon addition of ligand? How do this authors interprate this finding (i.e., what mechanism do they propose is active in the systems examined for this paper)?