Phosphorylation of Alkyl Radicals

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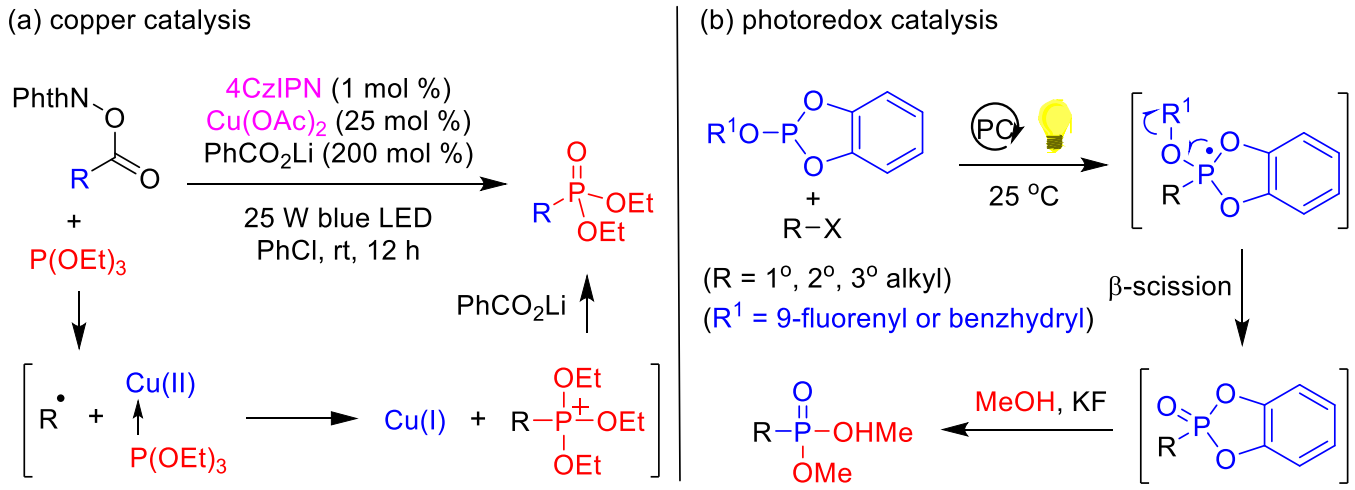
Organophosphorus compounds have found widespread applications in various areas ranging from biochemistry to ecology, medicine, agriculture, and materials science. A variety of methods have been developed for C(sp^3)–phosphorylation, including nucleophilic and electrophilic phosphorylation and phosphoryl radical addition onto unsaturated bonds. However, methods based on the phosphorylation of alkyl radicals remain elusive. Studies on the formations and properties of phosphoranyl radicals by Bentrude and others in the 1970s led to the conclusion that radicals such as methyl radical add to trivalent phosphorus reversibly while radicals such as isopropyl radical do not react at all.[1]



Our investigation on copper-catalyzed radical reactions led to the hypothesis of "copper-assisted phosphite transfer", based on which the copper-catalyzed decarboxylative phosphonylation of *N*-acyloxyphthalimides with trialkyl phosphites was successfully accomplished under mild conditions (Fig. 1a).[2a] Furthermore, our extensive study on alkyl radical addition to phosphites revealed that primary, secondary and even tertiary alkyl radicals add efficiently to 9-fluorenyl (or benzhydryl) *o*-phenylene phosphite. Thus, a radical variant to the Arbuzov reaction was successfully developed under photoredox-catalyzed conditions via radical addition–β-scission sequence (Fig. 1b).[2b] The extension of the above strategies to alkyl radical phosphinylation reactions will also be discussed.[3]

[1] (a) W. G. Bentrude, *Acc. Chem. Res.* **1982**, *15*, 117-125. (b) J. A. Rossi-Ashton, A. K. Clarke, W. P. Unsworth, R. J. K. Taylor, *ACS Catal.* **2020**, *10*, 7250-7261.

[2] (a) J. Yin, X. Lin, L. Chai, C.-Y. Wang, L. Zhu, C. Li, *Chem* **2023**, *9*, 1945-1954. (b) L. Chai, J. Wang, J. Yang, J. Yin, Z. Zhang, Y. Cheng, L. Zhu, X.-S. Xue, C. Li, *CCS Chem.* **2024**, *6*, 1312-1323.

[3] (a) Y. Cheng, J. Zhen, L. Chai, J. Wang, J. Yin, L. Zhu, C. Li, *Angew. Chem. Int. Ed.* **2024**, *63*, e202316764. (b) J. Wang, Y. Zhang, L. Zhu, X.-S. Xue, C. Li, *Angew. Chem. Int. Ed.* **2024**, *63*, e202400856. (c) L. Chai, Y. Cheng, L. Zhu, C. Li, *CCS Chem.* **2024**, accepted.