

論文の内容の要旨

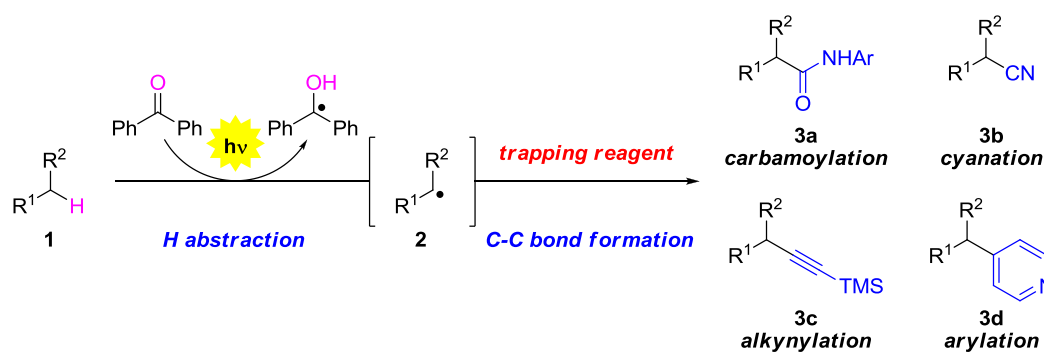
論文題目 : Development of Photochemically Induced Direct Transformation of C(sp³)-H Bonds

(光化学を利用した C(sp³)-H 結合の直接的変換反応の開発)

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Abstract

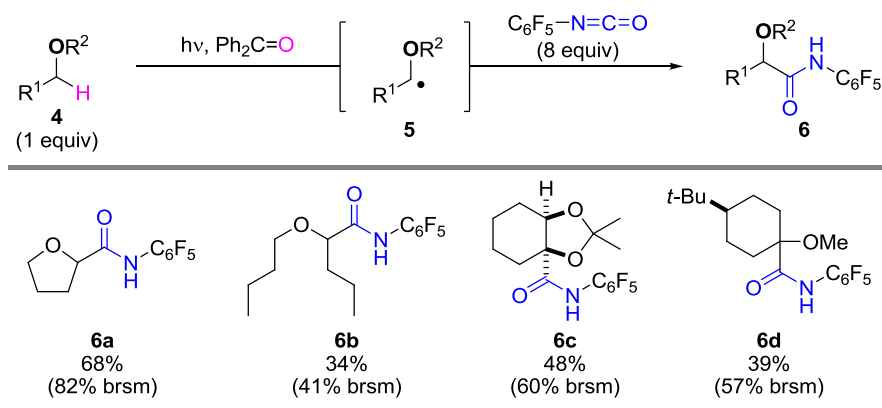
The carbon-carbon (C-C) bond forming reaction is one of the most fundamental transformations in synthetic organic chemistry. The direct transformation of C(sp³)-H bonds to C(sp³)-C bonds has especially attracted much interest in recent years from the viewpoint of streamlining the chemical synthesis. However, this extremely useful reaction has still remained challenging mainly due to the lack of general strategies for the selective transformation of C(sp³)-H bonds without affecting other functionalities. Here, the author reports four new methodologies for the intermolecular direct transformation of inert C(sp³)-H bonds to synthetically useful carbon units (Scheme 1). Namely, photochemically induced C-H carbamoylation, cyanation, alkynylation, and arylation have been achieved by utilizing the combination of benzophenone (Ph₂C=O) with a variety of radical acceptors.



Scheme 1. Photochemically induced radical C(sp³)-H functionalization

1. Photochemically induced C–H carbamoylation using isocyanate¹

The intermolecular carbamoylation of ethereal C–H bond was successfully developed using the combination of Ph₂C=O and pentafluorophenyl isocyanate (Scheme 2). The electron-rich ethereal C–H bond of **4** is selectively abstracted by photochemically activated Ph₂C=O, furnishing the α -alkoxy radical **5**. Then the carbon radical **5** attacks the central carbon of isocyanate to provide the amide **6**. Overall, the ethereal C–H bond is converted to a carbamoyl group in a single step. As well as cyclic and acyclic ethers (**6a** and **6b**), methine C–H bonds on oxy-functionalized carbocycles were also carbamoylated despite of the sterically-hindered around the reaction site (**6c** and **6d**). It is noteworthy that a tetra-substituted carbon center can be newly constructed on carbocycles.

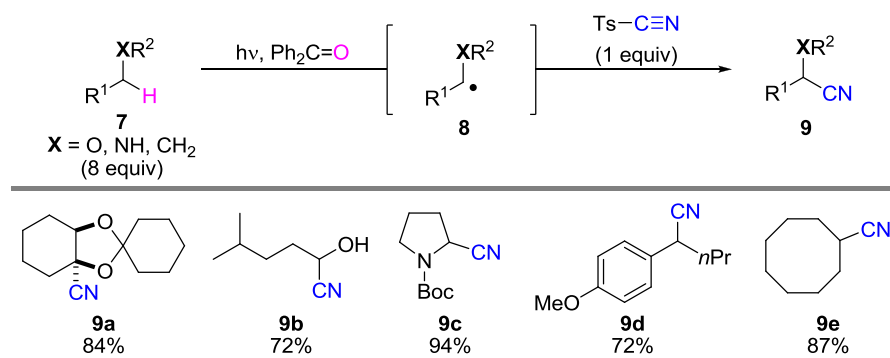


Scheme 2. Photochemically induced carbamoylation of ethereal C–H bonds

2. Photochemically induced C–H cyanation using tosyl cyanide^{2,3}

A novel photochemical protocol for the direct transformation of unreactive C(sp³)–H bonds to C(sp³)–CN bonds was developed by employing tosyl cyanide (TsCN) as a source of cyano group (Scheme 3). The C–H cyanation proceeds at ambient temperature with a broad applicability of starting materials including ether (**9a**), alcohol (**9b**), carbamate (**9c**), alkylbenzene (**9d**), and even alkane (**9e**). Overall, the cyanation preferentially took place at the most electron-rich C–H bond due to the electron-deficient nature of oxyl radical, which is photochemically generated from Ph₂C=O. On account of the operational simplicity and high predictability of the reaction site, the present protocol provides a powerful tool for a quick introduction of the cyano group, a highly valuable functionality in both organic synthesis and

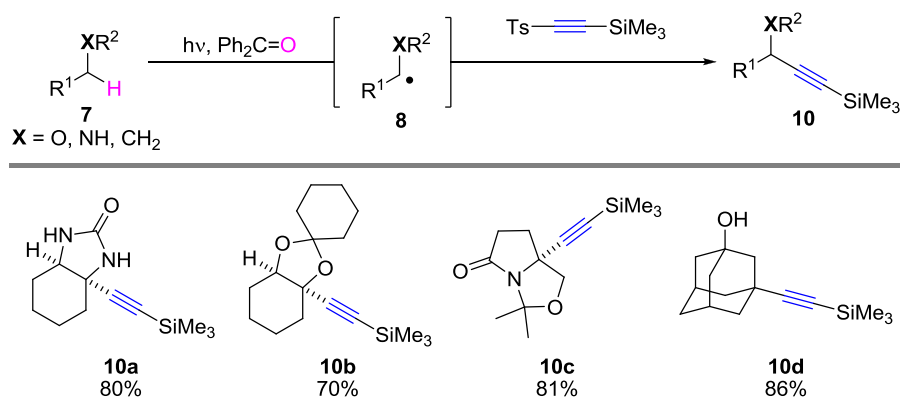
medicinal chemistry.



Scheme 3. Photochemically induced cyanation of C(sp³)-H bonds

3. Photochemically induced C-H alkylation using alkynyl sulfone⁴

Based on the analogy to TsCN, the photoinduced alkylation of inert C(sp³)-H bonds was achieved by utilizing 1-tosyl-2-(trimethylsilyl)acetylene and Ph₂C=O (Scheme 4). The present transformation enables the direct introduction of a synthetically useful acetylene unit into a wide variety of starting materials, such as protected diamine (**10a**) and diol (**10b**), lactam (**10c**), and alkane (**10d**). It is noteworthy that a tetrasubstituted carbon is newly installed in a highly efficient manner by the alkylation of methine C-H bond.

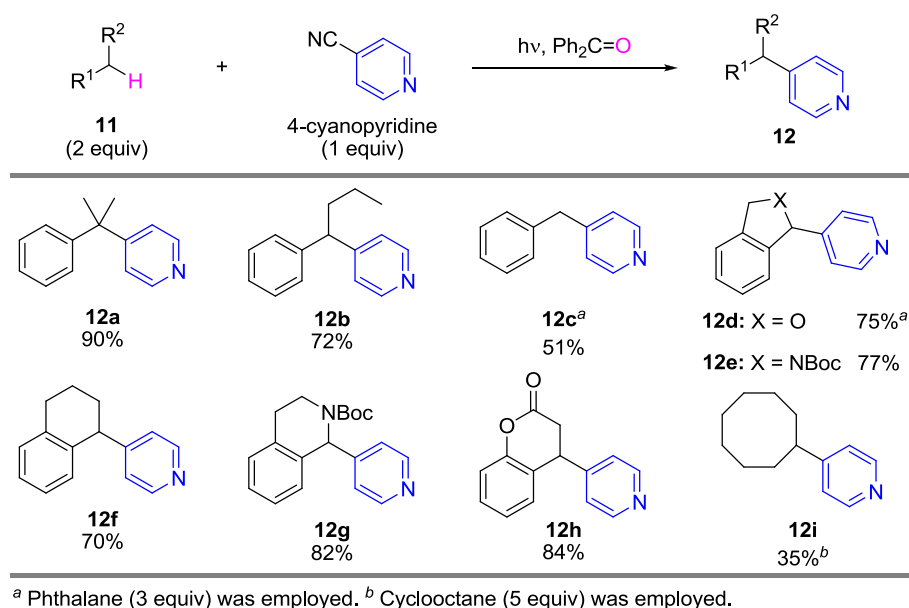


Scheme 6.4. Photochemically induced alkylation of C(sp³)-H bonds

4. Photoinduced coupling reaction of C(sp³)-H bonds and 4-cyanopyridine⁵

A photochemical coupling reaction of inert C(sp³)-H bonds and 4-cyanopyridine was developed in metal-free conditions (Scheme 5). A variety of benzylic C-H bonds was efficiently converted to a pyridine ring under the photoirradiation in the presence of Ph₂C=O

(**12a–h**). Furthermore, even the C–H bond of alkane was applicable to this transformation as well (**12i**). Regardless of the sterically congested nature, the methine C–H bond exhibited high reactivity toward the coupling reaction, affording a product equipped with a quaternary carbon (**12a**). The present protocol serves as a novel methodology for both the introduction of a pyridine ring into benzylic moiety and the preparation of 4-alkylpyridines.



Scheme 5. Photoinduced coupling reaction of C(sp³)–H bonds with 4-cyanopyridine

In conclusion, a series of photochemical reactions for the direct transformation of unreactive C(sp³)–H bonds to C(sp³)–C bond have been developed by employing Ph₂C=O as a common radical initiator. The introduced carbamoyl group, cyano group, alkynyl group, and pyridine ring can serve as versatile handles for further carbon elongations and functional group manipulations. Therefore, these newly developed protocols are highly valuable for achieving a streamlined synthesis of structurally complex molecules.

References

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