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Alkene homologation via visible light promoted hydrophosphination using triphenylphosphonium triflate

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A hydrophosphination reaction of alkenes with triphenylphosphonium triflate under photocatalytic conditions is described. The reaction is promoted by naphthalene-fused *N*acylbenzimidazole and is believed to proceed through intermediate formation of phosphinyl radical cation. The resulting phosphonium salts are directly involved in the Wittig reaction leading to homologated alkenes.

Addition of the P-H bond at the double bond of alkenes constitutes an atom economic way of synthesis of organophosphorus compounds.¹⁻³ Typically, these processes are performed starting from disubstituted phosphines, their oxides, phosphinic acids and alkyl phosphites (Scheme 1). While particular reaction conditions depend on the type of phosphorus reagent and alkene, the addition proceeds easily with electron deficient alkenes.² In case of unactivated double bonds, the reaction is more challenging to perform,³ and uncatalyzed thermal addition was described only in case of free phosphines R₂PH.⁴ The hydrophosphination of alkenes may be catalyzed by transition metal complexes,¹ but the most widely used activation methods are based on radical initiation and proceed via P-centered radicals.⁵ For this, classic activators such as AIBN,⁶ triethylborane,⁷ oxidizing metal salts,⁸ oxygen⁹ and UV light¹⁰ were employed. Development of photocatalysis allowed hydrophosphination to be promoted by visible light.^{11,12} Reactions of phosphonium salts with Michael acceptors, that is when phosphonium salt behaves as a source of free phosphine acting as nucleophile followed by protonation of carbanion, have also been described.13 Herein we report that easily prepared triphenylphosphonium triflate can be involved into radical hydrophosphination of unactivated alkenes, and the resulting phosphonium salts were used



° \ PPh₃

Scheme 1. Addition of the P-H bond to alkenes.

directly for the Wittig reaction.^{14,15} Importantly, in this process, olefins as feedstock reagents are directly converted into phosphonium salts that saves a step by avoiding the transformation of alkene-to-alkyl halide.¹⁶

The hydrophosphination is expected to involve the phosphonium radical cation as a key intermediate capable of adding at unactivated alkenes. Previously these species have been considered from a general mechanistic perspective.¹⁷ However, recently they have found synthetic applications for the homolytic abstraction of the hydroxy group from carboxylic acids and alcohols generating the corresponding radicals.¹⁸ A straightforward way of generating phosphonium radical cations involves single electron oxidation of phosphines, which may be achieved by using light activated ruthenium- or iridium-based catalysts.^{17c,18,19} In this work, we propose that the radical cation can be formed via proton coupled electron transfer (PCET)²⁰ using an organic photocatalyst.

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Our idea is based on application of organic photocatalysts, which we applied for the thiol-ene reaction.²¹ The proposed



Scheme 2. Proposed mechanism.

concept is shown in Scheme 2. The interaction of phosphonium salt with a photocatalyst generates a hydrogen-bonded complex, which under the action of light transforms into Pcentered radical cation **1** and a nitrogen-stabilized radical **2**. Addition of **1** at the double bond generates alkyl radical **3**. The latter intermediate abstracts hydrogen atom either from phosphonium cation, thereby regenerating radical cation **1**, or from aminyl species **2** with regeneration of the nitrogen catalyst.

4-Phenylbutene **5a** was selected as a model substrate and its reaction with triphenylphosphonium triflate **6** was evaluated. Additional amount (5 mol %) of free phosphine and a photocatalyst were added, and the reaction was irradiated with blue light for 16 h (Table 1). Tetrahydrofuran was used as solvent considering further transformations of the resulting phosphonium salts (*vide infra*). The reaction did not proceed in



a Determined by GC analysis using tetralin as internal standard. b Yield of 7a determined by ¹H NMR using trichloroethylene as internal standard of 9 and 0 and

the absence of photocatalyst. In the presence of 0.5 mol % of naphthaloylidenebenzimidazol (NBI)²² moderate conversion of 21% was observed within two hours, which reached 37% after overnight irradiation (entry 2). This phenomenon suggested catalyst deactivation as reaction proceeds, and this was the case with all evaluated catalysts. However, since NBI can be made from readily available precursors,^{21,22} it can be used in increased loadings. Rewardingly, with 3 mol % of the catalyst complete conversion was achieved within 16 hours (entry 3). 9-Phenylacridine (PhAcr), which was previously used in a PCET driven process,²³ was slightly less effective in this reaction (entry 9). We also evaluated a fluorinated iridium photocatalyst (Ir[dF(CF₃)ppy]₂(dtbpy)PF₆). This highly oxidizing complex was expected to initiate the chain process shown in Scheme 2 by oxidation of the phosphine into the radical cation 1. Though the reaction did work, incomplete conversions were observed even in the presence of increased amount of the phosphine (entries 5 and 6) and unidentified byproducts were observed. Correspondingly, NBI was used in further experiments. For a representative hydrophosphination reac-





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^{*a*} Isolated yields are shown. ^{*b*} Time for step (a) 16 h. ^{*c*} 1 equiv of HMDS was used. ^{*d*} For step (a), 5% of NBI, time 24 h. ^{*e*} For step (a), 5% of NBI, time 36 h. ^{*f*} 1.5 equiv of LiHMDS solution was used for deprotonation.

tion, a quantum yield of 0.05 was determined. This means that the process does not have the chain character, and the product is formed by interaction of radical **3** with aminyl species **2**.

To get more insights into the nature of the generation of phosphonium radical cation, a series of UV-vis absorption and fluorescence experiments for combinations of NBI and phosphonium triflate (6) were performed. These studies support the formation of a complex, which is believed to undergo the light induced PCET (see Supporting Information for details).

Under the optimized conditions, various alkenes were subjected to hydrophosphination reaction. We noted that hydrophosphination of unfunctionalized alkenes such as pentene, hexene, vinyl- and allylcyclohexane proceeded faster compared to that of model 4-phenylbutene **5a**, and for most of alkenes complete conversion was achieved within 4 hours. The resulting phosphonium salts **7** were directly involved into the Wittig reaction (Table 2). Thus, the mixture containing salts **7** was cooled to -30 °C and treated with *n*-butyl lithium in the presence of 0.3 equiv of hexamethyldisilazane, which removed the excess of butyllithium. Subsequent addition of a carbonyl compound and warming to room temperature furnished alkenes **8**.

Benzophenon was used in combination with light alkenes allowing for the isolation of non-volatile target products. The fact that hydrophosphination and Wittig reactions require different conditions (mildly acidic and strongly basic, respectively) imposes some limitations on the scope of functional groups. Alkenes bearing PMP, TIPS of thiocarbamate protected hydroxy group successfully provided expected products (compounds 8j,k,v). At the same time, 3-buten-1-ol and 4-peneten-1-ol protected with the benzyl group remained unreactive in hydrophosphination reaction, and the reason for such phenomenon is not clear. TBS and THP protecting groups on oxygen do not tolerate the acidic conditions of the hydrophosphination step. As carbonyl compounds. benzophenone and formaldehyde (as paraform) were typically used, though aromatic aldehydes were also successful (products 80,p). In case of formaldehyde, the overall result of the two-step process corresponds to the homologation of the starting alkene by one CH₂-fragment.²⁴

To support the radical character of the hydrophosphination process, a 1,6-diene was evaluated as a substrate affording cyclized phosphonium salt **9** as a single product (Scheme 3).



Scheme 3. Radical cyclization experiment.

In summary, a one pot method for the homologative transformation of alkenes is described. The reaction involves light mediated hydrophosphination and the Wittig reaction of intermediate phosphonium salts. The generation of the phosphonium radical cation is a key feature of the process.

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Conflicts of interest

There are no conflicts to declare.

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