Conference paper

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Photocatalytic hydrogenolysis of allylic alcohols for rapid access to platform chemicals and fine chemicals

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Abstract: A brief account of our recent work on the chemo-, regio- and stereoselective photocatalytic hydrogenolysis of allylic alcohols to alkenes promoted by palladium-loaded titanium oxide (Pd/TiO_2) photocatalysts is presented. Since methanol is employed as the reducing agent, the method does not involve stoichiometric generation of salt waste. The photocatalytic hydrogenolysis proceeds at room temperature, and is compatible with the presence of functional groups such as C=C double bonds and hydroxyl groups at non-allylic positions. The regioselectivity is predictable: the hydrogen atom is predominantly incorporated into the sterically less hindered carbon atom of the allylic moiety. This protocol should provide straightforward green access to a range of platform chemicals (exemplified by the two-step synthesis of propylene from glycerol) and fine chemicals [e.g. (*S*)-(+)-lavandulol from (*R*)-(−)-carvone] without the need for protection/deprotection steps.

Keywords: alkene; allyl alcohol; allylic alcohol; green chemistry; hydrogenolysis; ICGC-6; palladium; palladium-loaded titanium oxide; photocatalysis; propylene synthesis; reductive deoxygenation; titanium oxide.

Introduction

Reductive deoxygenation of alcohols is an essential step in the production of platform chemicals from biomass, because biomass-derived resources are generally oxygen-rich and removing oxygen atoms from such chemicals allows production of more easily handled, carbon/hydrogen-rich chemicals with higher solubility in organic solvents and lower boiling point [1, 2]. Direct cleavage of the C–O bonds of allylic alcohols to alkenes is a representative reductive deoxygenation that is important not only in the conversion of biomass-derived allylic alcohols, but also in the synthesis of complex organic molecules with olefin functionalities [3]. Because of its synthetic importance, hydrogenolysis of allylic alcohols to alkenes has been studied for decades, and catalytic methods for this reaction using cobalt complexes [4, 5], heteropolyacid ($H_3[PW_{12}O_{40}] \cdot nH_2O$) [6] or bismuth triflate [7], and stoichiometric methods using titanocene [8–11] or $NaBH_3CN/BF_3 \cdot OEt_2$ [12] are available without significant loss of C=C π-bonds. Those methods, however, require the use of stoichiometric salt additives, silicon, titanium, or boron reagents (Scheme 1). A greener method for directed cleavage of the C–O bonds of allylic alcohols to alkenes remains elusive.

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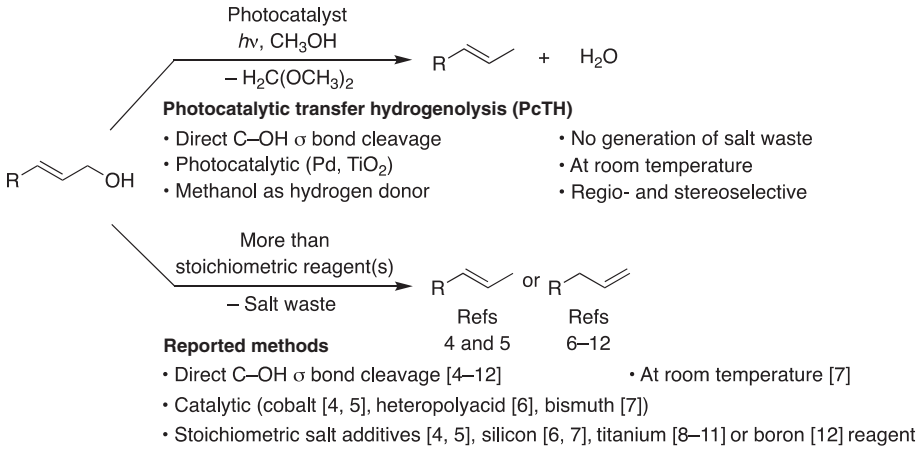


Scheme 1: PcTH and thermal hydrogenolysis of the C–O σ-bond of allylic alcohols. Inside the brackets are reference numbers.

In the course of our studies to explore selective synthetic methods using metal-loaded semiconductor photocatalysts [13–15], we have recently found that palladium-loaded titanium(IV) oxide (Pd/TiO_2) photocatalysts effectively promote hydrogenolysis of allylic alcohols to alkenes in methanol at room temperature (rt) under light irradiation (Scheme 1) [16]. As hydrogen atom(s) from methanol is incorporated in the alkene product in the photocatalytic process, we characterized this reaction as photocatalytic transfer hydrogenolysis (PcTH) [17, 18]. The PcTH of allyl alcohols is highly chemo- and redox-selective: hydrogenolysis of the C–O σ-bond predominates over reduction of the C=C π-bond and oxidation of the HC–OH bond. The regio- and stereoselectivity in the PcTH of substituted allylic alcohols are readily predictable. In this paper, we focus on our recent efforts in developing the PcTH of allylic alcohols in the context of production of platform chemicals and fine chemicals.

Results and discussion

Preparation of palladium-loaded titanium oxide

We chose palladium-loaded titanium oxide (Pd/TiO_2) photocatalyst for the PcTH of allylic alcohols because palladium nanoparticles and TiO_2 are privileged tools for catalytic conversion of allylic compounds [19] and photocatalytic hydrogen evolution from alcohols [20, 21], respectively. First, Pd/TiO_2 was prepared by impregnating TiO_2 [from Sigma-Aldrich, anatase–rutile mixture, <100 nm particle size (BET)] with an aqueous solution of $PdCl_2$, followed by drying under vacuum and reduction with $NaBH_4$ [22–24]. Inductively coupled plasma optical emission spectroscopy (ICP-OES) of digested samples of the Pd/TiO_2 showed that the palladium content was 4.78 ± 0.06 wt%. The presence of Pd nanoparticles loaded on TiO_2 (diameter: 4–7 nm) was confirmed by high-resolution transmission electron microscopy (HRTEM) and energy-dispersive X-ray spectrometry (EDX) (Fig. 1a and b). X-Ray photoelectron spectroscopy (XPS) analysis indicated that the valence number of the Pd nanoparticles was mainly Pd^0 (Fig. 1c) [16].

PcTH of allyl alcohol using Pd/TiO_2

Scheme 2 shows the result of our initial examination of PcTH of allyl alcohol (**1a**) using Pd/TiO_2. **1a** was smoothly converted to **2a** in 70 % yield with Pd/TiO_2 [**1a**/Pd (mol/mol) = 300] in CH_3OH in the presence of $TsOH \cdot H_2O$ as an additive under near-UV–vis light irradiation ($\lambda > 365$ nm) at 25 °C (Scheme 2). GC/MS analysis

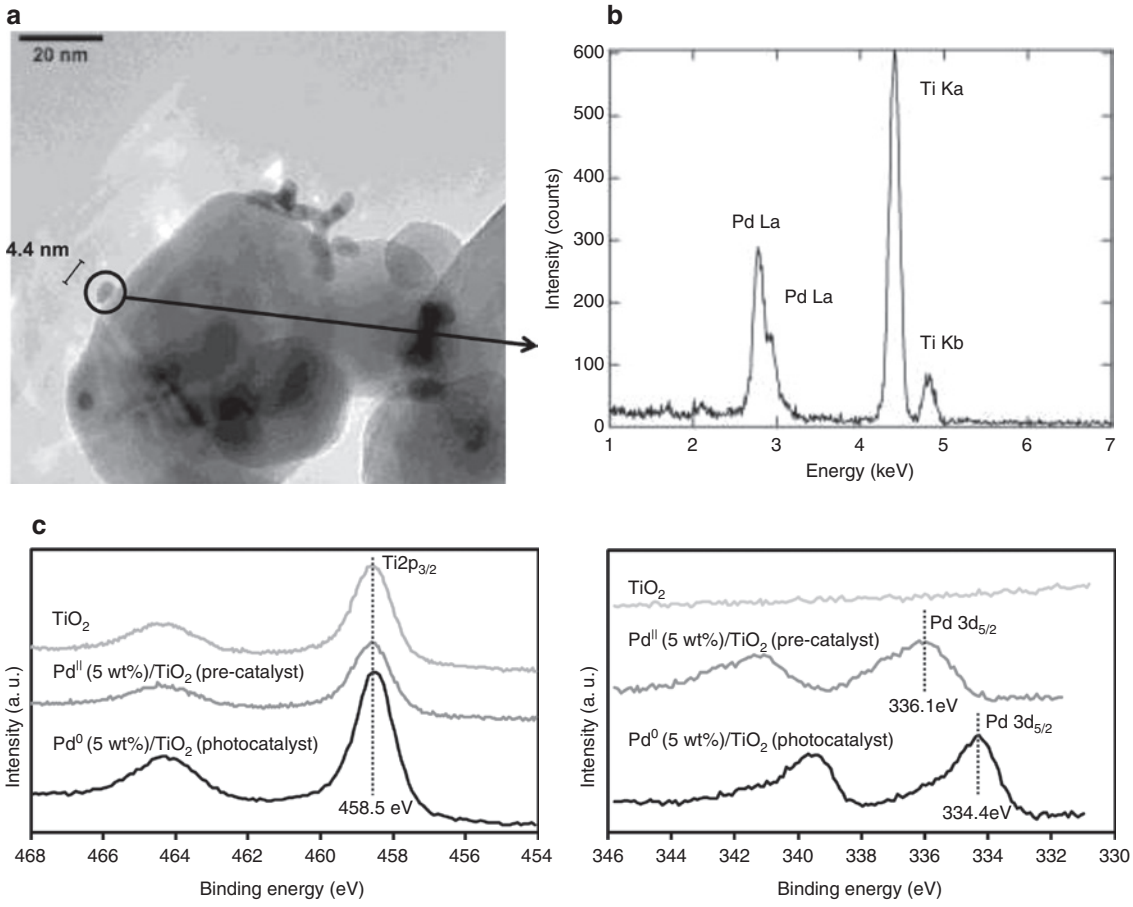
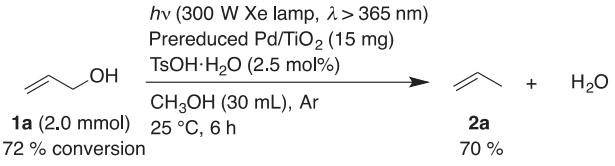


Fig. 1: (a) HRTEM, (b) EDX, and (c) XPS analyses of Pd/TiO_2.



Scheme 2: PcTH of **1a** to **2a** using Pd/TiO_2 under near-UV–vis light irradiation.

of the reaction mixture indicated concomitant formation of methylal and methoxymethanol. In the absence of any acidic additive, PcTH of **1a** gave **2a** in a lower yield. Under slightly acidic conditions with TsOH, the OH group of **1a** may be more readily adsorbed on the photocatalyst covered by a higher concentration of H^+, which could also activate the OH group more effectively, giving protonated **1a**. Pd, TiO_2, and near-UV light irradiation were all essential for PcTH to proceed.

GC monitoring of the product distribution revealed high selectivity of the PcTH for propylene generation (Fig. 2). PcTH of **1a** afforded **2a** in 94 % yield at $t = 9$ h. Hydrogen gas (H_2) generation was negligible before the complete consumption of **1a**. After consumption of **1a**, evolution of H_2 and reduction of **2a** to propane (**3a**) started, implying that the presence of **1a** kinetically suppresses (1) generation of H_2 gas; and (2) hydrogenation of the alkene of **1a** and **2a** on the Pd surface, both of which are otherwise favorable processes. This chemoselectivity is completely opposite to that observed in thermal catalysis over Pd nanoparticles under a hydrogen atmosphere [16].

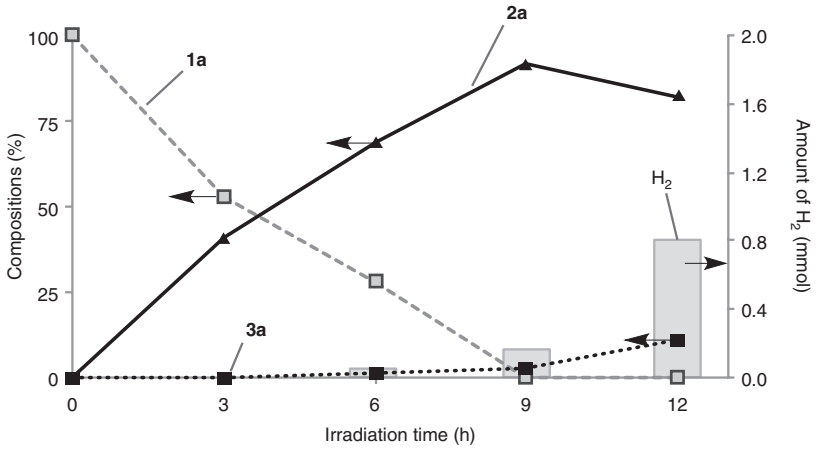


Fig. 2: GC monitoring of molar compositions of **1a**, **2a** and **3a**, and amount of H_2.

Catalyst recycling experiment

Catalyst recycling experiments (Fig. 3) indicated that (1) PcTH of **1a** using recovered photocatalyst gave **2a** without any appreciable decrease in yield; (2) the catalyst could be used at least five times; (3) throughout the recycling experiments, selectivity for producing **2a** over **3a** was consistently >99:1. The total turnover number through five runs calculated based on the amount of Pd loaded on TiO_2 was *ca*. 900 (mol/mol).

PcTH of γ-substituted allylic alcohols

In contrast to non-substituted allylic alcohol **1a**, PcTH of γ-substituted allylic alcohols raises issues of regioselectivity and stereoselectivity. For instance, hydrogenolysis of cinnamyl alcohol (**1b**) can potentially give stereoisomers of (*E*/*Z*)-*β*-methylstyrene [(*E*)-**2b** and (*Z*)-**2b**] and a regioisomer, allylbenzene (*iso*-**2b**). To our delight, however, after optimization of the reaction conditions, we found that PcTH of **1b** using Pd/TiO_2 and an acidic additive (0.5 mol%) selectively gave *E*-**2b** (93 % yield) together with a small amount of over-reduced product **3b** (7 %, Scheme 3). Amounts of other isomers (*Z*-**2b** and *iso*-**2b**) were below the detection limit based on the GC calibration line (<2 % yield). In this experiment, we used Pd/TiO_2 prepared by impregnating TiO_2

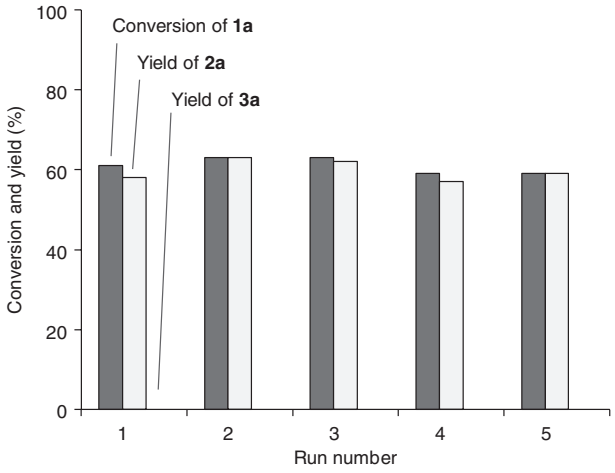
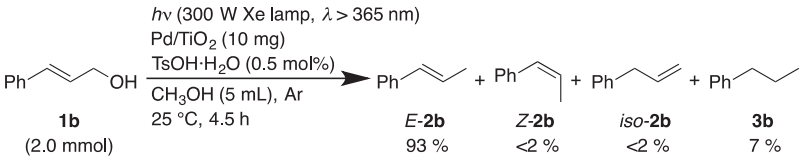


Fig. 3: Catalyst recycling experiment for PcTH of **1a** ($t = 4$ h).



Scheme 3: PcTH of **1b** using Pd/TiO_2 under optimized conditions.

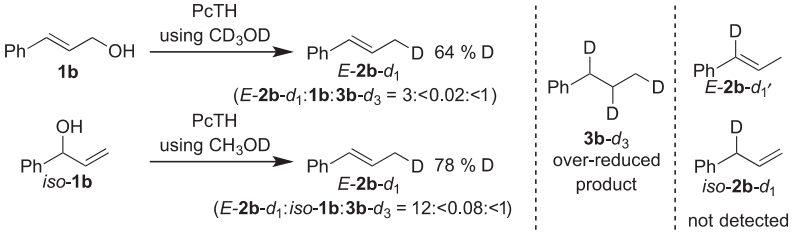
[Degussa Aeroxide® P25, anatase-rutile mixture, 21 nm particle size, 35–65 m^2/g surface area (BET)] with $PdCl_2(CH_3CN)_2$, without pre-reduction with $NaBH_4$ [25]. Again, we found that high chemoselectivity for C–O bond cleavage over C=C π-bond reduction is characteristic of this photocatalytic system: when the reaction mixture was left under a hydrogen atmosphere in the dark, hydrogenation of the C=C π-bond of **1b** afforded 3-phenylpropan-1-ol (86 % yield) and scant hydrogenolysis of the C–O bond of **1b** took place.

Deuterium labeling experiment

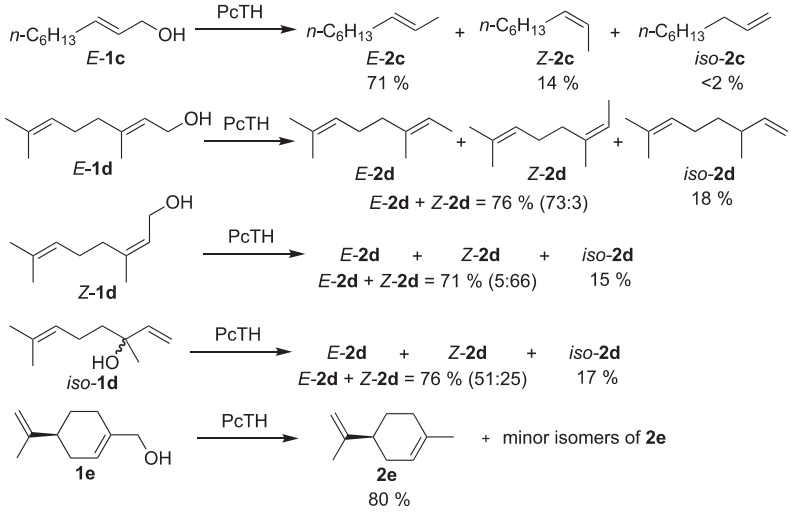
To explore the characteristics of the PcTH, deuterium-labeling experiments were conducted using deuterated methanol (CD_3OD) instead of CH_3OH (Scheme 4, above). ^1H and ^{13}C NMR analyses of the reaction mixture indicated that **1b** was converted to mainly *E*-**2b**-d_1 [*E*-**2b**-d_1 (64 % D):**1b**:**3b**-d_3 = 3:<0.02:<1]. Tri-deuterated **3b** (**3b**-d_3) was generated through over-reduction of *E*-**2b**-d_1. Since *E*-**2b**-d_1' and *iso*-**2b**-d_1 were not formed, the PcTH of **1b** appears to proceed via the S_N2 pathway, affording *E*-**2b**-d_1, rather than the S_N2' pathway followed by migration of the C=C double bond. In contrast, PcTH of 1-phenylallyl alcohol (*iso*-**1b**) using CH_3OD gave only *E*-**2b**-d_1 with high deuterium content (Scheme 4, below). This result suggests that *iso*-**1b** was reduced in the S_N2' manner and that protic deuterium of methanol-d_1 is predominantly used for reduction of *iso*-**1b** rather than C–H hydrogen at the methyl group of methanol-d_1. In other words, these results indicate that the protic hydrogen (or deuterium) is regioselectively incorporated into sterically less congested carbon, irrespective of the position of the OH group in the starting allylic alcohol. This predictability of regioselectivity in the hydrogenolysis of allylic alcohols is unprecedented [6].

Substrate scope

With the optimized conditions in hand, the substrate scope of the PcTH was investigated. A variety of allylic alcohols with aliphatic or aryl substituents underwent hydrogenolysis (selected examples are shown in Scheme 5). A simple aliphatic allylic alcohol *E*-**1c** was selectively converted to the corresponding *E*-**2c** (Scheme 5). PcTH of geraniol (*E*-**1d**) and nerol (*Z*-**1d**) stereospecifically gave the corresponding alkenes, *E*-**2d** and *Z*-**2d**, respectively (Scheme 5). In these cases, S_N2' reaction leading to *iso*-**2d** (15–18 %) occurred to a greater degree, compared with the cases of **1b** and *E*-**1c**. Similar to *iso*-**1b**, PcTH of secondary alcohol *iso*-**1d** proceeded via apparent S_N2' reaction to give a stereoisomeric mixture of two major products [*E*-**2d** and *Z*-**2d**



Scheme 4: Deuterium-labeling experiments. Conditions: **1b** or *iso*-**1b** (2 mmol), *hν* (λ > 365 nm), Pd/TiO_2 (15 mg), $TsOH \cdot H_2O$ (0.5 mol%), CD_3OD or CH_3OD (5 mL), Ar, 25 °C, 5 h.



Scheme 5: Selected results of PcTH of *E*-, *Z*-, and *iso*-allylic alcohols under similar conditions to those of Scheme 3 ($t = 5–10$ h).

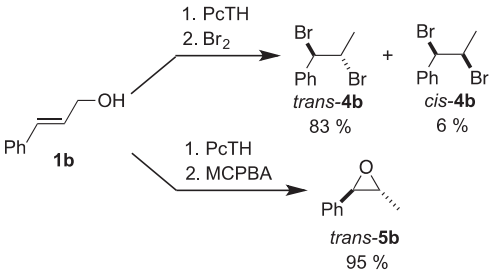
(51:25)] (Scheme 5). The reactivity is significantly higher than that in the reported cobalt catalysis, which was not effective for the reduction of *E*-**1d** to the corresponding alkene [5]. PcTH of (*S*)-perillyl alcohol (**1e**) for 10 h gave (*S*)-limonene (**2e**) in 80 % yield (Scheme 5). No racemization at the chiral carbon center of **1e** took place, and the presence of a C=C bond located distal from the allylic alcohol fragments of *Z*-**1d**, *iso*-**1d** and **1e** was fully tolerated.

Derivation of ene products

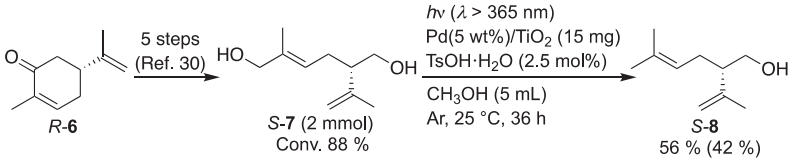
Alkene products obtained by the PcTH of allylic alcohols could be directly derivatized to more highly functionalized products by bromination and epoxidation (Scheme 6). PcTH of **1b** with Pd/TiO_2–methanol followed by bromination with Br_2 selectively afforded *trans*-**4b**, together with a small amount of *cis*-**4b**. Treatment with *m*-chloroperbenzoic acid (MCPBA) instead of Br_2 gave *trans*-**5b** stereospecifically.

Application to (*S*)-(+)-lavandulol synthesis

The high compatibility of PcTH with olefin functionalities encouraged us to attempt a short-step synthesis of (*S*)-(+)-lavandulol (*S*-**8**) via PcTH. Lavandulol is found in several kinds of essential oils and is a sex pheromone of mealybugs [26, 27]. It is used industrially as an additive for perfumes and flavors [28]. Koo et al. [29] recently reported a stereoselective synthesis of *S*-**8** from (*R*)-(−)-carvone (*R*-**6**) involving chemoselective but indirect deoxygenation of allylic alcohol *S*-**7** with retention of the homoallylic hydroxyl group (Scheme 7).



Scheme 6: Photocatalytic transfer hydrogenolysis–derivatization sequence.



Scheme 7: Synthesis of (*S*)-(+)-lavandulol (*S*-**8**) from (*R*)-(–)-carvone (*R*-**6**) employing PcTH.

Their method is superior in terms of ready availability of the starting material to other reported examples of racemic and stereoselective synthesis of lavandulol [28–34]. However, the key deoxygenation of *S*-**7** to *S*-**8** requires a tedious multi-step protection/deprotection sequence and stoichiometrically generates salt as a waste product [29].

We expected that our PcTH would cleave the allylic hydroxyl group rather than the homoallylic one of diol *S*-**7** (Scheme 7). Indeed, PcTH of *S*-**7** chemo- and regioselectively gave *S*-**8** as a major product with retention of the homoallylic hydroxyl group, C=C double bonds, and enantiomeric purity of the chiral center. The present single-step photocatalytic transfer hydrogenolysis thus makes it possible to skip the critical but tedious protection/deprotection steps in the previous route from *S*-**7** to *S*-**8** [29].

Conclusion

We describe a selective photocatalytic transfer hydrogenolysis (PcTH) reaction of allylic alcohols to afford alkenes, promoted by palladium-loaded TiO_2 (Pd/TiO_2) in CH_3OH under near-UV–vis light irradiation at room temperature. The photocatalyst is easily preparable and reusable. The hydrogen source for this reaction is methanol, and consequently, essentially no salt is generated as a wasteful product. PcTH of allyl alcohol opens up a straightforward synthetic route from glycerol to an important platform chemical, propylene. Alkene products of PcTH could be directly derivatized to more highly functionalized, synthetically useful compounds such as epoxides and dibromides. PcTH proceeded in either an S_N2 or S_N2' manner, in which a hydrogen atom was preferentially incorporated into the sterically less congested carbon of the allylic alcohol. This predictable regioselectivity is unprecedented among reported hydrogenolysis reactions of allylic alcohols [6]. Further, C=C double bonds and hydroxyl groups at non-allylic positions of substrates were fully tolerated under the reaction conditions. Such unique chemoselectivity should be useful for fine chemical synthesis, as illustrated by a short-step synthesis of (*S*)-(+)-lavandulol without the need for protection/deprotection steps. The PcTH strategy is expected to be useful for selective, direct and green access to a variety of platform chemicals and fine chemicals from renewable biomass resources and light energy.

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