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Photocatalytic transfer hydrogenolysis of allylic alcohols on Pd/TiO$_2$: A Shortcut to (*S*)-(+)-lavandulol

Yuki Takada,[a] Joaquim Caner,[b] Selvam Kaliyamoorthy,[a] Hiroshi Naka[a,b] and Susumu Saito* [a,b]

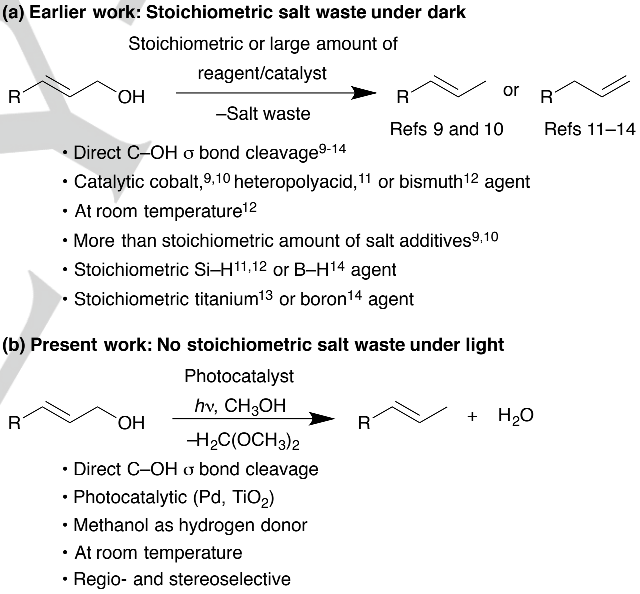
Abstract: We report herein a regio- and stereoselective photocatalytic hydrogenolysis of allylic alcohols to form unsaturated hydrocarbons employing a palladium(II)-loaded titanium oxide; the reaction proceeds at room temperature under light irradiation without stoichiometric generation of salt wastes. Olefin and saturated alcohol moieties tolerated the reaction conditions. Hydrogen atoms were selectively incorporated into less sterically congested carbons of the allylic functionalities. This protocol allowed a short-step synthesis of (*S*)-(+)-lavandulol from (*R*)-(–)-carvone by avoiding otherwise necessary protection/deprotection steps.

Introduction

Reductive deoxygenation is one of the most important methods for transformation of biorenewable resources into useful carbon feedstock.[1] Indeed, catalytic deoxygenation of alcohols via hydrodeoxygenation (HDO: hydrogenolysis of C–O σ bond) or deoxydehydration (DODH) followed by hydrogenation (apparent HDO), is a fundamental approach extensively studied in modern catalysis and is used to produce hydrocarbons as alternative biofuels.[1a,2] However, many of these processes require strenuous (> 150 °C) reaction conditions; in addition, two or more reaction steps are involved in the apparent HDO.

In contrast, hydrogenolysis of the C–O bonds of allylic alcohols, namely the HDO, offers direct access to the corresponding unsaturated hydrocarbons, which are useful building blocks for organic synthesis.[3] A range of allylic alcohols is available from many natural products (e.g., terpenoides)[4] and via catalytic multistep DODH of natural polyols.[5] It is a significant challenge to cleave the C–O σ-bond of allylic alcohols in the presence of hydrogen donors without accompanying side reactions of C=C π-bonds. Possible side reactions include double bond oxygenation (oxirane formation),[6] double bond reduction[7] and double bond isomerization.[7b,8]

Partly to this end, Funabiki *et al*. reported the hydrogenolysis of allylic alcohols with cobalt complex HCo(CN)$_5^{-3}$ under a hydrogen atmosphere.[9] In this reaction, the regioselectivity, S_N2 vs. S_N2' reaction, was altered by changing the ratio of potassium cyanide to cobalt chloride. The regioselectivity of this cobalt catalysis was later improved under milder reaction conditions.[10] In both cases, however, a perfect tolerance of ene groups and hydrogenolysis of γ-disubstituted allyl alcohols were not achieved; in addition, greater than stoichiometric amounts of salt additives were required. Additional systems that have been used for hydrogenolysis include: catalytic heteropolyacid ($H_3[PW_{12}O_{40}]\bullet nH_2O$);[11] bismuth triflate[12] with stoichiometric Et_3SiH and stoichiometric low-valent titanocene;[13] and $NaB(CN)H_3/BF_3\bullet OEt_2$.[14] Nevertheless, stoichiometric by-production of silyl-, titanium- or boron wastes is inevitable and migration of double bonds is not controllable. To date, the reactivity and selectivity of hydrogenolysis of unsymmetrical allylic alcohols, as well as the applicable substrate range, have been unpredictable. In addition, an unmet need persists to minimize byproducts so that a high standard of scalable production of chemicals can be met in next-generation industrial applications (Scheme 1a).



- Direct C–OH σ bond cleavage[9-14]
- Catalytic cobalt,[9,10] heteropolyacid,[11] or bismuth[12] agent
- At room temperature[12]
- More than stoichiometric amount of salt additives[9,10]
- Stoichiometric Si–H[11,12] or B–H[14] agent
- Stoichiometric titanium[13] or boron[14] agent

- Direct C–OH σ bond cleavage
- Photocatalytic (Pd, TiO$_2$)
- Methanol as hydrogen donor
- At room temperature
- Regio- and stereoselective

Scheme 1. Hydrogenolysis of allylic alcohols.
(a) Earlier work by others. (b) Present work: Direct photocatalytic transfer hydrogenolysis (PcTH).

In sharp contrast, our recent focus has been on photocatalysis at room temperature (rt) using a metal nanoparticle (NP)-loaded heterogeneous materials.[15] A novel protocol was previously demonstrated employing photocatalytic transfer hydrogenolysis (PcTH) for reductive deoxygenation of an allylic alcohol with palladium-loaded titanium(IV) oxide (Pd/TiO$_2$) in CH$_3$OH.[16,17] The photocatalysis is highly chemoselective (C–O σ-bond over C=C π-bond of allyl alcohol cleaved) and redox-selective (hydrogenolysis over oxidation of C–O of allyl alcohol). To the best of our knowledge, this was the first example of direct hydrogenolysis of an allylic alcohol to propylene using light energy. However, it was unclear whether the protocol could be used for regioselective PcTH of structurally

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[a] Y. Takada, S. Kaliyamoorthy, Dr. H. Naka, Prof. Dr. S. Saito
Graduate School of Science,
Nagoya University,
Chikusa, Nagoya 464-8602, Japan,
E-mail: saito.susumu@f.mbox.nagoya-u.ac.jp
[b] Dr. J. Caner, Dr. H. Naka, Prof. Dr. S. Saito
Research Center for Materials Science,
Nagoya University,
Chikusa, Nagoya 464-8602, Japan

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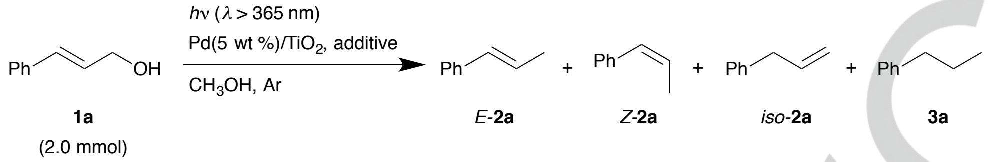
more intricate allylic alcohols while maintaining chemo- and redoxselectivity. We report herein for the first time the synthetic potential and application of PcTH to substituted allyl alcohols (Scheme 1b).

Results and Discussion

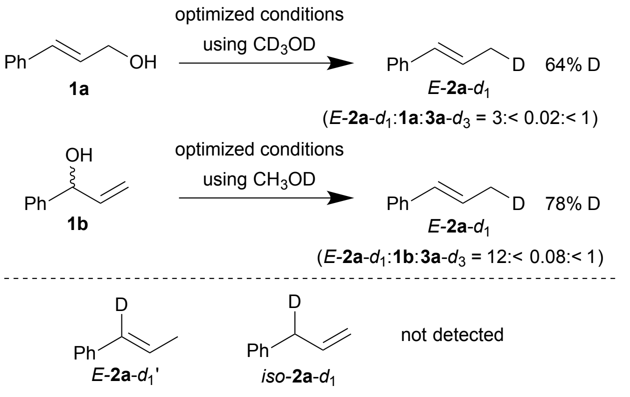
To begin, cinnamyl alcohol (**1a**) was used as a model substrate to optimize the reaction conditions (Table 1). After prescreening photocatalysts, we identified that $PdCl_2(CH_3CN)_2$-loaded TiO_2 (P25) (Pd(5 wt %)/TiO_2) selectively promoted PcTH to furnish *E*-**2a** (entry 1). Amounts of minor side products (*Z*-**2a**, *iso*-**2a** and **3a**) were less than the detection limit of a calibration line. These conditions proved to be superior to our previous conditions for the PcTH of an allylic alcohol[16,17] and other similar conditions (Table S1, ESI). The Pd loading on TiO_2 (P25) was varied to 1, 5 and 10 wt% (Table S1, entries 5 and 6), but a 5 wt% Pd resulted in a slightly higher yield of *E*-**2a** than the other two possible products. Decreasing the amount of $TsOH{\bullet}H_2O$ to 0.5 mol% resulted in a slight increase in yield (entry 2). Indeed, the lower amount of $TsOH{\bullet}H_2O$ gave the highest reaction rate, and *E*-**2a** was obtained in the highest yield with t = 4.5 h (entry 4). Therefore, the catalyst system shown in entries 2–5 was used as the optimized conditions for further studies. The PcTH proceeded in the absence of $TsOH{\bullet}H_2O$ but with a lower reaction rate (entries 6 and 7). Using the sodium salt of $TsOH{\bullet}H_2O$ resulted in only a slight decrease in yield (entry 8 vs. 2). A more dilute CH_3OH solution has a slight influence on the yield of *E*-**2a** (entry 9). Although the PcTH at 50 °C showed a higher reaction rate (entry 10), the yield of **2a**, however, was 77% with 11% of **3a**, whereas it proceeded more sluggishly at 0 °C without an improvement of selectivity (entries 11 and 12). In control experiments, hydrogen gas (H_2) was introduced to the reaction vessel with an expectation that it functions as a hydrogen source for reduction of both **1a** and $Pd^{II}Cl_2(CH_3CN)_2$

Table 1. Optimization of reaction conditions of PcTH[a]



Entry	Pd(5 wt %)/TiO_2 (mg)	CH_3OH (mL)	*T* (°C)	Additive (mol %)	Reaction time *t* (h)	Conv.[b] (%)	Yield[b] (%)			
							E-**2a**	*Z*-**2a**	*iso*-**2a**	**3a**
1	15	5	25	$TsOH{\bullet}H_2O$ (2.5)	2	38	36	–[c]	–[c]	–[c]
2	15	5	25	$TsOH{\bullet}H_2O$ (0.5)	2	46	40	–[c]	–[c]	–[c]
3	15	5	25	$TsOH{\bullet}H_2O$ (0.5)	4	90	79	–[c]	3	–[c]
4	15	5	25	$TsOH{\bullet}H_2O$ (0.5)	4.5	> 99	93	–[c]	–[c]	7
5	15	5	25	$TsOH{\bullet}H_2O$ (0.5)	5	> 99	65	–[c]	–[c]	28
6	15	5	25	none	2	28	29	–[c]	–[c]	–[c]
7	15	5	25	none	5	60	51	–[c]	–[c]	–[c]
8	15	5	25	TsONa (2.5)	2	41	36	–[c]	–[c]	–[c]
9	15	30	25	$TsOH{\bullet}H_2O$ (0.5)	2	40	32	–[c]	–[c]	5
10	15	30	50	$TsOH{\bullet}H_2O$ (2.5)	2	98	77	–[c]	3	11
11	15	5	0	$TsOH{\bullet}H_2O$ (0.5)	2	–[e]	16	–[c]	–[c]	4
12	15	5	0	$TsOH{\bullet}H_2O$ (0.5)	7	78	68	–[c]	–[c]	8
13[d]	15	5	25	$TsOH{\bullet}H_2O$ (0.5)	2	99	–[c]	–[c]	–[c]	10
14	0	5	25	$TsOH{\bullet}H_2O$ (2.5)	5	< 1	–[c]	–[c]	–[c]	–[c]

[a] Light source: 300 W Xe lamp with a cold mirror (λ > 365 nm). Pd(5 wt %)/TiO_2 ($Pd^{II}Cl_2(CH_3CN)_2$-loaded TiO_2) photocatalyst was made using P25 (Degussa Aeroxide® P25, from Sigma–Aldrich, anatase-rutile mixture, 21 nm particle size, 35–65 m^2/g surface area (BET)). [b] Determined by GC-MS (dodecane as an internal standard). [c] Not determined because the product was barely or not detected (less than < 2%). [d] Under H_2 instead of Ar without light irradiation. 3-Phenylpropan-1-ol was generated in 86% yield. [e] Not determined.



Scheme 2. PcTH of **1a** and **1b** using deuterated methanol.
Conditions: **1a** or **1b** (2 mmol), hν (λ > 365 nm), $PdCl_2(CH_3CN)_2$-loaded TiO_2 (Pd(5 wt%)/TiO_2) (15 mg), $TsOH{\bullet}H_2O$ (0.5 mol %), CD_3OD or CH_3OD (5 mL), 5 h, Ar, 25 °C. The products were analysed by ^1H and ^{13}C NMR. Yield (molar ratio) and deuteration ratio were determined by ^1H NMR. Major side products were diastereomers of **3a**-d_n (PhCH(D/H)CH(D/H)CH_2(D/H)) (n = 0–3)

loaded on TiO_2 (P25); however, almost no hydrogenolysis of the C–O bond tookplace even after t = 5 h (entry 13). The major product was 3-phenylpropan-1-ol, which was generated in favour of hydrogenation of the C=C π-bond of **1a**. Light irradiation in the absence of catalyst led to minimal conversion of **1a** (entry 14).

Considering mechanistic scenario, n (n = an integer) holes (nh^+) and n electrons (ne^-) are generated in TiO_2 photocatalysts upon light irradiation.[16] In a formal sense, CH_3OH is oxidized, giving $2e^-$ to holes ($2h^+$) on the surface of TiO_2 (Figure 1). Excited $2e^-$ of TiO_2 accumulate on the Pd NP surface and interact with $2H^+$ (apparently from CH_3OH) to give active hydrogen atoms adsorbed [2H(ad)] on Pd NP. Under slightly acidic conditions with TsOH, the OH group of allylic alcohol may be more readily adsorbed on Pd NP covered by a higher concentration of H^+, which could also activate the OH group more effectively, giving $R–OH_2^+$. Separately formed transient H(ad) (H^+ and $2e−$) on Pd NP seems to react with $R–OH_2^+$, which facilitates attack of H(ad) toward a carbon of $R–OH_2^+$ via S_N2 or $S_N2´$ manner. Allylic alcohols and CH_3OH would make a self-assembled monolayer-type alignment on Pd NP so that the alkyl and olefin groups could expose to the space distal from the NP surface. Indeed, a preceding report indicates that at high coverage of benzyl alcohol on Pd (111) surface, the alcohol adopts an upright structure (more likely standing up perpendicular to the surface, rather than sprawling on the surface), where only the alcohol function is bound to the Pd surface and the phenyl ring extends into vacuum.[18a,b] Indeed, benzyl alcohol underwent the hydrogenolysis of the C–O bond using Pd/TiO_2 under light.[18c,d] In contrast, Shon suggested that the hydrogenation/isomerization reactions of allyl alcohol in the presence of H_2 on alkanethiolate-capped Pd NP surface likely occur through a mono-σ-bonded Pd-alkyl intermediate followed by β-hydride elimination. When there is no H_2 present, a π-allyl Pd hydride mechanism is also suggested.[18e,f] Since hydrogenation and isomerization of, at least, the trisubstituted olefins of allylic alcohols *E*- and *Z*-**1g** (*vide infra*) are slower than the hydrogenolysis of their C–O bonds in the present PcTH, the mechanism shown in Figure 1 would be more favourable.

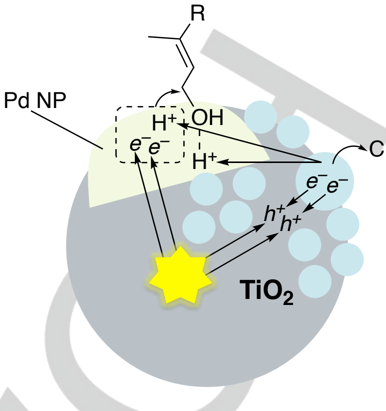
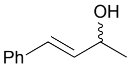
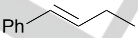
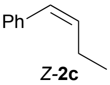
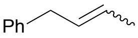
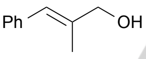
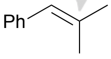
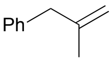
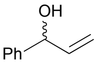
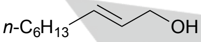
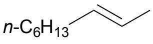
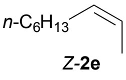
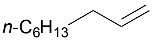
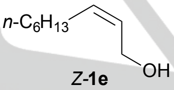


Figure 1. H^+ and $2e^-$ (in dotted square) would work as H^-. CH_3OH (small circles in light blue) loses $2e^-$ (which combine with $2h^+$) and $2H^+$ (which move to a surface of Pd NP and interact with $2e^-$ that came from light-excited sites (shining yellow star) of TiO_2 (a large circle in gray)).

Deuterated methanol (CD_3OD) was used instead of CH_3OH under the optimized conditions to get further insight into the characteristics of the PcTH reaction (Scheme 2). As a result, *E*-**2a**-d_1 was obtained from **1a** as the major product (*E*-**2a**-d_1 (64% D):**1a**:**3a**-d_3 = 3:< 0.02:< 1, t = 5 h). ^1H and ^{13}C NMR analysis indicated that over-reduced product **3a** was tri-deuterated. The yield of fully saturated hydrocarbons **3a**-d_n (n = 1–3) was comparable to that obtained previously (Table 1, entry 5).

Table 2. Substrate scope of PcTH[a]

Entry	Substrate	Reaction time t (h)	Products	Conv.[b]	Yield[b](%) $E + Z$ (ratio)[c]	Yield[b](%) *iso*
1[d]	 **1c**	2	 *E*-**2c** +  *Z*-**2c** +  *iso*-**2c**	69	61 (61:–[e])	–[e]
2	 **1d**	6	 **2d** +  *iso*-**2d**	99	90	7
3	 **1b**	3	*E*-**2a** + *Z*-**2a** + *iso*-**2a**	86[f]	67[f] (64:3)[f]	4[f]
4	 *E*-**1e**	5	 *E*-**2e** +  *Z*-**2e** +  *iso*-**2e**	> 99	85 (71:14)	–[e]
5	 *Z*-**1e**	5.5	*E*-**2e** + *Z*-**2e** + *iso*-**2e**	> 99	82 (43:39)	–[e]

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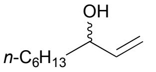
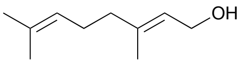
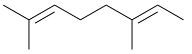
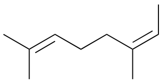
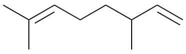
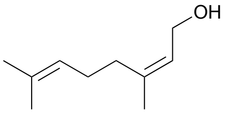
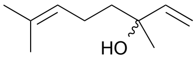
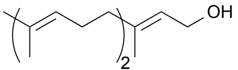
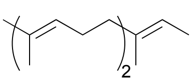
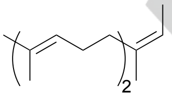
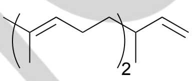
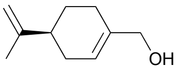
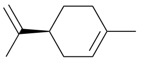
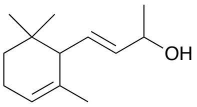
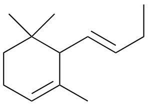
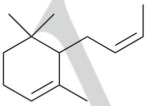
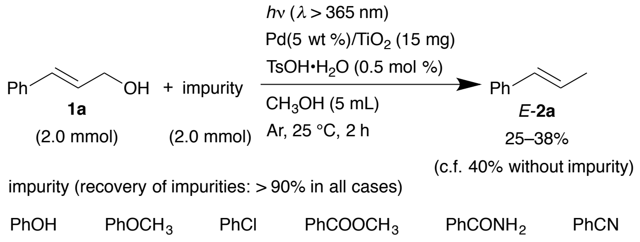
6[g]	 **1f**	5	*E*-**2e** + *Z*-**2e** + *iso*-**2e**	> 99	72 (57:15)	–[e]
7	 *E*-**1g**	6	 *E*-**2g** +  *Z*-**2g** +  *iso*-**2g**	> 99	76 (73:3)[h]	18
8	 *Z*-**1g**	6	*E*-**2g** + *Z*-**2g** + *iso*-**2g**	95	71 (5:66)[h]	15
9	 **1h**	6	*E*-**2g** + *Z*-**2g** + *iso*-**2g**	> 99	76 (51:25)[h]	17
10	 **1i**	5.5	 *E*-**2i** +  *Z*-**2i** +  *iso*-**2i**	> 99	81 (–[i]) (83)[j]	16
11[k]	 **1j**	10	 **2j** + isomers of **2j**	98[f]	80[f] (**2j**) + isomers[l]	
12	 **1k**	6	 **2k** or  *iso*-**2k**	< 10	–[e]	

[a] Conditions: allylic alcohol (2 mmol), CH_3OH (5 mL), Pd(5 wt%)/TiO_2 ($Pd^{II}Cl_2(CH_3CN)_2$-loaded TiO_2) (15 mg), $TsOH•H_2O$ (0.5 mol%), 300 W Xe lamp with a cold mirror (l > 365 nm), Ar atmosphere (1 atm), 25 °C unless otherwise specified. [b] Determined by ^1H NMR analysis (1,1,2,2-tetrachloroethane or benzene as internal standard). [c] The number in parentheses is molar ratio of the *E*/*Z* product determined by ^1H NMR analysis unless otherwise noted. [d] TsONa (2.5 mol %) was used instead of $TsOH•H_2O$. Negligible amount of 4-phenylbutan-2-ol and (3-methoxybutyl)benzene were detected. [e] Not determined because the product was barely or not detected. [f] Conversion and yield were determined by GC-MS (dodecane as an internal standard). [g] Nonan-3-one and nonan-3-ol were also observed in 17 and 14% yield, respectively. [h] Area ratio of *E*-**2g** and *Z*-**2g** analysed by GC-MS. [i] *Z*-isomer was not detected on ^{13}C NMR analysis. [j] Of isolated as a mixture of isomers. [k] 2.5 mol % of $TsOH•H_2O$ was used. [l] The structures of isomers were not confirmed. Area ratio of **2j**:isomers was 40:3 in GC-MS analysis.

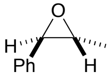
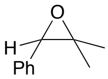
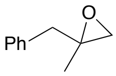
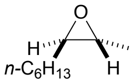
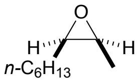
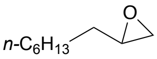
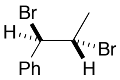
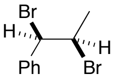
Given the absence of deuteration at the β and γ position of *E*-**2a** and based on the mechanistic scenario proposed in Figure 1, the PcTH of **1a** proceeded via an apparent S_N2 pathway giving *E*-**2a**-d_1, rather than $S_N2´$ followed by migration of the double bond.[19,20] In contrast, **1b** was converted solely to *E*-**2a**-d_1 using CH_3OD. Since it is highly unlikely that a π-allyl Pd intermediate was majorly involved in the catalytic cycle, **1b** reacted with an active hydrogen atom (H(ad)) through an apparent $S_N2´$ pathway in preference to an S_N2 pathway. These results suggest that, irrespective of the position of the OH group of **1a** and **1b**, H(ad) (hydride or H^+ + $2e^–$) favourably attacked less sterically congested carbons; in other words, the terminal positions of the main alkyl chain of **1a** and **1b** were consistently targeted. Such a predictable regioselectivity in hydrogenolysis of allylic alcohols is unprecedented.[11]

With the optimized PcTH conditions in hand, the substrate scope was investigated (Table 2). 2° alcohol **1c** underwent hydrogenolysis faster than **1a** (entry 1). In the PcTH of **1d**, **2d** was produced through the S_N2 pathway predominately (entry 2). As mentioned in the deuterium-labelling experiment (Scheme 2), PcTH of **1b** gave *E*-**2a** rather than *iso*-**2a** (entry 3). Aliphatic allylic alcohols in three different isomeric forms were tested (entries 4–6). *E*-**1e** was converted into the corresponding *E*-**2e** in a better yield than *Z*-**1e**, and the *Z*-isomer *Z*-**2e** was also detected. The selectivity of *Z*- vs. *E*-**2e** was low in the case of *Z*-**1e**, probably due to the isomerization of olefins occurring during the PcTH.[19,20] *E*-**2e** was generated as the major product from 2° alcohol **1f** through an apparent $S_N2´$-enriched hydrogenolysis (entry 6). Geraniol (*E*-**1g**) and nerol (*Z*-**1g)** were converted stereospecifically to the *E*-**2g** and *Z*-**2g**, respectively (entries 7 and 8). Both reactions were more contaminated with $S_N2´$ reaction products than when *E*-**1e** and *Z*-**1e** were used, providing *iso*-**2g** bearing a terminal olefin in a small amount (~15%). The isomeric 3° alcohol **1h** underwent an apparent $S_N2´$ reaction, giving a mixture of *E*-**2g** and *Z*-**2g** (3:1) as the two major products (entry 9). This is a stark contrast to the cobalt catalysis, in which hydrogenolysis of sterically congested *E*-**1g** and **1h** proceeded with minimal conversion.[10] Farnesol (**1i**) was chosen because of the higher boiling points of the corresponding hydrocarbon products, which facilitate easy separation and isolation by column chromatography (entry 10). The product distribution of isomeric structures was comparable to that obtained with *E*-**1g**. *E*-**2i** was obtained in an isolated yield of 83%, together with minor isomers *Z*-**2i** and *iso*-**2i**. PcTH of (*S*)-perillyl alcohol (**1j**) was completed by prolonging *t,* and an important fragrance, (*S*)-limonene (**2j**), was obtained in 80%



Scheme 3. Functional group compatibility test.
Yield and conversion obtained after PcTH were determined by GC-MS (dodecane as an internal standard).

Table 3. Derivation of ene products after PcTH of allylic alcohols[a]

Entry	1	Product, yield[b]		
1	**1a**	 *trans*-**4a** 95%		
2	**1d**	 **4d** 81%	 *iso*-**4d** 8%	
3[c]	*E*-**1e**	 *trans*-**4e** 56%	 *cis*-**4e** 2%	 *iso*-**4e** 10%
4	**1a**	 *trans*-**5a** 83%	 *cis*-**5a** 6%	

[a] PcTH conditions: allylic alcohol (2 mmol), CH_3OH (5 mL), $PdCl_2(CH_3CN)_2$-loaded TiO_2 (Pd(5 wt%)/TiO_2) (15 mg), TsOH•H_2O (0.5 mol%), 300 W Xe lamp with a cold mirror (λ > 365 nm), Ar atmosphere (1 atm), 25 °C, 4–6 h. Epoxidation (or dibromination) procedures: After filtration of the reaction mixture obtained by PcTH, the filtrate was washed with H_2O and extracted with $CHCl_3$ (or hexane), and the mixture was treated with MCPBA (2.9 mmol) at 0 °C for 3 h (or with Br_2 (20 mmol) at 0 °C for 12 h). See ESI for experimental details. The structures in the table show relative configuration. [b] Determined by ^1H NMR (1,1,2,2-tetrachloroethane as an internal standard). [c] (3-nonyloxiran-2-yl)methanol generated from starting allylic alcohol was also obtained in 28% yield.

yield (entry 11). Chiral GC-MS analysis showed that the chiral center of **1j** was retained after the PcTH. The C=C bonds distal from the reacting carbon also tolerated the PcTH conditions (entries 7–11). This result is markedly different from conventional hydrogenation of C=C π-bonds over a Pd/solid support under H_2 in the dark. Sterically congested **1k** was not converted to neither **2k** nor *iso*-**2k** (entry 12).

Whether other functional groups could tolerate the PcTH conditions was also investigated (Scheme 3). As a result, phenol, ether, chloroaryl, ester, amide, and nitrile groups of non-allylic alcohols essentially unreacted at least in a short light irradiation time (2 h).

To further probe functional group compatibility, a carbon–carbon triple bond was also tested under the PcTH conditions (Table S2, ESI). A propargylic alcohol (3-phenylprop-2-yn-1-ol) was used instead of allylic alcohols. Semi-hydrogenation of carbon–carbon triple bond first took place to give *Z*-**1a** as major product (58% after 5 h). The reaction that retards subsequent C=C bond reduction reminds us of the Lindlar's catalyst and recent Pd variants bearing similar functions at a high pressure of H_2;[21] unlike the Lindlar's catalyst, however, in this system under light, poisoning of Pd surface (with $Pb(OAc)_2$, $CaCO_3$, and/or organic substrates such as quinoline) is not required. Subsequent PcTH of the allylic C–O bond of *Z*-**1a** (and **1a**) similarly gave a mixture of *E*- and *Z*-**2a** (75% after 12.5 h). Because of possible isomerization of the olefin groups under near UV-Vis light,[19,20] *E/Z* selectivity was moderate upon a longer reaction time (up to *E*/*Z* = 31:44, see ESI).

To expand the synthetic application of PcTH, direct derivation of a set of olefinic products was performed on the crude mixture obtained after PcTH (Table 3). After removal of the photocatalyst by filtration, the filtrate was washed with H_2O and extracted with $CHCl_3$ or hexane. The $CHCl_3$ solution of a crude mixture of *E*-**2a**, *Z*-**2a** and *iso*-**2a** were subjected to further reactions (See ESI for experimental details). For instance, epoxidation of a mixture of ene products by *m*-chloroperbenzoic acid (MCPBA) furnished *trans*-**4a** in 95% yield (entry 1).[22] A minimal amount of *cis*-2-methyl-3-phenyloxirane and 2-benzyloxirane were also detected by ^1H NMR. The epoxidation took place stereospecifically. Likewise, epoxidation of crude olefinic compounds obtained by PcTH of **1d** and *E*-**1e** yielded epoxides **4d** and *trans*-**4e**, respectively, which were obtained as major products (entries 2 and 3). When crude ene products obtained by PcTH of **1a** were treated with Br_2 instead of MCPBA, an 83% yield of *trans*-**5a** was obtained (entry 4).

By taking advantage of the double bond compatibility under the PcTH reactions, the synthetic shortcut to (*S*)-(+)-lavandulol (*S*-**7**) from precursor diol **6** was demonstrated. Lavandulol is in an important class of monoterpenes mainly found in *lavandula* essential oils; it plays a pivotal role as a sex pheromone in some mealybugs.[23] In industrial applications, lavandulol is an important additive used to control the odour balance of perfumes and flavors.[24] Several racemic and stereoselective syntheses of lavandulol have been reported because of its importance.[24–26] These methods, however, require a variety of starting materials or suffer from low regioselectivity and tedious multistep reactions involving protection/deprotection steps. Recently, Koo *et al.* succeeded in a stereoselective eight-step synthesis of *S*-**7** from (*R*)-(–)-carvone,[26] which is frequently utilized as a chiral building block in asymmetric synthesis.[27] In Koo's synthesis, a protective activation of the key intermediate **6** is a critical step. However, the synthesis mandates stoichiometric generation of multiple (metallic) wastes (Scheme 4).[26]

Two different hydroxyl groups, allylic and homoallylic alcohols, are incorporated in **6**. Our expectation was that PcTH would selectively deoxygenate an allylic alcohol over a homoallylic alcohol. After diol **6** was prepared according to reported procedures,[26] it was subjected to PcTH under the optimized conditions except that a larger amount of TsOH (2.5 mol %) was used (Scheme 4). To our delight, *S*-**7** was obtained in 56% yield (isolated yield: 42%) through selective PcTH of the allylic alcohol. A minor side product, an isomer of *S*-**7** (5-methyl-2-(prop-1-en-2-yl)hex-5-en-1-ol), was also detected by ^1H and ^{13}C NMR analysis (16% yield). The chirality of *S*-**7** was retained from racemization, ascertained by chiral GC analysis.

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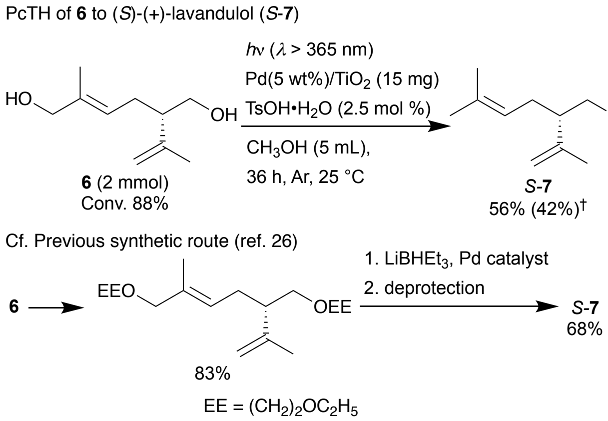
It should be noted that the protection-deprotection strategy critical for the previous total synthesis of *S*-**7**[26] was bypassed with PcTH, where both the homoallylic C=C bond and alcohol moieties effectively tolerated the PcTH conditions.



Scheme 4. Synthesis of (*S*)-(+)-lavandulol (*S*-**7**) from intermediate **6**. Yield and conversion obtained after PcTH were determined by ^1H NMR (1,1,2,2-tetrachloroethane as an internal standard). †Of isolated, purified product.

Conclusions

In conclusion, we have developed a selective photocatalytic transfer hydrogenolysis (PcTH) of allylic alcohols to furnish unsaturated hydrocarbons using palladium(II)-loaded TiO_2(P25) in CH_3OH under near-UV–Vis light at room temperature. The precatalyst is simply prepared by impregnating TiO_2 with a palladium(II) source; PcTH can immediately be started using the precatalyst without its calcination. The only reagent used was CH_3OH,[28] which is a cheap and sustainable solvent, hydrogen/electron donor, and hole scavenger in photocatalysis.[29] Owing to this efficient and green nature, salt wastes were not formed. In addition, simple removal of catalyst and solvent facilitated further derivation of the PcTH products to synthetically useful, functionalized compounds. It is now predictable that both the S_N2 or S_N2' reactions take place so that hydrogen atoms of CH_3OH and/or allylic alcohols are incorporated more favourably into the less sterically hindered carbon of starting materials. Many functional groups including C=C bonds, phenol, ether, chloroaryl, ester, amide, and nitrile groups of non-allylic alcohols well tolerate PcTH conditions by setting an appropriate light irradiation time. Application of PcTH to the rapid synthesis of (*S*)-(+)-lavandulol was also successfully achieved without protection/deprotection steps. We envisage that PcTH will further provide selective and direct routes to useful (chiral) platform- and fine chemicals, capitalizing on the renewability of biomass resources and the sustainability of light energy.

Experimental Section

Catalyst preparation

Pd(5 wt%)/TiO_2 ($PdCl_2(CH_3CN)_2$-loaded TiO_2): Pd(5 wt%)/TiO_2 ($PdCl_2(CH_3CN)_2$-loaded TiO_2) catalyst was prepared in a 1000 mL round-bottom flask covered with aluminum foil by impregnation of 6.06 g of TiO_2 (Degussa Aeroxide® P25) with a solution of $Pd(CH_3CN)_2Cl_2$ (0.319 g, prepared by refluxing $PdCl_2$ in CH_3CN) in a deionized H_2O/THF (5:1, 300 mL). The slurry was sonicated for 5 min and stirred using rotary evaporator under atmospheric pressure for 1 h at 50 °C. Then, solvent was removed under reduced pressure. The remaining solid was ground in a mortar and dried at 50 °C under oil pump vacuum for 7 h. The final amount of the solid ($PdCl_2(CH_3CN)_2$-loaded TiO_2) was 5.98 g.

PcTH of 1a employing Pd(5 wt%)/TiO_2 (Table 1, entry 3 (*t* = 4 h))

A cylindrical Pyrex glass vessel was charged with a cross-shaped magnetic stir bar, Pd(5 wt%)/TiO_2 (15 mg), cinnamyl alcohol (**1a**, 268 mg, 2.00 mmol), *p*-toluenesulfonic acid monohydrate (TsOH•H_2O, 1.9 mg, 0.01 mmol), *n*-dodecane (as internal standard, 50 μL) and anhydrous CH_3OH (5 mL). After sonication of the mixture (to fully disperse the photo-precatalyst), the reaction vessel was sealed with a rubber septum and the stirred suspension was immediately deaerated with a stream of Ar. After the Ar stream was stopped, the mixture of a closed system was irradiated with near-UV–Vis light (λ > 365 nm). After reaction time (*t*) of 4 h, the reaction mixture was sampled by a syringe and analyzed by GC-MS to determine the amount of **1a**, *trans*-b-methyl styrene (*E*-**2a**), *cis*-b-methyl styrene (*Z*-**2a**), 3-phenyl-1-propene (*iso*-**2a**) and propylbenzene (**3a**). The yields of **1a** (0.20 mmol, 90% conversion), *E*-**2a** (1.57 mmol, 79% yield) and *iso*-**2a** (0.052 mmol, 3% yield) were determined based on the corresponding calibration curves made with authentic samples and *n*-dodecane as an internal standard. The yields of *Z*-**2a** and **3a** were not determined because the amounts detected by GC were smaller than detection limit of the calibration curves (less than 2%). Minimal amounts of 3-phenylpropan-1-ol and benzaldehyde dimethyl acetal were also detected by GC-MS.

(*S*)-(+)-Lavandulol (*S*-7) synthesis through PcTH of lavandulol precursor 6

A cylindrical Pyrex glass vessel was charged with a cross-shaped magnetic stir bar, $PdCl_2(CH_3CN)_2$-loaded TiO_2 (15.0 mg), (*S*,*E*)-2-methyl-5-(prop-1-en-2-yl)hex-2-ene-1,6-diol (**6**, 341 mg, 2.00 mmol), *p*-toluenesulfonic acid monohydrate (TsOH•H_2O, 9.8 mg, 0.05 mmol), *n*-dodecane (50 μL) and dehydrated CH_3OH (5 mL). After sonication of the mixture (to fully disperse the photocatalyst), the reaction vessel was sealed with a rubber septum and the stirred suspension was immediately deaerated with a stream of Ar. After Ar stream was stopped the mixture of closed system was irradiated with near-UV–Vis light (λ > 365 nm). After *t* of 36 h, light irradiation was stopped. The mixture was analyzed directly by ^1H NMR and ^{13}C NMR to determine the yield based on integral ratios between the products and the internal standard (1,1,2,2-tetrachloroethane). (*S*)-(+)-lavandulol (*S*-**7**) and its stereoisomer (5-methyl-2-(prop-1-en-2-yl)hex-5-en-1-ol (**8**, structure of which was determined based on ^1H NMR and ^{13}C NMR) were obtained in 56% (1.12 mmol) and 16% (0.32 mmol) yield, respectively, and 12% (0.24 mmol) of starting material **6** was recovered. The mixture of PcTH was filtered through a Celite pad and the residue remained on the pad was washed with CH_2Cl_2. The filtrate was added to H_2O (15 mL) in a separatory funnel and the organic phase was extracted with CH_2Cl_2 (10 mL × 3). The combined organic phase was washed with aqueous NaCl and dried over Na_2SO_4. After filtration, the filtrate was evaporated *in vacuo* and the residue was purified by column chromatography on silica gel (hexane/ethyl acetate (EtOAc) = 25:1 to 10:1) to give (*S*)-(+)-lavandulol (*S*-**7**) as colorless oil with an isolated yield of 42% (129 mg, 0.82 mmol).

Supplemental results, experimental procedures and spectra data of compounds were available in ESI.

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Keywords: hydrogenolysis • photocatalysis • allylic alcohols • titanium oxide • palladium

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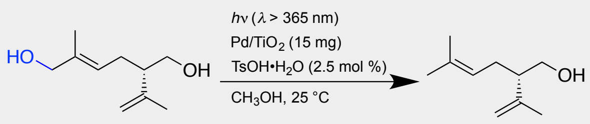

•Regio- and stereoselective direct C–OH σ bond cleavage without stoichiometric salt waste

We report herein a regio- and stereoselective photocatalytic hydrogenolysis of allylic alcohols to form unsaturated hydrocarbons employing a palladium(II)-loaded titanium oxide; the reaction proceeds at room temperature under light irradiation without stoichiometric generation of salt wastes. This protocol allowed a short-step synthesis of (S)-(+)-lavandulol from (R)-(–)-carvone by avoiding otherwise necessary protection/deprotection steps.

*Yuki Takada, Joaquim Caner, Selvam Kaliyamoorthy, Hiroshi Naka, Susumu Saito**

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Photocatalytic transfer hydrogenolysis of allylic alcohols on Pd/TiO_2: A Shortcut to (*S*)-(+)-lavandulol