Synthesis of anti-Markovnikov Alcohols via Epoxidation and Hydrogenation of Styrenes using Photocatalytically Generated Redox Equivalents

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We report an efficient method for a formal anti-Markovnikov addition of water to styrenes through photocatalytic generation of redox equivalents, using a gold-doped titanium dioxide (Au/TiO2) semiconductor as photocatalyst. Under irradiation with UV–A light, the photocatalytic activity of Au/TiO2 generates in situ under aerobic conditions hydrogen peroxide (H2O2) and under anaerobic conditions dihydrogen (H2). In the presence of oxygen and a Ru catalyst, the epoxidation of different styrene derivatives is achieved. Subsequently, regioselective reductive Pd-catalyzed epoxide opening in the absence of oxygen gives the corresponding 2-phenylethanol derivatives.

1. Introduction

TiO2-based semiconductor materials are used in photocatalytic processes, especially in applications for wastewater treatment and air purification.[1] In most cases, hydrogen peroxide and hydroxyl radicals are produced by irradiation of TiO2 with light under aerobic conditions. Among others, these species are mainly responsible for the oxidative degradation of pollutants. Besides that, TiO2 has attracted a lot of attention in photocatalytic energy production. It is considered one of the most promising materials for hydrogen generation from oxidation of water under inert conditions.[2] In contrast, the use of TiO2 as photocatalyst for organic synthesis remains less explored with considerably fewer reports.[3]

Herein, we report a specific application of TiO2 in the synthesis of 2-phenylethanol derivatives from the corresponding styrenes via epoxidation and subsequent reductive ring opening. TiO2 has already been reported as photocatalyst for the anti-Markovnikov hydration of aliphatic alkenes, however only in low yields and the method was not applied for vinyl arenes.[4] In particular, we are using a heterogeneous Au-doped TiO2 photocatalyst for the in situ production of H2O2 under oxygen atmosphere as well as H2 under an inert atmosphere in THF, in combination with a ruthenium-based catalyst for the epoxidation and a palladium-based catalyst for the epoxide opening. Scheme 1 summarizes the overall process. The deposition of gold nanoparticles on TiO2 is beneficial for the overall photocatalytic performance.[5] Due to the semiconductors intrinsic band gap of 3.2 eV for anatase and 3.0 eV for rutile, even non-doped TiO2 is capable of absorbing light in the ultraviolet region. This causes excitation of electrons into the conduction band, which can be used for reductive processes and holes in the valence band, which can be used for oxidative processes.[6] Deposition of metal nanoparticles results in better spatial charge separation (metal NP act as electron traps) and less prominent charge recombination, thus enhancing the photocatalytic performance of the material.[7] In this work, we show a photocatalytic alternative to classic synthetic strategies for 2-phenylethanol derivatives, which include Grignard reactions, Friedel-Crafts-type reactions, or biochemical approaches.[8] In contrast to those, our strategy is based on a two-step photocatalytic approach, with no need for stoichiometric amounts of metal reagents, due to the use of cheap and abundant organic solvents as terminal reductants. Additionally, our method is very safe, due to the in situ generation of H2O2 and H2. Thus, handling of the commonly used hazardous 30% aqueous H2O2 for the epoxidations and inflammable H2-gas under great pressure or in large reservoirs for the reduction is avoided. Alteration between H2O2- and H2-production can easily

Scheme 1. Schematic depiction of the synthesis of 2-phenylethanol from styrene in two steps. Left: Photocatalytic generation of H2O2 under an oxygen atmosphere and ruthenium-catalyzed epoxidation step. Right: Photocatalytic generation of H2 under an inert atmosphere and palladium-catalyzed regioselective epoxide opening.

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Supporting information for this article is available on the WWW under https://doi.org/10.1002/cptc.202000205

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be achieved by switching between aerobic and anaerobic conditions in the reaction vial. A convenient sample preparation strategy was developed, without the need for isolation of the intermediate epoxide. Both individual steps were optimized using the two most used modifications of TiO_2 (P25 and rutile) and we compare the catalytic activity of both materials.

2. Results and Discussion

2.1. Photocatalytic Generation of Redox Equivalents Using Au/TiO_2

Previous work has shown that Au/TiO_2 is suitable for the photocatalytic generation of H_2O_2 as well as H_2 from water or organic solvents. For both reactions, gold-doping was necessary to achieve sufficient amounts of H_2O_2 or H_2 in order to be applicable to organic reactions. Here we used two distinct Au/TiO_2-catalysts differing in the respective modification of the TiO_2 support material. In the following the two catalysts are referred to as Au/TiO_2 (rutile), where the supporting material was TiO_2 in the rutile modification, and Au/TiO_2 (P25), where the supporting material was TiO_2 in the P25 modification, which in itself is a mixture of 75%-85% anatase, 15% rutile and a small amount of amorphous phase.

Previous detailed investigations showed that no significant difference for H_2O_2 production between both modifications is observed. The H_2 production for both materials under various reaction conditions was quantified by measurement of the amount of H_2 in the gas phase of a reaction vial using head space-GC (HS-GC) after 1 hour of irradiation with light. To calculate the actual amount of hydrogen a calibration curve derived from the HS-GC-response for defined amounts of H_2 in the reaction vial was used assuming ideal gas behavior. The measurements showed linear behavior for at least up to 82 μmol (2 mL) of hydrogen. For a detailed description of the HS-GC set-up and the calibration procedure see Si (section 3, Scheme S1). Figure 1 shows the H_2 evolution activity under varying reaction conditions. In i) the amount of H_2 produced from 2 mg of either Au/TiO_2 (rutile) or Au/TiO_2 (P25) under 385 nm irradiation for 1 hour in different solvents is compared. In contrast to the similar performance of both materials for the H_2O_2-production, in this case the P25-modification clearly outperformed the rutile-modification in all solvents. This effect can be attributed to the high anatase content in the P25 support material, which has been reported by Murdoch et al. to exhibit a higher H_2-evolution activity compared to a purely rutile-based support material. Furthermore, the data shows that hydrogen evolution from pure THF is very inefficient. However, hydrogen production can be enhanced using a mixture of THF and water (10 μL per hour) or even more by using ethanol (59 μL per hour) or methanol (67 μL per hour). With all solvents, hydrogen generation is realized by reduction of protons that are derived from the oxidation of the corresponding solvent. Hydrogen evolution from sacrificial reductants (like alcohols) is well reported in literature. The use of THF as sacrificial reductant has been reported by Kisch in 1984. The adaptation of this process with our Au/TiO_2 system has been the topic of previous work.

Further optimization was done by adjustment of the irradiation wavelength and the catalyst loading (see iii)). The photocatalytic H_2-production using Au/TiO_2 is known to be driven by UV-light. As expected, utilizing shorter wavelengths significantly increased the amount of hydrogen produced from a THF/H_2O mixture (3/1), with only traces being detected at 400 nm, 10 μmol at 385 nm, and 41 μmol at 365 nm. Higher catalyst loadings also correlate to an increase in hydrogen production. With 10 mg of Au/TiO_2 (P25), which was the highest amount that was tested, 122 μmol of hydrogen were generated after 1 h of irradiation at 365 nm.

2.2. Synthetic Application of Photocatalytically Generated Redox Equivalents for the Synthesis of 2-Phenylethanol Derivatives

Based on these results, our aim was now to utilize the photocatalytic hydrogen peroxide and the hydrogen production by Au/TiO_2 in an organic synthesis sequence. The synthesis of 2-phenylethanol from styrene via the corresponding epoxide requires hydrogen peroxide for the first step and dihydrogen for the second step. In combination with suitable catalysts, aerobic conditions can be applied for H_2O_2 production and the synthesis of styrene oxide and subsequently inert conditions for H_2 production and the regioselective epoxide opening. The main challenge was to find catalyst systems that not only work for the individual reactions, but also allow for an efficient sequential coupling of both reaction steps.

![Figure 1](image-url)
2.2.1. Epoxidation of Styrenes Using Au/TiO₂ as H₂O₂ Source

After a quick screening of different epoxidation catalysts we optimized our reaction conditions with a catalytic system consisting of a combination of RuCl₃·H₂O and dipicolinic acid, which was reported earlier by Beller et al.[14] To be compatible with the photocatalytic in situ generation of H₂O₂ from THF the catalytic epoxidation system must tolerate THF as solvent, the use of H₂O₂ as oxidant (instead of frequently used peroxoacids), and show photostability under the irradiation conditions. Another aspect in favor of the RuCl₃·H₂O/dipicolinic acid system is the use of only three equivalents of H₂O₂ and the continuous addition under the reported conditions, which is mimicked by the continuous in situ generation in the photocatalytic approach.

The results of different reaction parameters under the photocatalytic conditions at the example of the epoxidation of para-fluorostyrene are given in Table 1. All reactions were carried out with 0.3 mmol of para-fluorostyrene in 1.5 mL of THF. Preliminary experiments have shown that the photocatalytic system is producing H₂O₂ in a steady state concentration resulting from the equilibrium between its generation and decomposition. This equilibrium turned out to be influenced by the Au/TiO₂-loading, with the catalyst in excess having a negative effect on the H₂O₂ concentration.[9] Therefore, the epoxide-yield using different amounts of Au/TiO₂ varies, with high catalyst loadings resulting in low epoxide yields (entry 1, 2 and 4). While after 16 h, comparable yields of 37% and 42% were achieved with 1.5 mg and 2.5 mg, using 5 mg a yield of only 35% was achieved even after significantly prolonged reaction time. From our experiments, 2 mg were concluded to be the ideal catalyst loading for the given reaction volume. For the RuCl₃·H₂O and dipicolinic acid loadings, very similar results as described by Beller et al. were obtained.[14] Only minor deviations in the yield were observed for different RuCl₃·H₂O loadings with the best results for 0.1 mg (<0.1 mol% calculated for RuCl₃·H₂O and 0.3 mmol substrate; see entries 3–6). A bigger effect was observed varying the amount of dipicolinic acid, where the product yield could be increased by using up to 8 mol% of the ligand. The use of higher amounts of dipicolinic acid did not enhance the yield any further (entries 7–9). Prolongation of the reaction time to 24 h led to full conversion and a yield of 65% of the epoxide-product (entry 10). While H₂O₂-production is enhanced by shorter irradiation wavelengths, the product yield was highest for 400 nm under otherwise equal conditions (entries 11–14). The low yields using 455 nm can be attributed to the significantly lower H₂O₂ production under blue-light irradiation. In contrast, shorter wavelengths lead to an increase in side-reactions, as can be seen by the higher substrate conversion at lower overall product yields. Besides low amounts of (para-fluorophenyl)acetaldehyde (<10%), which is also reported by Beller et al.[14] to be a side product, the photocatalytic conditions apparently lead to further side product formation. Unfortunately, we could not identify the nature of the side-products, but we assume that the irradiation is causing polymerization reactions of the fluorostyrene-monomers. The use of 400 nm constitutes the best compromise between efficient H₂O₂ production and suppression of side reactions (entry 13). Performing the reaction under our optimized conditions, but with Au/TiO₂ (P25) instead of Au/TiO₂ (rutile) showed that both catalyst modifications lead to the same product yield (compare entry 15 and 8). Noteworthy to mention here is that upon deviation from the optimized conditions usually the rutile modification showed a slightly better performance. This may be due to minor differences in the effectiveness in H₂O₂ production. Therefore, the scope of the reaction was explored using only the rutile modification.

Continuous addition of the substrate via syringe pump did not reduce the amount of side reactions (entry 16). Finally, control reactions without RuCl₃·H₂O or dipicolinic acid showed the necessity of both for the epoxide formation (entry 17 and 18). Interestingly the presence of only dipicolinic acid still leads to substrate consumption, however with a low conversion of 25%. In contrast to that, in presence of only RuCl₃·H₂O, 65% of the substrate was consumed, while only trace amounts of the desired product were observed.

| Table 1. Optimization of reaction conditions for the epoxidation of para-fluorostyrene. |
|-----------------------------------------|----------|--------------------|-----|-----|-----|
| **Entry** | **Au/TiO₂** | **RuCl₃·H₂O** | **Dip. ac.** | **λ** | **Conv.** | **Yield** |
|           | [mg]      | [mg]            | [mol%] | [nm] | [%]      | [%]      |
| 1         | 2.5       | 0.1             | 7      | 385  | 14.5     | 85       | 42       |
| 2         | 1.5       | 0.1             | 7      | 385  | 14.5     | 81       | 37       |
| 3         | 1.5       | 0.05            | 7      | 385  | 22       | 78       | 29       |
| 4         | 1.5       | 0.1             | 7      | 385  | 22       | 77       | 35       |
| 5         | 1.5       | 0.2             | 7      | 385  | 22       | 76       | 29       |
| 6         | 1.5       | 0.4             | 7      | 385  | 22       | 78       | 28       |
| 7         | 1.0       | 0.1             | 6      | 400  | 20       | 85       | 50       |
| 8         | 1.0       | 0.1             | 8      | 400  | 20       | 92       | 58       |
| 9         | 1.0       | 0.1             | 10     | 400  | 20       | 92       | 59       |
| 10        | 1.0       | 0.1             | 8      | 400  | 20       | 92       | 59       |
| 11        | 1.0       | 0.1             | 4      | 385  | 16       | 100      | 41       |
| 12        | 1.0       | 0.1             | 4      | 385  | 16       | 90       | 46       |
| 13        | 1.0       | 0.1             | 4      | 400  | 16       | 85       | 47       |
| 14        | 1.0       | 0.1             | 4      | 455  | 24       | 43       | 25       |
| 15        | 1.0       | 0.1             | 8      | 400  | 20       | 95       | 58       |
| 16        | 1.0       | 0.1             | 4      | 385  | 24       | 82       | 44       |
| 17        | 2.0       | 0.1             | 8      | 400  | 24       | 25       | 0        |
| 18        | 2.0       | 0.1             | 0      | 400  | 24       | 65       | 3        |

[a] Conversion and yield were determined by quantitative NMR analysis using para-fluorotoluene as internal standard. [b] Au/TiO₂ (P25) was used instead of Au/TiO₂ (rutile). [c] Addition of the substrate as a solution in THF via syringe pump (0.15 mM, 2.0 mL, flowrate: 200 µL/h).

2.2.2. Reductive Epoxide Opening Using Au/TiO₂ as H₂ Source

In the same way as for the epoxidation catalyst, hydrogenation catalysts were screened. As a result, two palladium catalysts turned out to be promising candidates for the epoxide opening reaction, Pd(OAc)₂ and Pd(0)EnCat (encapsulated palladium nanoparticles). With both catalysts, regioselective ring opening
to the anti-Markovnikov product was achieved in trial reactions and no significant deviation in the performance between both catalysts could be observed. The scope was investigated using Pd(OAc)$_2$ as catalyst due to the simplicity of the set-up and a lower overall Pd loading. Consequently, in the following, only the optimization using Pd(OAc)$_2$ is shown (see Table 2). A comparison to the Pd(0)EnCat system can be found in the supporting information (Section 2, Table S1).

At first it was tested whether Pd(OAc)$_2$ can be used in THF as catalyst for the regioselective ring opening of styrene oxides under standard conditions using an H$_2$-balloon. As expected, this was possible with the desired alcohol as the main product and ethylbenzene as the only side product detected via GC. In contrast to that, running the reaction in methanol or ethanol, which would provide larger amounts of H$_2$ (see Figure 1), led to the formation of alcohol adducts as the main product via a nucleophilic attack of the alcohol during the ring opening reaction (analyzed via GC-MS). In situ generation of H$_2$ and nucleophilic attack of the alcohol during the ring opening reaction (analyzed via GC-MS).

In order to use conditions similar to the previous epoxidation reaction RuCl$_3$H$_2$O and dipicolinic acid from the solution, the reaction mixture is extracted with 1.5 mL of DEE to remove excess NaOH from the organic phase. The organic phase is then concentrated under reduced pressure to around 0.5 mL and can then be used for the epoxide opening reaction. For the detailed procedure, see the general procedure in the SI (section 2, Table S2).

After the work-up process the epoxide opening was performed, using Pd(OAc)$_2$ or Pd(0)EnCat. In both cases regioselective ring opening to the anti-Markovnikov product was observed, with the only side product being small amounts of para-fluoro-ethylbenzene. The reaction conditions were optimized in regard to the time required for full conversion of the epoxide. The optimization of the reaction conditions for Pd(OAc)$_2$ is depicted in Table 3. The comparison to Pd(0)EnCat can be found in the SI (section 2, Table S2).

### Table 2. Evaluation of Pd(OAc)$_2$ as ring opening catalyst.

| Entry | H$_2$ source and reaction conditions | Solvent | Product formation |
|-------|-------------------------------------|---------|------------------|
| 1     | H$_2$-balloon                       | THF     | yes              |
| 2     | H$_2$-balloon or Au/TiO$_2$ + irrad. | MeOH or ETOH | no    |
| 3     | Au/TiO$_2$ + irrad.                 | THF     | no               |
| 4     | Au/TiO$_2$ + irrad.                 | THF/H$_2$O 3/1 | yes  |
| 5     | Au/TiO$_2$ + irrad. + RuCl$_3$H$_2$O | THF/H$_2$O 3/1 | no    |
| 6     | Au/TiO$_2$ + irrad. + after epoxida-| THF/H$_2$O 3/1 | no    |

### Table 3. Optimization of the reaction conditions for the epoxide opening using Pd(OAc)$_2$.

| Entry | Conditions | t (full conv.) [h] |
|-------|------------|-------------------|
| 1     | 5 mg Au/TiO$_2$ (P25), 1.2 mol % Pd(OAc)$_2$, 365 nm | > 24 |
| 2     | 10 mg Au/TiO$_2$ (P25), 2.2 mol % Pd(OAc)$_2$, 385 nm | > 18 |
| 3     | 10 mg Au/TiO$_2$ (P25), 2.2 mol % Pd(OAc)$_2$, 365 nm | 18 |
| 4     | 5 mg Au/TiO$_2$ (P25), 1.8 mol % Pd(OAc)$_2$, 365 nm | 15 |
| 5     | 10 mg Au/TiO$_2$ (rutile), 2.2 mol % Pd(OAc)$_2$, 365 nm | > 24 |
| 6$^d$ | 10 mg Au/TiO$_2$ (P25), 2.2 mol % Pd(OAc)$_2$, 365 nm | n.d. |

[a] Successive epoxidation and epoxide opening without work-up protocol.
All reactions were performed after the epoxidation reaction using 0.3 mmol para-fluorostyrene and the work-up procedure (unless otherwise stated). The results are in accordance with the results from the screening for the highest H$_2$-generation activity. The fact that higher AuTiO$_2$ loadings and irradiation with a shorter wavelength led to a higher H$_2$-evolution, allowed to shorten the reaction time for full substrate conversion (entries 1–3). Adjusting the amount of Pd(OAc)$_2$ showed, that using 1.8 mol% was sufficient for full conversion after 15 h (entry 4). While lower amounts of Pd(OAc)$_2$ caused slower substrate conversion, larger amounts also slowed down the reaction by increased light absorption, due to darkening of the reaction mixture. Catalytic activity is also observed using AuTiO$_2$ (rutile), but product formation is significantly slower, which can be attributed to the lower H$_2$-evolution from the rutile modification. Finally, entry 6 shows the attempt of direct epoxidation and epoxide opening without intermediate work-up process. In this case, no detectable epoxide consumption was observed after 24 h.

### 2.2.3. Scope and Limitations of the Two-Step Process

With the optimized conditions for both reaction steps and a work-up procedure in hand, we investigated the scope of the reaction. Yields for the epoxidation were determined by NMR-analysis using trichloroethylene (TCE) as internal standard (values in blue and in brackets in Table 4). The overall yield after both steps was determined by isolation of the products (values in pink). Most substrates gave moderate epoxide yields between 42% and 71%. The yields for the epoxide opening can be determined indirectly from the epoxidation yields and the yields of the isolated products.

In general, the performance of the ring opening reaction was better than that of the epoxidation, with the corresponding yields ranging between 60% and 85% (not directly given in the Table). Para-fluorostyrene gave an overall yield of 50% of the corresponding primary alcohol 3a, with yields for the individual steps being 65% for the epoxidation and 77% for the ring opening. Very similar yields were obtained with unsubstituted styrene (3b), as well as a trimethylsilyl group in para position (3e), with each giving the product in a yield of 49% after both steps. Compound 3c with a methyl group in para position was obtained in an overall yield of 48%, but the epoxidation step was less efficient with only 57%. A phenyl substituent in the para position (3d) caused the overall yield to drop to 35%, while the epoxidation step went equally well with 58%. Furthermore, an electron pushing acetoxy group gave the final product in a yield of only 28% with a corresponding epoxide yield of 48%. Substitution at the double bond is tolerated. The best results in the epoxidation step were achieved for cis- and trans-β-methylstyrene with 71% (2g) and 66% (2h). After ring opening 3g was obtained with a yield of 67% and 3h with 42%. At the same time, α-methylstyrene (3i) gave slightly lower yields with 56% and 37%, respectively. Substitution of the methyl group with a more sterically hindered phenyl group resulted in yields of 42% and 28% (3j).

### Table 4. Scope of the reaction. The yields in pink correspond to the final products after both reaction steps, the yields in blue and in brackets correspond to the yield of the epoxide intermediate.

| Compound | Epoxide Yield | Ring Opening Yield |
|----------|---------------|--------------------|
| 3a       | 50% (85%)     |                    |
| 3b       | 49% (65%)     | 48% (57%)          |
| 3c       | 35% (58%)     | 28% (48%)          |
| 3d       | 67% (71%) (cis) | 37% (56%) (trans) |
| 3e       | 42% (66%)     | 28% (42%)          |
| 2k       | 20%           |                    |
| 2l       | 0%            |                    |
| 2m       | 85%           |                    |
| 2n       | 45%           |                    |
remaining. This can be rationalized by the electron withdrawing effect of the CF₃ group, deactivating the double bond for the reaction with H₂O₂. In the case of 2l, full substrate conversion was observed, while no epoxide formation could be detected. Most likely, the electron donation from the methoxy substituent is activating the double bond for unwanted side reactions. Compounds 2m and 2n are examples of substrates with reasonable yields of the corresponding epoxides, while not being suited for the epoxide opening. In both cases, the reactants decomposed and the corresponding primary alcohols could not be isolated.

2.3. Reactor Design for Heterogeneous Photocatalytic Reactions

A new photo reactor setup was designed for running several heterogeneous reactions simultaneously under reproducible conditions. In contrast to homogeneous systems, reproducible stirring conditions are of importance in heterogeneous systems. Unlike homogeneous catalysts, even distribution of heterogeneous material has to be achieved by thorough stirring. Thereby, insufficient stirring can cause the heterogeneous material to precipitate, decreasing interaction between catalyst and reagents and causing a nontransparent layer at the bottom of the vial. By blocking off most of the light, this is inhibiting the photocatalytic reaction. On the other hand, violent stirring can cause splashing of the reaction mixture, distributing the heterogeneous material over the lid and the sides of the glass vial, ultimately removing it from the reaction medium. Our setup consists of a multi-spot magnetic stirrer with 15 individual stirring centers and a tailor-made LED plate with a cooling element on top (Figure 2). A reproducible stirring quality is ensured as the reaction vials and the stirring centers are concentric. Temperature control is achieved by water cooling through a metal cooling block that is placed directly on top of the LEDs holding the reaction vials. Irradiation of the samples is done from the plain bottom side of the glass vials.

Alteration of the irradiation wavelength is possible by exchange of the LED base plate.

3. Conclusion

In conclusion, a series of 2-phenylethanol derivatives has been synthesized via epoxidation of the corresponding styrenes and subsequent reductive ring opening. In both reaction steps, the corresponding redox equivalents in the form of H₂O₂ and H₂ were generated in situ using Au/TiO₂ as photoredox catalyst. Alteration between hydrogen peroxide and hydrogen production is achieved by the application of aerobic or anaerobic conditions. Operating under oxidative and reductive reaction conditions shows the versatility of the gold-doped TiO₂ catalyst. While a one-pot reaction could not be achieved, both individual steps were optimized to give satisfactory yields and a procedure for sequential epoxidation and epoxide opening has been developed. However, further simplification of the process can be envisaged using more compatible homogeneous catalytic systems or using a heterogeneous epoxidation catalyst and filter techniques.

Experimental Section

General Procedures

General Procedure: Epoxidation

A 5 mL crimp cap vial equipped with Au/TiO₂, dipicolinic acid and a stirring bar was capped and the atmosphere was exchanged 3 times with oxygen. After addition of 1.5 mL of a solution of RuCl₃·xH₂O in oxygen saturated THF, the corresponding styrene (0.3 mmol, 1.0 equiv.) was added with the help of a Hamilton syringe. Subsequently, the reaction mixture was ultrasonicated for 5 minutes. An oxygen balloon was connected to the vial via a thick needle through the septum of the crimp cap. Finally, the reaction mixture was stirred at 400 rpm and irradiated with 400 nm LEDs for 24 h.
General Procedure: Work-Up

After the epoxidation reaction, 2 mL of a 2 M NaOH solution were directly added to the vial through the septum of the crimp cap. The mixture was extracted with DEE (3 x 1 mL) and the combined organic phases were transferred to another crimp cap vial. Residues of the sodium hydroxide solution were washed with 1 mL of a 3/1 mixture of water and brine, followed by a final washing step of the water phase with 1.5 mL of DEE. The combined organic phases were evaporated via a thick needle through the septum of the crimp cap and the mixture was concentrated to an overall volume of around 0.5 mL following a standardized procedure (40 °C, 5 min at 750 mbar, then 3 min at 300 mbar).

General Procedure: Epoxide Opening

After the reaction was stopped the reaction mixture was transferred to a sintered glass funnel (lower vacuum assembly) containing a layer of a few millimetres of MgSO₄, followed by a final washing step of the atmosphere was exchanged for N₂. After ultrasonication for 5 min, the samples were irradiated for 15 h using 365 nm LEDs.

The mixture was extracted with DEE (3 x 1 mL) and the combined organic phases were transferred to another crimp cap vial. Residues of the sodium hydroxide solution were washed with 1 mL of a 3/1 mixture of water and brine, followed by a final washing step of the water phase with 1.5 mL of DEE. The combined organic phases were evaporated via a thick needle through the septum of the crimp cap and the mixture was concentrated to an overall volume of around 0.5 mL following a standardized procedure (40 °C, 5 min at 750 mbar, then 3 min at 300 mbar).

Acknowledgements

This work was supported by the German Science Foundation (DFG, KO 1537/18-1). Open access funding enabled and organized by Projekt DEAL.

Conflict of Interest

The authors declare no conflict of interest.

Keywords: anti-Markovnikov addition · epoxidation · photocatalysis · redox equivalents · semiconductors

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**Test the water**: The anti-Markovnikov addition of water to styrene is realized by the photocatalytic in situ generation of redox equivalents using Au/TiO$_2$ as photocatalyst. By sequential epoxidation and regioselective epoxide opening various 2-phenylethanol derivatives are obtained from the corresponding styrenes. Alteration between H$_2$O$_2$ and H$_2$ production for the corresponding reaction step is achieved applying either aerobic or anaerobic photocatalysis conditions, respectively.

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**Synthesis of anti-Markovnikov Alcohols via Epoxidation and Hydrogenation of Styrenes using Photocatalytically Generated Redox Equivalents**