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

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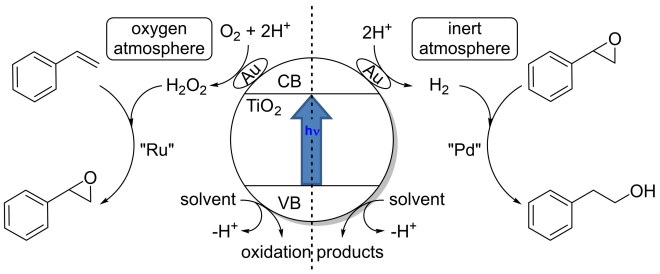
We report an efficient method for a formal anti-Markovnikov addition of water to styrenes through photocatalytic generation of redox equivalents, using a gold-doped titanium dioxide (Au/TiO_2) semiconductor as photocatalyst. Under irradiation with UV–A light, the photocatalytic activity of Au/TiO_2 generates in situ under aerobic conditions hydrogen peroxide (H_2O_2) and under anaerobic conditions dihydrogen (H_2). 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

TiO_2-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 TiO_2 with light under aerobic conditions. Among others, these species are mainly responsible for the oxidative degradation of pollutants. Besides that, TiO_2 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 TiO_2 as photocatalyst for organic synthesis remains less explored with considerably fewer reports.[3]

Herein, we report a specific application of TiO_2 in the synthesis of 2-phenylethanol derivatives from the corresponding styrenes via epoxidation and subsequent reductive ring opening. TiO_2 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 TiO_2 photocatalyst for the in situ production of H_2O_2 under oxygen atmosphere as well as H_2 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



Scheme 1. Schematic depiction of the synthesis of 2-phenylethanol from styrene in two steps. Left: Photocatalytic generation of H_2O_2 under an oxygen atmosphere and ruthenium-catalyzed epoxidation step. Right: Photocatalytic generation of H_2 under an inert atmosphere and palladium-catalyzed regioselective epoxide opening.

deposition of gold nanoparticles on TiO_2 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 TiO_2 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 H_2O_2 and H_2. Thus, handling of the commonly used hazardous 30% aqueous H_2O_2 for the epoxidations and inflammable H_2-gas under great pressure or in large reservoirs for the reduction is avoided. Alteration between H_2O_2- and H_2-production can easily

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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/TiO2

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.[9] 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[9] 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.[10] 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.[11] The use of THF as sacrificial reductant has been reported by Kisch in 1984.[12] The adaptation of this process with our Au/TiO_2 system has been the topic of previous work.[9]

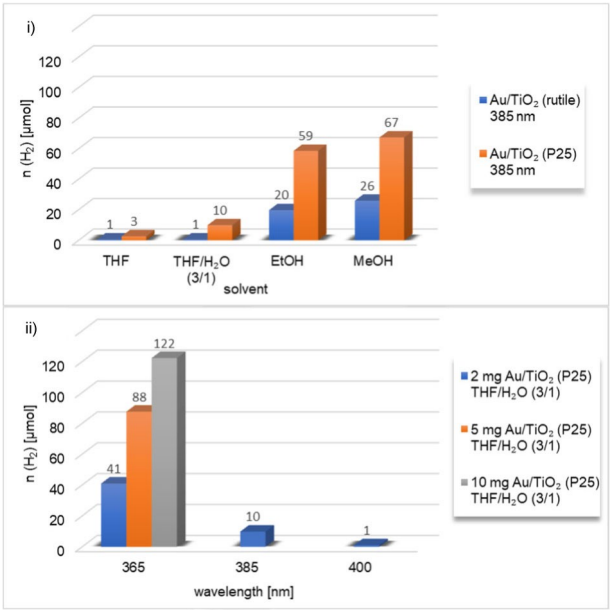


Figure 1. Influence of TiO_2 modification, amount of catalyst, solvent and irradiation wavelength on the amount of H_2 produced after 1 h of irradiation. i) Comparison of Au/TiO_2 (rutile) and Au/TiO_2 (P25) in different solvents (2 mL). ii) Comparison of irradiation wavelength and amount of Au/TiO_2 (P25).

Further optimization was done by adjustment of the irradiation wavelength and the catalyst loading (see ii)). The photocatalytic H_2-production using Au/TiO_2 is known to be driven by UV-light.[13] 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

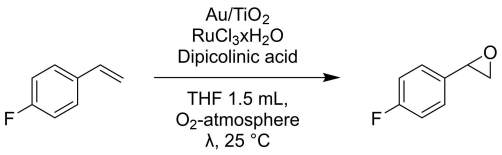
Based on these results, our aim was now to utilize the photocatalytic hydrogen peroxide and the hydrogen production by Au/TiO_2 in an organic synthesis sequence. The synthesis of 2-phenylethanol from styrene via the corresponding epoxide requires hydrogen peroxide for the first step and dihydrogen for 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.

2.2.1. Epoxidation of Styrenes Using Au/TiO_2 as H_2O_2 Source

After a quick screening of different epoxidation catalysts we optimized our reaction conditions with a catalytic system consisting of a combination of $RuCl_3xH_2O$ and dipicolinic acid, which was reported earlier by Beller et al.[14] To be compatible with the photocatalytic in situ generation of H_2O_2 from THF the catalytic epoxidation system must tolerate THF as solvent, the use of H_2O_2 as oxidant (instead of frequently used peroxoacids), and show photostability under the irradiation conditions. Another aspect in favor of the $RuCl_3xH_2O$/dipicolinic acid system is the use of only three equivalents of H_2O_2 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 H_2O_2 in a steady state concentration resulting from the equilibrium between its generation and decomposition. This equilibrium turned out to be influenced by the Au/TiO_2-loading, with the catalyst in excess having a negative effect on the H_2O_2 concentration.[9] Therefore, the epoxide-yield using different amounts of Au/TiO_2 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 $RuCl_3xH_2O$ 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 $RuCl_3xH_2O$ loadings with the best results for 0.1 mg (<0.1 mol% calculated for $RuCl_3{\cdot}5H_2O$ 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 H_2O_2-prodction 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 H_2O_2 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 H_2O_2 production and suppression of side reactions (entry 13). Performing the reaction under our optimized conditions, but with Au/TiO_2 (P25) instead of Au/TiO_2 (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 effectivity in H_2O_2 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 $RuCl_3xH_2O$ 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 $RuCl_3xH_2O$, 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/TiO_2 [mg]	$RuCl_3xH_2O$ [mg]	dip. ac. [mol%]	λ [nm]	t [h]	Conv. [%][a]	Yield [%][a]
1	2.5	0.1	7	385	14.5	85	42
2	1.5	0.1	7	385	14.5	81	37
3	5	0.05	7	385	22	78	29
4	5	0.1	7	385	22	77	35
5	5	0.2	7	385	22	76	29
6	5	0.4	7	385	22	78	28
7	2	0.1	6	400	20	85	50
8	2	0.1	8	400	20	92	58
9	2	0.1	10	400	20	92	59
10	2	0.1	8	400	24	100	65
11	2	0.1	4	365	16	100	41
12	2	0.1	4	385	16	90	46
13	2	0.1	4	400	16	85	47
14	2	0.1	4	455	24	43	25
15[b]	2	0.1	8	400	20	95	58
16[c]	2	0.1	4	385	24	82	44
17	2	0	8	400	24	25	0
18	2	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/TiO_2 (P25) was used instead of Au/TiO_2 (rutile). [c] Addition of the substrate as a solution in THF via syringe pump (0.15 mM, 2.0 mL, flowrate: 200 μL/h).

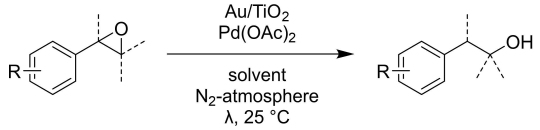
2.2.2. Reductive Epoxide Opening Using Au/TiO_2 as H_2 Source

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

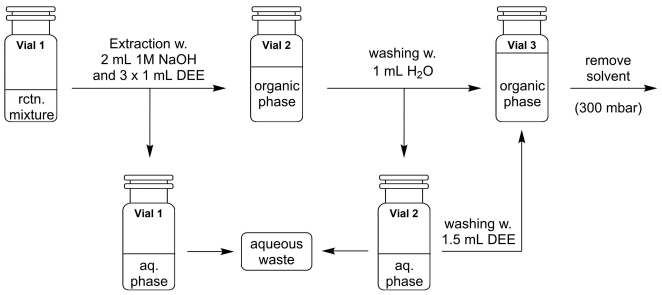
to the anti-Markovnikov product was achieved in trial reactions and no significant deviation in the performance between both catalysts could be observed. The scope was investigated using $Pd(OAc)_2$ as catalyst due to the simplicity of the set-up and a lower overall Pd loading. Consequently, in the following, 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 with Au/TiO_2 and irradiation did not lead to significant substrate conversion in pure THF. However, due to the synergistic effect of a mixture of water and THF generating higher amounts of H_2, product formation could be observed under irradiation with 365 nm. In order to use conditions similar to the previous epoxidation reaction $RuCl_3xH_2O$ and dipicolinic acid were added in entry 5, under otherwise identical conditions as in entry 4. Unfortunately, this led to the formation of an unidentified side product. In a similar way, sequential epoxidation and ring opening (entry 6) suffered from low epoxide conversions and side product formation. Thus, the ideal scenario of a direct coupling by simple switching from oxidative to reductive conditions by exchanging the atmosphere is not possible, due to the incompatibility of the catalytic systems for epoxidation and epoxide opening. At the same time, complete isolation of the epoxides between the reactions is not desirable due to low chemical stability and relatively high volatility of some of the styrene oxide derivatives. Therefore, a quick and simple washing protocol was developed. A visualization of the protocol is given in Scheme 2.

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_2O 3/1	yes
5	Au/TiO_2 + irrad. + $RuCl_3xH_2O$ + acid	THF/H_2O 3/1	no
6	Au/TiO_2 + irrad. + after epoxidation	THF/H_2O 3/1	no

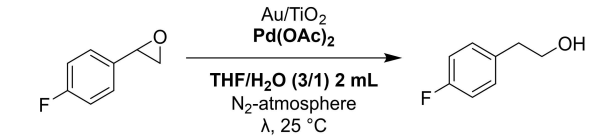


Scheme 2. Depiction of the work-up protocol.

In order to separate $RuCl_3xH_2O$ and dipicolinic acid from the solution, the reaction mixture is extracted with 2 mL of a 1 M NaOH-solution and 3×1 mL of diethylether (DEE). Both are directly added to the reaction vial via syringe. Due to the miscibility gap between THF and water under basic conditions, the organic phase can easily be separated and transferred into a new glass-vial. In this step, the heterogeneous Au/TiO_2 remains in the aqueous phase. Subsequently the organic phase is washed with 1 mL of H_2O in order to remove excess NaOH from the organic phase. Too basic conditions should be avoided for the reduction step as the photocatalytic H_2-generation is hampered in basic medium. In a last washing step, the aqueous phase is extracted with 1.5 mL of DEE to minimize loss of organic material. Afterwards the organic solution is 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 experimental section.

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 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[a]	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.

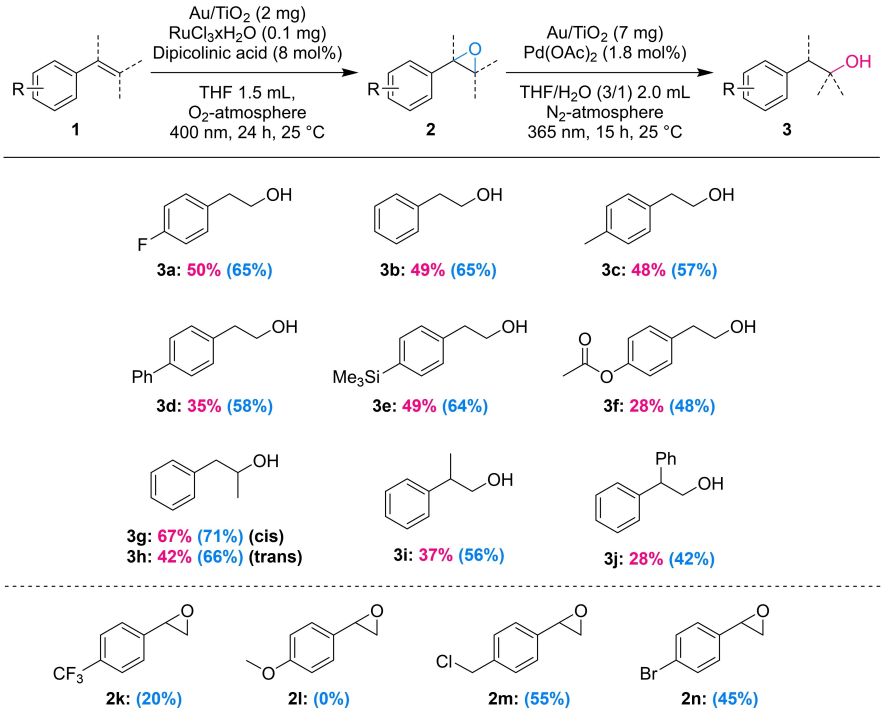
All reactions were performed after the epoxidation reaction using 0.3 mmol *para*-fluorostyrene and the work-up procedure (unless otherwise stated). The results are in accordance with the results from the screening for the highest H_2-generation activity. The fact that higher $AuTiO_2$ loadings and irradiation 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**). Limitations for this reaction system can be seen in the bottom row of Table 4. In the case of **2k** the epoxide yield after 24 h of irradiation was only 20% with around 65% of substrate

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.



remaining. This can be rationalized by the electron withdrawing effect of the CF_3 group, deactivating the double bond for the reaction with H_2O_2. 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 heterogenous 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 H_2O_2 and H_2 were generated in situ using Au/TiO_2 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 TiO_2 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/TiO_2, 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 $RuCl_3xH_2O$ 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.

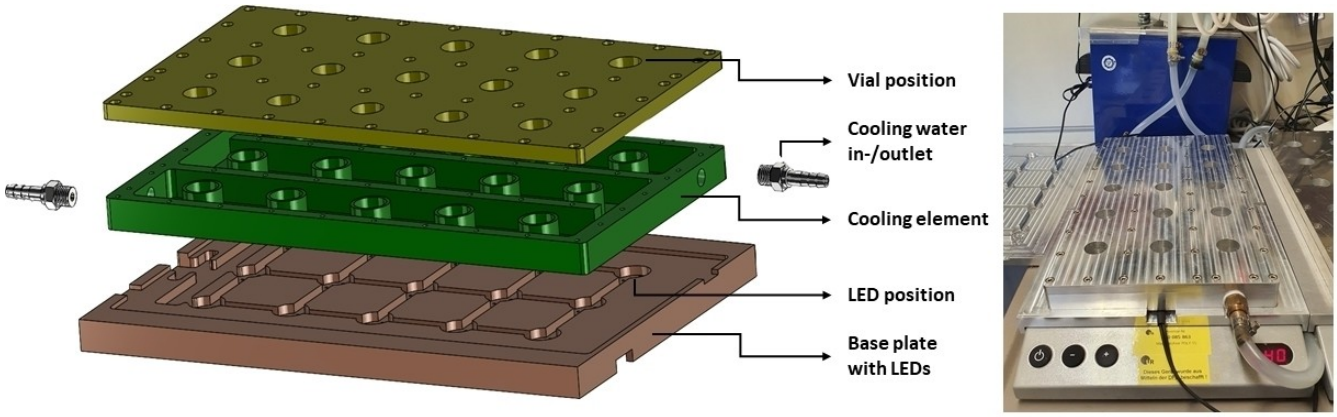


Figure 2. Reactor design for heterogeneous reactions. Left: Design drawing of the LED plate and cooling element of the 15-spot reactor. Right: Picture of the reactor including magnetic stirrer, LED plate and cooling system.

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 (3×1 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

Reaction with $Pd(OAc)_2$: After the work-up, 2 mL of a solution of $Pd(OAc)_2$ in THF/water (3/1) was added to the remainder. After addition of Au/TiO_2 and a stirring bar the vial was closed again and the atmosphere was exchanged for N_2 9 times (15 s at 300 mbar, then 5 s N_2). After ultrasonication for 5 min, the samples were irradiated for 15 h using 365 nm LEDs.

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 $MgSO_4$ and the reaction vial was washed with *ca.* 25 mL of THF. After stirring of the mixture for a few minutes, the filtrate was directly collected in a connected round bottom flask. After evaporation of the solvent, the crude product was purified via automated flash column chromatography.

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Conflict of Interest

The authors declare no conflict of interest.

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