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Photo-Induced Dihydroxylation of Alkenes with Diacetyl, Oxygen, and Water

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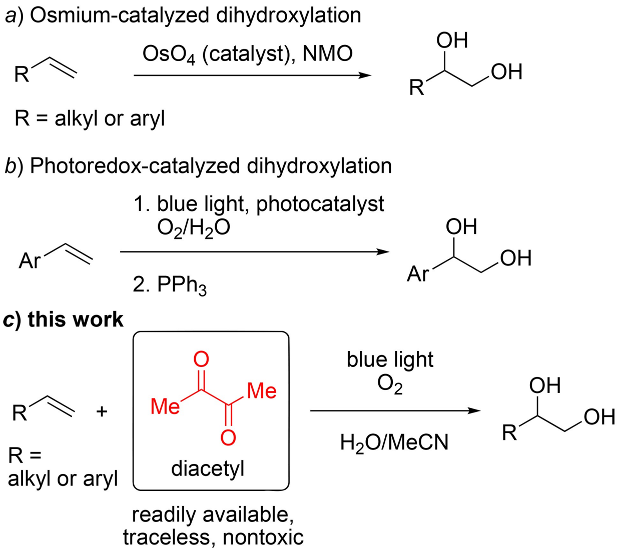
Dedicated to Professor *E. Peter Kündig* on the occasion of his 75th birthday

Herein reported is a photo-induced production of vicinal diols from alkenes under mild reaction conditions. The present dihydroxylation method using diacetyl (= butane-2,3-dione), oxygen, and water dispenses with toxic reagents and intractable waste generation.

Keywords: alkenes, diacetyl, dihydroxylation, photochemistry, water.

Introduction

A 1,2-diol motif is prevalent in natural products, pharmaceutical compounds, and functional materials. Dihydroxylation of alkenes offers a straightforward access to 1,2-diols.[1–5] Osmium tetroxide is often utilized as a catalyst for direct dihydroxylation despite of its high toxicity (*Scheme 1,a*). Asymmetric variants of the osmium-catalyzed reaction are also available.[6] Another classical method is given by the *Prevost–Woodward* reaction, in which stoichiometric amounts of iodine and a silver salt are used, generating a lot of wastes.[7,8] The sustainability of chemical processes has become a major issue facing synthetic chemists. It is highly desired to develop an alternative method of dihydroxylation which dispenses with toxic reagents and intractable waste generation. *Lu* reported a dihydroxylation reaction which uses oxygen, water, visible light, and an acridinium photoredox catalyst (*Scheme 1,b*).[9] It proceeds through a radical pathway under mild reaction conditions; however, the eligible substrates are limited to styrene derivatives. Herein described is a benign protocol for dihydroxylation which uses diacetyl (=butane-2,3-dione), oxygen, water, and visible light. All components are readily available, nontoxic, and easily disposable (*Scheme 1,c*). Noteworthy is that not only styrene derivatives but also ordinary aliphatic alkenes are eligible substrates for the present photoinduced dihydroxylation reaction.



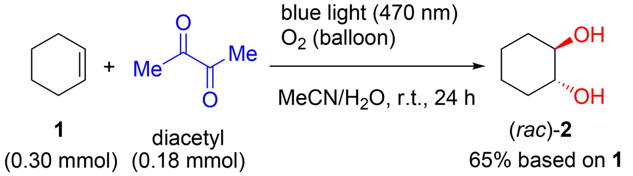
Scheme 1. Dihydroxylation reactions of alkenes.

Supporting information for this article is available on the WWW under https://doi.org/10.1002/hlca.202000228

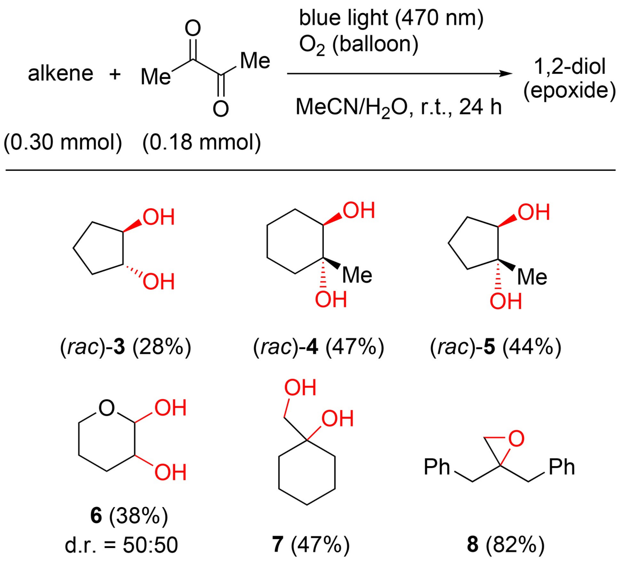
Results and Discussion

An acetonitrile/water (4:3 *v/v*, 7 mL) solution of cyclohexene (**1**, 0.30 mmol) and diacetyl (0.18 mmol) was irradiated with blue light (470 nm) under oxygen (1 atm) at ambient temperature. After 24 h, the mixture was subjected to chromatographic purification, which afforded *trans*-1,2-cyclohexanediol (**2**) in 65% yield based on **1** (*Scheme 2*). Both light and oxygen were indispensable for the reaction. Other 1,2-diketones such as 3,4-hexadione, benzil (1,2-diphenylethane-1,2-dione), and 1,2-cyclohexanedione also gave **2**, albeit in lower yields (<5%–57%).

The dihydroxylation reaction was examined using other aliphatic alkenes (*Scheme 3*). 1-Methyl-1-cyclohexene and 1-methyl-1-cyclopentene afforded the corresponding *trans*-1,2-diols **4** and **5** in 47% and 44% yields, respectively. Methylidenecyclohexane gave 1,2-diol **6** in 47% yield. Cyclic hemiacetal **7** was obtained from 3,4-dihydropyran in 38% yield. On the other hand, 2-benzyl-3-phenyl-1-propene gave rise to epoxide **8** instead of 1,2-diol.

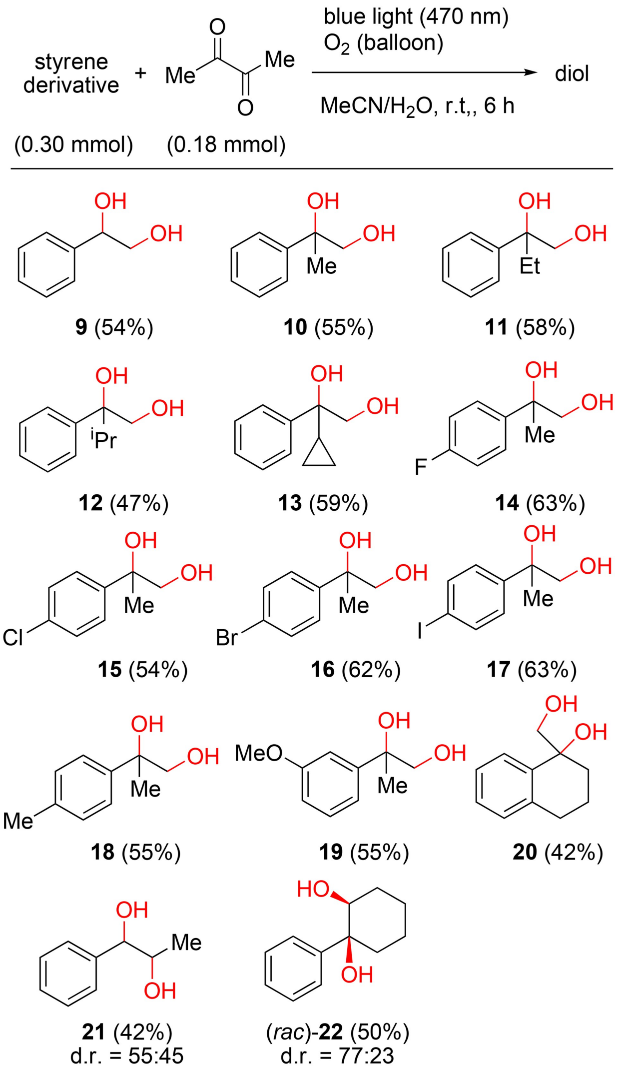


Scheme 2. Visible light-induced dihydroxylation of alkenes with diacetyl, oxygen, and water.



Scheme 3. Dihydroxylation of aliphatic alkenes.

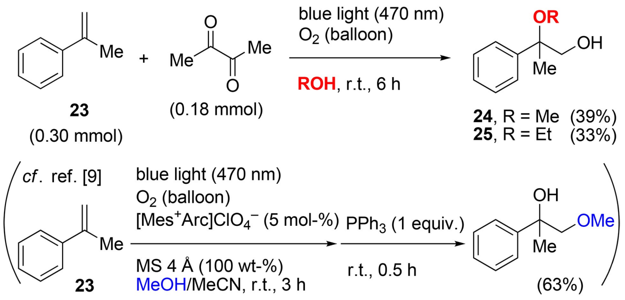
Next examined were styrene derivatives (*Scheme 4*). When styrene was subjected to the dihydroxylation reaction, the corresponding diol **9** was obtained in 54% yield together with a small amount of α-hydroxyacetophenone (*ca.* 7% yield). It was assumed that the latter compound was produced by further oxidation of the diol **9**. α-Substituted styrenes were also suitable substrates. Sterically hindered α-isopropylstyrene participated in the reaction to afford the 1,2-diol **12** in 47% yield. When α-cyclopropylstyrene was subjected to the dihydroxylation reaction, the 1,2-diol **13** was obtained and no ring-opening product was detected. This result indicated that the reaction pathway involving a benzylic radical species was unlikely.[10] Halogenated styrene derivatives successfully underwent the dihydroxylation reaction keeping the carbon–halogen bond intact (**14**–**17**). Although a



Scheme 4. Dihydroxylation of styrene derivatives.

carbon–iodide bond is particularly labile upon photoirradiation,[11] that of 4-iodo-β-methylstyrene remained under the reaction conditions; the diol **17** was obtained in 63% yield together with 4′-iodoacetophenone (*ca.* 29% NMR yield). Electron-donating substituents such as methyl (**18**) and methoxy (**19**) groups were allowed on the phenyl ring. On the other hand, 4-trifluoromethylstyrene failed to give a diol. (*E*)-β-Methylstyrene and 1-phenyl-1-cyclohexene afforded a mixture of diastereomers **21** and **22** because the benzylic stereogenic center was labile enough to epimerize via a benzylic cation under the reaction conditions.[12]

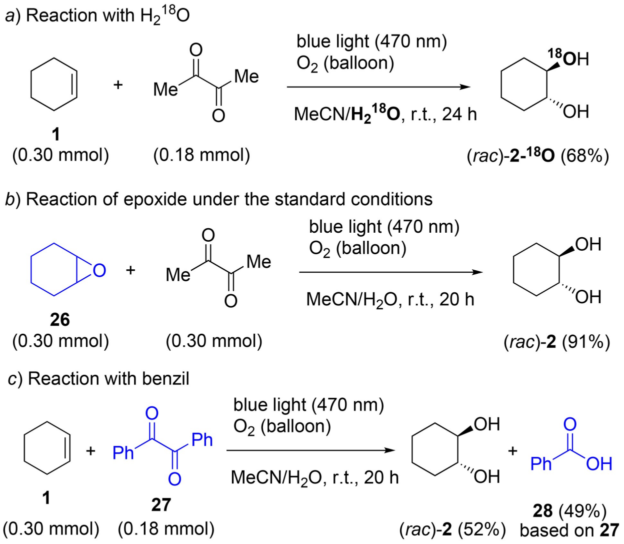
Hydroxyalkoxylation of styrene derivatives took place when alcoholic solvents were used (*Scheme 5*). 2-Methoxy-2-phenyl-1-propanol (**24**) was produced from α-methylstyrene (**23**) in 39% yield when methanol was used as the solvent. The reaction in ethanol afforded 2-ethoxy-2-phenyl-1-propanol (**25**) in 33% yield, being in contrast to the previous photo-induced dihydroxylation reaction, which showed an opposite regioselectivity, giving 1-alkoxy-2-phenyl-2-propanol from **23**.[9]



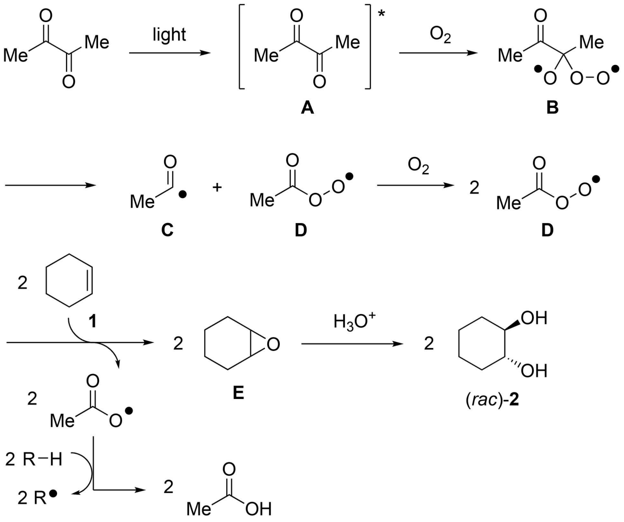
Scheme 5. Hydroxyalkoxylation of alkene **23**.

In order to gain mechanistic insights, the dihydroxylation reaction of **1** was performed in water-^{18}O. The product **2-*^{18}O*** incorporated only one ^{18}O isotope, which was confirmed by high resolution mass spectrometry (*Scheme 6,a*). Next, we followed a course of the reaction of cyclohexene **1** by using gas chromatography, which detected cyclohexene oxide (**26**) albeit as a very minor peak. We supposed intermediacy of the epoxide **26**, and subjected isolated **26** to the present reaction conditions. Ring-opening hydration occurred, and the diol **2** was obtained in 91% yield (*Scheme 6,b*). Next, benzil (**27**) was used in place of diacetyl in the dihydroxylation reaction of alkene **1**, and its end product was tracked down. Benzoic acid (**28**) was obtained together with the diol **2** (*Scheme 6,c*).

It has been reported that alkenes are epoxidized when irradiated with UV light in the presence of diacetyl under an oxygen atmosphere.[13,14] Combining this precedent result with the observation of the epoxide **26** in the reaction of **1**, we proposed the reaction pathway involving intermediacy of an epoxide. Diacetyl is excited upon photoirradiation,[15,16] and the following intersystem crossing generates a triplet state of diacetyl **A**, which reacts with triplet oxygen to furnish biradical species **B** (*Scheme 7*).[17] β-Scission of **B** produces acetyl radical **C** and acetylperoxyl radical **D**. The acetyl radical **C** couples with oxygen to generate another acetylperoxyl radical **D**.[18] As a whole, two acetylperoxyl radicals **D** arise from diacetyl.



Scheme 6. Mechanistic experiments.



Scheme 7. Plausible reaction pathway.

They epoxidize alkene **1** to afford the corresponding epoxide **E**, which undergoes acid-mediated ring opening by water, giving rise to the diol **2**.[19,20] The generation of benzoic acid (**28**) in the experiment shown in *Scheme 6,c* suggests that the generated acetoxy radical species would abstract a hydrogen atom from solvent or the substrate to generate acetic acid, which acidifies the reaction media. Another conceivable mechanistic scenario is that the acetoxy radical would undergo a sequence of decarboxylation/radical coupling to generate ethane and related compounds.[18]

Conclusions

An indirect, but reliable method to obtain *trans*-1,2-diols from alkenes is given by a sequence of epoxidation and the following ring opening with water.[21–23] However, the conventional method requires peroxy compounds, which are highly explosive in general, as a necessary oxidant. We developed the dihydroxylation reaction which possesses the following advantages. *1*) The reaction conditions are mild and environmentally benign, excluding toxic or explosive reagents, instead employing visible light, molecular oxygen, and diacetyl. *2*) Not only styrene derivatives but also aliphatic alkenes participate in the reaction. The present reaction serves as a greener and safer option of dihydroxylation reactions, although the product yields are moderate.

Experimental Section

A Typical Procedure for Dihydroxylation of Cyclohexene (**1**)

A balloon filled with oxygen was attached to a 30 mL glass *Schlenk* tube equipped with a stirrer bar. The *Schlenk* was evacuated and refilled with oxygen, which was repeated three times. Then, anhydrous acetonitrile (4.0 mL), distilled water (3.0 mL), cyclohexene (**1**, 25.4 mg, 0.31 mmol), and diacetyl (15.3 mg, 0.18 mmol, 0.6 equiv.) were added to the *Schlenk* through a syringe. The mixture was stirred under photoirradiation (470 nm) at room temperature for 24 h. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (ethyl acetate) to afford *trans*-1,2-cyclohexanediol (**2**) as white solids (23.2 mg, 0.20 mmol, 65 % yield).

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Author Contribution Statement

Y. M. and *M. M.* designed the experiments and wrote the manuscript. *Y. M.* and *D. I.* carried out the experiments.

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