Green Chemistry Experiment: A Template-Directed [2+2] Photodimerization Conducted in the Solid State

Introduction

A misconception often encountered in organic chemistry is that all organic reactions that produce covalent bonds (*e.g.* C-C single bonds) must occur in solution (*i.e.* liquid phase). This is not true. In fact, organic reactions can occur without solvent. From an environmental perspective, such **solvent-free reactions** are desirable since they eliminate the use of organic solvents (*e.g.* chloroform). Organic solvents are typically toxic and can pollute the environment (*e.g.* damage to ozone layer). The area of organic chemistry that is concerned with the reduction of organic solvents in chemical synthesis and, more generally, the reduction of environmental pollutants in synthetic chemistry is known as **green chemistry**.

In this experiment, you will conduct an organic reaction in a solvent-free medium. Specifically, you will conduct a reaction in an organic crystal. You will use a molecule, referred to as a **chemical template**, to assemble two reactant molecules, using noncovalent forces in the form of **hydrogen bonds**, in a process known as a **co-crystallization**. The reactants will be positioned by the template to undergo a [2+2] cycloaddition reaction. The solid-state reaction will occur by irradiating the crystals with ultraviolet (UV) radiation, in a **photochemical reaction**, and will result in the formation of two carbon-carbon single bonds (C-C bonds). Sources of the UV-energy to induce the solid-state reaction will include a photochemical reactor and the sun.

Background

Recall that there are three states of matter: gas phase, liquid phase, and solid state. In going from the gas phase to the solid state, the space between molecules decreases dramatically. In both the gas and liquid phase, molecules are 'free' to move by a process known as diffusion. In contrast, molecules in the solid state are in a static environment, being 'frozen' in position. A familiar example is H_2O (Figure 1a). The gaseous form of H_2O is steam; the liquid form of H_2O is water; and the solid form of H_2O is ice. Weak bonds known as hydrogen bonds hold together the H_2O molecules in ice and water. Each hydrogen bond consists of an H-atom of one H_2O molecule that interacts with a lone pair of an O-atom of a second H_2O molecule through an

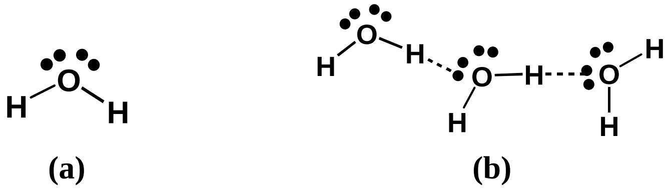

(a) (b)

Figure 1. (a) water and (b) two O-H···O hydrogen bonds involving three water molecules.

electrostatic attraction (denoted: O-H···O bond) (Figure 1b). In effect, the hydrogen bond acts as ‘glue’, allowing the H_2O molecules to ‘stick’ together.

The solid state is a desirable medium to conduct an organic reaction since the reaction does not require solvent. For a reaction to occur in the solid state, reactant molecules must be arranged in close proximity. Typically, reactants must be separated < 4.2 Å (1 Å $= 1 \times 10^{-10}$ m). For comparison, the length of a C-C bond is 1.54 Å. Reactive sites separated > 4.2 Å are too far apart to react.

[2+2] Photodimerization

The reaction that you will study in this experiment is a **[2+2] cycloaddition reaction**. A cycloaddition reaction is a reaction where unsaturated chemical functionalities add, or **dimerize**, to give a molecule with atoms arranged in a cyclic structure. The Diels-Alder reaction is an example of a cycloaddition reaction, which gives a cyclohexene product. Here, you will study a cycloaddition reaction between two *trans* C=C bonds, which react to produce a four-membered ring known as a **cyclobutane ring** (Figure 2). Each C-atom of a C=C bond is sp^2 hybridized. In a cycloaddition reaction involving two C=C bonds, it is overlap between *p*-orbitals that permits four π-electrons, two from each π-bond (hence, the term: ‘[2+2]’) to form two C-C bonds. UV-light (denoted: *hv*) provides the energy for the reaction to occur.

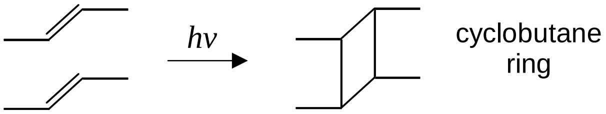


Figure 2. Photoreaction involving two *trans* C=C bonds to give a cyclobutane ring.

[2+2] Photodimerization in the Solid State

In the late 1960’s, Gerhard Schmidt of the Weizmann Institute, Israel, provided rules that describe how C=C bonds should be arranged in the solid state to undergo a [2+2] cycloaddition reaction. Schmidt revealed that the C=C bonds must:

(1) adopt a parallel orientation, and
(2) be separated by < 4.2 Å

These geometry criteria place the C=C bonds close enough for the *p*-orbitals of the two C=C bonds to overlap. Unfortunately, most organic molecules that possess C=C bonds do not crystallize with the C=C bonds arranged in a suitable position to react. This is related to the fact that packing in the solid state is largely based on the shapes of molecules. Since organic molecules are available in a variety of shapes, it is difficult to expect that every molecule in organic chemistry will crystallize in the special arrangement, outlined by Schmidt, to react.

Template-Directed Solid-State Reaction

One way to organize a molecule in the solid state to undergo a [2+2] photodimerization is to use a chemical template. A template is a molecule that assembles, using noncovalent bonds (*e.g.* hydrogen bonds), two molecules in a position for a chemical reaction, yet is not part of the final product (Figure 4). A familiar example of a chemical template is deoxyribonucleic acid, or DNA.

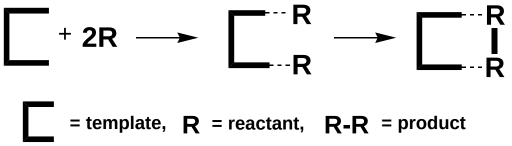
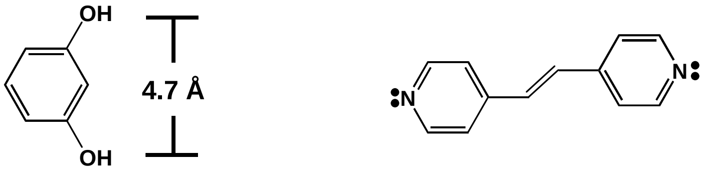


Figure 4. Schematic representation of a chemical template.

The chemical template that we will study in this experiment is 1,3-benzenediol, or resorcinol (Figure 5a). Similar to H_2O, resorcinol possesses two O-H groups, located in the 1- and 3-positions of the benzene ring. The separation distance between the two oxygen atoms of resorcinol is 4.7 Å.



(a) **(b)**

Figure 5. Structure of (a) resorcinol and (b) *trans*-1,2-bis(4-pyridyl)ethylene (4,4'-bpe).

The reactant that we will study is *trans*-1,2-bis(4-pyridyl)ethylene, hereafter referred to as 4,4'-bpe (Figure 5b). This molecule consists of a pyridine ring attached to each C-atom of a C=C bond. The two pyridine rings of 4,4'-bpe adopt a *trans* configuration about the C=C bond.

To use resorcinol to assemble 4,4'-bpe in the solid state for a [2+2] photodimerization, we will employ a method known as a **co-crystallization**. In a co-crystallization, two molecules are crystallized <u>at the same time</u> to produce a stoichiometric solid that is made up of each molecule. The co-crystallization can be conducted with or without the use of solvent. In this experiment, you will conduct the co-crystallization without solvent by grinding the two components together using a **mortar-and-pestle**. Molecules form co-crystals because of attractive noncovalent forces between the molecules.

Specifically, we will co-crystallize resorcinol with 4,4'-bpe in a 1:1 ratio. The co-crystallization will permit two molecules of resorcinol to interact with two molecules 4,4'-bpe by way of four O-H···N hydrogen bonds (Figure 6). The positioning of the O-H groups, along with the hydrogen bonds, will produce a **molecular assembly** in the solid state, of formula 2(resorcinol)·2(4,4'-bpe), wherein the C=C bonds of 4,4'-bpe are arranged parallel and separated by 3.7 Å, an ideal position for a photodimerization. UV-irradiation of the co-crystal will produce the cyclobutane product tetrakis(4-pyridyl)cyclobutane (Figure 7). In this way, we will utilize a chemical template to direct a [2+2] photodimerization in the solid state.

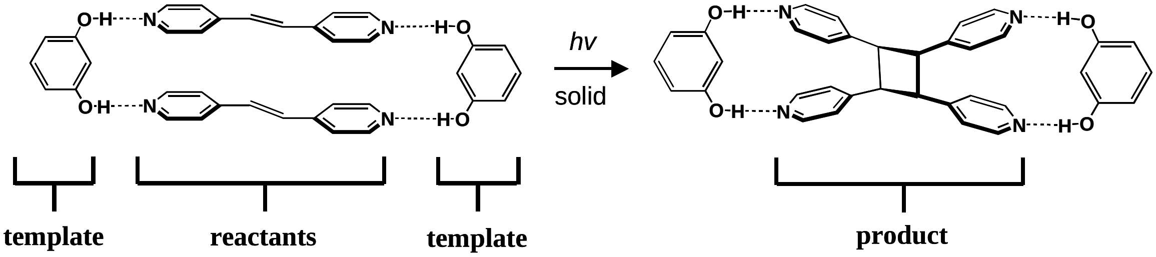


Figure 6. Schematic of the photoactive molecular assembly 2(resorcinol)·2(4,4'-bpe).

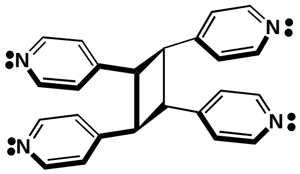


Figure 7. Structure of tetrakis(4-pyridyl)cyclobutane.

Procedure

Day 1

A. Preparation of Reactive Cocrystals

Cocrystals of 2(resorcinol)·2(4,4'-bpe) and Melting Point

Weigh 180 mg of the 4,4'-bpe that you purified in the Wittig lab and 120 mg of resorcinol. Place both solids in a clean and dry mortar from your mortar-and-pestle apparatus. Grind the two solids together for a period of 25-30 minutes. Pay particular attention to having the two solids thoroughly mix together. Collect the resulting fine powder.

Obtain a melting point of your co-crystals of 2(resorcinol)·2(4,4'-bpe). Save an appropriate amount of sample for TLC analysis on Day 2.

B. Sample Preparation for Photoreaction

Place 100 mg of your cocrystals of 2(resorcinol)·2(4,4'-bpe) evenly between two pre-cut transparency films, which will be provided by your TA. Make sure that you spread the sample evenly between the two sheets. Stick the transparency films together using four pieces of masking tape (one at each corner). Be sure to label your sample by writing your section number and your drawer number, along with your initials, on the masking tape.

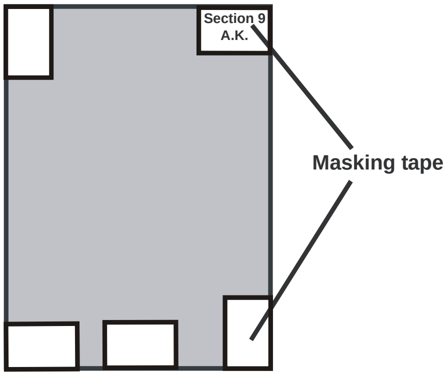


Figure 8. Schematic representation of the transparency assembly.

C. Photoreaction

Provide your TA with the transparency sample that contains your cocrystals. Your sample will be placed in a photoreactor. The photoreactor consists of a mercury lamp that emits broadband (*i.e.* many different wavelengths) UV-energy of high intensity (Figure 9). The sample will be placed in the photoreactor for a period of approximately 15 hours.

Figure 9. The mercury lamp used for the solid-state photoreaction.

Day 2

Collect your photoreacted sample from your TA.

A. Sample Analysis

With the UV reaction now complete, it is time to analyze your sample, as well as the material used prior to the photoreaction.

TLC Analysis

Prepare a TLC plate will four lanes involving your co-crystals of 2(resorcinol)·2(4,4'-bpe) (before photoreaction), your 4,4'-bpe, resorcinol, and your photoreacted sample. All solutions should be prepared in a 10:1 mixture of ethyl acetate and ethanol that is also used as the eluent. Analyze the spots on the TLC plate using both UV light and iodine vapors.

^{1}H NMR Spectroscopy and Melting Point

Prepare a sample of your photoreacted sample for ^{1}H NMR analysis (to be handed-in to your TA at the end of Day 2). Additionally, obtain a melting point of your photoreacted sample.

B. Recovery of the Photoproduct

Weigh the remaining amount of your photoreacted sample and place the sample in a 25 mL Erlenmeyer flask. To the flask add 15 mL of 1 M NaOH solution and heat the mixture on a hot water bath (70-80 °C) for 20 minutes. Vigorously stir the mixture with a stir bar while heating. Extract the cyclobutane product 4,4'-tpcb from the resulting yellow-green aqueous solution using three 20 mL portions of dichloromethane. Dry the collected organic layers over $MgSO_4$. Transfer the solution to a pre-weighed round-bottom flask and remove the solvent using a rotary evaporator (*caution*: do not discard the aqueous solution). Record the weight of the cyclobutane photoproduct 4,4'-tpcb.

C. Recovery of the Template

Acidify the remaining aqueous layer in the extraction funnel with 10 % HCl solution until the solution shows a clear acid reaction (litmus, pH = 2) and becomes yellow or faintly red. Extract the resorcinol with three 20 mL portions of diethyl ether and dry the organic layers over sodium sulfate. Place the dried ethereal solution in a pre-weighed round-bottom flask and remove the solvent using a rotary evaporator. Record the weight of the recovered resorcinol template.

D. TLC Analysis of Isolated Product and Template

Prepare a TLC plate with four lanes involving resorcinol, the TA standard of the photoproduct, the recovered photoproduct, and the recovered template using an ethyl acetate:ethanol (10:1) mixture as the eluent. Analyze the spots on the TLC plate using both UV light and iodine vapors.

Results and Discussion

From all the information that you have at your disposal (*i.e.* TLC, ^{1}H NMR, melting points) discuss whether or not the photoreaction occurred. Give an explanation as to why the photoreaction was or was not successful. For convenience, report the reactivity in the order of your TLC analyses. Do not forget to include literature values where appropriate.

Report the percent yield of the photoreaction and the percent recovery of the photoproduct and template. Hint: The percent yield of the photoreaction can be determined directly from the intensities of the peaks in your ^{1}H NMR spectrum of your photoreacted sample. Be sure to include all NMR data in Appendix B of your report.

In this experiment, the resorcinol template used hydrogen bonds to organize the reactants in the solid state for the photoreaction. What is the typical strength (in kJ/mole) of a hydrogen bond? Compare this energy to that of a C-C bond.

List two ways in which this experiment can be considered environmentally-friendly.

Please include a critical evaluation of this experiment as a separate page at the end of your report (after the Appendices). Suggestions for improvement are the most helpful, but you may comment on any aspect of the experiment. This page will be removed and not returned.

References

[2+2] Photodimerization in the Solid State

Schmidt, G.M.J. Photodimerization in the Solid State. *Pure Appl. Chem.* **1971**, *27*, 647-678.

Co-crystallization and Template-Directed Solid-State Reactivity

MacGillivray, L.R.; Reid, J.L.; Ripmeester, J.A. Supramolecular Control of Reactivity in the Solid State Using Linear Molecular Templates. *J. Am. Chem. Soc.* **2000**, *122*, 7817-7818.

Green Chemistry

Anastas, P.T.; Warner, J.C. *Green Chemistry: Theory and Practice*; Oxford University Press: Oxford, UK, 1998.

Name: ____________________________ Section:_____________________________

ID #: ____________________________ Date: ______________________________

Cocrystal:

2(resorcinol)·2(4,4’-bpe)

melting point of 2(resorcinol)·2(4,4’-bpe) (^{o}C) : __________________

Photoreacted sample:

melting point (after photoreaction) (^{o}C) : __________________

percent yield of photoreaction (%): __________________

R_f values and identities of spots: __________________

Recovered Photoproduct and Template:

percent recovery of photoproduct (%) : __________________

percent recovery of template (%) : __________________

R_f values and identities of spots: __________________