

Note:

- During the attendance check a sticker containing a unique code will be put on this exam.
- This code contains a unique number that associates this exam with your registration number.
- This number is printed both next to the code and to the signature field in the attendance check list.

Organic Photochemistry

Exam: CH3038 / Endterm **Date:** Thursday 3rd March, 2022
Examiner: Prof. Thorsten Bach **Time:** 08:30 – 10:00

	P 1	P 2	P 3	P 4	P 5	P 6	P 7	P 8
I								

Working instructions

- This exam consists of **16 pages** with a total of **8 problems**. Please make sure now that you received a complete copy of the exam. Detaching pages from the exam is prohibited.
- The total amount of achievable credits in this exam is 100 credits.
- Allowed resources:
 - one **non-programmable pocket calculator**
 - one **analog dictionary** English ↔ native language

No molecule models are allowed.

Cheating and cheating attempts will result in the candidate failing the exam.

- Do not write with red or green colors nor use pencils.
- Physically turn off all electronic devices, put them into your bag and close the bag.
- You may only use the distributed paper to give your answers; no additional sheets are allowed. There is additional space at the end of the exam but make sure to clearly indicate which question you are answering. **Short answers please!**
- Every correct and fully answered problem will be awarded the number of credits shown. It is possible to obtain only a fraction of the credits if the answer is not completely satisfactory.
- Consider the relative and absolute configuration of molecules, unless otherwise noted.

Left room from _____ to _____ / Early submission at _____

Problem 1 Multiple Choice Questions (14 credits)

There is only **one** correct answer option. Please answer multiple choice questions in the following way:

Mark correct answers with a cross



To undo a cross, completely fill out the answer option



To re-mark an option, use a human-readable marking



a) The Stokes shift...

- describes the shift of wavelength between absorption and emission.
- increases the distance of core coordinates between two states.
- cannot be determined experimentally.
- reduces the energy difference between triplet and singlet state.

b) Which statement regarding quantum chemical calculations is true?

- A full CI approach can only be solved for more than six heavy atoms.
- Excited state calculations are more demanding and costly than ground state calculations.
- All of these statements are true.
- Wavepacket dynamics are less sophisticated than adiabatic dynamics.

c) In an enone-alkene [2 + 2] photocycloaddition, which substituents on the alkene partner will favor a head-to-head regioselectivity?

- SMe, CF₃, CO₂Et, CN
- CN, CO₂Me, CF₃, COMe
- COMe, CN, OMe, Et
- OEt, NEt₂, CO₂Me, COMe

d) A chiral catalyst in enantioselective, photochemically initiated electrocyclic ring openings controls...

- the dis- or conrotatory pathway of the reaction.
- the torque selectivity.
- the thermal or photochemical pathway of the reaction.
- none of the other options.

e) Which of the following compounds usually present an inefficient intersystem crossing from the S₁ to the T₁ states?

- carbonyl compounds
- photosensitizers
- olefins
- transition metal complexes

f) In the flavin-catalyzed photooxidation of benzylic alcohols, why does the reduction-pathway of the photoexcited RFTA* in its singlet state ($^1k_{ET}$) not lead to any product formation (vs. the productive pathway from the triplet state)?

- The formed intermediate is not stable enough.
- Oxidation of the alcohol only works from the triplet state.
- Reduction of RFTA* only works from the triplet state.
- Back electron transfer (BET) is too rapid, so the excited state is quenched.

g) What is the reason for the redox activity of the excited state of catalysts like $[\text{Ru}(\text{bpy})_3]^{2+}$?

- Charge transfer interactions between ligands and substrate
- None of the other options
- Spatial separation of charge within the ligand
- Spatial separation of charge within the molecule d and f orbitals
- Spatial separation of charge between molecules

h) Which compound presents the lowest bond dissociation energy (BDE) for (at least) one of the C–H bonds?

- benzaldehyde
- tetrahydrofuran
- cyclohexene
- triethylamine

i) A follow-up reaction of an ATRA of a halide and an alkene can usually be triggered by...

- a base leading to the elimination product (cross-coupling).
- an acid leading to the elimination product (cross-coupling).
- another photoredox cycle which leads to the activation of the C–X bond and another addition of the alkene (cross-polymerization).
- addition of a Pd-catalyst, leading to β -H elimination after oxidative addition (Heck-type cross-coupling).

j) An essential factor for the design of multicatalytic procedures is...

- the compatibility of all catalysts and substrates throughout the reaction cycles.
- the compatibility of all catalysts and substrates during excitation.
- none of the other options.
- the compatibility of all catalysts and substrates regarding their redox potential.

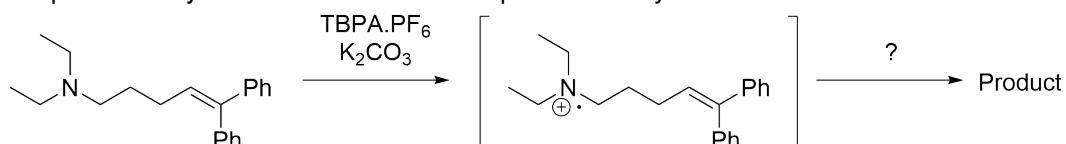
k) Which one of these radicals is **not** an efficient abstractor for XAT?

- C(sp²)-centered radical
- Sn-centered radical
- Si-centered radical
- α -aminoalkyl radical

l) What is one of the major advantages of combining metal-photocatalysis with cross-coupling catalysis compared to standard cross-coupling reactions?

- The combination of e.g. Ni and Ir allows an irradiation with a longer wavelength, i.e. lower energy. Therefore, green LEDs can be easily employed.
- Using photoredox-catalysis, radicals can easily be generated and single electron transmetalation has a low activation barrier. Therefore, heating or adding bases is not required.
- Reactions using light need an overall lower activation energy as the molecules stay on an excited hypersurface. Therefore, even alkyl fluorides are suitable reactants.
- Reactions with light are in general labelled as green, sustainable chemistry. Therefore, they are better received in the scientific community.

m) The depicted diethyl amino radical cation will predominantly...



- form the α -amino radical at the ethyl chain selectively.
- form the iminium ion at the ethyl chain selectively.
- form a mixture of α -amino radical regioisomers.
- undergo an intramolecular cyclization reaction.

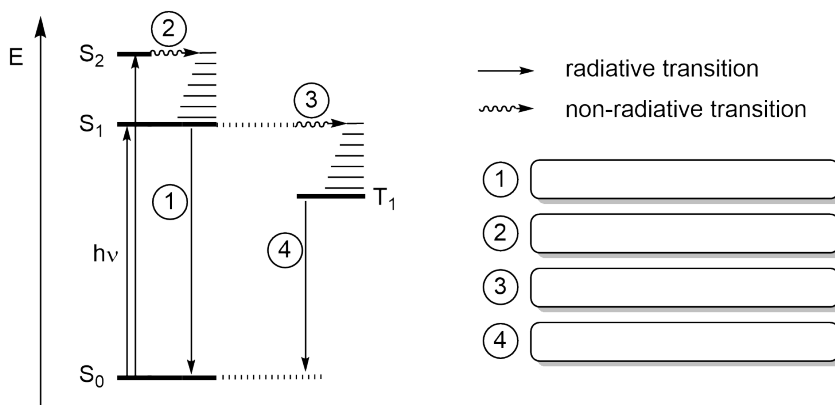
n) Which sentence is **incorrect** for photochemical reactions in the solid state?

- The symmetry of the substrate packing is determining the observed regioselectivity.
- The symmetry of the substrate packing is determining the observed stereoselectivity.
- They usually occur with maximum molecular movement.
- They usually occur with minimal molecular movement.

Problem 2 Fundamentals of Theory and Spectroscopy (18 credits)

To successfully conduct photochemical reactions, fundamental processes and properties of organic and organometallic compounds upon irradiation need to be studied and understood.

a) The Jablonski diagram schematically illustrates the electronic states of a molecule and transitions between them. One example of such a diagram is shown below (S = singlet state, T = triplet state). Fill out each box with the proper scientific term of the corresponding transition.



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b) Fermi's golden rule describes the transition rate from one electronic state to another one. In this context, briefly explain the "energy gap law" and give the typical time scale on which those processes occur.

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c) Name **two** different types of pericyclic reactions and provide a corresponding reaction example (thermal or photochemical).

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d) Transient absorption spectroscopy is a useful method to understand photophysics and -chemistry. Name **one** outcome that can be obtained by recording transient absorption spectra for different delay times.

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e) The Born-Oppenheimer approximation is important for the solution of the Schrödinger equation. Please give a brief qualitative description of this principle and how it helps to solve the Schrödinger equation.

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f) You would like to determine the quantum yield of a photocatalyzed reaction. Therefore, you want to irradiate a sample solution (volume = 2.5 mL) in a cuvette with a suitable LED with $\lambda_{max} = 420$ nm (irradiated area = 1.0 cm²) and detect the energy of the light that has passed the solution (i.e. transmitted).

With only solvent in the cuvette (without substrate and catalyst), you measure an energy output of the LED of 120 550 $\mu\text{W cm}^{-2}$. With your sample solution (substrate and catalyst), you measure an energy of 5590 $\mu\text{W cm}^{-2}$. After exactly 60 min, you take a sample of the solution and determine via calibrated GC analysis that the product concentration was 42.1 $\mu\text{mol mL}^{-1}$.

Calculate the energy of a photon at 420 nm, the mol of absorbed photons after 60 min and the quantum yield of product formation. Provide all numbers with three significant digits.

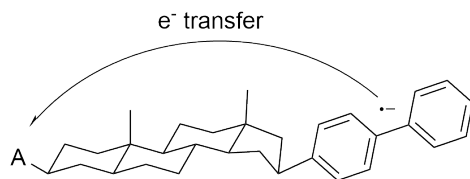
Useful constants: Avogadro constant = $6.0221 \times 10^{23} \text{ mol}^{-1}$, Planck constant = $6.6261 \times 10^{-34} \text{ J s}$, speed of light = $299.79 \times 10^6 \text{ m s}^{-1}$.

• $E_{\text{photon}}(420 \text{ nm}) =$

• $n_{\text{photons}} =$

• $\phi =$

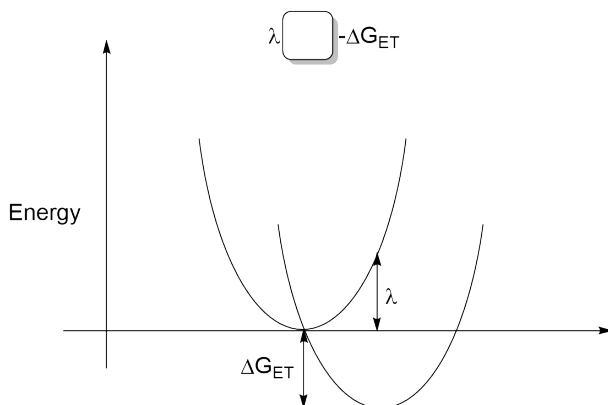
g) The Marcus inverted region was proven to exist experimentally by performing an electron transfer reaction from a biphenyl radical anion donor (D) to different acceptor moieties (A) across a rigid steroid scaffold. The concept of the Marcus inverted region of electron transfer ($D^- - A$ to $D - A^-$) can be explained qualitatively by drawing the energy potentials of reactants and products along the total reaction coordinate as a pair of parabolas.



Draw the missing sets of intersecting parabolas, so that all three sets represent three examples of electron transfer with increasing exergonicity (ΔG_{ET}). Include arrows to show ΔG_{ET} and λ in the three sets of parabolas: 1) exergonic electron transfer, in the normal (non-inverted) region; 2) barrierless electron transfer; 3) Marcus inverted region electron transfer.

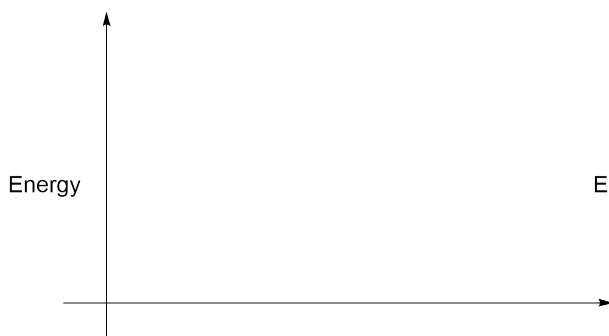
Write above each set of parabolas whether λ is larger ($>$) than, smaller ($<$) than, or equal ($=$) to $-\Delta G_{ET}$.

Barrierless electron transfer



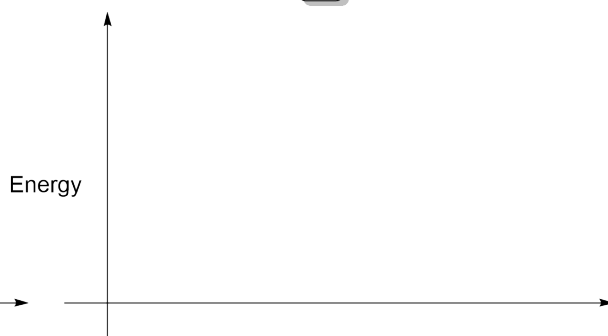
Exergonic electron transfer
(non inverted)

$$\lambda > -\Delta G_{ET}$$



Marcus inverted Region
electron transfer

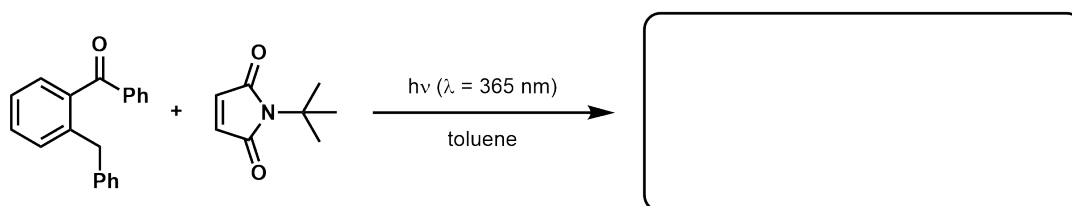
$$\lambda < -\Delta G_{ET}$$



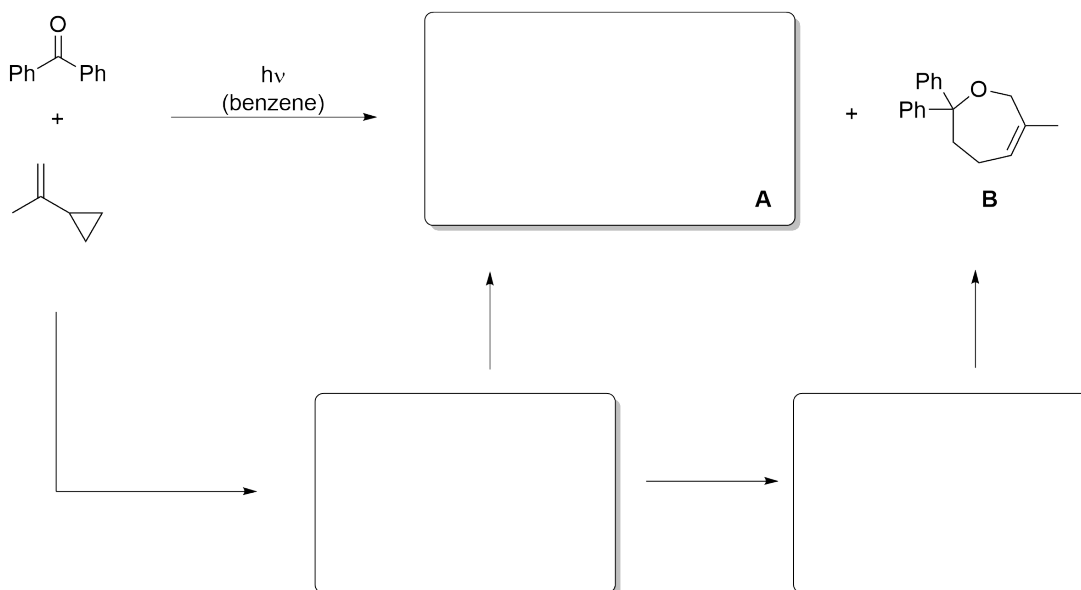
Problem 3 Direct Excitation (7 credits)

Many photochemical processes are induced upon absorption of light by an organic substrate.

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- a) In the following reaction, a reactive intermediate is formed after intramolecular hydrogen abstraction, which then undergoes a reaction with the depicted olefin. Draw the structure of the product. *Hint: The endo-diastereomer is obtained.*



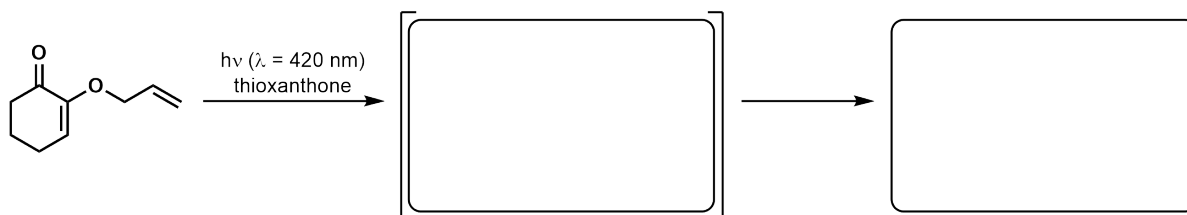
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- b) Irradiation of benzophenone in the presence of the shown alkene yields a product mixture of **A** and **B**. What structure would you expect for product **A**? Give the common intermediate for both products as well as an intermediate that explains how product **B** can be formed.



Problem 4 Photocatalysis (18 credits)

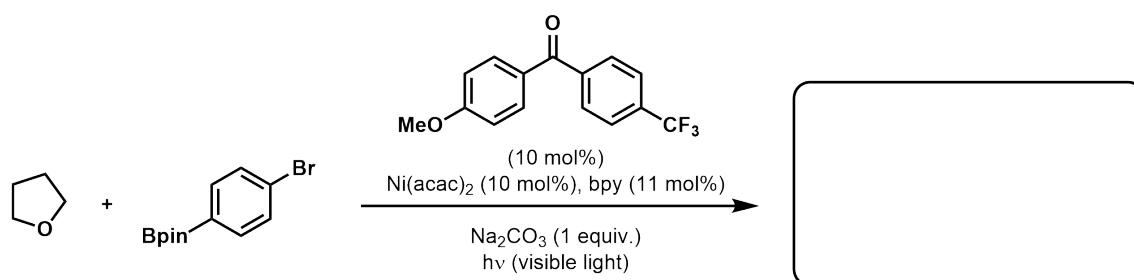
Both organic and organometallic catalysts have significantly expanded the repertoire of photochemical reactions.

a) Draw the structure of the diradical intermediate and the product of this reaction. *Hint: A strained ring system is being formed.*



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b) Hydrogen abstraction is a useful process in photocatalysis. Draw the structure of the product.



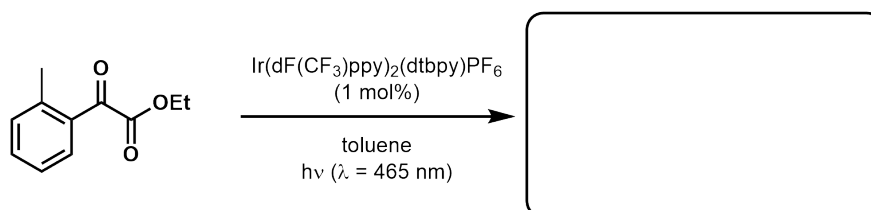
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c) Fill in the missing structures with the correct relative configuration. *Hint: Methylene blue is a triplet sensitizer.*



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d) When the depicted compound is sensitized, a reaction named after two chemists occurs. Draw the structure of the main product.



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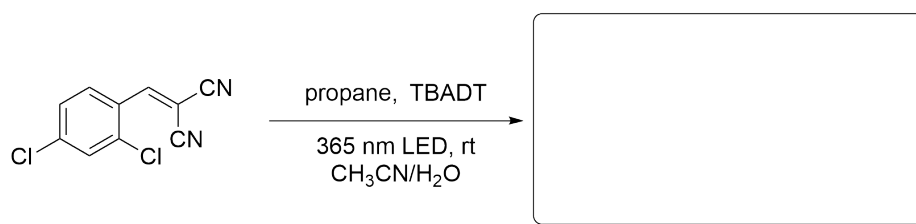
e) The following lactone undergoes a reaction when irradiated with visible light in the presence of the nicotinamide-dependent ketoreductase LKADH. This enzyme is a dehydrogenase stemming from the bacterium *Lactobacillus kefir* with NADH in its active site. Under the reaction conditions, the promiscuous photoenzymatic activity gives predominantly the (*R*)-enantiomer. Draw the product, and briefly explain why the stereoselectivity is observed and why visible light can be used instead of UV light.



Explanation:

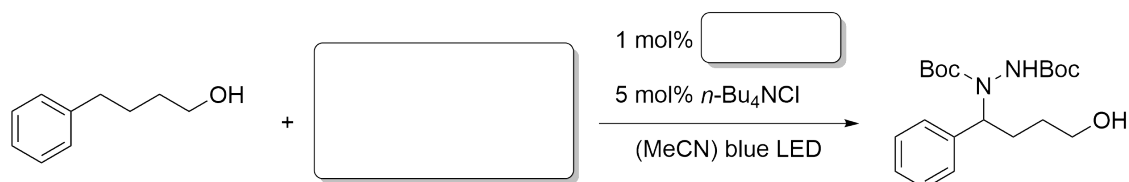
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f) Decatungstate photocatalysis can be used to functionalize C(sp³)-H bonds of light hydrocarbons. Draw the product you would expect from the reaction below.



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g) In the following reaction, δ -functionalized products are obtained through photoinduced ligand-to-metal charge transfer catalysis. Provide a suitable reagent and a possible catalyst that can coordinate to the alcohol, allowing for a productive reaction.



Problem 5 Basics of Photoredox Catalysis (9.5 credits)

Some fundamental aspects are relevant for various photoredox-catalyzed reactions.

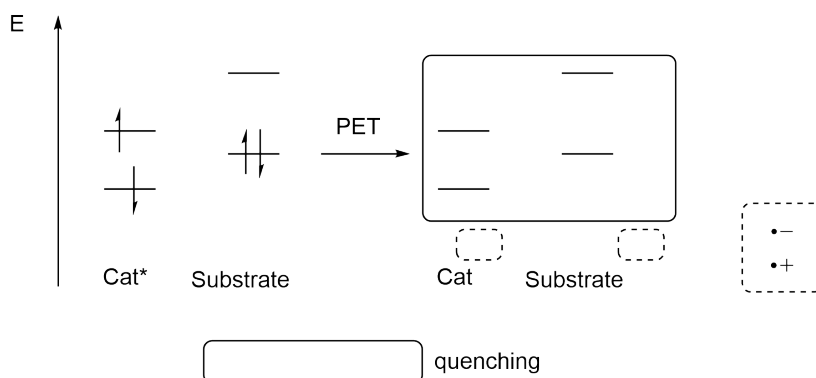
a) The transition metal photocatalysts $[\text{Ru}(\text{bpy})_3]^{2+}$ is one of the most frequently applied catalysts for photoredox and sensitization processes in organic synthesis. Name **two** (photo)physical properties of this photocatalyst. Also explain why the related compound $[\text{Fe}(\text{bpy})_3]^{2+}$ does not show such (photo)physical properties.

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- two properties of $[\text{Ru}(\text{bpy})_3]^{2+}$:
- difference of $[\text{Fe}(\text{bpy})_3]^{2+}$:

b) Transition metal and organic photocatalysts (e.g. $[\text{Ru}(\text{bpy})_3]^{2+}$ or eosin Y) can participate in photoredox processes. Below you find a scheme demonstrating a photoinduced electron transfer (PET) between an excited catalyst (Cat^*) and a general substrate. Please complete the scheme by filling in electrons (as arrows) and the elements given in the dashed box on the right. Name the type of quenching represented in this scheme.

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c) Amine radical cations are highly reactive and can be found in photoredox reactions. Draw and name the species that you would expect if an amine radical cation reacts with a base. Also name **one** typical subsequent reaction type that that species can undergo.

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d) What does the abbreviation "conPET" stand for? Name an example in which this process is used.

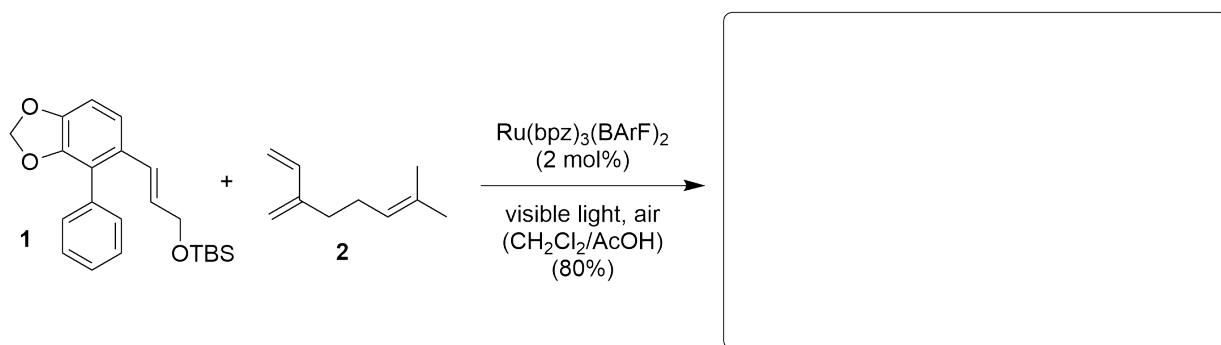
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Problem 6 Photoredox Chemistry (13 credits)

Through photoredox catalysis, a plethora of chemical reactions have been made feasible.

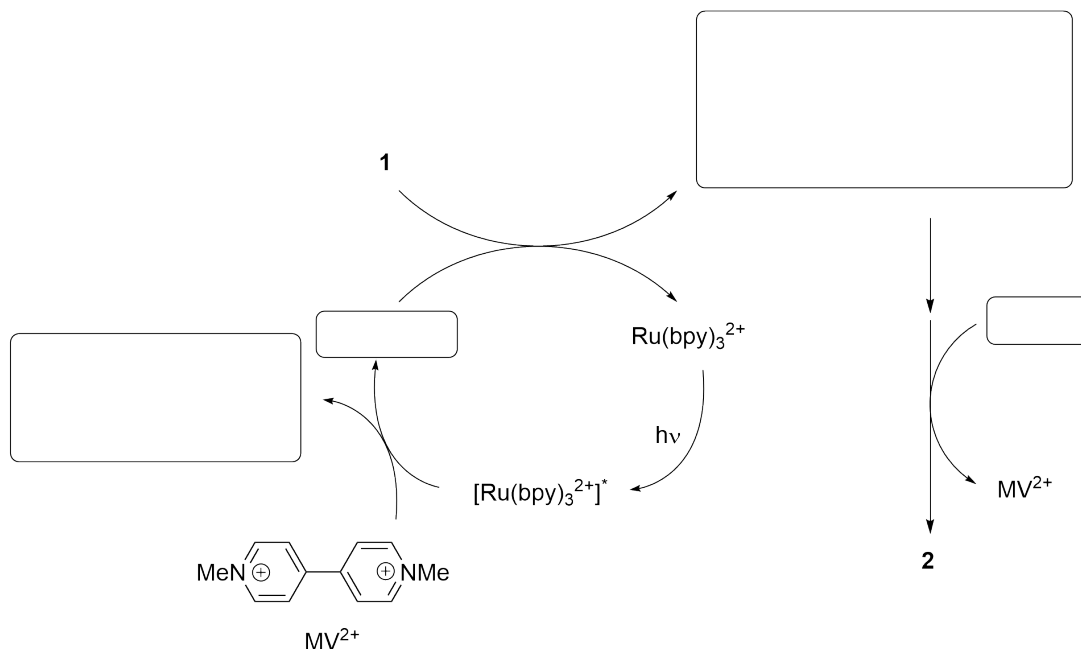
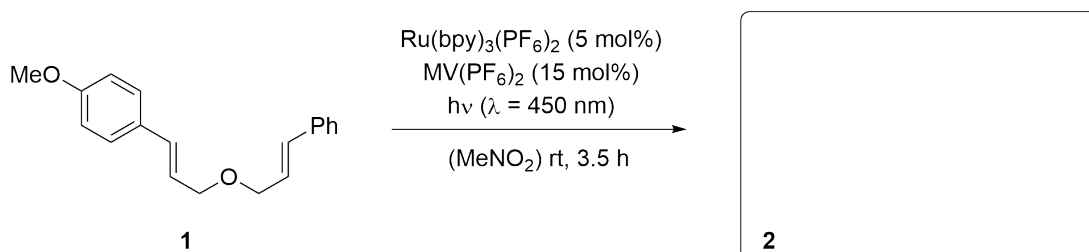
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a) The Yoon group became intrigued by the structure of the natural product *Heitziamide A*. Inspired by its biosynthesis, the total synthesis comprised a photocatalytic reaction of the *trans*-fagaramide derivative **1** and the monoterpene myrcene (**2**). Provide the structure of the product with the correct relative configuration.

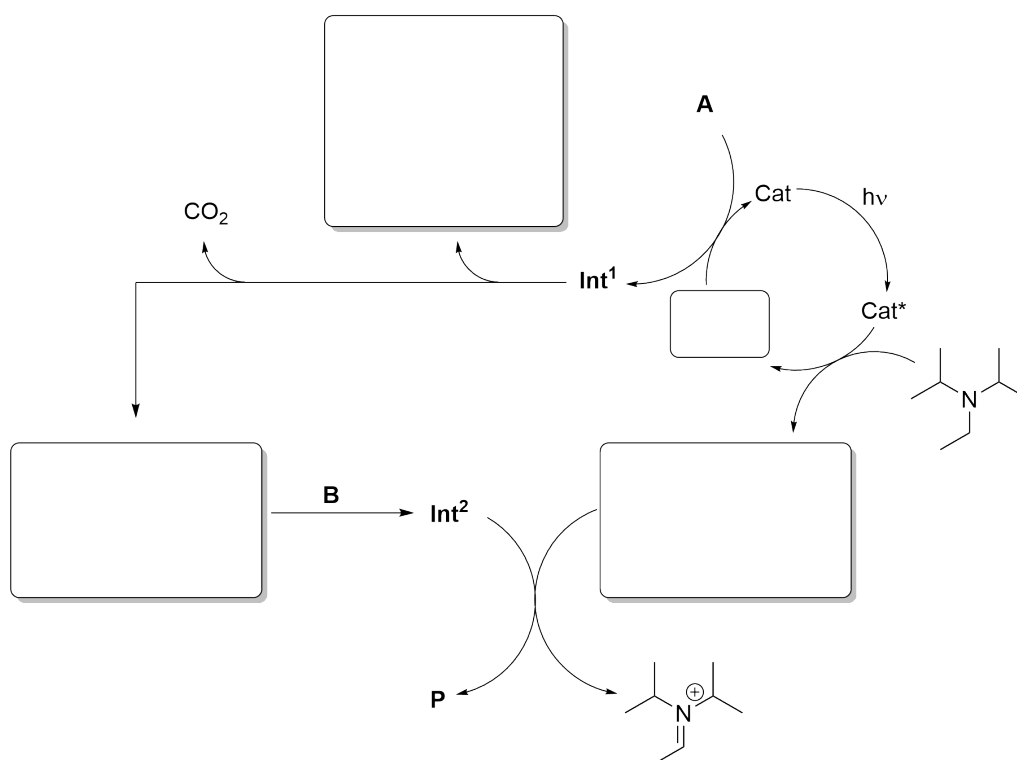
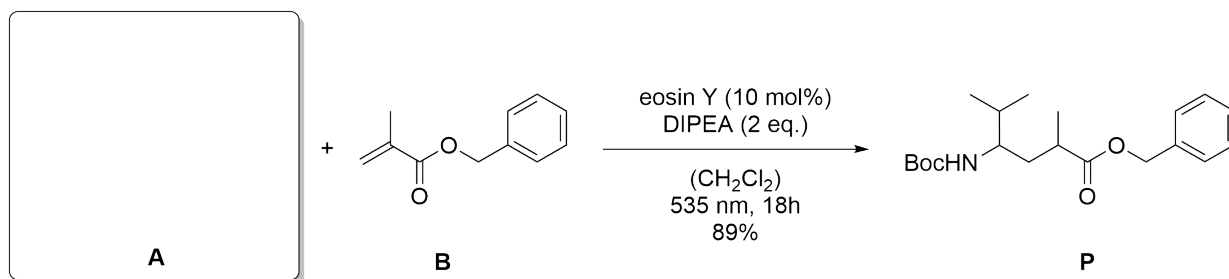


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b) A styrene derivative is irradiated in the presence of a ruthenium catalyst and a bipyridinium salt. Draw the structure of the **bicyclic** product that is formed by this reaction and give a mechanistic explanation. Neglect the configuration of the product.



c) In the presence of visible light, eosin Y (a photocatalyst) can reach an excited state that reacts with an amine like diisopropylethylamine (DIPEA). In the example below, the quenched catalyst initiates a reaction of **A**, which ultimately undergoes a transformation with benzyl methacrylate (**B**) to product **P**. Provide the structure of the starting material **A** and fill in the boxes below with the correct intermediates. **Int¹** and **Int²** are reactive intermediates that may or may not be ions.

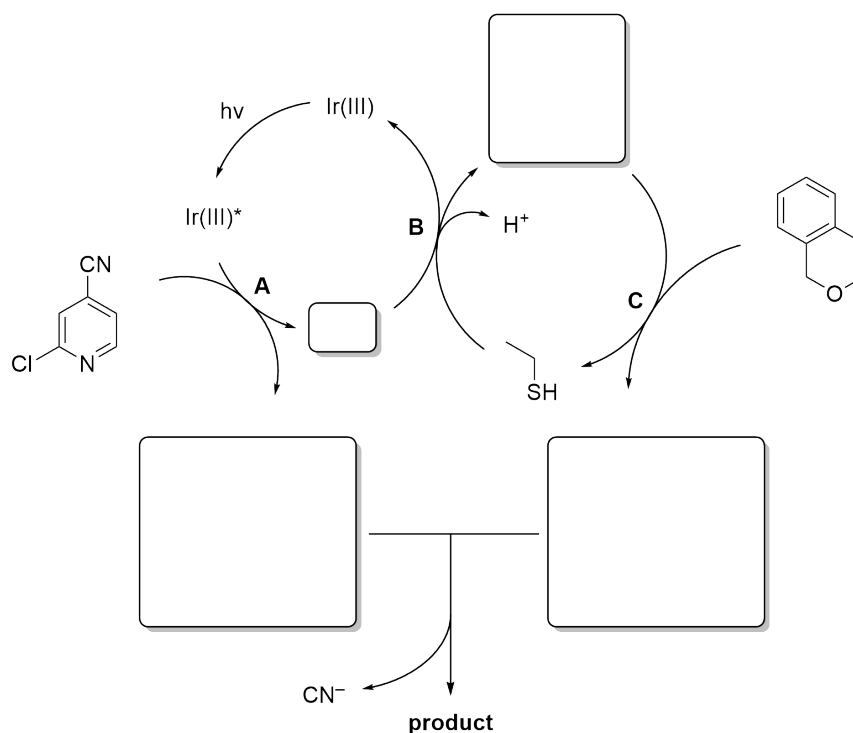
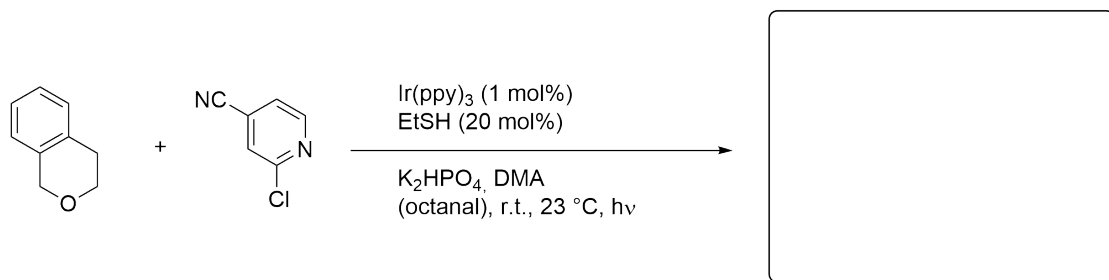


Problem 7 Multicatalysis (9 credits)

In some cases, a multicatalysis approach is employed for specific reactivity in photochemistry.

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a) The group of MacMillan reported an example of photoredox-chalcogen-multicatalysis. The transformation is enabled by the interplay of an iridium(III) complex, serving as a photoredox catalyst, and a thiol to couple benzylic ethers with pyridines. Fill out the gaps of the multicatalytic cycle and draw the product. What are the intermolecular processes **A**, **B** and **C** called?



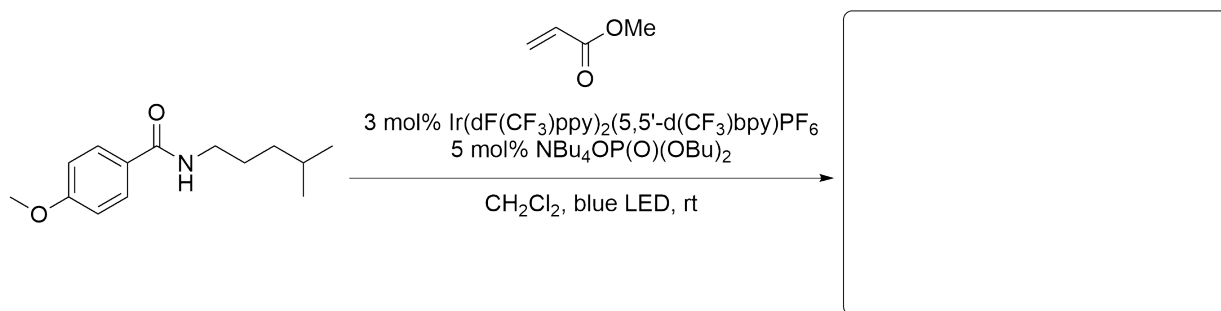
A:

B:

C:

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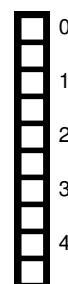
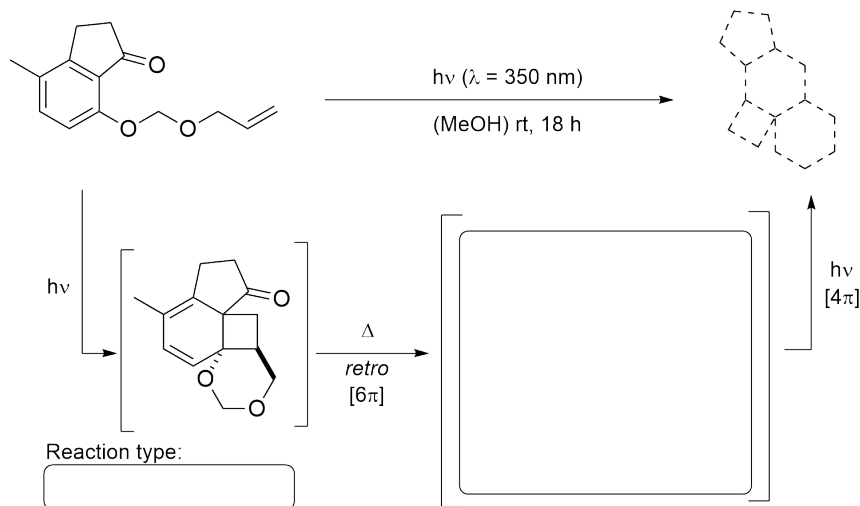
b) The N–H bond of *N*-arylamides can be cleaved homolytically via concerted proton-coupled electron transfer (PCET). Draw the product of the following reaction.



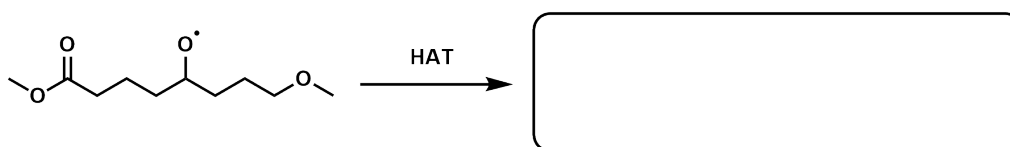
Problem 8 Diversity in Reactivity (11.5 credits)

Organic photochemistry gives rise to a diverse set of chemical reactions.

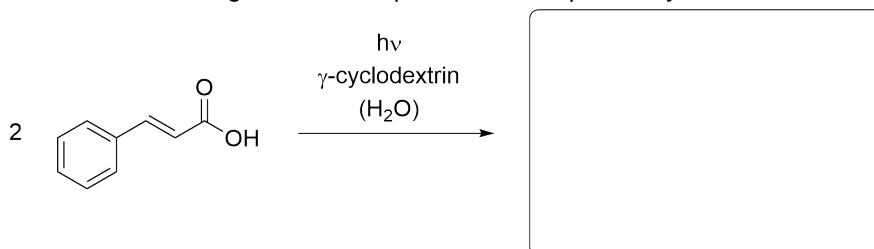
a) Photochemical reaction cascades are useful tools to construct complex molecular scaffolds. Below you can find an example transformation involving two photochemical steps and one thermal step. Please give the name of the first photochemical transformation and draw the product of the subsequent thermal pericyclic reaction. For the last photochemical reaction, the product scaffold is already given. Fill in all bonds, atoms and substituents, while observing the correct relative configuration.



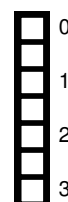
b) Considering polar effects, which radical intermediate will be obtained upon intramolecular HAT?



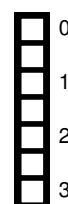
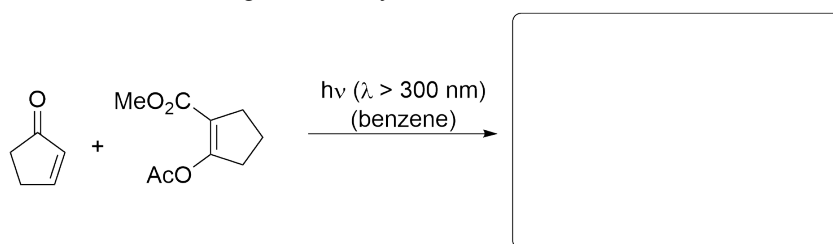
c) In the presence of γ -cyclodextrin, two molecules of cinnamic acid dimerize to the *syn*-head-to-head product upon irradiation with UV-light. Draw the product and explain why this reaction is diastereoselective.



Explanation:



d) Give the missing structure in the shown photochemical transformation after direct irradiation under consideration of the diastereo- and regioselectivity.



Additional space for solutions—clearly mark the (sub)problem your answers are related to and strike out invalid solutions.

A large, empty rectangular box with a thin black border, occupying most of the page. It is intended for students to write their solutions to the problems on the page.