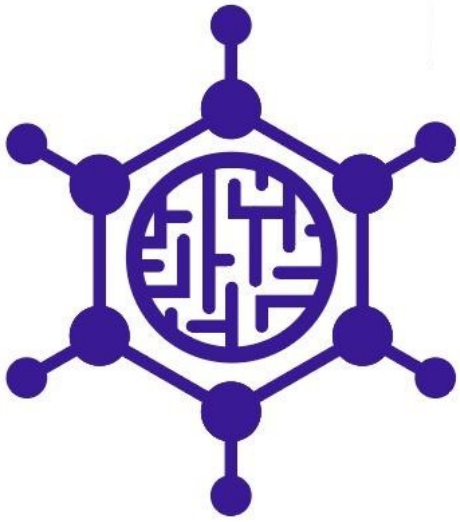


Instructions

(Prelims Round)

29 June 2021

1. The duration of the exam is 6 hours. However, an additional time of 2 hours might be taken without incurring any penalty. This net duration of 8 hours is **inclusive** of any unforeseen delays in scanning and uploading. The **hard** deadline is set at **10 PM IST, 29th June 2021**. Any submission after that will not be considered. Only one submission per team will be allowed.

2. We highly encourage you to start the process of submitting your answers in the Google form (see below) by 9:00 PM IST. Late submissions, in any case, will not be accepted. If you face persisting network issues during submission, inform us immediately by email (**chemenigma.pravega@gmail.com**) or call Anubhav at +**91 8777752927**.

3. This paper contains 15 questions in total, including 8 short answer questions

and 7 long answer questions. There are **29 pages** in this question paper.

4. Mention question number and title (which is given at the beginning of each question) clearly. We advise writing the question number at the middle of the page to avoid it being cut out during scanning. Answer all subparts of a question together and begin each question in new page. Clearly mention the subpart number for each question.

5. Clearly write your name(s), the name of your institute, as well as your registered email ids at the beginning of the answer script.

6. Do not submit multiple documents. If you have both typed and handwritten answers, compile your documents as a **single** pdf or word file.

7. It is preferred that you name the file as "Participant 1 Full Name_Participant 2 Full Name" (in case of team participation) or "Participant Full Name" (in case of individual participation).

8. Show your steps clearly for both short answer questions and long answer questions. Do not skip steps to receive full credit. Partial credit may be awarded for an incomplete solution or progress towards a solution.

9. In case of any clarification required kindly mail us. We will try our best to clarify. Even after that, if you feel you have any comments regarding the question (for example, incompleteness, incorrectness, etc.) you can mention that in your answer clearly with all the reasons why you think so. If we feel that you claim is correct, scoring will be done accordingly. But the first priority should be getting it clarified from us.

10. You are free to do beyond what is asked to do in the question (though it will not be considered for evaluation). You are also free to add any comments in your answer regarding any question.

11. The exam is open book. You may consult any non-living sources such as books, internet etc but you must cite the sources if you use them. In case you fail to do so, you will be penalised on grounds of plagiarism, and it may even lead to disqualification of the team.

12. If there are any corrections to any question, those will be informed to you over mail.

Submissions **MUST** be made using the form
https://bit.ly/ChemenigmaPrelimsSubmission

Best of Luck!

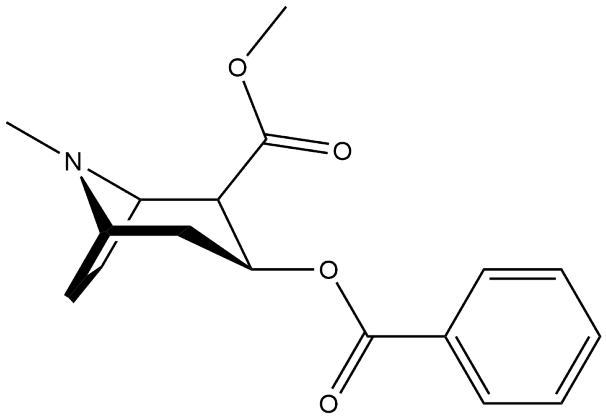
Questions

215 points

1 (*45 points*) Short Answer Questions

1.1

Given below is a stimulant drug (Compound A) whose production and distribution is illegal in most countries. To keep the use of the drug in check, a variety of chemical field tests are used for its detection in suspected samples.

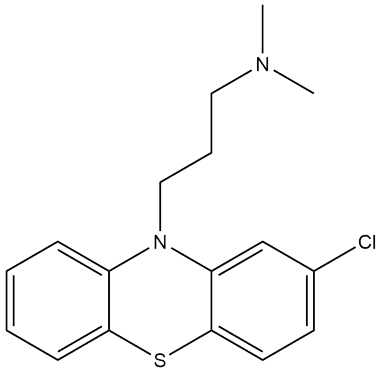


One such test uses the reagent : cobalt(II) thiocyanate trihydrate $Co(SCN)_2(H_2O)_3$ in presence of glycerol. Reaction of Compound A and the reagent gives a blue precipitate which is Step 1 of the detection test. In Step 2, addition of HCl causes disappearance of the blue ppt, and in the last step, chloroform is added and the blue colour reappears in the lower - organic region, confirming the presence of Compound A.

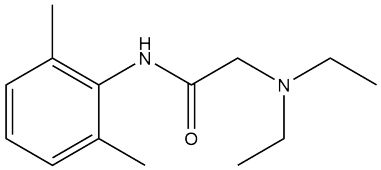
(a) It is observed that in Step 1 - Compound A and the reagent form a complex (blue ppt) in molar ratio of 2:1. Also it was observed that after filtering out the ppt, the resultant filtrate did not give blood red colour with Fe^{3+}. Predict the possible structure of such a complex. If the complex shows geometrical isomerism, predict which of the isomers would be more stable.

(*3 points*)

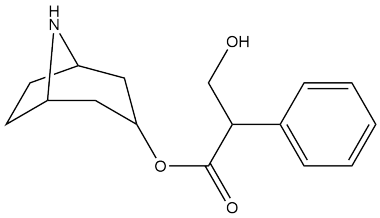
(b) Some more examples of drugs are given below:



Compound B



Compound C



Compound D

It is observed that Compound B and C, being structurally very different from Compound A, give a very similar reaction in Step 1 of the above test. Thus it can potentially be a false positive for our test. However, Compound D, being structurally somewhat similar, does not produce any complex with cobalt thiocyanate. Can you explain these observations?

(*4 points*)

(c) Usually, Compound A is transported in the form of its chloride salt. What would happen if we add hot aqueous NaOH solution to this salt?
Also predict if the obtained solution would still give a complex with cobalt thiocyanate.

(*3 points*)

1.2

The square planar coordination complex of diamminedichloroplatinum (II) has two geometric isomers – *cis* and *trans* commonly known as cisplatin and transplatin respectively. Certain sets of chemical reactions were performed on two samples A and B of the compound diamminedichloroplatinum (II). Assume that the samples

do not contain any impurities and are purely either cis or *trans*.

$$\text{Sample A: A} \xrightarrow{Ag_2O/H_2O} \text{X} \xrightarrow{H_2C_2O_4} \longrightarrow \text{Y}$$

The mass of $H_2C_2O_4$ that reacted was 5/3rd the mass of A.

$$\text{Sample B: B} \xrightarrow{{S_2O_3}^{2-}\text{ (in equimolar amounts as B)}} \text{P} \xrightarrow{\text{excess }{S_2O_3}^{2-}} \text{Q}$$

The compound Q was found to be $[Pt(S_2O_3)_2]^{2-}$
Identify A and B. (*5 points*)

1.3

Cobalt is known to form dihydrate, tetrahydrate, and hexahydrate complexes in aqueous medium. The probability of an ion to form a complex is inversely proportional to the spin energy of the ion in the complex. 182.84 g of a cobalt sulphate salt containing cobalt ions in 2+ and 3+ state was found to absorb 80.49 grams of water on crystallisation. Find the fraction of Co^{2+} ions in the sample. Report up to 2 decimal places.
(Atomic masses in amu: H:1, O:16, Al:27, S:32, Co:59)

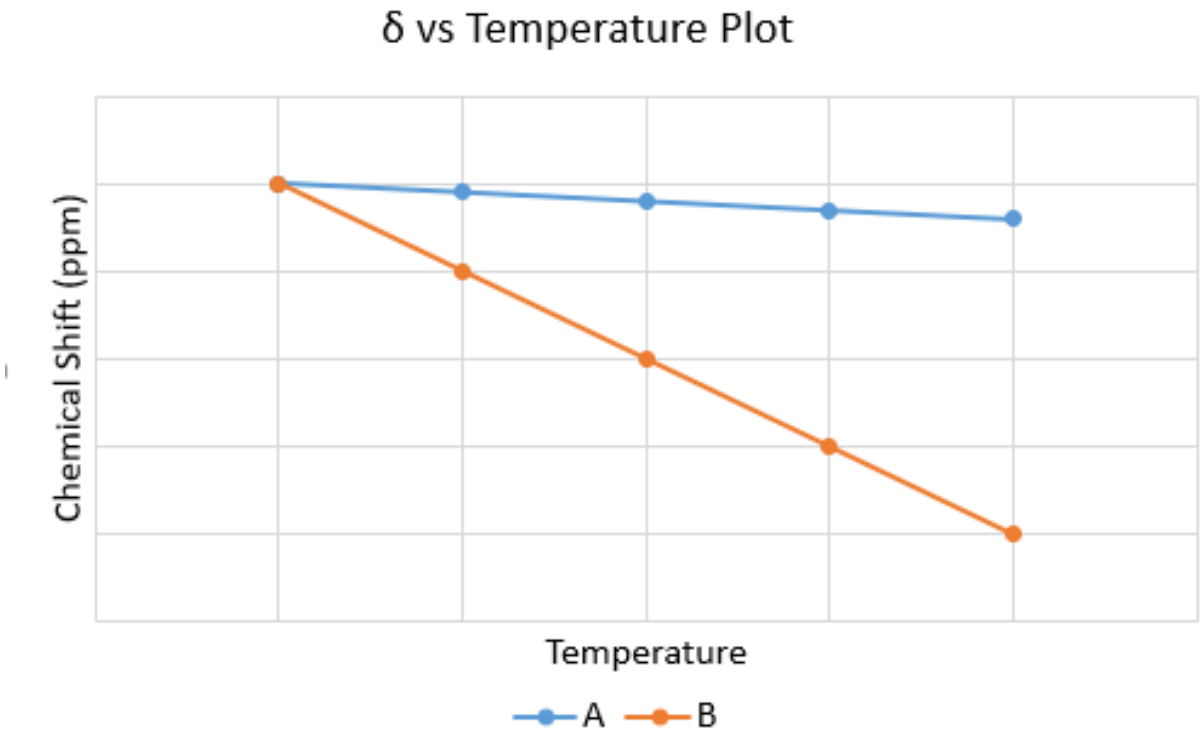
(*5 points*)

1.4

A molecule X has molecular weight of 94 u gives violet colour with $FeCl_3$. On reaction of X with acetic anhydride in the presence of Sodium Acetate, we obtain a compound Y.
Now,

$$\text{Y} \xrightarrow[\text{ii) aq} \cdot \text{ HCl}]{\text{i) cat} \cdot \text{ AlCl}_3} \text{A} + \text{B}$$

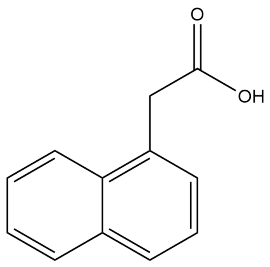
'A' and 'B' are two isomeric products formed and their relative yield depends on the conditions of the reaction. ^{1}H NMR spectra of dilute solutions of A and B in CCl_4 showed the following trend for the chemical shift (δ) of the most downfield proton with temperature (concentrations kept constant):



State the reason for this trend and explain why compound B shows a much steeper slope than compound A. Also identify the products A and B. (*6 points*)

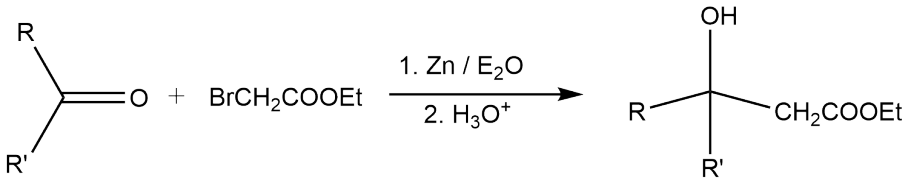
1.5

1-Naphthaleneacetic acid(NAA) is a synthetic plant hormone in the auxin family and is an ingredient in many commercial plant rooting horticultural products; it is a rooting agent and used for the vegetative propagation of plants from stem and leaf cuttings. It is also used for plant tissue culture.

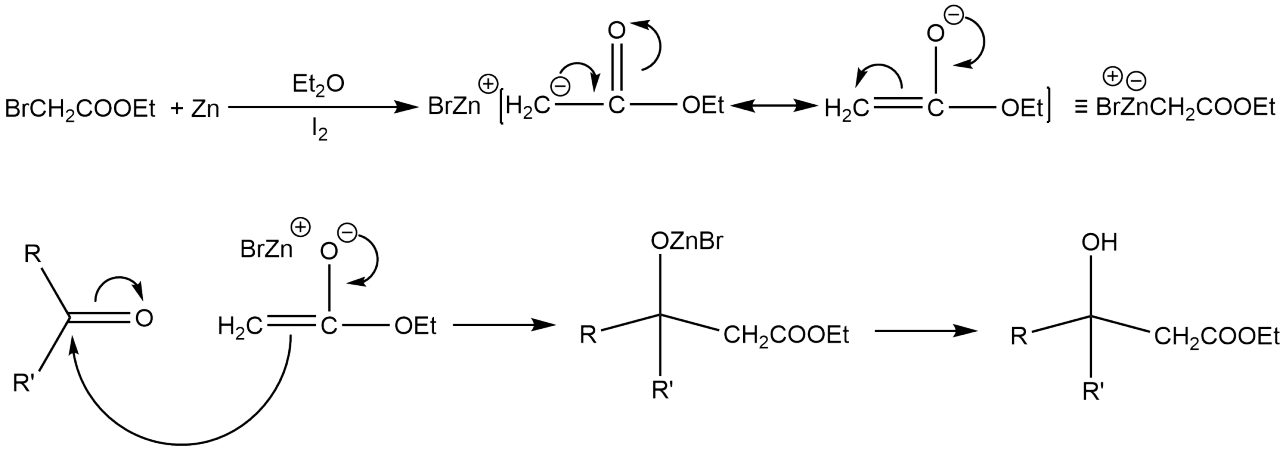


NAA

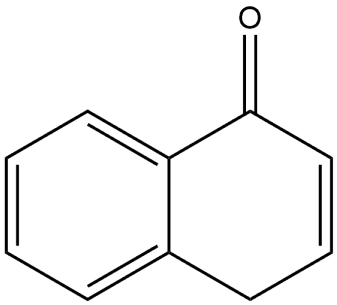
Synthesis of NAA is one of the applications of Reformatsky Reaction. Reformatsky reaction involves the preparation of β-hydroxyesters by the treatment of a reactive organic halide e.g., α haloester or its vinyl homologue with a carbonyl carbon in the presence of zinc metal in dry ether and subsequent hydrolysis. Zinc is activated by adding traces of iodine.



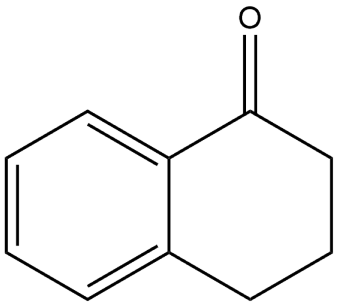
Mechanism :



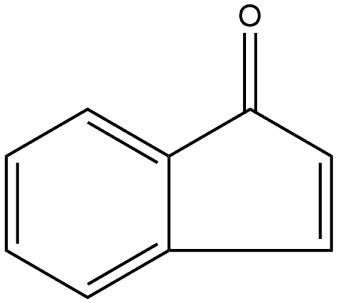
From the above information, determine which of the following is the primary reactant for the synthesis of NAA?



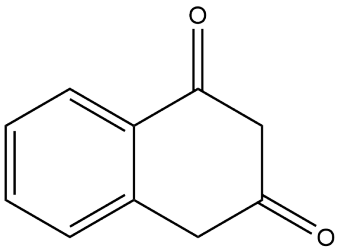
(a) Option A



(b) Option B



(c) Option C



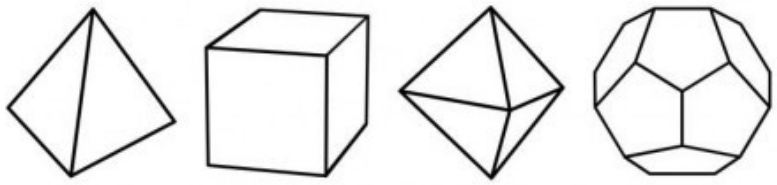
(d) Option D

(*5 points*)

1.6

A transformation, called T say, of a polyhedron is done as follows: A new polyhedron is made by constructing pyramids on all the faces. The resultant polyhedron is then 'dualised' i.e. a new polyhedron is made where vertices correspond to faces and vice-versa. One consequence of dualisation is that the number of faces and vertices are reversed as compared to the original polyhedron. Which of the following platonic solids could give rise to the C_{60} fullerene if the transformation T is applied?
(a) Tetrahedron
(b) Cube
(c) Octahedron
(d) Dodecahedron
Also give a one-line, if not one-phrase reasoning.

(*5 points*)



1.7

Consider a substance X. It is known that the change in chemical potential of 1 mole X in its gaseous phase is 10 times of X in liquid phase on isothermal compression from 1 bar to 10 bar. Assume X behaves ideally in its gaseous state. Determine the molar volume of X in its liquid phase. (*5 points*)

1.8

The zero-point energy of a molecule is the energy with which it vibrates even at zero kelvin. This zero-point energy possessed by the molecule is in some cases higher than the energies of the individual bonds present in the molecule. For instance, the zero-point energy of n-hexane is close to 530 kJ/mol and the energy required to break a C-C or C-H bond is around 400 kJ/mol. Should these molecules not decompose spontaneously? (*5 points*)

2 (*170 points*) Long Answer Questions

2.1 (*20 points*) A little bit of everything

Terpenoids are the largest group of secondary plant metabolites. Camphor is a terpenoid commonly used in lots of creams, ointments and lotions. It can also cause toxicity in children. It can be modified to give some very interesting ligands. Thus, its synthesis and chemistry have been very widely studied.

2.1.1

Its synthesis involves a not-so-obvious isomerisation step that converts compound A to B:

Compound A

Compound B

(a) Propose a mechanism for this. Justify each step of the mechanism.

(*2 points*)

(b) You might think it would be easy to make camphor by ozonolysis of B. But it's not used in the industrial synthesis due to the formation of a lactone. Draw the structure of the lactone. Show the mechanism of its formation for extra credit.

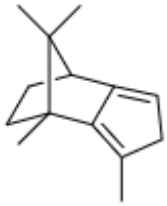
(*2 points*)

2.1.2

From compound B, camphor is synthesised. From the vinyl lithium derivative of camphor, a camphor derived cyclopentadiene X is formed when reacted with a

compound with chemical formula C_4H_6O and whose protons show chemical shifts of 6.298, 6.211, 5.908 and 2.286 ppm (the list is exhaustive). Show the mechanism of this reaction.

Vinyl lithium derivative



Compound X

(*5 points*)

2.1.3

The compound X after reaction with n-BuLi forms metal complexes. Consider the following complexes: $FeCl_2X_2$ and $CuCl_2X_2$ where X is the ligand formed in part 2. If both compounds are colourless, odourless and have very similar chemical properties, what analytical method can you use to distinguish between the two?

(*3 points*)

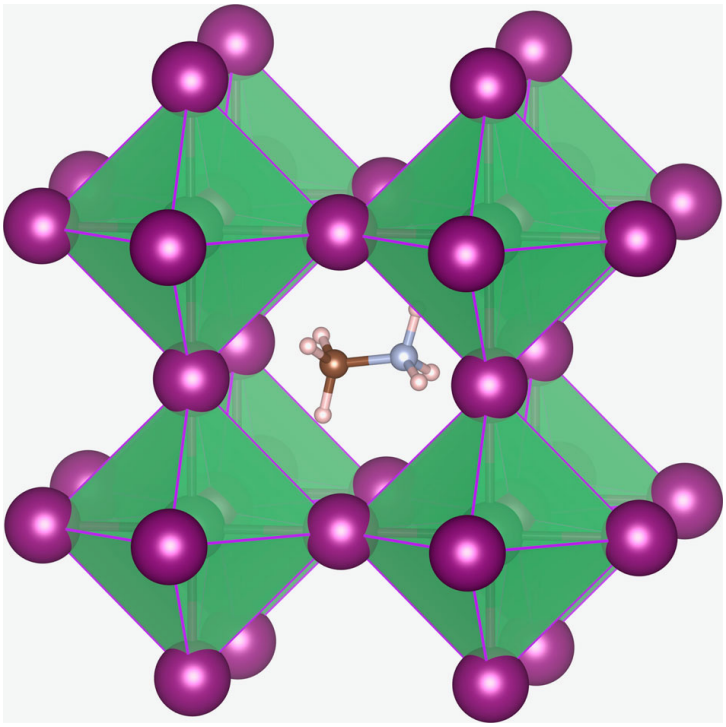
2.1.4

In an experiment, camphor was subjected to ionisation followed by neutralisation of the radical cation and the products were frozen in an inert matrix and IR analysed. The spectrum suggested the presence of the enol form of camphor. To confirm or refute this hypothesis, the IR spectrum of the enol might be calculated. Considering the molecule to be rigid, roughly draw all the conformers (Newman projection not required) that might be considered for IR calculation. These conformers are the stationary points on the potential energy surface of the molecule. The stationary point with the lowest energy will be considered for the calculation. Which conformer might that be?

(*8 points*)

2.2 *(30 points)* Shine bright like a perovskite

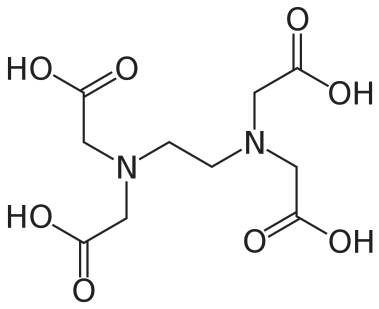
LEDs play an essential role in lives today. There has been interest in utilizing lead halide perovskite semiconductors for light emitting applications. They exhibit bright luminescence with tunable-bandgap. These LEDs are found to approach the efficiency close to those of commercial LEDs. However, owing to halide segregation, efficient and colour-stable red luminescence has not yet been realized.
In an experiment to produce colour-stable red-emission , ligand treatment was applied on the pervoskite crystals. Generally these pervoskite structures have the stoichiometry of ABX_3 where A is an organic ammonium or alkali metal cation, B is a group 14 cation, and X represents the halide ions.
In this demonstration $MAPb(I_xBr_{1-x})_3$ was utilised, where MA is methylammonium.



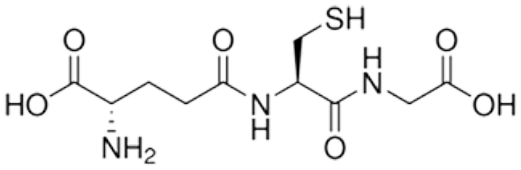
Structure of perovskites

2.2.1

For ligand treatment two ligands E and G as shown below were used.



Ligand E



Ligand G

Treatment of the crytals with both E and G was determined to be the most favourable. The E+G treated nanocrystals were observed to be smaller than untreated nanocrystals. In addition, the I:Br ratio decreased from 2:1 to 2:3 in the treated nanocrystals. The treated crystals show that the ligands suppress the halide segregation and improve band gap stability. In semiconductors, removal of defects improves properties and leads to a greater electronic stability.
Answer the following questions:

(a) Try to explain the action of E+G treatment based on the above information. Try to connect with the important role of such ligands in medicine to treat heavy metal poisoning.

(*3 points*)

(b) Try to explain why E+G ligand treatment is better than application of E along or G alone. A metric to quantify the effect of E and G are the surface bonding energies. Surface binding energy of E was calculated to be -1.60 eV and that of G to be -1.85 eV. In essence, try to explain how the application of E and G together effect the surface binding energies.

(*4 points*)

2.2.2

A significant issue that affects the perovskite crystals under illumination is halide segregation. In essence, in these mixed halide perovskites, excitation can either drive an electron-hole pair excitation or else lead to local halide rearrangement which leads to formation of halide-rich regions, i.e., iodine and bromine rich regions (where the above x approaches 1 for iodine), which alter the optical properties. The iodine rich regions have a lower band gap, which leads to red-shifting of the emission.
Now answer the following questions:

(a) What type of crystal defect are responsible for the halide segregation?

(*2 points*)

(b) Based on the answer to the previous question, try to formulate why does

E+G ligand application suppress halide segregation (possible thermodynamics of crystal defects?).

(*6 points*)

2.2.3

Now, to consider the light emitting properties of the perovskite crystal, assume that upon application of current, an electron-hole pair is formed. Assume hole is identical to an electron in every way except charge. Now, when the electron-hole pair is formed, it is trapped in the void occupied by the methylammonium ion. Let this void be approximated using a particle in a box model with the box being formed by the octahedrally coordinated Pb^{2+} ions. Assume they are in the lowest energy state. Light is emitted when the electron-hole pair recombine.
Based on this, answer the following:

(a) Using this simplistic model, calculate the wavelength of light emitted from $MAPbI_3$ crystal. Base on the information given on iodine rich regions forming, is the calculated wavelength accurate? If not, using the same model, explain what inaccuracies could lead to this error. (Given information: Ionic radius of Pb^{2+} = 1.19Å, Ionic radius of I^- = 2.02Å, mass of electron/hole = 9.1×10^{-31} kg, Take standard value of any other constants.)

(*8 points*)

(b) Based on this mechanism, explain why bromine-rich regions have a lower wavelength than iodine-rich regions? Explain how varying the parameter x in $MAPb(I_xBr_{1-x})_3$ can help in tuning the band gap of the perovskite LED.

(*5 points*)

(c) Using this model and and the properties discussed above, suggest another application of these perovskite crystals.

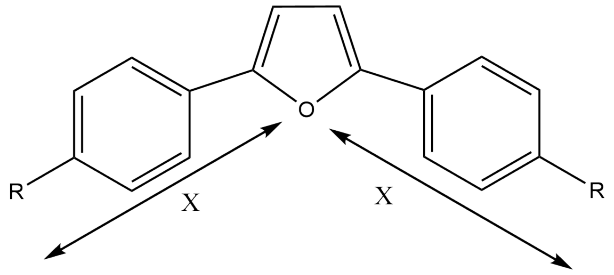
(*2 points*)

2.3 *(7 points)* Curved Binders

A variety of molecules are observed to bind to the minor groove of DNA. The best minor-groove binders are generally bent planar oligomers, which give them a crescent-shape. The curvature is one of many factors that affect the binding strength. They have found extensive uses in DNA molecular recognition, and are providing clinically useful drugs against diseases as as diverse as cancer and sleeping sickness.

2.3.1

Consider an example of the above:

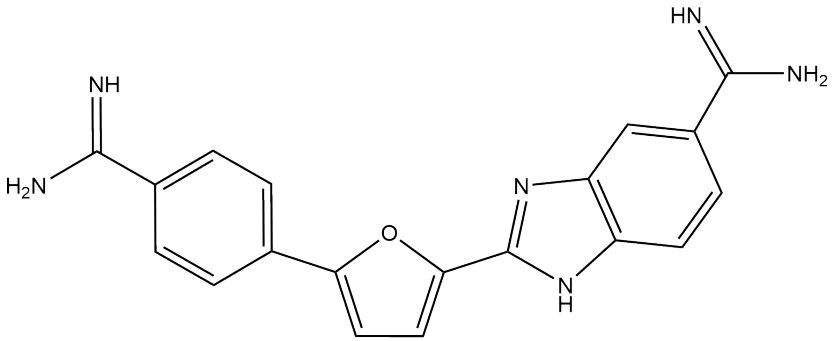


Can you come up with a model as simple as possible to estimate the radius of curvature of the above molecule? (Estimate X using the following assumptions and estimate radius of curvature : Bond lengths (pm) : C-C = 154 pm for single bonds; C-C in benzene = 139 pm)

(*4 points*)

2.3.2

Below is another example of such a compound :



Suppose the O in the furan ring is replaced with S. Predict what will happen to the curvature of the molecule. How do you think it will impact the minor groove binding strength of the molecule?

(*3 points*)

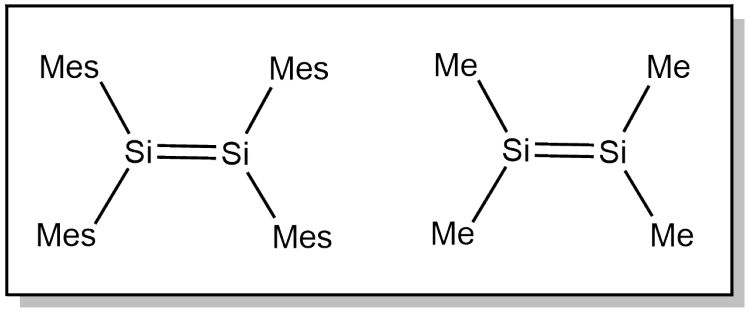
2.4 *(30 points)* The 'p'–riodic Table

The exploration of organic chemistry, i.e. "the chemistry of carbon", has dominated the efforts of chemists over the past two centuries. During this same time frame, the chemistry of the remaining elements in the p-block has garnered much less attention. This deficiency was further exacerbated by the fact that, in contrast to carbon for which the chemistry is dominated by the tetravalent state, many other p-block elements form multiple valencies and oxidation states with distinctive reactivity patterns. This leaves our understanding of the chemistry of the other p-block elements far short of that established for carbon. **The following problems for you to solve celebrate the unique and colourful chemistry of the "neglected ones", i.e. the non-carbon p-block elements!**

2.4.1

The stabilization of heavier main group element compounds having multiple bonding has been a central research theme in organometallic chemistry for almost 30 years. It was recognized from the early work, particularly in Group 14, that the multiple bonding of the heavier elements differs from that seen for the lightest group members. The lightest member of Group 14 is carbon, whose well-studied chemistry provides good contrast to that of the heavier congeners.

(a) Refer to the following diagram:

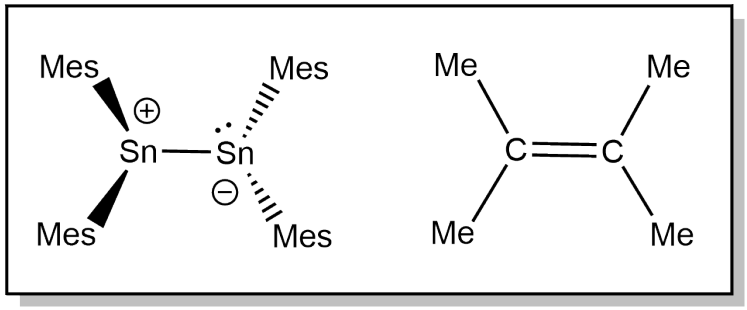


The compound on the left has been isolated and characterized, but that on the right has remained elusive. What might be the reason behind it?

(*3 points*)

(b) Whereas alkenes adopt a planar geometry, the heavier Group 14 analogs,

$R_2E{=}ER_2$ (R = alkyl or aryl; E = Si, Ge, Sn, or Pb) deviate from planarity, reflecting a change in bonding pattern. Rationalize this observation with a logical bonding model accompanied by a rough molecular orbital energy diagram.
Note: The following schematic can serve as a hint to the answer!

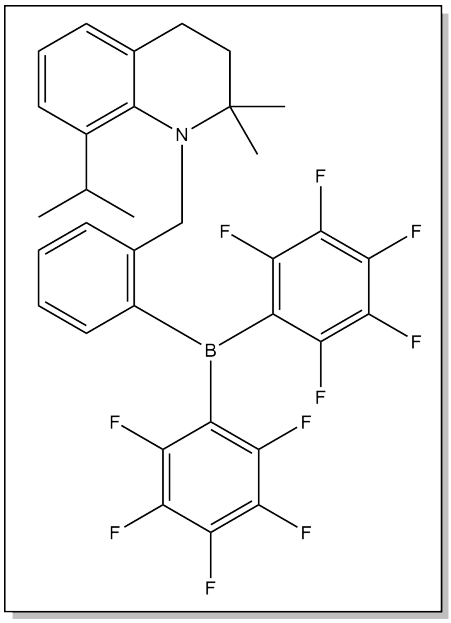


(5 points)

(c) Consider the heavier Group 14 alkene analogs, i.e. $R_2E{=}ER_2$ (E = Sn, or Pb) again. If R = N,N-difluoroamide group, what kind of structure do you expect it to have and why? If R = $C(SiMe_3)_3$ group, will your answer change? Why/why not?
Hint: Apply the same model you have developed in answering 1.(b).
(3 + 2 = 5 points)

2.4.2

For many years, it was believed that the combination of a Lewis base and Lewis acid resulted in the formation of a Lewis acid-base adduct, and consequently the neutralization quenched the donor-acceptor ability of Lewis pairs. This paradigm changed in 2006 with the discovery of "frustrated Lewis pairs" (FLPs). Early on, it was recognized that not all Lewis base/Lewis acid combinations form strong adducts. FLP denotes the combination of a bulky Lewis base with a bulky, electrophilic Lewis acid. It evades self-quenching but act cooperatively to heterolytically cleave the strong H−H bond. In this manner, FLP's effect a reaction that is normally attributed to the chemistry of transition-metal surfaces or homogeneous transition-metal complexes. Dihydrogen activation rapidly led to the development of metal-free FLP-catalyzed hydrogenations. FLP frequently involves a **Group 13** element and a **Group 15** element. A typical N/B intramolecular FLP is shown below:



(a) Suggest a mechanism of dihydrogen activation by FLP along with a rough sketch of relevant molecular orbitals.

(*4 points*)

(b) Can you think of some alternative mechanism? Discuss in brief. You don't need to provide any diagram here.

(*2 points*)

(c) Suppose you want to determine whether a particular FLP system is following the first mechanism proposed by you or the second one. Write the experimental design pointwise and briefly.

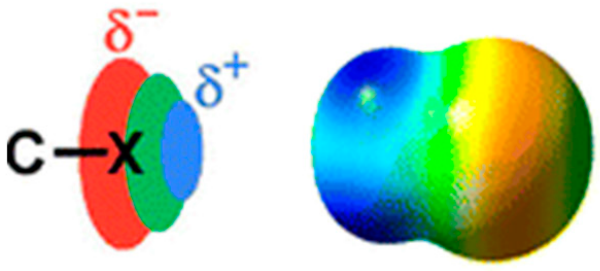
(*6 points*)

(d) The separation of saturated (i.e. paraffins) and unsaturated (i.e. olefins) hydrocarbons is critical to industries such as petroleum refining. How do you think an FLP system can help the industry in this regard?

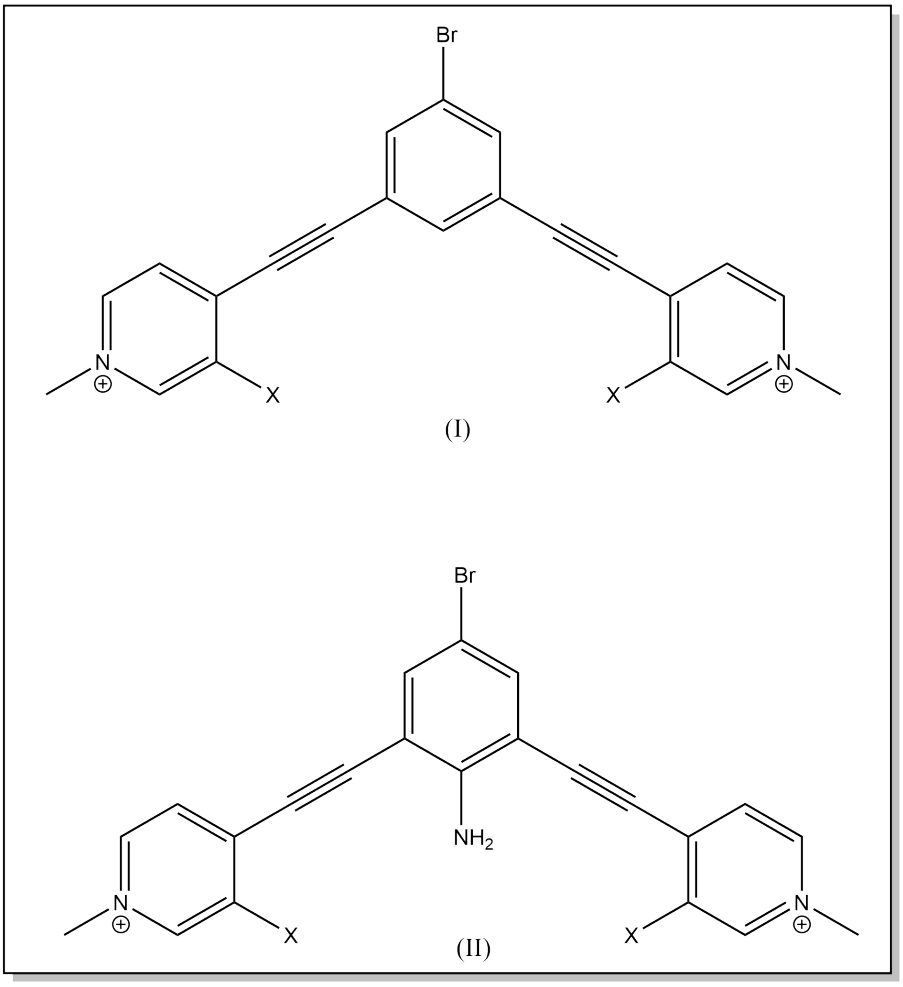
(*2 points*)

2.4.3

Group 17 elements, i.e. the halogens, are typically considered as sites of high electron density because of their high electronegativity. In compounds wherein the halogen atom is involved in the formation of one covalent bond, there is a region of higher electron density which forms a belt orthogonal to the covalent bond, and a region of lower electron density (known as σ-hole), mainly in the heavier halogens. The latter can form attractive interactions with electron-rich sites (i.e. nucleophiles). An IUPAC recommendation issued in 2013 defined these interactions as "halogen bonds" (i.e. XB).



(a) Bisethynylpyridinium halogen bonding receptors can bind anions and neutral Lewis bases in a bidentate fashion. In the following diagram, X denotes halogen (i.e. X = F, Cl, Br, or I).



Out of the receptors (I) and (II), which one would chelate to chloride better and why? This effect is the most pronounced for which X?

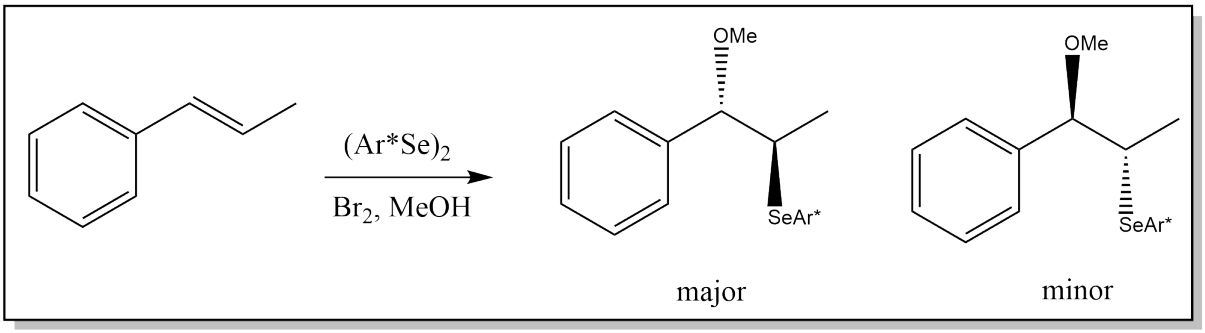
(4 + 2 = 6 points)

(b) "If X were iodine, the receptor would prefer SH^- to OH^- as the ligand." Is this a correct statement? Explain briefly.

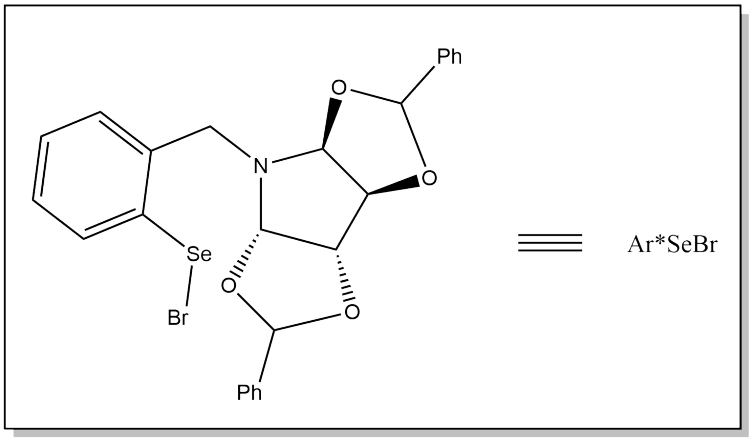
(*2 points*)

2.4.4

Analogous to the XB exhibited by Group 17 elements, **Group 16** elements participate in chalcogen bonding (ChB)! In the last few years, intra- as well as inter-molecular ChB has increasingly been exploited in solution, most notably in anion recognition/transport as well as in organocatalysis.
Diselenides with a chiral pyrrolidine moiety have been seen to catalyze the asymmetric methoxyselenylation of *trans*-β-methylstyrenes:



Explain the role of ChB in obtaining a good diastereomeric excess in the above reaction (under optimized conditions).
Hint: The effective reagent is shown below.



(*3 points*)

2.4.5

The "nobility" of **Group 18** elements has fascinated humans for millennia, and you probably are not an exception. According to you, Ne and He have not been forced to form genuine (i.e. primary) chemical bonds in neutral entities to this day. To your

surprise, your friend provides the counterexample of a peculiar entity described in literature: HNeF! How would you reestablish your point?

(*2 points*)

2.5 *(20 points)* This is 'Gibb'-erish

Gibbs Free Energy (G) is one of many thermodynamic potentials and is especially useful when looking at chemical systems. It is a Legendre Transformation of the Internal Energy (U) and defined as $G = U + PV - TS$.

2.5.1

Suppose water is undergoing solidification at $-10°$C. It is given that the vapour pressures of the liquid and solid states are 286.5 Pa and 260 Pa respectively at $-10°$C. It is also given that the molar volume of supercooled water is 1.80×10^{-5} m^3mol^{-1} and that of ice is 2.00×10^{-5} m^3mol^{-1} at $-10°$C. Find the change in Molar Gibbs Free Energy for the above-mentioned process.

(*8 points*)

2.5.2

The Gibbs Free Energy of a chemical system is useful when dealing with chemical equilibrium of reactions. At equilibrium, Gibbs Free energy is minimized. Consider the following isomerization reaction: A $\rightleftharpoons$ B
It is known that the Gibbs Free Energy of B is lower than that of A. Thus, the system to minimize the Gibbs Free Energy should lead to formation of B and at equilibrium, since Gibbs Free Energy is minimum, B should be present exclusively with no trace of A. Does this seem intuitive to you? Is the above assertion, correct? If not, please state mathematically as well as with sound physical reasoning, why not?

(*5 points*)

2.5.3

In a semiconductor p-n junction diode, doping is used as a technique to induce carriers in the p-type (holes as majority charge carriers) and n-type (electrons as majority charge carriers) layers. For example, Phosphorous is doped into Silicon for n-type doping and Aluminium is doped into Silicon for p-type doping. Can you show that a p-n junction is thermodynamically unstable? Assume here that doping is similar to forming a solid solution of the dopant in the host material.

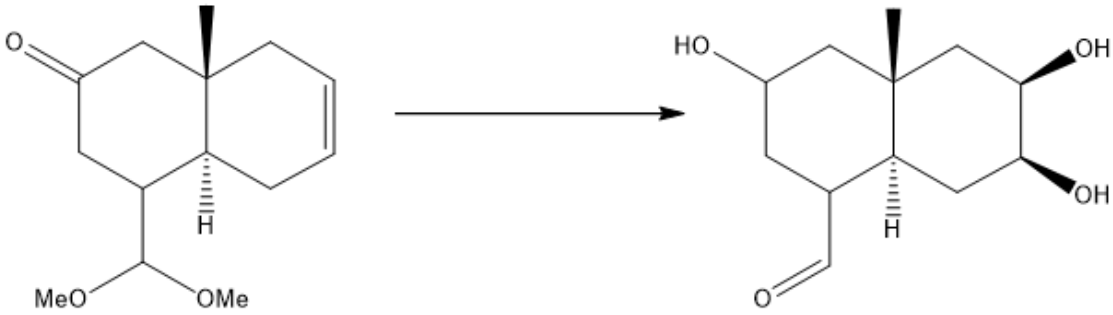
(*7 points*)

2.6 *(40 points)* The Stereochemical Demon

Stereochemistry is one of the most fascinating aspects in Organic Chemistry. To a practising organic chemist, nothing can be probably more exciting than playing with molecular models and molecular geometries. This question aims to explore some of the fascinating aspects of stereochemical control of organic reactions, particularly conformational analysis, stereoelectronic effects and stereoselectivity. So, buckle your seat belts to enjoy the ride!

2.6.1

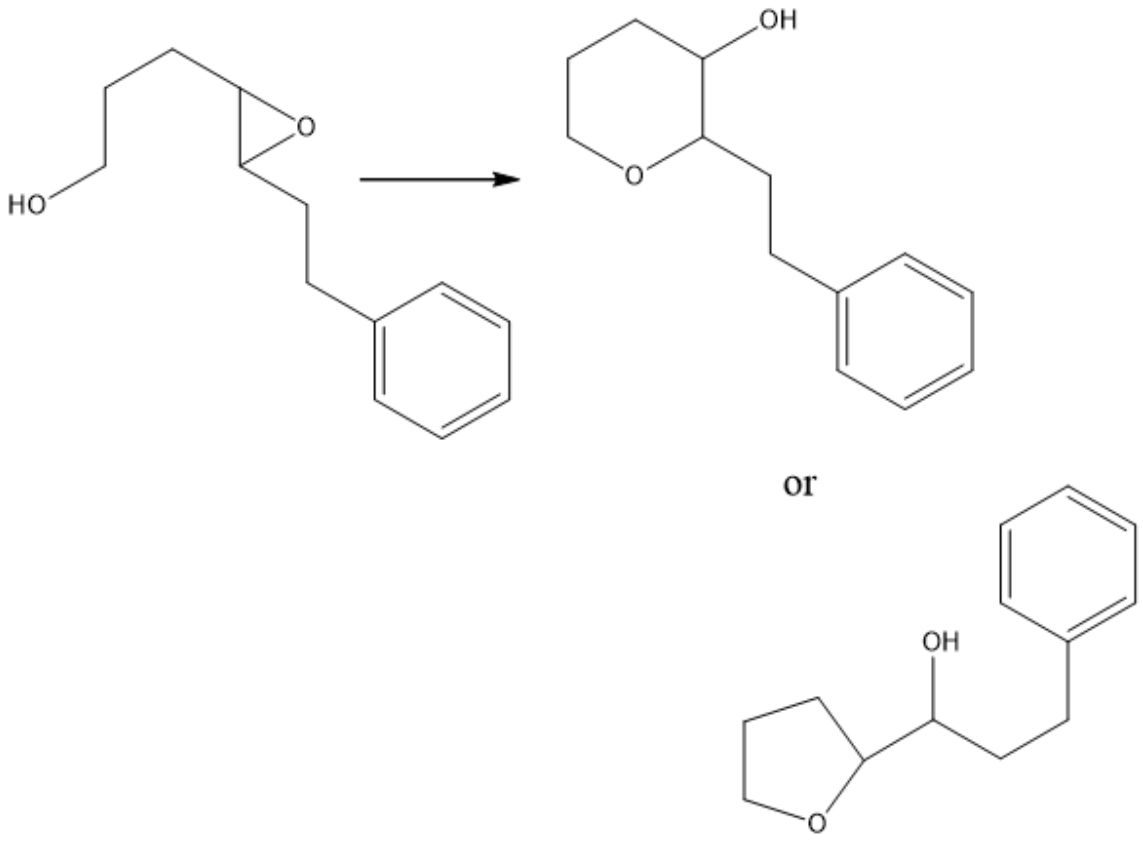
Carry out the following transformation is as few steps as possible. Provide rationale for the stereochemistry and chemoselectivity in each step of transformation. Also justify your choice of reagents (by explaining why other equally possible alternatives do not work),



(5 points)

2.6.2

The acid-catalyzed cyclization of trans epoxide yields a single kinetic product.

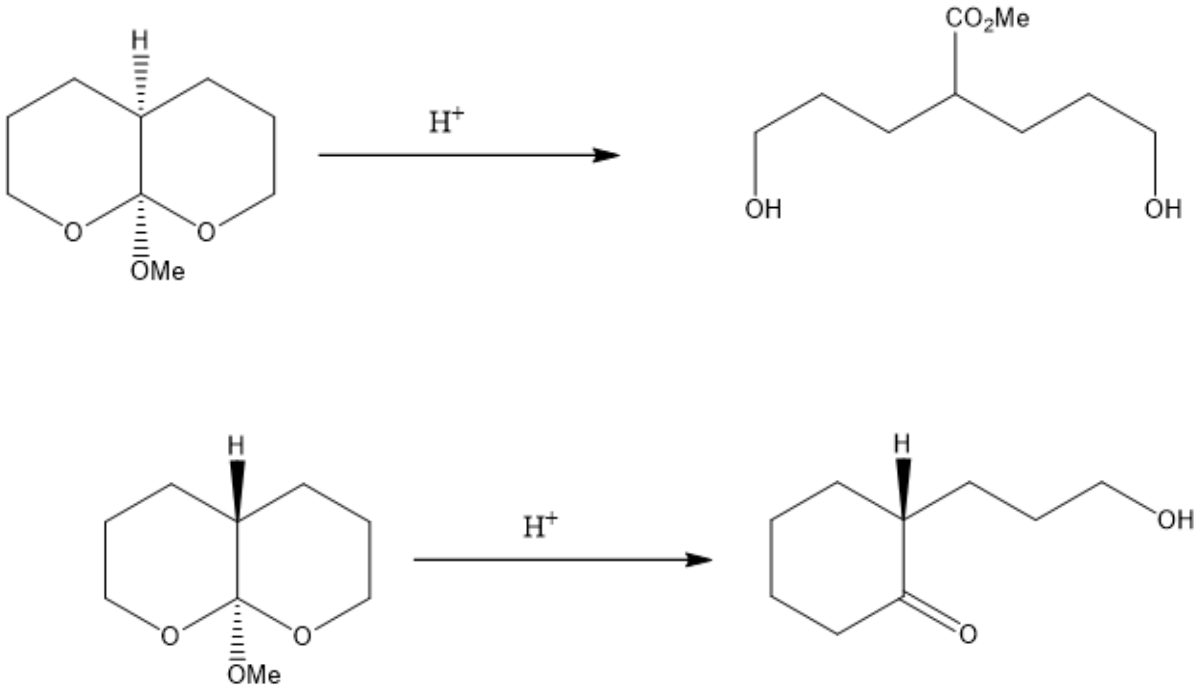


Predict the kinetic product of this reaction and its stereostructure (relative stereochemistry). Assume carbonium ions are not involved in this transformation. Provide an explanation that accounts for the selectivity of this process. The question might look very scary, but indeed is simple. Just a warm-up exercise on cyclizations!

(*4 points*)

2.6.3

The hydrolysis of cyclic orthoesters appears to be dominated by stereoelectronic factors.

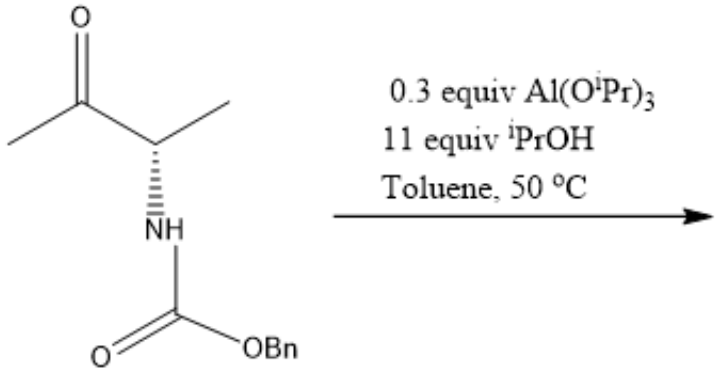


Please provide an explanation for why the *cis*-compound (first reaction above) undergoes hydrolysis to give hydroxy ester, and why the *trans*-compound provides lactone (second reaction above). Try to think in terms of orbitals and their influence on reactivity. As an additional hint, you might also note that the first reaction above is slower than the second. Furthermore, the first reaction is slower than the second. Also, the first reaction above actually leads to a mixture of both the hydroxy ester as well as the lactone (given in second reaction). The former dominates, and it suffices for you to explain its formation.

(*10 points*)

2.6.4

Predict the product with correct stereochemistry and rationalize its stereochemistry.

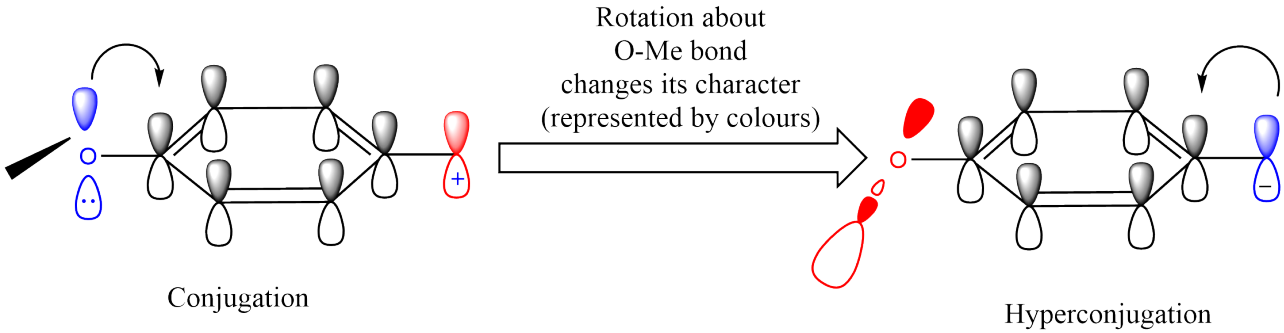


Would the outcome of the reaction be any different if the reaction was carried out at a pH of 1? Justify your answer in not more than 2 sentences. *(4+2 = 6 points)*

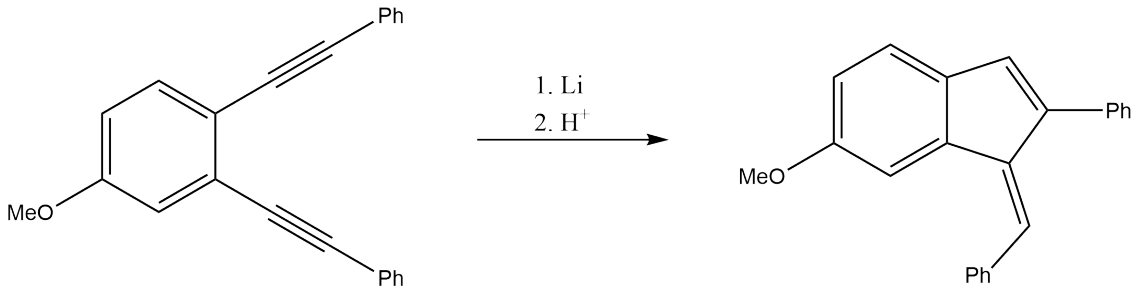
2.6.5

Chameleonic behaviour of functional groups is not uncommon in chemistry. In fact, chemical reactions routinely convert donors into acceptors.

One of the most widely known chameleonic groups is the methoxy group. The chameleonic nature of the methoxy group is represented below:



Rotation of the *p*-OMe substituent has profound stereoelectronic consequences for the regioselectivity of reductive cyclization. Consider the following reaction.



The lithium in the reaction above merely serves as a reducing agent.
Using the information given above, state whether the given reaction is possible or not. You need not consider whether it actually occurs or not, you just need to consider the feasibility of the reaction. Please note that methoxy group can stabilize a positively charged centre para to it extremely well. Hence, the more negatively charged centre might be expected to be preferably located meta to the methoxy group, to prevent destabilization due to +R group.

(*5 points*)

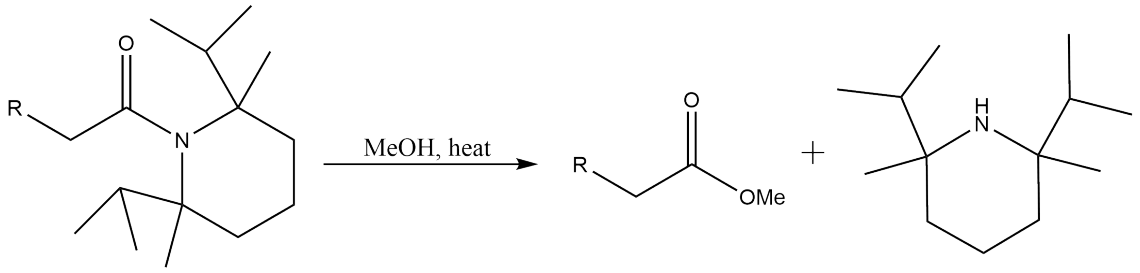
2.6.6

Suppose I carry out the same reaction as above. However, just out of curiosity, I substitute the methoxy group with a $-OCF_3$ substituent. The remainder of the structure of the reactant remains unaltered. Can you predict the product of the reaction then? How would this reaction differ from the previous one? Please provide a **very brief** justification for your answer.

(*6 points*)

2.6.7

Consider the reaction below:



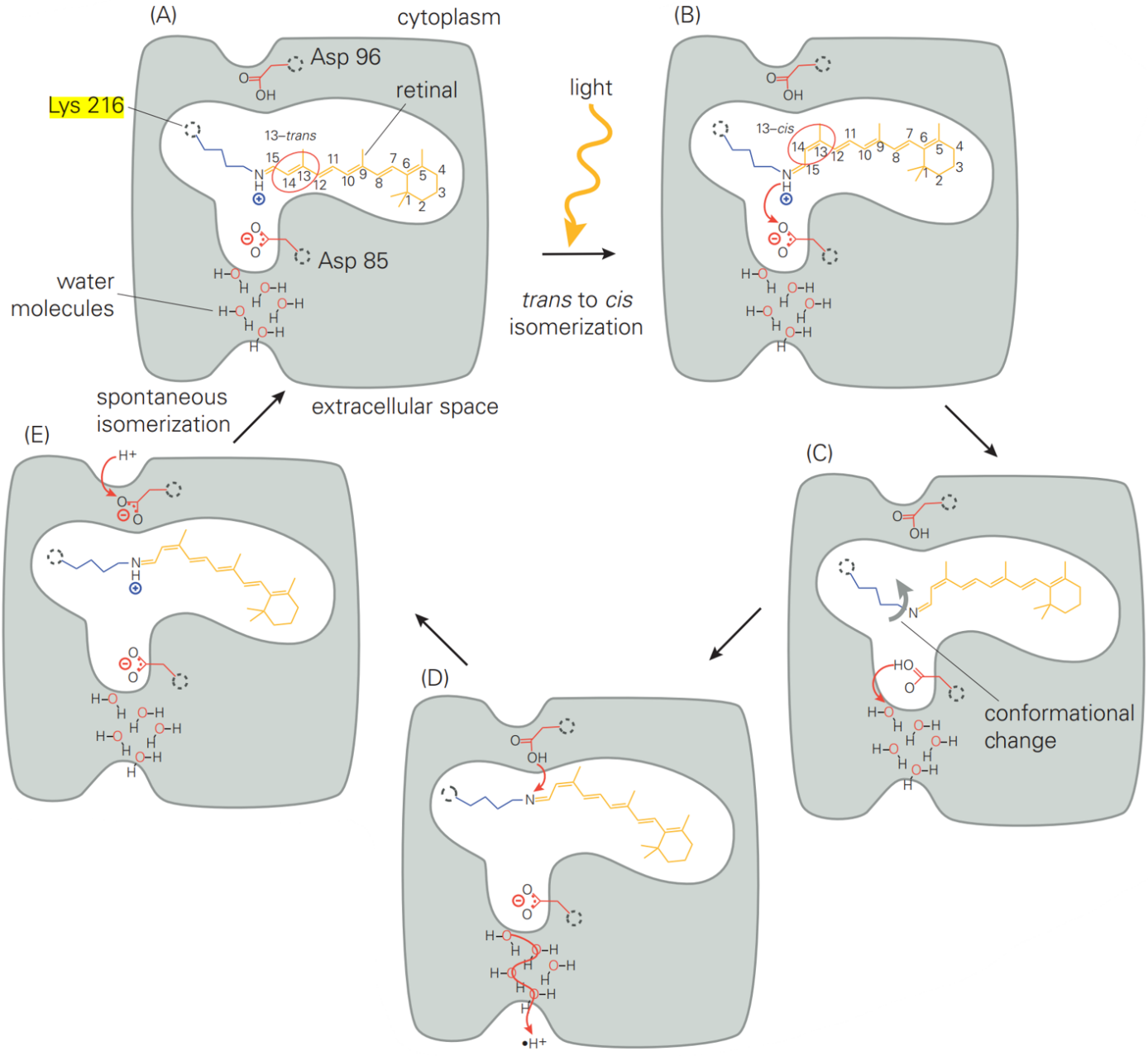
As you must we aware of, amides are extremely unreactive towards nucleophilic attack at carbonyl group. In this context, does the reaction above seem feasible? Explain your opinions briefly.

(*4 points*)

2.7 *(13 points)* Protonein

2.7.1

Following is the schematic of the directional proton transfer mechanism in a particular cell. The amino acids labelled are a part of a protein, embedded in which is the retinal molecule (retinal has been magnified for clarity).



You are a part of a group of independent researchers who want to develop two mutated variants – X216 in which the 216th residue is changed from lysine to leucine and X85 in which 85th residue changed from aspartic acid to asparagine. The project aims to analyse the biochemical role of the amino acids at the respective residues by finding answers to the following questions –

(a) Would the binding of retinal with the protein in X216 mutant be affected?
(*2.5 points*)

(b) Would the pathway of proton transfer be able to continue normally for X85, ignoring the possibility of alternate routes?
(*2.5 points*)

The development of mutants however is not within your budget. An organisation identifies your potential and is ready to fund your project if you can predict the answers to (a) and (b) and explain your predictions, to prove your research does have a basis. Do it.

2.7.2

Assume the organisation does fund you and you complete your research successfully and are back from a vacation to Hawaii. A group of biologists meanwhile, working on the same cell, isolated the retinal conjugated protein domain, to study pH dependent and light independent (implies no photoisomerization) reactions. The protonated state, P*, was found to absorb at a peak of 520 nm (spectrophotometric analysis) and the unprotonated state, P at 460 nm. Plotting the ratio of absorbances, they found deprotonation to be favoured at a neutral pH in aqueous media (assume no other interaction occurs between water molecules and the protein). Surprisingly though, yield of the titration decreases at high pH. To make things weirder, the team detects rapid synthesis of a new form, P^a, which absorbs at 395 nm. Baffled, they approach your gang to sort this out. Your team works out the mechanism given below:

- $$P^* + H_2O \rightleftharpoons P + H_3O^+$$
  (both forward and backwards reactions are first order wrt each reactant)
- $$P^* + OH^- \rightleftharpoons P^{**}$$
- $$P^{**} + P^* \longrightarrow P^a$$

In writing answers to the following questions, you're free to use as many variables as long as you define them clearly.

(a) Write the equation for the rate of disappearance of P*. (no extra points for solving/trying to solve)

(*4 points*)

(b) An excess of alkaline solution of pH $\approx$ 14 is poured into the protonated protein-retinal complex (P^*) suspension. Make reasonable approximations to your equation in (a) and find the half-life of P* in the solution. Assume the ones mentioned above are the only reactions that occur.

(*4 points*)
