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Most questions are taken from some research papers or/and questions from some courses of the IISc UG curriculum. References have been given accordingly.

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## Questions

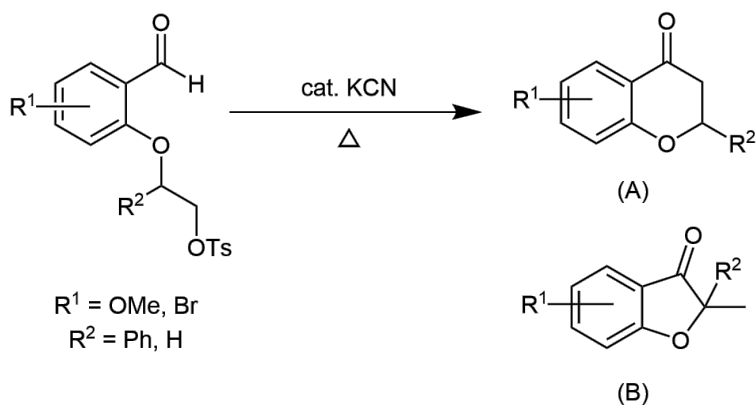
100 points (+3 bonus points)

# 1 (25 (+1 bonus) points) RRR: Reactions, Reagents and Rearrangements

## 1.1 Catalysis

Ref: He, J. M.; Zheng, J. Y.; Liu, J.; She, X. G.; Pan, X. F. *Org. Lett.* **2006**, *8*, 4637. We have taken only the concepts like rearrangements, etc., from this paper.

Mr. G. Sharma aspires to be a synthetic organic chemist and works as a research associate (RA) in a research lab. He is currently focusing on reacting two electrophiles. He is motivated by amazing reactions like Benzoin condensation, Baylis-Hillman reaction, etc. Before getting into the lab, he thought of reading some recent interesting articles and apply them to his work in the future. He got stuck on the products of a reaction. Major products depended on the substituents researchers used, **not** only on the functional group. Assuming that the given reagent *cat.* KCN works here as it is in the benzoin condensation. Explain which R<sup>2</sup> substitution would give which product (in major amount) with a proper mechanism (further, assume that KCN is soluble in the solvent used in the reaction).



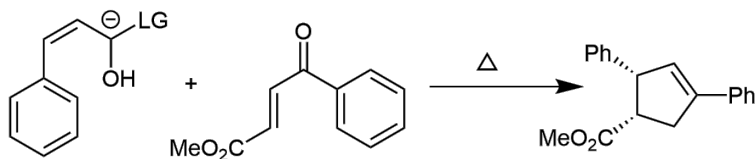
(3 points)

## 1.2 Cascade reaction

Ref: Chiang, P.-C.; Kaeobamrung, J.; Bode, J. W. *J. Am. Chem. Soc.* **2007**, *129*, 3520. We have taken only the concepts like rearrangements, etc., from this paper.

A cascade reaction is a chemical process where at least two consecutive reactions happen, where the following reaction depends on the functionality formed in the previous reaction. These are useful because there is a lesser amount of work-up required to isolate the final desired product. Examples of these reactions are Robinson annulation, etc. Below reaction is an observation of getting a very

unexpected product In the below reaction, LG denotes a leaving group. (*Exact structure and reactivity is beyond the scope of the exam*). Explain the product formation. (*Hint: carbonyl carbon will be intercepted with the anion given in the reactant followed by a famous rearrangement*)



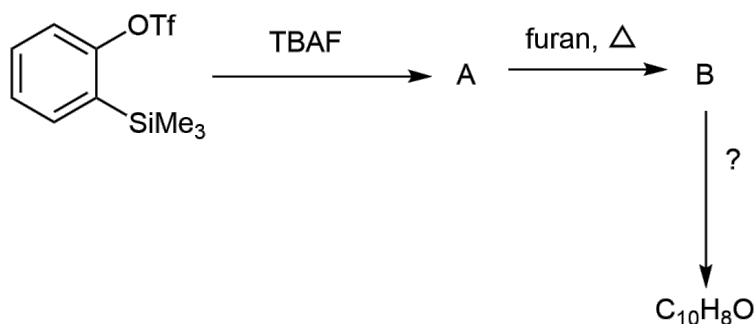
(5 points)

### 1.3 No solvent reaction!

**Ref:** It is taken from a UG Chem course.

Few kinds of intermediates are fascinating and promising to get compounds that would be very difficult to get via other methods, and sometimes solvent is not even required. Below one is an example. The end product of the below reaction is used to make a chiral ligand that is very useful in asymmetric synthesis. Mention the missing reagent/step and explain all the products/intermediates (including A and B) with proper mechanisms.

**Note:** The intended compound with intended hints was  $\alpha$ -naphthol and properties of  $\beta$ -naphthol were given in the original question paper by mistake.



(4 points)

### 1.4 Metals in organic chemistry?!

**This sub-question was our creativity only.**

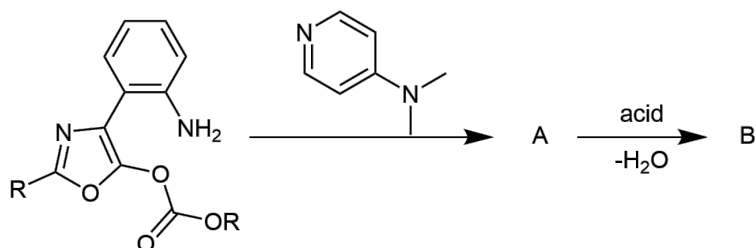
Ms. Parveen is an organic chemist. She usually uses transition metals containing reagents in her work. Nowadays, she is focusing on a reaction.

A compound with CAS no. **626-02-8** is treated with 3-bromoprop-1-ene in KOH to obtain the compound (A) that undergoes one more famous rearrangement upon heating, and compound (B) is obtained, followed by treatment with  $\text{Pd}(\text{OAc})_2$  and triethanolamine to get the final compound (C). Draw the structure of A, B, and C and mention the most acidic proton of C. (4 points)

### 1.5 Spirooooo!

**This sub-question was our creativity only.**

Mrs. S. Mallik. works on the synthesis of spiro compounds, their optical activity, and their applications. So, she conducted the below reaction. Here, the pyridine derivative catalyzes the reaction, followed by cyclization. Draw the mechanism.



(3 points)

### 1.6 Listen: Stereo Hearts (feat. Adam Levine)

**Ref: It is taken from a UG Chem course.**

Ms. Aprajita is a PhD student. During her TA duties, the instructor told her to frame questions on stereochemistry, and she came up with the below one. After framing the question, the instructor told her to perform the reaction in the lab. So, she took **cyclopentanone**, and after one/two step(s), she obtained **methyl 2-oxocyclopentane-1-carboxylate (A)**.

- (a) Mention that one/two step(s) reaction to obtain (A). (1 point)

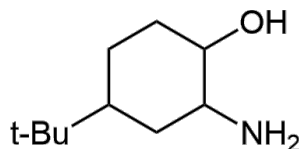
After this, she used  $\text{LiAlH}_4$ , followed by a reaction with  $\text{TsCl}$ , pyridine, and then treated with a base to get compound (B). Somehow, she obtained two products.

- (b) Write the two possible products (B) and explain them with a proper mechanism. (2 points)

### 1.7 Not following the herd

**This sub-question was inspired from the book: Jonathan Clayden Nick Greeves Stuart G Warren - Organic chemistry-Oxford University Press (2012)**

Ms. Samiksha Saini is also a Ph.D. student. She works on optically active organic compounds. She was preparing compound (A) and wanted to measure the amount of each stereoisomer possible.



**Note: Absolute configuration of the C atom connecting t-Bu group is fixed, i.e., either one of R and S should be considered while solving the question. Apologies for any confusion.**

- (a) Write all possible stereoisomers possible in chair form. *Consider the t-Bu group in the equatorial position in all possible isomers.* (1 point)

People usually use High-Performance Liquid Chromatography (HPLC) to know the ratio of stereoisomers formed, and if possible, they try to get the structure of any of the isomers. Using this, they get the amount of isomers formed. But she thinks of trying to use a different method. She treated 2 mmol of the mixture of isomers of (A) with  $\text{NaNO}_2, \text{HCl}$  and obtained three kinds of products, one aldehyde (1.2 mmol), 1 ketone (0.6 mmol), and one oxirane-containing compound. (*assuming 100% conversion*)

- (b) Write the structure of isomers with the corresponding products and their amount (in %). Explain with a mechanism which isomer favors which product. (2 points)

Bonus: Write the name of the reaction. (1 point)

## 2 (16 points) Dimension is critical?!!

**This question was compiled from various sources like [this](#) etc. and then modified in this present form.**

The concept of the critical radius is very important in diverse fields of chemistry and biology — from simple phenomena of phase transition like solidification to polymerization of actin subunits to form cytoskeletal elements, etc. Here, we'll try to have a very brief idea about why nucleation to a particular dimension is necessary to enable further growth.

Here, we'll talk about a very simple case of solidification.

- (a) Let's first consider,  $G_L$  = Gibbs energy of liquid per unit volume,  $G_S$  = Gibbs energy of solid per unit volume.

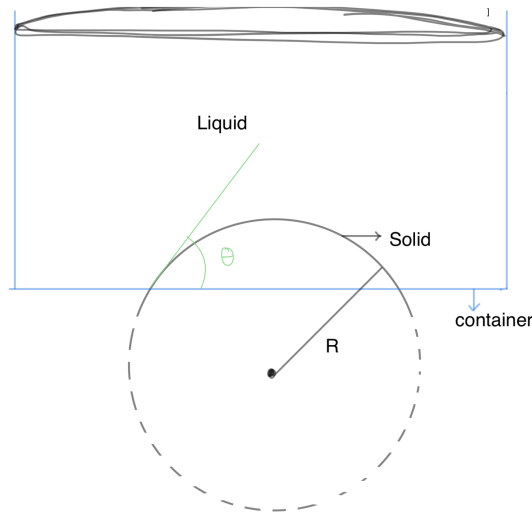
If a solid sphere of radius  $r$  is formed within the liquid of the same compound. What is the change in the Gibbs energy? *considering only the contribution of*

the Gibbs energy of liquid and solid; what's the condition (Answer, based on temperature) that solidification becomes a spontaneous process. (2 points)

- (b) Observation: If you cool down slowly to 0 °C, it is possible that you won't even see a bit of ice. So, Gibbs energy (per unit volume of solid and liquid) is not the only factor that contributes to the net change in Gibbs energy for the formation of the solid ball of radius  $r$  within its liquid. What is the other factor that is contributing to the net change in Gibbs energy  $\Delta G_{net}$ ? [ $\Delta G_{net}$  = net change in Gibbs energy for the formation of solid ball of radius  $r$  within its liquid]. (3 points)
- (c) For which value of  $r$ ,  $\Delta G_{net}$  has its maximum value? Can it be called the critical radius? Justify your answer. (3 points)
- (d) Now, Assuming that  $\Delta H$  and  $\Delta S$  for the solid to the liquid transformation is independent of temperature. Explain the relation between the ease of solidification and temperature. (2 points)

Now, let's discuss nucleation that is aided by some other surface or defects. Consider a situation where a solid is forming in the bottom of the container, i.e., the solid has a surface shared with the container also.

- (e) Derive an expression for the net change in Gibbs energy for the process. For ease of calculation, consider the picture below.



$R$ =radius of curvature

$$\text{volume of solid part} = \frac{4}{3}\pi R^3 \times \left( \frac{2 - 3\cos\theta + \cos^3\theta}{4} \right)$$

(4 points)

- (f) What's the critical radius in this case? (1 point)
- (g) In which case is more amount of solid required for successful nucleation?

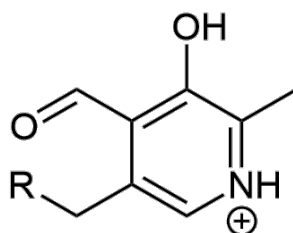
(1 point)

### 3 (8 (+2 bonus) points) 'On'-'Off' molecular switch

Ref: D. Wilson, N. R. Branda, *Angew. Chem. Int. Ed.* 2012, 51, 5431–5434

Mr. S. Srinivasan is interested in chemical biology and looks for molecules that are biologically important, and their reactivities are explained by basic chemistry. Recently, he was reading an article and encountered a molecule.

Consider the below molecule, the biologically active form of vitamin B<sub>6</sub>; it is an enzyme cofactor responsible for amino acid metabolism in organisms. Consider the deprotonated form of the carboxylic acid group in the molecule for (b) and (d) sub-parts.

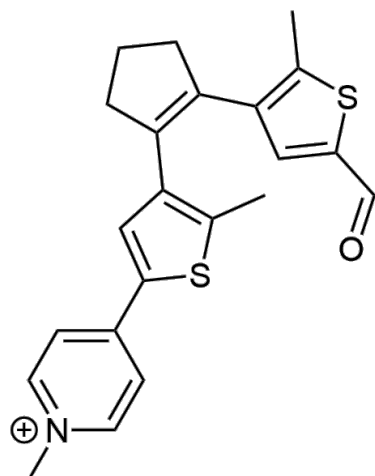


Compound A

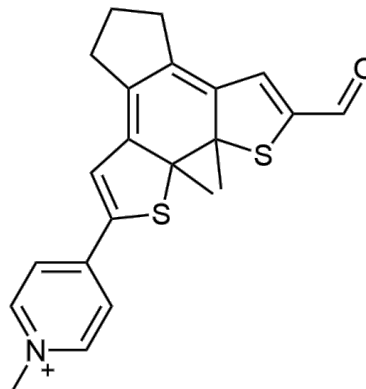
It forms imine with amino acids.

- Write the product (imine) with the reaction mechanism of the above compound (A) reacting with alanine. (2 points)
- Mention the most acidic hydrogen of imine in part (a) with a proper explanation. (1 point)

We know about the efficiency of the above imine acting as a base and responsible for the enormous range of reactions it catalyzes. Now, researchers thought to make a mimic of this. So, they come up with the below molecule (B).



Compound B



Compound C

Molecule (B) converts into (C) upon irradiation with UV light and comes to (B) again upon shining visible light. Now, he is trying to figure out how it can happen.

- (c) Propose a mechanism for converting (B) to (C) photochemically and justify the steps. (2 points)

Bonus: Assign the R, S to all chiral centers of compound (C) with proper explanation. (2 points)

Note the presence of aldehyde in (C) as same as in the case of (A); it reacts with amino acids also and forms imine (D).

- (d) Write the most acidic hydrogen of imine (D) with a proper explanation. (1 point)

- (e) Provide a method to monitor the formation of imine (D) and briefly describe the protocol to perform in the lab (No need to provide very minute details).

*Hint: Conjugate base of imine (D).* (1 point)

Let us end this question with an ‘easier’ sub-question.

- (f) Indicate which is in ‘On’ and which one is in ‘Off’ state between (B) and (C) with a reasonable explanation. (1 point)

#### 4 (20 points) Light-matter interaction

Coupling molecules into an optical cavity can change their various properties, such as electron transport, superconductivity, chemical reactivity, etc. In this question, we’ll discuss the basics of chemistry, which deals with this phenomenon — that is, polariton chemistry. In quantum optics, to study atoms/molecules coupled to an optical cavity, many model Hamiltonians are well-known, one of them being the



Jaynes-Cummings Hamiltonian. Now, we'll see how we can get some insight into this step by step. First, let's define the matter Hamiltonian as:

$$\hat{H}_M = \hat{\mathbf{T}} + \hat{V}(\hat{\mathbf{x}}) = \sum_j \frac{1}{2m_j} \hat{\mathbf{p}}_j^2 + \hat{V}(\hat{\mathbf{x}}_j),$$

where,  $\hat{\mathbf{p}}_j = -i\hbar\nabla_j$ . We denote electronic coordinate with  $\hat{\mathbf{r}}$  and nuclear coordinate with  $\hat{\mathbf{R}}$ . Now, considering a finite subset of electronic states  $|\psi_\alpha(\mathbf{R})\rangle$ , where there are total  $N$  matter states, we define the following projection operator.

$$\hat{\mathcal{P}} = \sum_{\alpha=1}^{\mathcal{N}} |\psi_\alpha(\mathbf{R})\rangle\langle\psi_\alpha(\mathbf{R})|,$$

Note that  $\hat{\mathcal{P}}$  here defines the truncation of full Hilbert space.

- (a) Let's discuss a general case. Say,  $|a\rangle$  is an arbitrary ket (normalized) in the ket space spanned by the eigenkets of some observable. Now, we define an operator  $|a\rangle\langle a|$  and name it as a projection operator. Justify the name of the operator. (hints: take any ket and apply the operator). Show that  $\sum_a |a\rangle\langle a| = 1$  where  $\{|a\rangle\}$  is a complete orthonormal basis. (2 + 1 points)
- (b) Write the dipole moment operator in the truncated Hilbert space; use the states  $|\psi_\alpha(\mathbf{R})\rangle$  as a basis. [Hint: any operator  $\hat{x}$  can be expressed as

$$\sum_i \sum_j |a_i\rangle\langle a_i|\hat{x}|a_j\rangle\langle a_j|$$

So you only need to calculate  $\hat{\mathcal{P}}\hat{\mu}\hat{\mathcal{P}}$ . use the notation  $\mu_{ij}$ =element in the  $i$ th row and  $j$ th column.] (1 point)

- (c) We can diagonalize the same dipole matrix to obtain

$$\hat{\mathcal{P}}\hat{\mu}\hat{\mathcal{P}} = \sum_{\nu}^{\mathcal{N}} \mu_{\nu\nu}(\mathbf{R}) |\phi_\nu\rangle\langle\phi_\nu|,$$

where,

$$|\phi_\nu\rangle = \sum_{\alpha}^{\mathcal{N}} c_{\alpha}^{\nu}(\mathbf{R}) |\psi_{\alpha}(\mathbf{R})\rangle,$$

Find an expression for  $c_\alpha^v(\mathbf{R})$ , and assume orthogonality of the basis kets. (1 point)

- (d) When a molecule is coupled to a cavity, the Hamiltonian of the molecules interacting with the cavity can be written as follows (under single mode and long wavelength approximation)  $\hat{H}_{d.E.}$ :

$$\hat{H}_M + \hbar\omega_c(\hat{a}^\dagger\hat{a} + \frac{1}{2}) + i\omega_c\hat{\boldsymbol{\mu}} \cdot \mathbf{A}_0(\hat{a}^\dagger - \hat{a}) + \frac{\omega_c}{\hbar}(\hat{\boldsymbol{\mu}} \cdot \mathbf{A}_0)^2.$$

Where the last three terms come from the photon Hamiltonian.  $\hat{a}^\dagger$  and  $\hat{a}$  are the creation and the annihilation operators. Now, we define a unitary transformation as

$$\hat{U}_0 = \exp\left[-i\frac{\pi}{2}\hat{a}^\dagger\hat{a}\right].$$

Calculate the transformed Hamiltonian  $\hat{U}_0\hat{H}_{d.E.}\hat{U}_0^\dagger$ . (5 points)

This transformed Hamiltonian is a very famous Hamiltonian that is used extensively nowadays for polariton chemistry studies.

- (e) Suppose we have an atom with 2 levels, i.e.,  $|g\rangle, |e\rangle$ , where they are ground and excited states, respectively. Now, for this atom, we define creation and annihilation operators  $\sigma^*$  and  $\sigma$  with the following properties:

$$\sigma^*|g\rangle = |e\rangle$$

$$\sigma^*|e\rangle = 0$$

$$\sigma|g\rangle = 0$$

$$\sigma|e\rangle = |g\rangle$$

guess the two operators (try to think in very simple terms involving  $|g\rangle, |e\rangle$ ) (3 points)

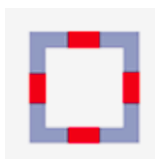
- (f) Write the dipole moment operator in the following subspace  $\hat{\mathcal{P}} = |g\rangle\langle g| + |e\rangle\langle e|$ . Consider that molecule has no permanent dipole and use part (b) of this question. (3 points)
- (g) Replace the dipole moment operator in the expression of Hamiltonian that you got as the answer for part (d) with the expression you got in part (f). (3 points)
- (h) Ignore the  $\omega_c(\mathbf{A}_0 \cdot \boldsymbol{\mu}_{eg})^2$  term. Write the expression. This is the Rabi Hamiltonian which, under rotating wave approximation, it gives you the Jaynes-Cummings Hamiltonian. (1 point)

## 5 (14 points) Chemistry beyond molecules!!!

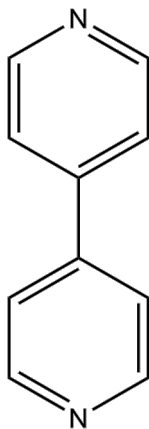
Ref: R. Chakrabarty, P. S. Mukherjee, P. J. Stang *Chem. Rev.* 2011, 111, 6810. Some of the sub-questions are made from this review article.

Supramolecular chemistry is a very exciting interdisciplinary field that deals with mostly non-covalent interaction as opposed to traditional chemistry. Biological systems, whose functioning depends a lot on these, are many times the inspiration for supramolecular research. Important concepts advanced by supramolecular chemistry include molecular self-assembly, molecular folding, molecular recognition, host-guest chemistry, mechanically-interlocked molecular architectures, and dynamic covalent chemistry.

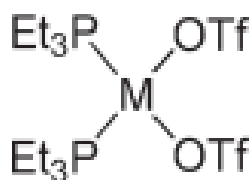
Here, we'll see how researchers design discrete structures using supramolecular chemistry. Metal-ligand coordination bonds can be used for this purpose. Note that the structures of ligands must be rigid to generate a particular structure selectively. For example, with 90-degree acceptor and 180-degree donor units, square structures can be prepared.



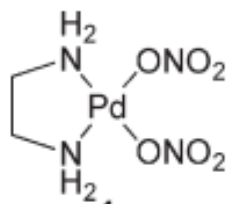
where the red-colored one is a donor and the grey-colored one is an acceptor. Now, this 180-degree donor can be some ligand with two donor sites at an angle of 180-degree; for example:



Whereas, 90-degree acceptor can be prepared using cis-blocked transition metal complexes, with examples being:



A) M=Pd or Pt because of square planar geometry.



B)

(a) Can you guess why a and b are called cis-blocked acceptors (1 point)

(b) What are the thermodynamic parameters that play a major role in “cis-blocking” in case of a and b (try to think of different parameters for both of them which are playing the most important roles). Elaborate your answer

(2 points)

(c) What are the different 2D shapes possible by using combination of

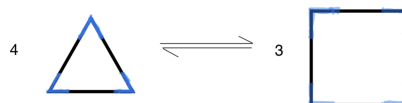
A. 180° acceptor with i. 60° ii. 109° iii. 120° donors

B. 120° acceptor with i. 60° ii. 180° donors.

Isn't it simple geometry?!

(2.5 points)

(d) Now, let's discuss dynamic equilibrium between different shapes formed by the same building blocks. Suppose we have a 90° acceptor and linear donor. In many cases, an equilibrium like this is observed:



Ligands are shown in black, whereas cis-blocked metal acceptors are shown in blue.

A. What thermodynamic factors favor the formation of triangles and squares, respectively? Elaborate your answer. (2 points)

- B. Which structure will be favored if the concentration of the components is increased? (2 points)
- C. Which structure will be favored if the temperature of the structure is increased? (2 points)
- (e) In the last part, we discuss some 3D architectures. Suppose we're again using cis-blocked Pd acceptors, but the ligand, this time, can donate from three sites symmetrical in structure and planar at an angle of  $120^\circ$  from each other. If we claim that an octahedron-like structure is formed with 6 acceptors occupying the vertices, can you tell how many ligands will be used? Can you draw a rough sketch of the structure? (2.5 points)

## 6 (10 points) Maths Ugh...!

**Ref: McQuarrie, Donald A., and John D. Simon. Physical Chemistry: A Molecular Approach. University Science Books, 1997; and a UG Chem course.**

Researchers employ some techniques to investigate the influence of temperature on the equilibrium constant of a reaction. In these experiments, the temperature of the mixture at equilibrium is abruptly altered while maintaining constant pressure. As a result of this sudden temperature change, the chemical system reacts by transitioning to a new equilibrium state that aligns with the new temperature.

- (a) Write the relation between the equilibrium constant with temperature. (1 point)



Consider the above reaction, where symbols have their usual meanings, i.e.,  $k$  denotes rate constants. Let us denote the change in conc. of substance  $i$  due to perturbation in temperature with  $\Delta i$ .  $\Xi$  denotes the time required for  $\Delta[B]$  to decay to  $\frac{1}{e^2}$  of its initial value.

- (b) Derive the relation between  $\Xi$  and both rate constants assuming first-order kinetics. (3 points)
- (c) Plot  $[B]$  v/s  $t$  showing the initial and the final concentration of  $[B]$ , assuming first-order kinetics and  $\Delta_r H^\circ > 0$ . (2 points)

After getting tired of these equations, a researcher decides to perform a reaction and tries to understand the order of reaction w.r.t. reactants. He found the rate of formation of B and decay of A as follows:

$$\frac{dA}{dt} = -k(10^{-3} + [B])[A]$$

Assume that the reaction follows eqn (1) (stoichiometry). Initially, he started with  $[A] = 0.1M$ ,  $[B] = 0$  and found  $k = 1$  per sec.

- (d) By doing calculations, draw a conclusion about the completion of the reaction in finite time. (4 points)

## 7 (7 points) It is Lab time!!!

**This question was our creativity only.**

Ms. Jyotika Das is a UG student working as an intern in a research lab. She is outstanding in the lab. She was performing a condensation reaction. She started with a compound (A) that gives a positive Tollens test and (B) that gives a foul smell after treating it with chloroform with an alkali. She got some fascinating results.

She decided to monitor the reaction after 24 hrs. of setting up the reaction. She made three spots on the TLC plate, each for (A), (B), and reaction mixture ( $R_x$ ). She got **three** spots from the  $R_x$  (ignore any spot at baseline). She was confused about whether the reaction was completed. She took the  $R_x$  and evaporated the solvent after the work-up and then dissolved 20 mg of the residue in a solvent and submitted it for  $^1H$  NMR. She found that there is no mixture and the desired product is there. (*State your assumptions clearly.*)

- (a) Explain why she would obtain three spots with a proper reaction mechanism provided that  $^1H$  NMR suggests no mixture. (3 points)
- (b) Provide a modification with the reason in the protocol she followed for TLC monitoring. (Write about the reagent that should be used to obtain a satisfying result.) (2 point)
- (c) Guess with a reason what solvent she used for  $^1H$  NMR sample submission. (1 point)

She was pleased with the above results and carried out a few more reactions with the obtained compound.

*(End this question with an easier sub-question)*

- (d) She wanted to have monosubstitution at methylene carbon (flanked by carbonyls) of diethyl malonate that would be obtained by reaction with the above product. Suggest a method. (1 point)