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CANADIAN CHEMISTRY OLYMPIAD | OLYMPIADE DE CHIMIE DU CANADA

2020 Take Home Exam

Deadline: 12 noon EST on Friday, April 3rd, 2020

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Introduction:

The purposes of the Canadian Chemistry Olympiad program is to provide high school students with the opportunity to study and test themselves on advanced Chemistry topics and to prepare students for competition at the International Chemistry Olympiad. The questions on the take-home exam are questions from the advanced topics identified by the IChO hosts. For IChO 2020, Turkey will be hosting. There are 25 problems posted on the IChO 2020 website, seven of these problems are part of the Take home exam.

Please note that CCO participants should tackle these problems **independently**. Your ability to use critical thinking and advanced problem solving techniques will be essential if the CCO selection committee selects you for the IChO team. After completing and submitting the Take home exam, you should continue to solve the rest of the 25 problems.

All of the reference material you need to solve the questions precedes the questions on this exam.

The take home problems are due Friday, April 3rd at 12 noon Eastern Standard Time (EST). The CCO will not accept late submissions. Please ensure that all of your answers are legible and clearly organized. The CCO evaluators may not evaluate illegible or disorganized answers. Please ensure that you print your name is clearly at the top of every page. Scan your test, put CCO Take Home Exam – your name (First and Last) in the subject line and send the exam as one pdf file to both jpittlainsbury@utschools.ca and bussierg@chem.ubc.ca (in the same email).

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Reference Material: Please note that all of the reference material for the 25 questions on the preparatory problems is part of this take home exam. You may not need to use all of the reference materials to solve the problems on this CCO take home exam.

Physical Constants and Equations:

Avogadro's constant, $N_A = 6.0221 \times 10^{23} mol^{-1}$

Boltzmann constant, $k_B = 1.3807 \times 10^{-23} JK^{-1}$

Universal gas constant, $R = 8.3145\ JK^{-1}mol^{-1} = 0.08205\ atm\ L\ K^{-1}mol^{-1}$

Speed of light, $c = 2.9979 \times 10^{8} ms^{-1}$

Planck's constant, $h = 6.6261 \times 10^{-34}\ J\ s$

Faraday constant, $F = 9.6485 \times 10^{4}\ C\ mol^{-1}$

Mass of electron, $m_e = 9.10938215 \times 10^{-31}\ kg$

Standard pressure, $P = 1\ bar = 10^5\ Pa$

Atmospheric pressure, $P_{atm} = 1.01325 \times 10^5\ Pa = 760\ mmHg = 760\ torr$

Zero of the Celsius scale, $273.15\ K$

1 picometer (pm) = $10^{-12}\ m$; $1A^0 = 10^{-10}\ m$; 1 nanometer (nm) = $10^{-9}\ m$

$1\ eV = 1.6 \times 10^{-19}\ J$

$1\ cal = 4.184\ J$

$1\ amu = 1.66053904 \times 10^{-27}\ kg$

Charge of an electron: $1.6 \times 10^{-19}\ C$

Ideal gas equation: $PV = nRT$

Enthalpy: $H = U + PV$

Gibbs free energy: $G = H - TS$

$\Delta G = \Delta G^0 + RTlnQ$

$\Delta G^0 = -RTlnK$

$= -nFE^0_{cell}$

Entropy change:

$\Delta S = \frac{q_{rev}}{T}$, where q_{rev} is heat for the reversible process

$\Delta S = nRln\frac{V_2}{V_1}$ (for isothermal expansion of an ideal gas)

Nernst equation: $E = E^0 + \frac{RT}{nF} ln \frac{C_{ox}}{C_{red}}$

Energy of a photon: $E = \frac{hc}{\lambda}$

Integrated rate law

Zero order: $[A] = [A]_0 - kt$

First order:

$ln[A] = ln[A]_0 - kt$

Second order:

$$\frac{1}{[A]} = \frac{1}{[A]_0} + kt$$

Arrhenius equation: $k = Ae^{-E_a/RT}$

Equation of linear calibration curve: $y = mx + n$

Standard deviation:

$$s = \sqrt{\frac{\sum_{x=1}^{N}(x_1 - \bar{x})^2}{N-1}}$$

Lambert–Beer equation: $A = \varepsilon lc$

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Periodic Table of Elements

1																	18
1 H 1.008	2		atomic number Symbol atomic weight									13	14	15	16	17	2 He 4.003
3 Li 6.94	4 Be 9.01											5 B 10.81	6 C 12.01	7 N 14.01	8 O 16.00	9 F 19.00	10 Ne 20.18
11 Na 22.99	12 Mg 24.31	3	4	5	6	7	8	9	10	11	12	13 Al 26.98	14 Si 28.09	15 P 30.97	16 S 32.06	17 Cl 35.45	18 Ar 39.95
19 K 39.10	20 Ca 40.08	21 Sc 44.96	22 Ti 47.87	23 V 50.94	24 Cr 52.00	25 Mn 54.94	26 Fe 55.85	27 Co 58.93	28 Ni 58.69	29 Cu 63.55	30 Zn 65.38	31 Ga 69.72	32 Ge 72.63	33 As 74.92	34 Se 78.97	35 Br 79.90	36 Kr 83.80
37 Rb 85.47	38 Sr 87.62	39 Y 88.91	40 Zr 91.22	41 Nb 92.91	42 Mo 95.95	43 Tc -	44 Ru 101.1	45 Rh 102.9	46 Pd 106.4	47 Ag 107.9	48 Cd 112.4	49 In 114.8	50 Sn 118.7	51 Sb 121.8	52 Te 127.6	53 I 126.9	54 Xe 131.3
55 Cs 132.9	56 Ba 137.3	57-71	72 Hf 178.5	73 Ta 180.9	74 W 183.8	75 Re 186.2	76 Os 190.2	77 Ir 192.2	78 Pt 195.1	79 Au 197.0	80 Hg 200.6	81 Tl 204.4	82 Pb 207.2	83 Bi 209.0	84 Po -	85 At -	86 Rn -
87 Fr -	88 Ra -	89-103	104 Rf -	105 Db -	106 Sg -	107 Bh -	108 Hs -	109 Mt -	110 Ds -	111 Rg -	112 Cn -	113 Nh -	114 Fl -	115 Mc -	116 Lv -	117 Ts -	118 Og -

57 La 138.9	58 Ce 140.1	59 Pr 140.9	60 Nd 144.2	61 Pm -	62 Sm 150.4	63 Eu 152.0	64 Gd 157.3	65 Tb 158.9	66 Dy 162.5	67 Ho 164.9	68 Er 167.3	69 Tm 168.9	70 Yb 173.0	71 Lu 175.0
89 Ac -	90 Th 232.0	91 Pa 231.0	92 U 238.0	93 Np -	94 Pu -	95 Am -	96 Cm -	97 Bk -	98 Cf -	99 Es -	100 Fm -	101 Md -	102 No -	103 Lr -

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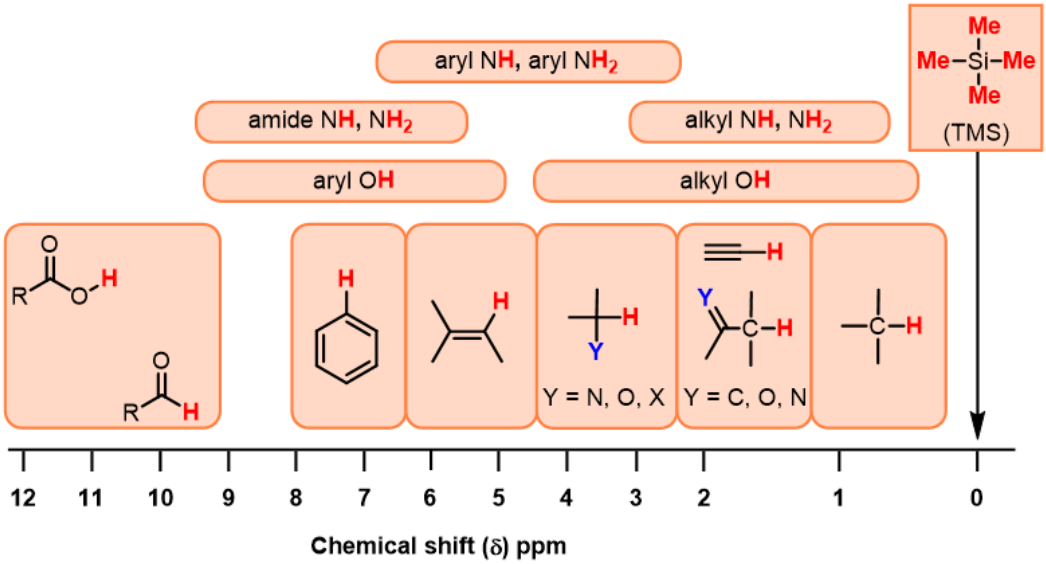
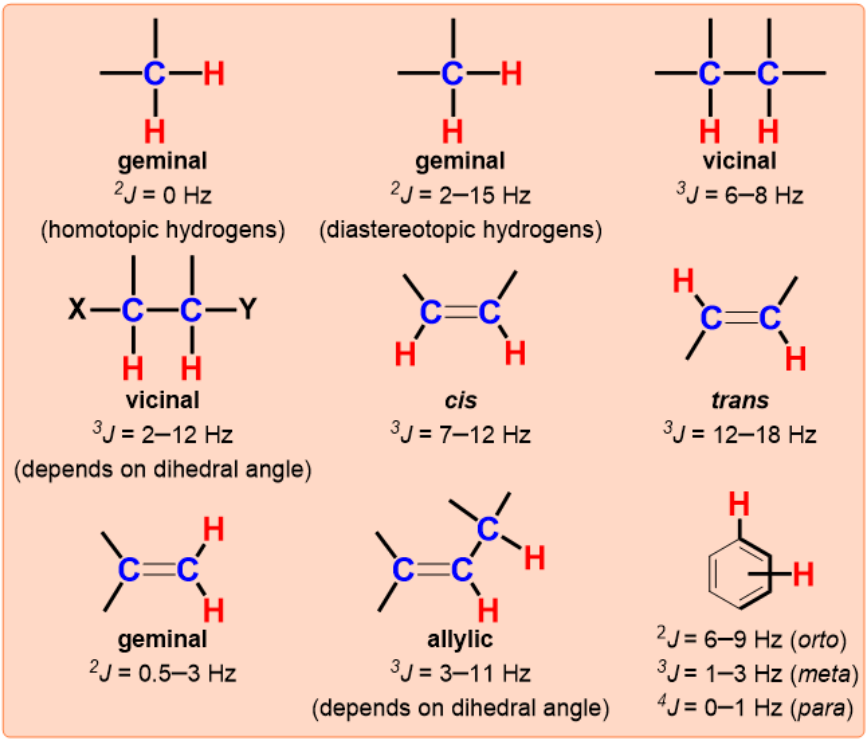
^{1}H NMR Chemical Shifts



Typical Coupling Constants



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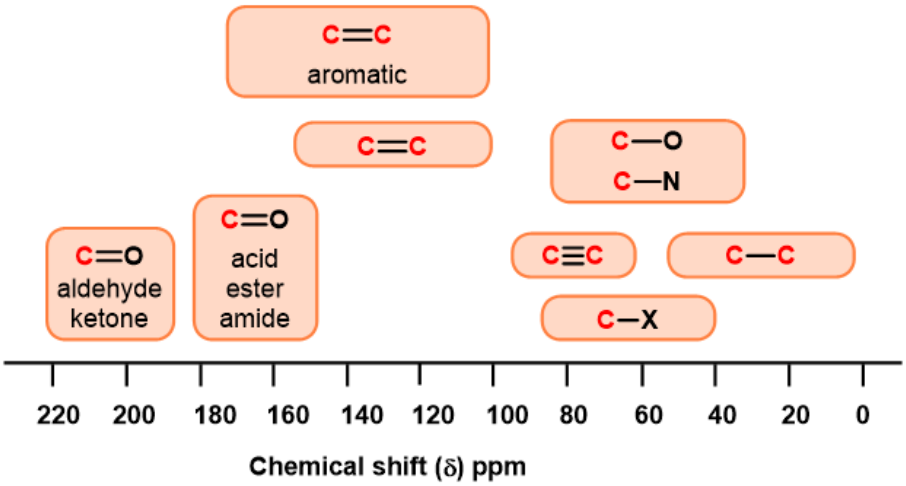
^{13}C NMR Chemical Shifts



IR Absorption Frequency Table

Functional Group	Type of Vibration	Absorption Frequency Region (cm^{-1})	Intensity
Alcohol			
O–H	(stretch, H–bonded)	3600–3200	strong, broad
	(stretch, free)	3700–3500	strong, sharp
C–O	(stretch)	1150–1050	strong
Alkane			
C–H	stretch	3000–2850	strong
	bending	1480–1350	variable
Alkene			
=C–H	stretch	3100–3010	medium
	bending	1000–675	strong
C=C	stretch	1680–1620	variable
Alkyl Halide			
C–F	stretch	1400–1000	strong
C–Cl	stretch	800–600	strong
C–Br	stretch	600–500	strong
C–I	stretch	500	strong
Alkyne			
C–H	stretch	3300	strong, sharp
C≡C	stretch	2260–2100	variable, not present in symmetrical alkynes
Amine			
N–H	stretch	3500–3300	medium (primary amines have two bands; secondary have one band, often very weak)
C–N	stretch	1360–1080	medium-weak

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N–H	bending	1600	medium
Aromatic			
C–H	stretch	3100–3000	medium
C=C	stretch	1600–1400	medium-weak, multiple bands
Carbonyl			
C=O	stretch	1820–1670	strong
Acid			
C=O	stretch	1725–1700	strong
O–H	stretch	3300–2500	strong, very broad
C–O	stretch	1320–1210	strong
Aldehyde			
C=O	stretch	1740–1720	strong
C–H	stretch	2850–2820 & 2750–2720	medium, two peaks
Amide			
C=O	stretch	1690–1640	strong
N–H	stretch	3500–3100	unsubstituted have two bands
	bending	1640–1550	
Anhydride			
C=O	stretch	1830–1800 &1775–1740	two bands
Ester			
C=O	stretch	1750–1735	strong
C–O	stretch	1300–1000	two bands or more
Ketone			
acyclic	stretch	1725–1705	strong
cyclic	stretch	3-membered - 1850	strong
	stretch	4-membered - 1780	strong
	stretch	5-membered - 1745	strong
	stretch	6-membered - 1715	strong
	stretch	7-membered - 1705	strong
α,β-unsaturated	stretch	1685–1665	strong
conjugation moves absorptions to lower wavenumbers			
aryl ketone	stretch	1700–1680	strong
Ether			
C–O	stretch	1300–1000 (1150–1070)	strong
Nitrile			
C≡N	Stretch	2260–2210	medium
Nitro			
N–O	stretch	1560–1515 & 1385–1345	strong, two bands

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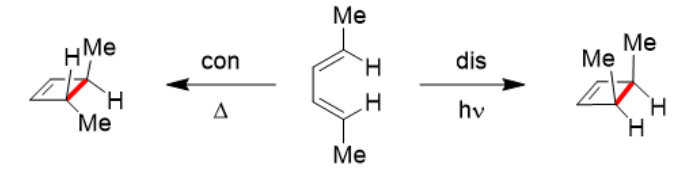
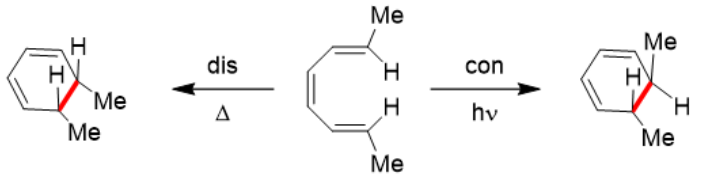
Question 1: Woodward-Hoffmann Rules and Pericyclic Reactions

The **Woodward–Hoffmann rules** (or the **pericyclic selection rules**), developed by Robert B. Woodward and Roald Hoffmann, are used to rationalize or predict some stereochemical aspects and the activation energy of pericyclic reactions. They are for all classes of pericyclic reactions (and their reverse 'retro' processes), such as cycloadditions, sigmatropic shift, electrocyclization, ene, and cheletropic reactions.

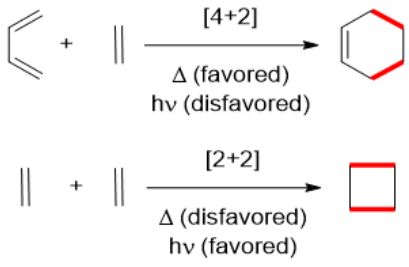
Woodward–Hoffmann rules for electrocyclic reactions		
System	**Conditions**	**Motion**
$4n$	thermal (Δ)	conrotatory (con)
	photochemical (hν)	disrotatory (dis)
$4n+2$	thermal	disrotatory
	photochemical	conrotatory



trans-isomer (2*E*,4*E*)-hexa-2,4-diene *cis*-isomer



cis-isomer (2*E*,4*Z*,6*E*)-octa-2,4,6-triene *trans*-isomer



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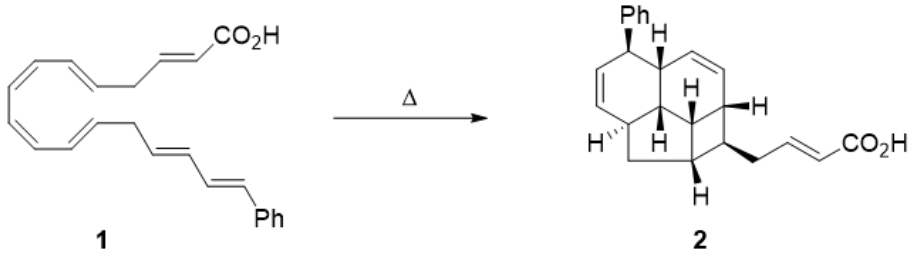
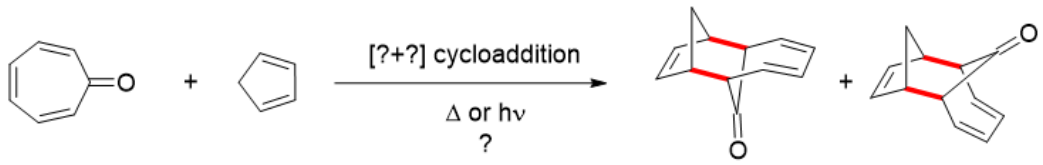
10.1. Thermal reaction of compound **1** results in the formation of endiandric acid **2** by a series of pericyclic reactions. **Show** all steps and **classify** their pericyclic processes.



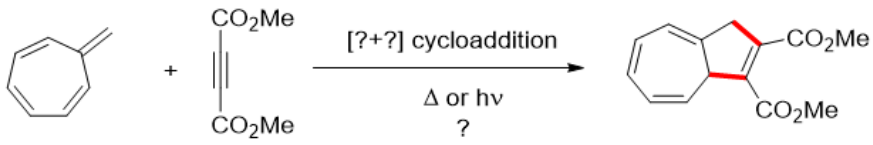
1 **2**
endiandric acid B

How many π electrons are involved in the following reactions? Are these reactions thermally or photochemically allowed according to the Woodward–Hoffmann rules?

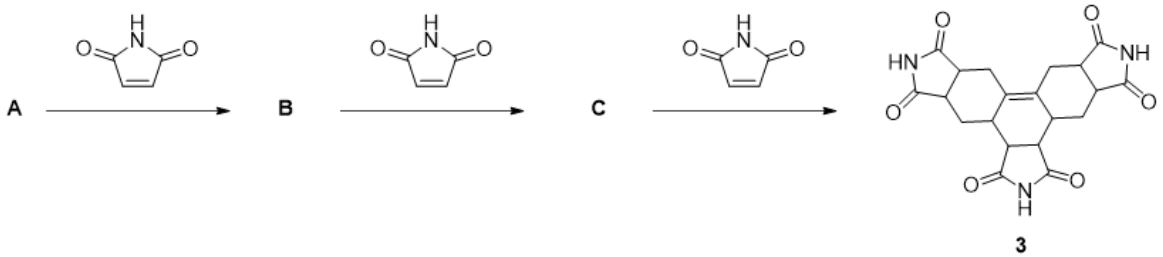
10.2.



10.3.



10.4. Domino Diels–Alder reaction of **A** with succinimide results in the formation of adduct **3**. **Draw** the structures of **A**–**C**.



3

10.5. The following reaction scheme illustrates the synthesis of *endo*-isomer of benzenoid tetracyclic hydrocarbon **I** starting from *o*-xylene. Br_2-elimination of tetrabromo-*o*-xylene **D**

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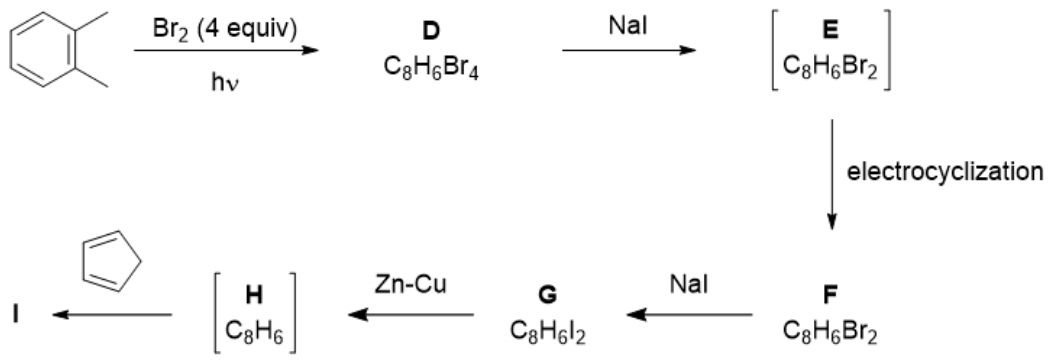
with sodium iodide leads to a reactive intermediate which undergoes a 4π electrocyclization to yield compound **F**. **Draw** the structures of intermediates and products **D**–**I**.



***retro*-Diels–Alder Reaction**

The *retro*-Diels–Alder (*r*DA) reaction is the reverse of the Diels–Alder reaction, i.e., the formation of diene and dienophile from cyclohexene. Generally, an *r*DA reaction is initiated by heating. In some cases, low temperature is sufficient for this transformation, depending on the nature of the substrate.

10.6. Cyclopentadienes are very useful synthetic intermediates in the fields of organic and coordination chemistry. Parent (unsubstituted) cyclopentadiene is obtained by the thermal decomposition of dicyclopentadiene. However, substituted cyclopentadienes are generally unstable due to the facile migration of the endocyclic double bonds. Consequently, practical and general methods for the synthesis of substituted cyclopentadienes are limited. In the following reaction scheme, the synthesis of a substituted cyclopentadiene derivative is given. Besides *r*DA, some steps also involve the *inverse*-Diels–Alder reaction, which is a cycloaddition between an electron-rich dienophile and an electron-poor diene (such as tetrazine **4**), through the interaction of the HOMO orbital of dienophile and the LUMO orbital of diene.

Draw the structures of the intermediates and products **J**–**N**.

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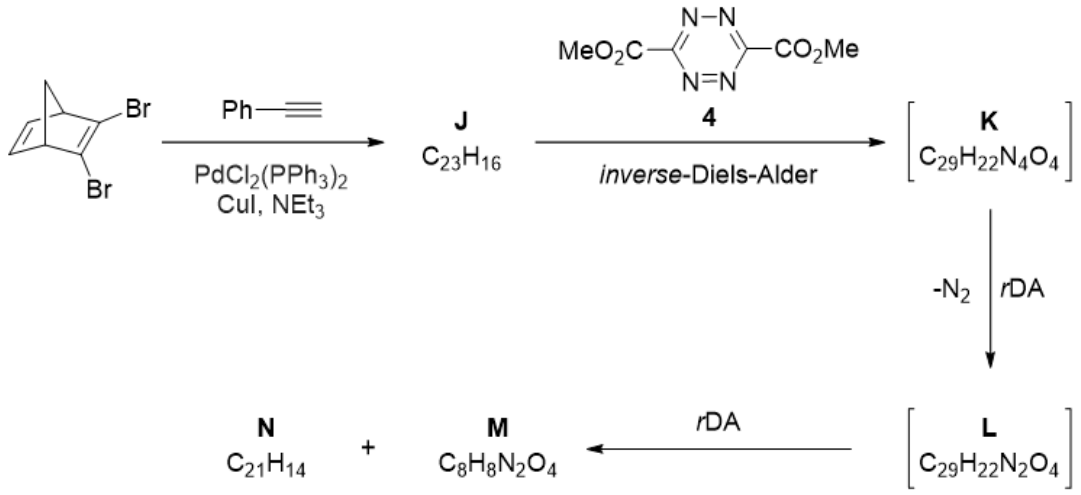
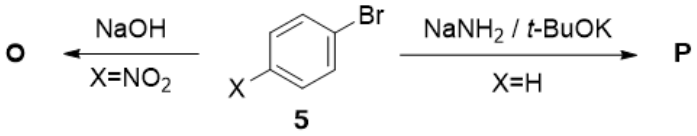


10.7. Nucleophilic aromatic substitution reactions constitute an important class of reactions in synthetic organic chemistry. In the following scheme, the reactions of aryl halide **5** proceed via two different kinds of intermediates in presence of a cyclic 1,3-diene depending on the reaction conditions and the nature of the substituent on the aromatic ring. **Draw** the structures of products (**O** and **P**), and **discuss** possible intermediates responsible for the formation of these products.



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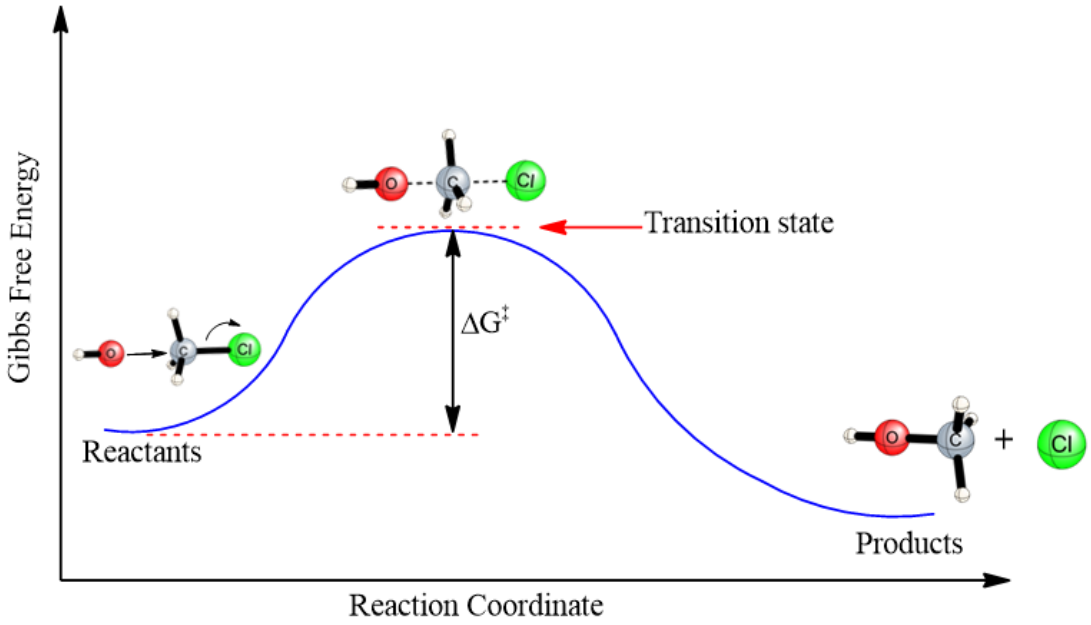
Question 2: Rate Constant Models and Kinetic Isotope Effect

Transition state theory (TST) is a very helpful model to explain the reaction rates of elementary chemical reactions. The TST assumes a quasi-equilibrium between reactants and transition state.



Reaction: $HO^- + CH_3Cl \longrightarrow [HO\text{----}CH_3\text{----}Cl]^{\ddagger} \longrightarrow CH_3OH + Cl^-$

Similar to the Arrhenius model, the TST proposes the following temperature-dependent rate constant expression:

$$k_{TST} = \frac{k_B T}{h} \exp\left[-\frac{\Delta G^{\ddagger}}{RT}\right]$$

where, k_B is the Boltzmann constant, h is the Planck constant, and $\Delta G^{\ddagger}$ is the activation free energy.

The TST rate constant introduces a simple temperature-dependent factor instead of Arrhenius factor A. Further, the TST model allows us to better understand the activation energy concept and build a bridge between the theory and experiment. Moreover, the TST activation free energy is a temperature dependent parameter instead of Arrhenius temperature independent E_a.

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For the decomposition of an organic compound obeying first-order reaction kinetics, the following rate constant values are obtained at given temperatures:

t (°C)	10	30	50	70
k/10⁻⁴ (s⁻¹)	1.1408	17.2075	185.5042	1515.7157

21.1. Using the Arrhenius model, **calculate** the activation energy.

21.2. **Calculate** the Arrhenius factor A.

21.3. **Calculate** the half-life of the organic compound at 75 °C.

21.4. Assume that the rate constants provided obey the TST model, instead of the Arrhenius model. Then, **calculate** activation free energy at 30 °C.

21.5. Assume that the rate constant obtained from both Arrhenius and TST models are equal to each other. Then, **derive** expressions for activation enthalpy and entropy in terms of the activation energy and the Arrhenius factor.

21.6. Using the expressions obtained, **calculate** the activation enthalpy at 80 °C.

The kinetic isotope effect (KIE) is the change in the reaction rate of a chemical reaction when one of the atoms in the reactants, generally hydrogen, is replaced by one of its isotopes, generally deuterium. KIE is generally utilized in organic chemistry in a procedure called as "deuterium labelling" by changing one or more hydrogen(s) with deuterium(s).

One of the common theoretical approaches to explain KIE is the primary KIE. In the primary KIE approach, it is assumed that the change in reaction rate is a quantum chemical effect that primarily results from heavier isotopes having lower vibrational frequencies compared to their lighter counterparts. Hence, one may assume that the TST model is valid, and the change in the activation free energy arises solely from the change in the zero-point vibrational energies (ZPVEs). Therefore, we may write the following equation:

$$\frac{k_H}{k_D} = \frac{\exp\left[(ZPVE(R,H) - ZPVE(TS,H))/RT\right]}{\exp\left[(ZPVE(R,D) - ZPVE(TS,D))/RT\right]}$$

where k_H and k_D are the rate constants of reactions including hydrogen and deuterium, respectively, $ZPVE(R,H)$ and $ZPVE(R,D)$ are the ZPVE values of the reactants including hydrogen and deuterium, respectively, and $ZPVE(TS,H)$ and $ZPVE(TS,D)$ are the ZPVE values of TSs including hydrogen and deuterium, respectively.

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For a thermal decomposition of an organic compound, the difference between ZPVE values of deuterium including TS (TS-D) and hydrogen including TS (TS-H) is -2.3 kJ/mol. Further, the ZPVE value of hydrogen including reactant (R-H) is 3.0 kJ/mol higher than that of deuterium including reactant (R-D).

21.7. **Calculate** the $\frac{k_H}{k_D}$ value at 298.15 K.

21.8. **Calculate** the $\frac{k_H}{k_D}$ value at 330.0 K.

21.9. If the rate constant k_H is 2.5×10^2 and k_D is 2.2×10^2 , then what is the temperature.

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Question 3: Acridine Orange/DNA Binding Interactions

Acridine orange (AO) is a fluorescent dye that binds to DNA via an intercalative mode of binding. AO can insert itself into the DNA base pairs. Interactions of intercalating agents such as AO with DNA have been widely studied, and complexation can be followed with spectrometric titrations by varying the DNA-to-dye ratio. Stock solutions of DNA can be standardized spectrophotometrically (ε = 13,200 mol dm^{-3} cm^{-1} at 260 nm for a molar DNA concentration, C_{DNA}, expressed in base pairs.)

24.1. <u>Give</u> an expression to calculate the pure DNA concentration from an absorbance reading at 260 nm from a UV spectrum of solution containing DNA (quartz cuvette length: 1.0 cm).

The interaction between DNA and AO to form the AO–DNA complex can be expressed by the following reaction:

$$AO + DNA \rightleftharpoons AO - DNA,$$

whose equilibrium constant is

$$K = \frac{[AO-DNA]}{[AO][DNA]} \qquad (1)$$

Where [DNA], [AO] and [AO-DNA] are equilibrium concentrations.

24.2. <u>Provide</u> a mass balance expression for the overall AO concentration (C_{AO}) at equilibrium conditions.

Binding of AO to DNA can be followed by recording fluorescence intensity (F). Both AO and AO–DNA complex display a maximum emission intensity at λ_{em} = 520 nm. In dilute solutions, concentration is proportional to F. Therefore, quantitative estimation of complexation can be determined by using F.

$$F = \varphi_i \times C_i$$

where φ_i is the fluorescence constant and C_i is the concentration for species i.

24.3. <u>Provide</u> an expression for the overall F in terms of φ and concentrations of AO and of DNA at equilibrium.

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Consider that initially there is only AO in the measuring cell displaying an emission at λ_{em} = 520 nm, and finally at equilibrium both AO and AO–DNA complex have emission at the same wavelength. $F - \varphi_{AO}\, C_{AO} = \Delta F$, and $\varphi_{AO-DNA}\, \varphi_{AO} = \Delta\varphi$ is given.

24.4. <u>Show that</u> $\Delta F = [AO - DNA]\Delta\varphi$.

The binding equilibrium constant for AO intercalation to DNA (ignore AO self-aggregation and dimerization) can be determined from the equation:

$$\frac{C_{AO}}{\Delta F} = \frac{1}{\Delta\varphi} + \frac{1}{\Delta\varphi K}\frac{1}{[DNA]} \qquad (2)$$

24.5. <u>Derive</u> equation (2) starting from equation (1).

Spectrofluorometric titration is performed by adding increasing amounts of the DNA directly into the cell containing the AO. Each time DNA is added, the fluorescence intensity at λ_{em} = 520 nm, where only free and bound AO have emission, is recorded.

C_{AO} (mol dm^{-3})	C_{DNA} (mol dm^{-3})	F_{520} (a.u.)*
1.857×10^{-7}	6.535×10^{-6}	162
1.832×10^{-7}	1.032×10^{-5}	188
1.800×10^{-7}	1.521×10^{-5}	210
1.725×10^{-7}	2.671×10^{-5}	240
1.604×10^{-7}	4.516×10^{-5}	260

* a.u. is arbitrary unit

24.6. <u>Calculate</u> the equilibrium binding constant for AO–DNA using the data given in the Table above. Assume that there is no AO self-aggregation or dimerization. Take $\varphi_{AO} = 5.00 \times 10^8$ mol dm^{-3}, and [DNA] ≅ C_{DNA}.

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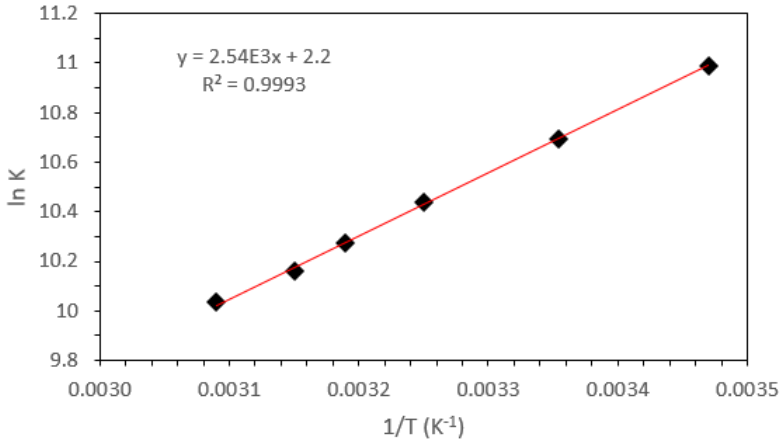

24.7. Given that $K = e^{-\frac{\Delta G^\circ}{RT}}$ and the plot above, **calculate** the values of ΔrH°, ΔrS°, and ΔrG° for the complexation of AO with DNA at 25 °C. (Assume that ΔrH° and ΔrS° do not change with the temperature.)

AO can undergo some self-aggregation (dimerization) at higher concentrations. The quantitative analysis of the dimerization can be expressed as follows:

$$2D \underset{k_d}{\overset{k_f}{\rightleftharpoons}} D_2$$

Here D represents AO monomer while D_2 represents dimeric AO, and k_f and k_d are the rate constants for dimer formation and dimer dissociation, respectively. According to that reaction, AO concentration dependence of the relaxation time, τ, which represents the time passed for a system to reach the new equilibrium when a sudden change is applied, is expressed by the relationship:

$$\frac{1}{\tau} = k_d + 4k_f C_{AO}$$

Data for dimerization of AO at 25 °C are given in the Table below.

$10^6\ C_{AO}$ (mol dm^{-3})	10^5 Relaxation time, τ (s)
2.50	2.32
4.50	2.27
8.00	2.18
11.0	2.11

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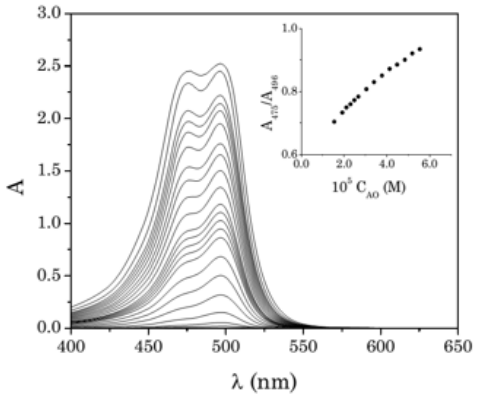
24.8. **Calculate** the values of k_d and k_f.

The absorbance spectra of AO derivative at various concentrations (0 to 7.3×10^{-5} mol dm^{-3}) in water are shown in the Figure below. The spectra indicate that two absorbance peaks exist: one at 496 nm and the other at 475 nm. The inset gives the ratio of absorbance peaks (A_{475}/A_{496}) as a function of AO concentration.



24.9. **Choose** correct statement(s) according to the absorbance spectra of the AO derivative.

- ☐ The band observed at 496 nm is attributed to the monomeric form.
- ☐ If there were only the monomeric form, the ratio of absorbance peaks (A_{475}/A_{496}) would remain constant.
- ☐ To reduce dimerization, the concentration of AO should be reduced.

24.10. If the initial concentration of AO is 1.0×10^{-5} mol dm^{-3}, then **calculate** the dimer fraction at equilibrium.

$$2D \underset{k_d}{\overset{k_f}{\rightleftharpoons}} D_2$$

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Question 4: Particle in a Box Problem: Free Electron Model

The particle in an one-dimensional box model is a crude approximation for conjugated molecules. In this model, π electrons are assumed to move freely over the carbon framework of conjugated bonds. Therefore, this model is also called the free electron model (FEM). The length of the box may be approximated via $L = n_C \times 1.40$ Å, where L is the box length and n_C is the number of carbons. Furthermore, the Pauli principle is applied when electrons are filled to the energy levels. The energy of a particle in an one-dimensional box can be written as follows:

$$E_n = \frac{n^2 h^2}{8mL^2}$$

where m is the mass of the particle, h is the Planck constant, and n is a positive integer.

For the 1,3,5,7-octatetraene molecule assuming FME:

18.1. <u>Draw</u> an energy diagram, fill the electrons, and calculate orbital energies.

18.2. <u>Calculate</u> the total π energy of the molecule.

18.3. <u>Determine</u> the wave length of the light (in nm) that require to excite an electron from the highest occupied molecular orbital (HOMO) to the lowest unoccupied molecular orbital (LUMO).

For two-dimensional conjugated systems, we may use the particle in a two-dimensional box model. In this case the total energy can be written as follows:

$$E_{n_1,n_2} = \frac{h^2}{8m}\left(\frac{n_1^2}{L_1^2} + \frac{n_2^2}{L_2^2}\right)$$

where L_1 and L_2 are the lengths and n_1 and n_2 are the quantum numbers of the first and second dimensions, respectively.

Graphene is a sheet of carbon atoms in the form of a two-dimensional hexagonal lattice in which one atom forms each vertex.

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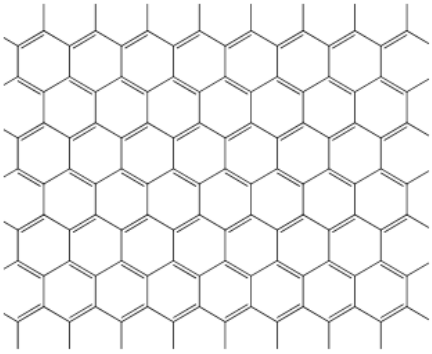

For a square shaped graphene sheet with $L_1 = L_2 = 11$ Å:

18.4. The distance between two adjacent carbons in the hexagonal 6-carbon unit is approximately 1.4 Å. **Calculate** the number of electrons in a (11 Å × 11 Å) sheet of graphene. For this problem you may ignore edge electrons. (Area of a regular hexagon with a side of L is $A = \frac{3\sqrt{3}}{2} L^2$).

18.5. **Calculate** the energy of the HOMO.

18.6. **Calculate** the energy of the LUMO.

18.7. The difference between energies of the LUMO and HOMO is called the band gap (E_g). **Calculate** the band gap.

The models for a particle in a one- and two-dimensional box can be extended to a three-dimensional rectangular box of dimensions L_1, L_2, and L_3, yielding the following expression for the allowed energy levels:

$$E_{n_1,n_2,n_3} = \frac{h^2}{8m}\left(\frac{n_1^2}{L_1^2} + \frac{n_2^2}{L_2^2} + \frac{n_3^2}{L_3^2}\right),$$

where n_1, n_2, and n_3 are the quantum numbers of the first, second, and third dimensions, respectively. For a particle in a cubic box of length L:

18.8. **Give** the expressions for the five different lowest energies.

18.9. **Draw** a diagram showing all the five energy levels. **Indicate** degeneracy of each level.

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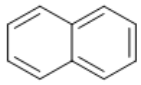
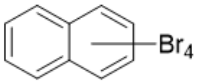
Question 5: NMR, Symmetry, and Structural Analysis

Naphthalene halides: Key compounds for many applications

Besides benzene, naphthalene is one of the best-known aromatic hydrocarbons. Therefore, the chemistry of naphthalene (**1**) has been extensively studied and many naphthalene derivatives have been synthesized. Halogen derivatives of this kind of compound are key for many transformations. For this reason, nearly all halogenated derivatives of naphthalene are known in the literature. Both ^{1}H and ^{13}C NMR spectra of symmetric compounds are characteristic, and allow researchers to exclude possible non-symmetrical structures to analyze the correct structures. Let us consider naphthalene tetrabromide isomers **2**.



1
Naphthalene



2
Naphthalene tetrabromides

9.1. **Draw** the structures of all naphthalene tetrabromide(s) with 3 signals in ^{13}C NMR and one signal (singlet) in ^{1}H NMR spectra.

9.2. **Draw** the structures of all naphthalene tetrabromide(s) with 5 signals in ^{13}C NMR spectra.

9.3. **Draw** the structures of all naphthalene tetrabromide(s) with 6 signals in ^{13}C NMR and a doublet (J = 8–9 Hz) in ^{1}H NMR spectra.

9.4. **Draw** the structures of all naphthalene tetrabromide(s) with 6 signals in ^{13}C NMR and a doublet (J = 1.5–2.0 Hz) in ^{1}H NMR spectra.

Dynamic NMR: fast transformation between tautomeric forms and identical nuclei in NMR

Bullvalene (**3**) is very suitable for degenerate Cope rearrangements. Without counting enantiomers, the number of possible valence tautomers of a bullvalene with ten distinguishable positions is 10!/3 = 1,209,600. This arrangement enables all carbon and hydrogen atoms to appear equivalent on the NMR timescale. At sufficiently high temperature, both ^{1}H NMR and ^{13}C NMR spectra of bullvalene show only one signal, average to a rounded peak. However, at −60 °C, as Cope rearrangements do not take place, olefinic and aliphatic protons are observed separately.

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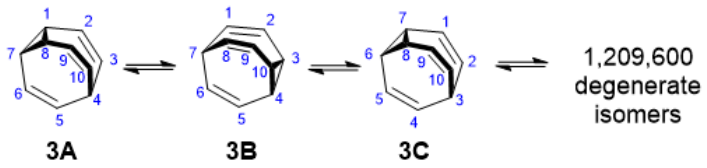


3A **3B** **3C**

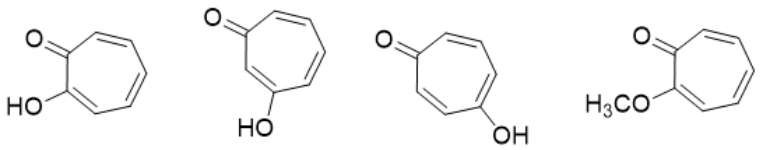
Bullvalene

9.5. At low temperature, ignoring any Cope rearrangement, **how many** carbon signals do you expect from the ^{13}C NMR spectrum of bullvalene?

Label identical carbon atoms with letters **a**, **b**, **c**… on the molecular structure.

9.6 Owing to fast tautomerism, some molecules give clearer spectra due to apparent symmetry. In light of this information, how many signals do you expect from the ^{13}C NMR spectra of the following compounds?

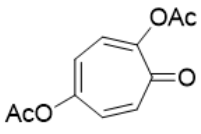
1*H*-imidazole 1-methyl-1*H*-imidazole



α-tropolone β-tropolone χ-tropolone 2-methoxtropone

9.7. In the literature, it has been shown that the tropolone diacetate derivative **4** has fewer signals than expected in ^{13}C NMR spectroscopy.

Draw reasonable resonance structure(s) and/or transformation(s) responsible for this symmetry. How many signals do you expect for this molecule in the ^{13}C NMR spectrum?



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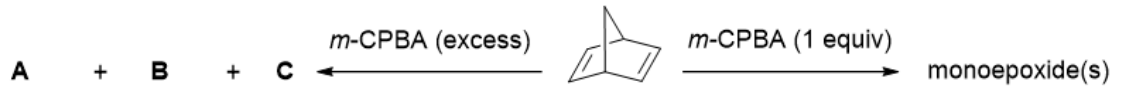
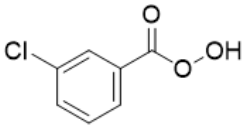
Stereochemistry of the epoxidation reaction of bicyclic alkenes.

9.8. Considering the following pieces of information, **draw** the structures of all possible stereoisomers formed under the given reaction conditions.

Hint: A and **B** are isomers with 3 signals and **C** is an isomer with 4 signals in ^{13}C NMR spectroscopy.



m-CPBA = *m*-Chloroperoxybenzoic acid



9.9. **Draw** the structures of the stereoisomer(s) formed under the given reaction conditions. How many signals do you expect for the epoxide product(s) in ^{13}C NMR spectra?

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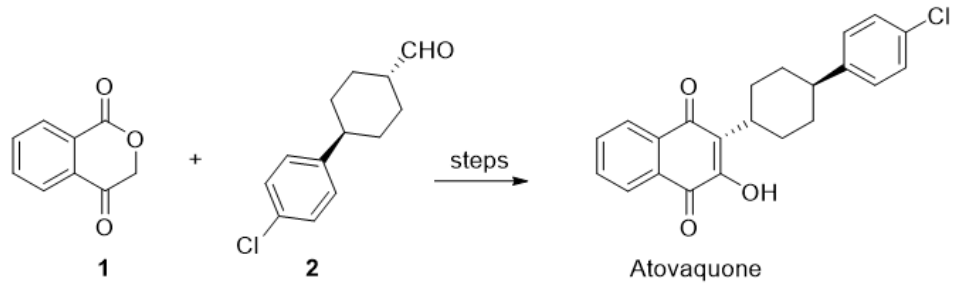
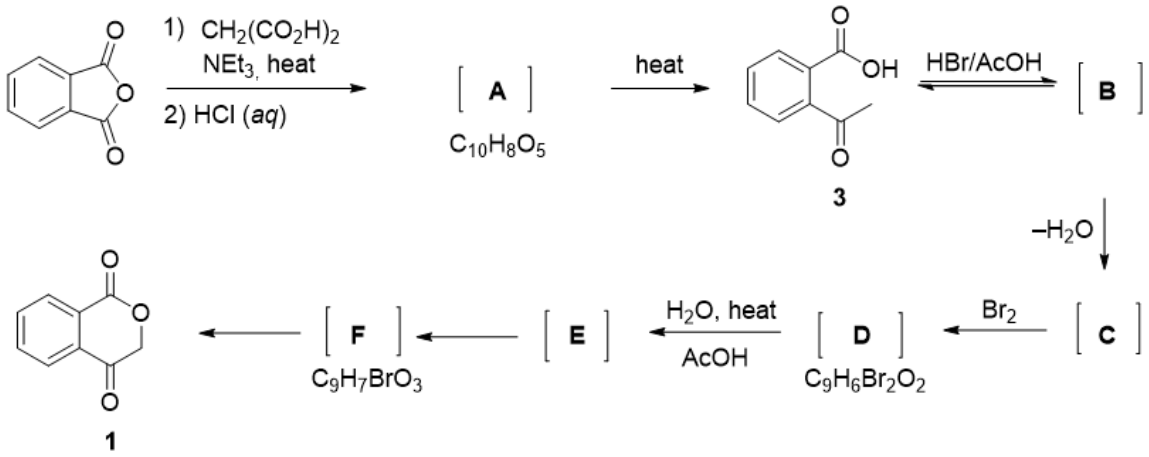
Question 6: Atovaquone

Atovaquone, an approved drug, is used to treat pneumocystosis and malaria. Ketoester **1** and aldehyde **2** are key compounds in the synthetic process of atovaquone.



6.1. The synthesis of key compound ketoester **1** is shown below. A mixture of phthalic anhydride and Et_3N is treated with diacid. Gas evolution is observed during this period. Treatment of the reaction mixture with *aq*. HCl solution provides formation of acid **3** through intermediate **A** with two carboxylic acid groups. Acid **3** is converted to the isomeric intermediate **B**, containing both hemiacetal and ester functionalities, followed by dehydration to the alkene **C**, which is then brominated to give **D** under acidic condition. Dibromide **D** undergoes solvolysis in a hot mixture of H_2O/AcOH to give tertiary carbocation intermediate **E**, which is then trapped with water to give intermediate hemiacetal **F**. Finally, rearrangement of intermediate hemiacetal **F** provides key compound **1**.

*Note: The square brackets denote that the product was not isolated but reacted further without purification. The conversion of **3** to **1** is a one-pot reaction that involves a series of reactions occurring one after another in the same vessel without isolation and purification of intermediates.*



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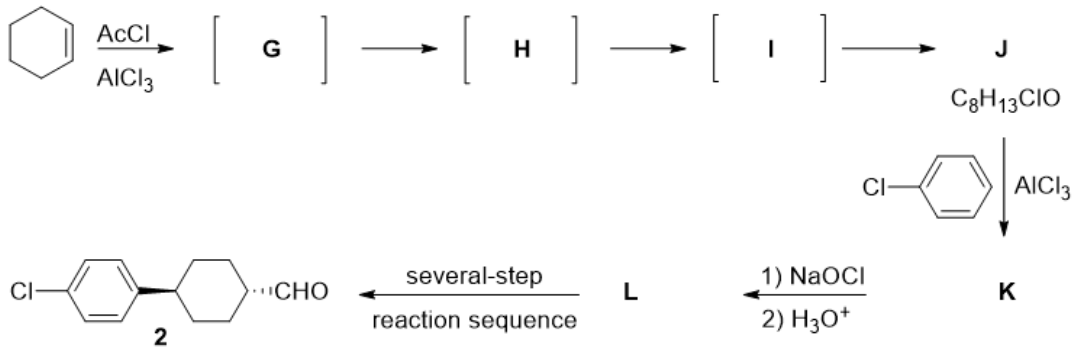
Spectroscopic data for intermediates **B** and **C**: **B:** ^{1}H NMR δ = 7.86–7.52 (4H), 4.13 (bs, 1H, exchangeable with D_2O), 1.97 (s, 3H). **C:** ^{1}H NMR δ = 7.92–7.58 (4H), 5.24 (m, 2H); ^{13}C NMR δ = 166.8, 151.8, 139.0, 134.4, 130.4, 125.3, 125.1, 120.6, 91.3; MS m/z = 146.0

Draw the structure of intermediates **A**–**F** in the synthesis of **1**.

6.2. The synthesis of aldehyde **2** starts from cyclohexene by key steps including Friedel–Crafts acylations, haloform, reduction, and oxidation. Friedel–Crafts acylation of cyclohexene with acetyl chloride yields chlorocyclohexyl methyl ketone **J.** Reaction of cyclohexene with acetyl chloride produces an initial carbocation **G** that undergoes two successive Wagner–Meerwein hydride migrations to form isomeric carbocations **H** and **I**, respectively. Trapping of carbocation **I** with chloride ion produces **J**, the Friedel–Crafts reaction of which with chlorobenzene provides **K**. Haloform reaction of methyl ketone **K** using sodium hypochlorite (NaOCl) gives the corresponding acid **L**. Acid **L** is converted into the aldehyde **2** in a several-step reaction sequence.

Draw structure of isomeric carbocations **G**–**I** formed in this reaction.



6.3. Are these carbocations chiral?

G	☐	Yes
	☐	No
H	☐	Yes
	☐	No
I	☐	Yes
	☐	No

6.4. **Draw** the structure of **J**–**L**.

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6.5. **Choose** all correct statements for **L**.

- ☐ **L** has 4 stereoisomers.
- ☐ **L** is a chiral compound.
- ☐ **L** is an achiral compound.
- ☐ **L** is a meso compound.
- ☐ **L** has 2 stereoisomers.
- ☐ Stereoisomers of **L** are diastereomers of each other.
- ☐ Stereoisomers of **L** are enantiomers of each other.

6.6. Which of the following compound(s) result(s) in the haloform reaction of **K**?

- ☐ CH_2Cl_2
- ☐ CH_3Cl
- ☐ $CHCl_3$
- ☐ CCl_4

6.7. Which of the following reagents are appropriate to form aldehyde **2** from **L**?

Choose all correct reactions.

- ☐ **L** $\xrightarrow[2)\ (COCl)_2,\ DMSO,\ NEt_3]{1)\ a)\ LiAlH_4\ b)\ H_3O^+}$ **2**
- ☐ **L** $\xrightarrow[2)\ a)\ DIBAL\text{-}H\ (1\ equiv),\ -78\ ^\circ C\ b)\ H_3O^+]{1)\ CH_3OH/H^+}$ **2**
- ☐ **L** $\xrightarrow[2)\ CrO_3/H_3O^+]{1)\ NaBH_4/EtOH}$ **2**
- ☐ **L** $\xrightarrow[2)\ HONHMe\cdot HCl,\ NEt_3\ 3)\ DIBAL\text{-}H\ (1\ equiv),\ -78\ ^\circ C\ b)\ H_3O^+]{1)\ SOCl_2}$ **2**
- ☐ **L** $\xrightarrow[2)\ CrO_3/H_3O^+]{1)\ EtOCOCl,\ NEt_3}$ **2**

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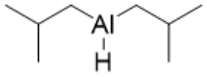
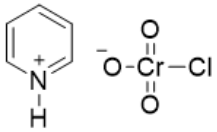
☐ **L** $\xrightarrow[2)\ NaBH_4/EtOH\ 3)\ PCC]{1)\ EtOCOCl,\ NEt_3}$ **2**

☐ **L** $\xrightarrow[2)\ DIBAL\text{-}H\ (1\ equiv),\ -78\ ^\circ C\ b)\ H_3O^+]{1)\ EtOCOCl,\ NEt_3}$ **2**

AcCl
Acetyl chloride



DIBAL-H
Diisobutylaluminium hydride



PCC
Pyridinium chlorochromate

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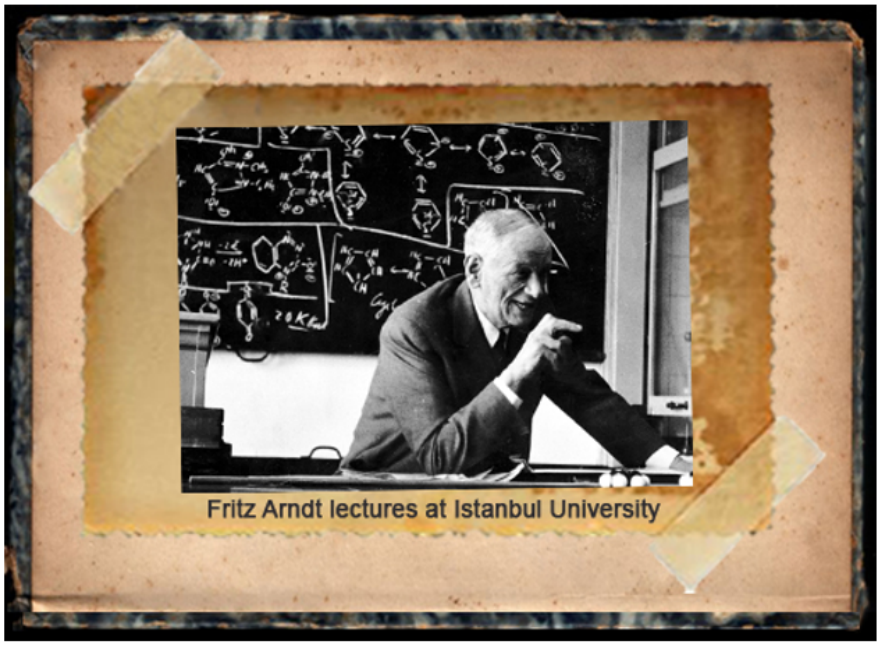
Question 7: Arnt-Eistert Homologation

Fritz Georg Arndt (6 July 1885–8 December 1969) was a German chemist who had a great influence on the development of chemistry in Turkey. He was employed for two decades of his professional life at Istanbul University in two distinct periods. He discovered the Arndt–Eistert synthesis with Bernd Eistert. The Arndt–Eistert synthesis is the chemical reaction for one-carbon homologation (i.e. the conversion of RCO_2H to RCH_2CO_2H) of carboxylic acids and is called the homologation process. In the Arndt–Eistert homologation, the key step is the Wolff rearrangement of diazoketones to ketenes, which can be achieved thermally, photochemically, or by silver (I) catalysis. The reaction is conducted in the presence of nucleophiles such as water, alcohols, or amines to capture the ketene intermediate to yield carboxylic acids, esters, or amides, respectively. In this problem, synthesis of indolizidine alkaloids is studied.


Fritz Arndt lectures at Istanbul University

5.1. As depicted in the scheme below, the synthesis of indolizidines 167B and coniceine could be easily and concisely achieved from β,γ-unsaturated ester **B**. The key step (**A** → **B**) is the Wolff rearrangement. Compound **C** has a lactam core, which is a bicyclic heterocycle containing a six-membered ring fused to a saturated five-membered ring, one of the bridging atoms being nitrogen.

Draw the structures of **A**–**D** without any stereochemical detail.

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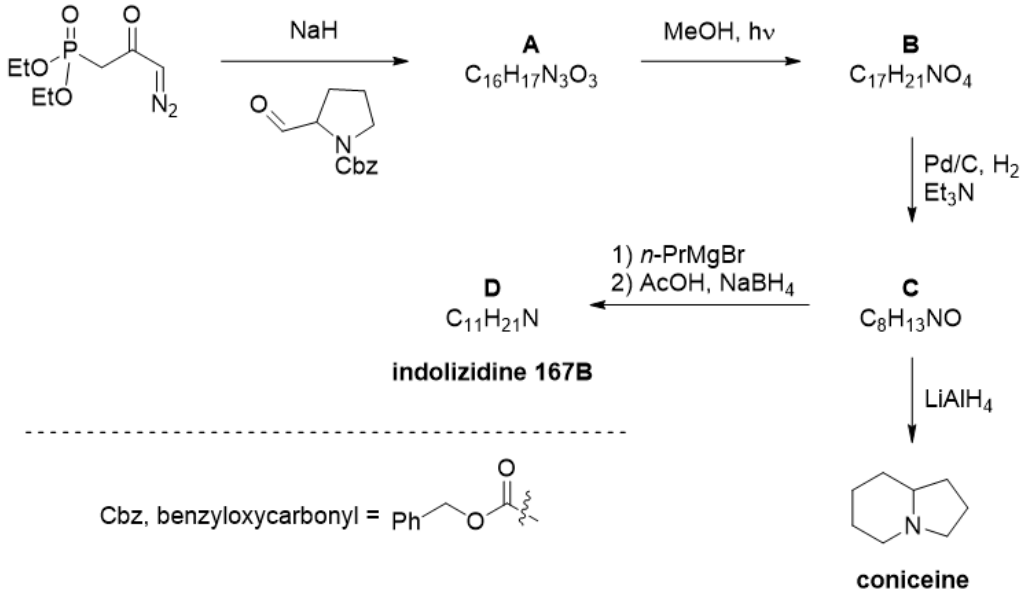

5.2. In the Arndt–Eistert homologation reaction, an α-diazo ketone can undergo photochemical Wolff rearrangement to form α-ketocarbene via nitrogen extrusion. This intermediate undergoes a 1,2-alkyl shift to give the ketene product.

Draw the structures of the α-ketocarbene and ketene intermediates in the second step (**A** → **B**).

5.3. Addition of propylmagnesium bromide to compound **C**, followed by AcOH/$NaBH_4$, is the last step in the total synthesis of indolizidine 167B.

Draw the structure of an intermediate ($\mathbf{C_{11}H_{20}N^+}$) in the fourth step (**C** → **D**).

5.4. An alternative synthesis of coniceine is depicted below. **Draw** the structures of **E**–**J**.

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