

IChO 2006

Theory problems and solutions · Gyeongsan, Korea · 11 theory problems with complete solutions

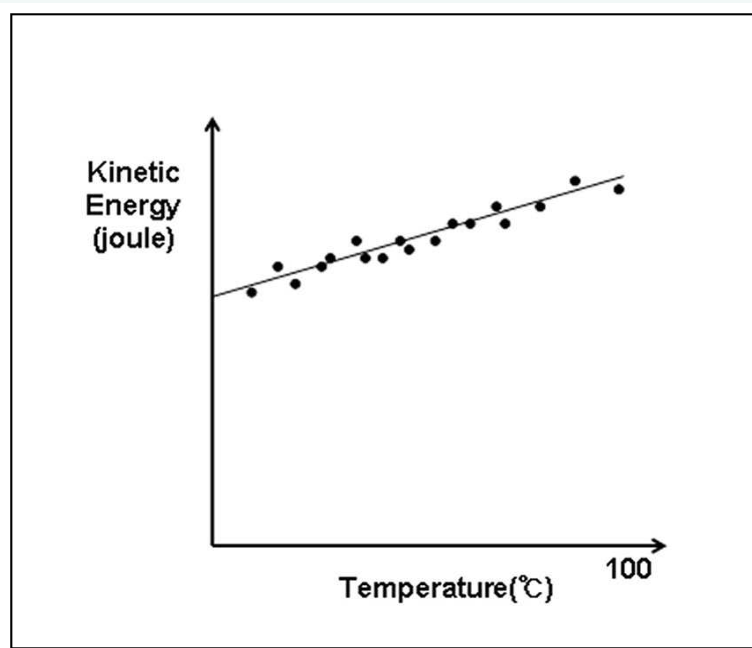
eulersolve.org/icho/2006/

Problem 1: Avogadro's number

Spherical water droplets are dispersed in argon gas. At 27 °C, each droplet is 1.0 micrometer in diameter and undergoes collisions with argon. Assume that inter-droplet collisions do not occur. The root-mean-square speed of these droplets was determined to be 0.50 cm s^{-1} at 27 °C. The density of a water droplet is 1.0 g cm^{-3} .

1.1 Calculate the average kinetic energy ($mv^2/2$) of this droplet at 27 °C. The volume of a sphere is given by $(4/3) \pi r^3$ where r is the radius.

If the temperature is changed, then droplet size and speed of the droplet will also change. The average kinetic energy of a droplet between 0 °C and 100 °C as a function of temperature is found to be linear. Assume that it remains linear below 0 °C.



At thermal equilibrium, the average kinetic energy is the same irrespective of particle masses (equipartition theorem).

The specific heat capacity, at constant volume, of argon (atomic weight, 40) gas is $0.31 \text{ J g}^{-1} \text{ K}^{-1}$.

1.2. Calculate Avogadro's number without using the ideal gas law, the gas constant, Boltzmann's constant).

Answers

- 1.1: $\overline{E}_k = 6.5 \times 10^{-21} \text{ J}$ per droplet.
- 1.2: $N_A = 5.7 \times 10^{23} \text{ mol}^{-1}$.

Solution

1.1

The droplet radius and density in SI units are

$$r = \frac{1.0 \times 10^{-6}}{2} = 5.0 \times 10^{-7} \text{ m}, \quad \rho = 1.0 \times 10^3 \text{ kg m}^{-3}.$$

Its mass is therefore

$$m = \rho \frac{4\pi r^3}{3} = (1.0 \times 10^3) \frac{4\pi}{3} (5.0 \times 10^{-7})^3 = 5.236 \times 10^{-16} \text{ kg}.$$

The root-mean-square speed is

$$v_{\text{rms}} = 0.50 \text{ cm s}^{-1} = 5.0 \times 10^{-3} \text{ m s}^{-1}.$$

Since $v_{\text{rms}}^2 = \langle v^2 \rangle$, the average translational kinetic energy is

$$\begin{aligned} \overline{E}_k &= \frac{1}{2} m \langle v^2 \rangle = \frac{1}{2} m v_{\text{rms}}^2 \\ &= \frac{1}{2} (5.236 \times 10^{-16}) (5.0 \times 10^{-3})^2 \\ &= 6.545 \times 10^{-21} \text{ J}. \end{aligned}$$

To two significant figures,

$$\boxed{\overline{E}_k = 6.5 \times 10^{-21} \text{ J}}.$$

1.2

In the classical treatment used in this problem, the mean translational kinetic energy extrapolates to zero at absolute zero. Consequently, the stated linear temperature dependence has the form

$$\overline{E}_k = aT,$$

where T is the absolute temperature. At 27 °C,

$$T_0 = 300.15 \text{ K},$$

so the energy increase per particle per kelvin is

$$a = \frac{d\overline{E}_k}{dT} = \frac{\overline{E}_k(T_0)}{T_0} = \frac{6.545 \times 10^{-21}}{300.15} = 2.181 \times 10^{-23} \text{ J K}^{-1}.$$

By the stated equipartition principle, an argon atom has the same average translational kinetic energy as a droplet at the same temperature. Thus the same value of a applies to each argon atom.

Argon is monatomic, so its thermal energy in this classical treatment is translational kinetic energy. At constant volume, the molar heat capacity is therefore

$$C_{V,m} = \frac{dU_m}{dT} = N_A \frac{d\bar{E}_k}{dT} = N_A a.$$

The supplied specific heat capacity gives

$$C_{V,m} = (0.31 \text{ J g}^{-1} \text{ K}^{-1})(40 \text{ g mol}^{-1}) = 12.4 \text{ J mol}^{-1} \text{ K}^{-1}.$$

Hence

$$\begin{aligned} N_A &= \frac{C_{V,m}}{a} = \frac{C_{V,m} T_0}{\bar{E}_k(T_0)} \\ &= \frac{(12.4 \text{ J mol}^{-1} \text{ K}^{-1})(300.15 \text{ K})}{6.545 \times 10^{-21} \text{ J}} \\ &= 5.687 \times 10^{23} \text{ mol}^{-1}. \end{aligned}$$

To two significant figures,

$$\boxed{N_A = 5.7 \times 10^{23} \text{ mol}^{-1}}.$$

The solution was checked against the official solution. Where this solution differs from the official solution, the official solution contains an error or a misprint.

Problem 2: Detection of hydrogen

Hydrogen is prevalent in the universe. Life in the universe is ultimately based on hydrogen.

2.1 There are about 1×10^{23} stars in the universe. Assume that they are like our sun (radius, 700,000 km; density, 1.4 g cm^{-3} ; 3/4 hydrogen and 1/4 helium by mass). Estimate the number of stellar protons in the universe to one significant figure.

In the 1920s Cecilia Payne discovered by spectral analysis of starlight that hydrogen is the most abundant element in most stars.

2.2 The electronic transition of a hydrogen atom is governed by $\Delta E(n_i \rightarrow n_f) = -C(1/n_f^2 - 1/n_i^2)$, where n is principle quantum number, and C is a constant. For detection of the $\Delta E(3 \rightarrow 2)$ transition (656.3 nm in the Balmer series), the electron in the ground state of the hydrogen atom needs to be excited first to the $n = 2$ state. Calculate the wavelength (in nm) of the absorption line in the starlight corresponding to the $\Delta E(1 \rightarrow 2)$ transition.

2.3 According to Wien's law, the wavelength (λ) corresponding to the maximum light intensity emitted from a blackbody at temperature T is given by $\lambda T = 2.9 \times 10^{-3} \text{ m K}$. Calculate the surface temperature of a star whose blackbody radiation has a peak intensity corresponding to the $n = 1 \rightarrow n = 2$ excitation of hydrogen.

The ground state of hydrogen is split into two hyperfine levels due to the interaction between the magnetic moment of the proton and that of the electron. In 1951, Purcell discovered a spectral line at 1420 MHz due to the hyperfine transition of hydrogen in interstellar space.

2.4 Hydrogen in interstellar space cannot be excited electronically by starlight. However, the cosmic background radiation, equivalent to 2.7 K, can cause the hyperfine transition. Calculate the temperature of a blackbody whose peak intensity corresponds to the 1420 MHz transition.

2.5 Wien generated hydrogen ions by discharge of hydrogen gas at a very low pressure and determined the e/m value, which turned out to be the highest among different gases tested. In 1919, Rutherford bombarded nitrogen with alpha-particles and observed emission of a positively charged particle which turned out to be the hydrogen ion observed by Wien. Rutherford named this particle the "proton". Fill in the blank.

Official English text of the problem.

Answers

- **2.1:** 1×10^{80} stellar protons, including protons within helium nuclei.
- **2.2:** 121.5 nm, the Lyman- α absorption wavelength.
- **2.3:** 2.4×10^4 K.
- **2.4:** 1.4×10^{-2} K, using the supplied wavelength form of Wien's law.
- **2.5:** ${}^{14}_7\text{N} + {}^4_2\text{He} \longrightarrow {}^{17}_8\text{O} + {}^1_1\text{H}$. The emitted particle is a proton, the hydrogen-1 cation, [1H+].

Solution

2.1

For this estimate, take hydrogen to be hydrogen-1 and helium to be helium-4, with molar masses approximately 1 g mol^{-1} and 4 g mol^{-1} , respectively. Use $N_A = 6.022 \times 10^{23} \text{ mol}^{-1}$.

The radius of each star is

$$R = 700,000 \text{ km} = 7.00 \times 10^{10} \text{ cm}.$$

Its mass is therefore

$$\begin{aligned} M_{\star} &= \rho \frac{4\pi R^3}{3} \\ &= (1.4 \text{ g cm}^{-3}) \frac{4\pi}{3} (7.00 \times 10^{10} \text{ cm})^3 \\ &= 2.011 \times 10^{33} \text{ g}. \end{aligned}$$

Each hydrogen nucleus contains one proton, and each helium nucleus contains two. Thus the number of protons per star is

$$\begin{aligned}
N_{p,\star} &= \frac{(3/4)M_{\star}}{1 \text{ g mol}^{-1}}N_{\text{A}} + 2 \frac{(1/4)M_{\star}}{4 \text{ g mol}^{-1}}N_{\text{A}} \\
&= (2.011 \times 10^{33} \text{ g}) (0.75 + 0.125) \frac{6.022 \times 10^{23}}{\text{g}} \\
&= 1.060 \times 10^{57}.
\end{aligned}$$

Multiplying by the number of stars gives

$$N_{p,\text{universe}} = (1 \times 10^{23})(1.060 \times 10^{57}) = 1.060 \times 10^{80}.$$

To one significant figure,

$$\boxed{N_{p,\text{universe}} = 1 \times 10^{80}}.$$

2.2

The energy change of the atom in the $3 \rightarrow 2$ emission transition is

$$\Delta E_{3 \rightarrow 2} = -C \left(\frac{1}{4} - \frac{1}{9} \right) = -\frac{5C}{36}.$$

The emitted photon therefore has positive energy

$$\frac{hc}{\lambda_{32}} = \frac{5C}{36}.$$

For absorption from $n = 1$ to $n = 2$,

$$\Delta E_{1 \rightarrow 2} = -C \left(\frac{1}{4} - 1 \right) = \frac{3C}{4} = \frac{hc}{\lambda_{12}}.$$

Taking the ratio eliminates h , c , and C :

$$\frac{\lambda_{32}}{\lambda_{12}} = \frac{3/4}{5/36} = \frac{27}{5}.$$

Hence

$$\lambda_{12} = \frac{5}{27}(656.3 \text{ nm}) = 121.537 \dots \text{ nm},$$

so

$$\boxed{\lambda_{12} = 121.5 \text{ nm}}.$$

This is the Lyman- α line in the ultraviolet.

2.3

Using the wavelength found in 2.2 and the supplied Wien constant,

$$T = \frac{2.9 \times 10^{-3} \text{ m K}}{121.537 \times 10^{-9} \text{ m}} = 2.3861 \times 10^4 \text{ K}.$$

The Wien constant has two significant figures, giving

$$\boxed{T = 2.4 \times 10^4 \text{ K}}.$$

2.4

First convert the transition frequency to a wavelength, using $c = 2.998 \times 10^8 \text{ m s}^{-1}$:

$$\nu = 1420 \text{ MHz} = 1.420 \times 10^9 \text{ s}^{-1},$$

$$\lambda = \frac{c}{\nu} = \frac{2.998 \times 10^8 \text{ m s}^{-1}}{1.420 \times 10^9 \text{ s}^{-1}} = 0.2111 \text{ m}.$$

This is the approximately 21 cm hydrogen line. Applying the wavelength form of Wien's law supplied in 2.3,

$$T = \frac{2.9 \times 10^{-3} \text{ m K}}{0.2111 \text{ m}} = 1.374 \times 10^{-2} \text{ K}.$$

Therefore,

$$\boxed{T = 1.4 \times 10^{-2} \text{ K}}.$$

The 2.7 K background can still supply photons at this frequency because a blackbody emits over a continuous range of wavelengths.

2.5

The incident alpha-particle is a helium-4 nucleus, $[^4\text{He}+2]$. The emitted proton is a hydrogen-1 cation, $[^1\text{H}+]$.

Taking the nitrogen target to be nitrogen-14, write the reaction with an unknown residual nucleus:



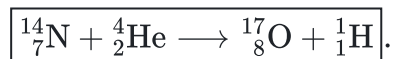
Conservation of nucleon number gives

$$14 + 4 = A + 1 \quad \Rightarrow \quad A = 17.$$

Conservation of nuclear charge gives

$$7 + 2 = Z + 1 \quad \Rightarrow \quad Z = 8.$$

Atomic number 8 identifies oxygen, so the residual nucleus is oxygen-17. The completed reaction is



Both sides contain 18 nucleons and total nuclear charge $+9e$. The equation describes a nuclear transformation; electron shells and chemical bonding are not specified.

The solution was checked against the official solution.

Problem 3: Interstellar chemistry

Early interstellar chemistry is thought to have been a prelude to life on Earth. Molecules can be formed in space via heterogeneous reactions at the surface of dust particles, often called the interstellar ice grains (IIGs). Imagine the reaction between H and C atoms on the IIG surface that forms CH. The CH product can either be desorbed from the surface or further react through surface migration with adsorbed H atoms to form CH₂, CH₃, etc.

Depending on how energetically a molecule "jumps" from its anchored site, it either leaves the surface permanently (desorption) or returns to a new position at the surface (migration). The rates of desorption and migratory jump follow the Arrhenius formula, $k = A \exp(-E/RT)$,

where k is the rate constant for desorption or migratory jump, A the jumping frequency, and E the activation energy for the respective event.

3.1 Desorption of CH from the IIG surface follows first-order kinetics. Calculate the average residence time of CH on the surface at 20 K. Assume that $A = 1 \times 10^{12} \text{ s}^{-1}$ and $E_{\text{des}} = 12 \text{ kJ mol}^{-1}$.

3.2 Consider the shortest time it would take for one CH unit to move from its initial position to the opposite side of an IIG by successive migratory jumps. Assume that the activation energy for migration (E_{mig}) is 6 kJ mol^{-1} , and the IIG is a sphere with a $0.1 \mu\text{m}$ radius. Each migratory jump laterally advances the molecule by 0.3 nm . Show work and choose your answer from (a) – (e) below.

(a) $t \leq 1 \text{ day}$

(b) $10 \text{ days} \leq t \leq 10^2 \text{ yr}$

(c) $10^3 \text{ yr} \leq t \leq 10^6 \text{ yr}$

(d) $10^7 \text{ yrs} \leq t \leq 10^{10} \text{ yr}$

(e) $t \geq 10^{11} \text{ yr}$

3.3 Consider the reaction of CO with H_2 to form H_2CO . The activation energy on a metal catalyst is 20 kJ mol^{-1} that is produced by formaldehyde at a rate of 1 molecule/s per site at 300 K. Estimate the rate of formaldehyde formation per site if the reaction takes place at 20 K.

3.4 Which is a set of all true statements? Circle one.

(a) Most CH species are desorbed from the IIG surface before encountering other reactants by surface migration.

(b) IIGs can assist transformation of simple molecules to more complex ones in interstellar space.

(c) For a reaction on the IIG to occur at an appreciable speed during the age of the Universe ($1 \times 10^{10} \text{ yr}$), the reaction energy barrier must be absent or negligible.

☐ (a) ☐ (b) ☐ (c) ☐ (a, b) ☐ (a, c) ☐ (b, c) ☐ (a, b, c)

Official English text of the problem.

Answers

- **3.1:** $\tau \approx 2.2 \times 10^{19} \text{ s} \approx 7.0 \times 10^{11} \text{ yr}$.
- **3.2:** $t \approx 4.9 \times 10^6 \text{ s} \approx 57 \text{ days}$; choose **(b)**.
- **3.3:** Formaldehyde (C=O) formation rate: $r_{20} \approx 1.8 \times 10^{-49} \text{ molecules s}^{-1} \text{ site}^{-1}$.
- **3.4:** Circle **(b, c)**, within the problem's thermal Arrhenius model.

Solution

Use $R = 8.314 \text{ J mol}^{-1} \text{ K}^{-1}$ and $1 \text{ yr} \approx 3.156 \times 10^7 \text{ s}$.

3.1 — Average residence time

The adsorbed species is methylidyne, CH, SMILES [CH]. Its attachment to the grain is not represented by this SMILES.

For first-order desorption, the probability that a molecule remains adsorbed after time t is

$$P(t) = e^{-k_{\text{des}} t}.$$

Therefore its mean residence time is

$$\tau = \int_0^{\infty} P(t) dt = \frac{1}{k_{\text{des}}}.$$

The desorption rate constant is

$$\begin{aligned} k_{\text{des}} &= A \exp\left(-\frac{E_{\text{des}}}{RT}\right) \\ &= (1.0 \times 10^{12} \text{ s}^{-1}) \exp\left[-\frac{12000 \text{ J mol}^{-1}}{(8.314 \text{ J mol}^{-1} \text{ K}^{-1})(20 \text{ K})}\right] \\ &= 4.55 \times 10^{-20} \text{ s}^{-1}. \end{aligned}$$

Thus

$$\tau = \frac{1}{k_{\text{des}}} \approx 2.2 \times 10^{19} \text{ s} \approx 7.0 \times 10^{11} \text{ yr}.$$

This is the mean lifetime; the half-life would instead be $(\ln 2)/k_{\text{des}}$.

3.2 — Shortest migration time

Use the same temperature and jumping frequency as in 3.1. The migration rate constant is

$$\begin{aligned} k_{\text{mig}} &= (1.0 \times 10^{12} \text{ s}^{-1}) \exp\left[-\frac{6000}{8.314 \times 20}\right] \\ &= 2.13 \times 10^{-4} \text{ s}^{-1}. \end{aligned}$$

The mean waiting time per jump is consequently

$$\tau_{\text{jump}} = \frac{1}{k_{\text{mig}}} = 4.69 \times 10^3 \text{ s}.$$

The shortest surface path between opposite points of a sphere is half a great circle:

$$L = \pi r = \pi(0.1 \times 10^{-6} \text{ m}) = 3.14 \times 10^{-7} \text{ m}.$$

If every jump advances along this path, the required number of jumps is

$$N \approx \frac{L}{\ell} = \frac{3.14 \times 10^{-7} \text{ m}}{0.3 \times 10^{-9} \text{ m}} = 1.05 \times 10^3.$$

Hence the shortest-path travel-time estimate is

$$\begin{aligned} t &= N\tau_{\text{jump}} = \frac{N}{k_{\text{mig}}} \\ &\approx 4.91 \times 10^6 \text{ s} \\ &\approx 56.8 \text{ days} \approx 0.156 \text{ yr}. \end{aligned}$$

Thus

$$\text{Choose (b): } 10 \text{ days} \leq t \leq 10^2 \text{ yr.}$$

This estimate assumes that all jumps advance toward the opposite point. Random migration generally requires more jumps.

3.3 — Formaldehyde formation at 20 K

The balanced reaction is



The species are carbon monoxide, CO, [C-]#[O+]; molecular hydrogen, H₂, [H][H]; and formaldehyde (methanal), H₂CO, C=O.

Assuming the same activation energy and effective rate prefactor at both temperatures, the Arrhenius rate ratio is

$$\frac{r_{20}}{r_{300}} = \exp \left[-\frac{E_a}{R} \left(\frac{1}{20 \text{ K}} - \frac{1}{300 \text{ K}} \right) \right].$$

Substituting $E_a = 20000 \text{ J mol}^{-1}$,

$$\frac{r_{20}}{r_{300}} = \exp \left[-\frac{20000}{8.314} \left(\frac{1}{20} - \frac{1}{300} \right) \right] = e^{-112.26} = 1.76 \times 10^{-49}.$$

Since $r_{300} = 1 \text{ molecule s}^{-1} \text{ site}^{-1}$,

$$r_{20} \approx 1.8 \times 10^{-49} \text{ molecules s}^{-1} \text{ site}^{-1}.$$

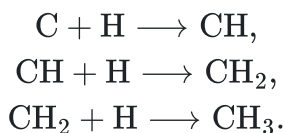
3.4 — Evaluation of the statements

(a) False. Migration is enormously faster than desorption:

$$\frac{k_{\text{mig}}}{k_{\text{des}}} = \exp \left(\frac{E_{\text{des}} - E_{\text{mig}}}{RT} \right) = \exp \left(\frac{6000}{8.314 \times 20} \right) \approx 4.7 \times 10^{15}.$$

Thus, in the absence of reaction, a methylidyne species can make approximately 4.7×10^{15} migratory jumps on average before desorbing. Migration provides extensive opportunity to encounter other adsorbed reactants.

(b) True. The grains retain reactants and permit encounters through surface migration. Successive hydrogen additions can build more complex species:



Here carbon and hydrogen atoms have SMILES [C] and [H]; methylene, CH₂, has SMILES [CH2]; and the methyl radical, CH₃, has SMILES [CH3]. These equations describe species on the surface. The SMILES do not specify their surface bonding or spin multiplicities.

(c) True in the intended thermal-activation model. At 20 K, even the 20 kJ mol⁻¹ barrier in 3.3 makes the reaction negligible over the stated age of the Universe. The expected number of formaldehyde molecules formed per site in that time is

$$\begin{aligned} r_{20} t_{\text{Universe}} &= (1.76 \times 10^{-49} \text{ s}^{-1} \text{ site}^{-1})(10^{10} \times 3.156 \times 10^7 \text{ s}) \\ &\approx 5.6 \times 10^{-32} \text{ site}^{-1}. \end{aligned}$$

Appreciable thermally activated chemistry therefore requires an absent or sufficiently small reaction barrier.

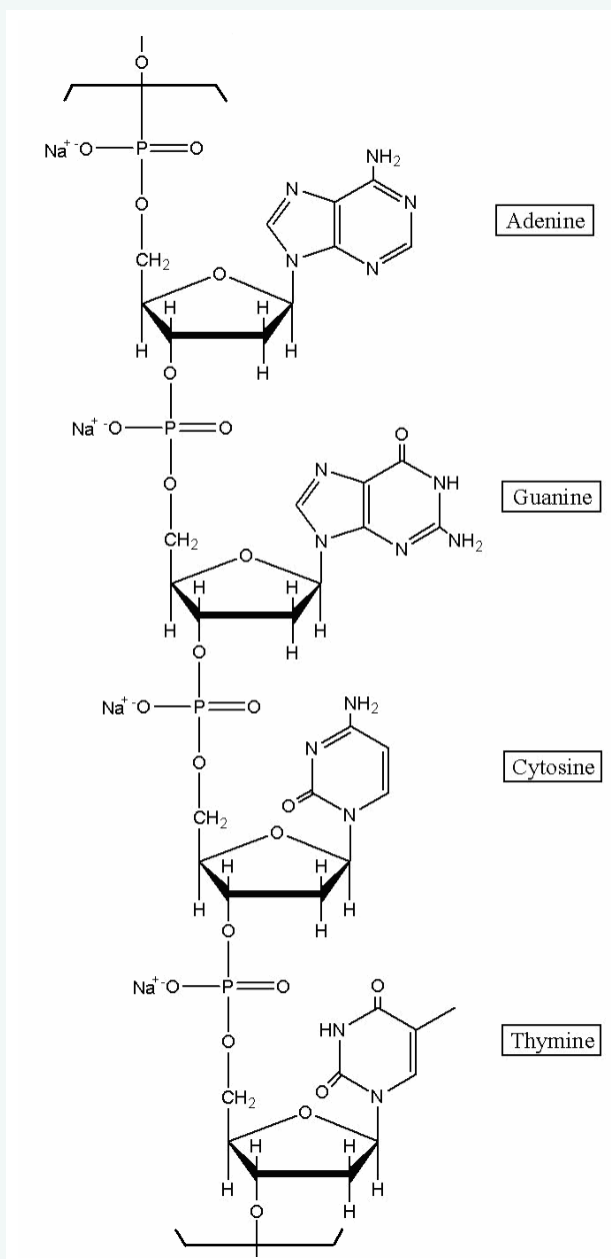
Consequently, circle

(b, c) .

The solution was checked against the official solution.

Problem 4: The Chemistry of DNA

4.1 In 1944 Oswald Avery isolated a genetic material and showed by elemental analysis that it was a sodium salt of deoxyribonucleic acid. A segment of DNA with formula mass of 1323.72 is shown.



Assuming that equimolar amounts of the four bases are present in DNA, write the number of H atoms per P atom. Calculate (to 3 significant figures) the theoretical weight percentage of H expected upon elemental analysis of DNA.

4.2 Chargaff extracted the separated bases and determined their concentrations by measuring UV absorbance. The Beer-Lambert law was used to obtain the molar concentration. Chargaff discovered the following molar ratio for bases in DNA:

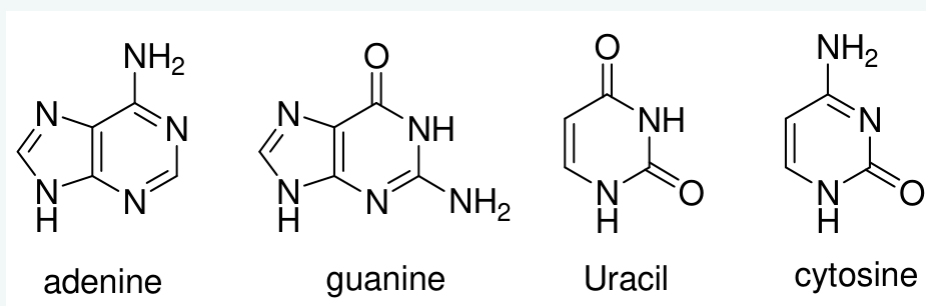
adenine to guanine = 1.43	thymine to cytosine = 1.43
adenine to thymine = 1.02	guanine to cytosine = 1.02

Chargaff's discovery suggested that the bases might exist as pairs in DNA. Watson and Crick mentioned in their celebrated 1953 paper in *Nature*: "It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material."

Draw structures of the specific pairing found in DNA. Indicate hydrogen bonds. Omit the sugar-phosphate backbone.

4.3 Mutation can occur through base pairings different from the above. Draw structures of any three alternative base pairs.

4.4 The plausibility of the formation of purine and pyrimidine bases in the prebiotic atmosphere of the Earth from HCN, NH₃, and H₂O has been demonstrated in the laboratory. Write the minimum number of HCN and H₂O molecules required for formation of the following compounds.



Official English text of the problem.

Answers

- **4.1: 11.25 hydrogen atoms per phosphorus atom;** theoretical hydrogen content **3.43% by mass.**
- **4.2: Adenine–thymine**, with **two** hydrogen bonds, and **guanine–cytosine**, with **three** hydrogen bonds. Structures and precise hydrogen-bond assignments are given below.
- **4.3:** Three examples are **guanine–thymine wobble**, **imino-adenine–cytosine**, and **guanine–adenine** pairs, each with the two hydrogen bonds specified below.
- **4.4:** Minimum numbers of molecules per molecule of base:

Base	HCN	H ₂ O
Adenine	5	0
Guanine	5	1
Uracil	4	2
Cytosine	4	1

Solution

4.1 — Hydrogen content of sodium DNA

The pictured structure is an internal sodium DNA segment with sequence 5'-AGCT-3'. Its chain-fragment SMILES, including the sugar stereochemistry and sodium counterions, is:

```
*P(=O)([O-])OC[C@H]1O[C@@H](n2cnc3c(N)ncnc32)C[C@H]1OP(=O)
([O-])OC[C@H]1O[C@@H](n2cnc3c(=O)[nH]c(N)nc32)C[C@H]1OP(=O)
([O-])OC[C@H]1O[C@@H](n2ccc(N)nc2=O)C[C@H]1OP(=O)([O-])OC[C@H]1O[C@@H]
(n2cc(C)c(=O)[nH]c2=O)C[C@H]1O*. [Na+].[Na+].[Na+].[Na+]
```

The first * represents the preceding residue's 3' oxygen, and the last represents the following phosphate phosphorus. These placeholders lie outside the counted segment.

Each sugar residue has seven carbon-bound hydrogen atoms: one, two, one, one, and two on C1', C2', C3', C4', and C5', respectively. The internal sodium phosphodiester groups contribute no additional hydrogen atoms.

Each attached base has one fewer hydrogen than its corresponding free base because its glycosidic attachment replaces an N-H hydrogen.

Attached base	Hydrogen atoms on base	Hydrogen atoms on sugar	Total
Adenine	4	7	11
Guanine	4	7	11
Cytosine	4	7	11
Thymine	5	7	12
Total	17	28	45

Thus the segment contains 45 hydrogen atoms and four phosphorus atoms:

$$\frac{N_H}{N_P} = \frac{45}{4} = 11.25.$$

The counted segment has composition C₃₉H₄₅N₁₅Na₄O₂₄P₄, consistent with the supplied formula mass.

Using $M(\text{H}) = 1.008 \text{ g mol}^{-1}$,

$$\text{Hydrogen mass percentage} = \frac{45(1.008 \text{ g mol}^{-1})}{1323.72 \text{ g mol}^{-1}} \times 100\% = 3.4267\%.$$

To three significant figures,

$$3.43\% \text{ hydrogen by mass}.$$

4.2 — Normal complementary base pairs

The ratios adenine/thymine and guanine/cytosine are both approximately unity. These suggest the complementary stoichiometries $A:T = 1 : 1$ and $G:C = 1 : 1$. The hydrogen-bond donors and acceptors of the depicted bases support these pairings.

The required covalent structures are:

Base	SMILES
Adenine (A)	<chem>Nc1ncnc2[nH]cnc12</chem>
Thymine (T)	<chem>Cc1c[nH]c(=O)[nH]c1=O</chem>
Guanine (G)	<chem>Nc1nc2[nH]cnc2c(=O)[nH]1</chem>
Cytosine (C)	<chem>Nc1cc[nH]c(=O)n1</chem>

These are free-base SMILES. In DNA, the hydrogen at N9 of a purine or N1 of a pyrimidine is replaced by the sugar attachment. Those attachment sites do not participate in the hydrogen bonds listed here.

For the requested drawings, place the paired bases approximately coplanar, with their Watson–Crick edges facing each other. Draw a dashed line from each indicated donor hydrogen to its acceptor:

Pair	Hydrogen-bond donor	Acceptor
A–T	Adenine N6–H	Thymine O4
A–T	Thymine N3–H	Adenine N1
G–C	Cytosine N4–H	Guanine O6
G–C	Guanine N1–H	Cytosine N3
G–C	Guanine N2–H	Cytosine O2

Here N6 of adenine, N4 of cytosine, and N2 of guanine are the exocyclic amino nitrogens; the numbered oxygen atoms are carbonyl oxygens.

Therefore, **A–T has two hydrogen bonds**, while **G–C has three**. The SMILES specify covalent connectivity; the table specifies the intermolecular hydrogen bonds and the arrangement required for the drawings.

4.3 — Three alternative base pairs

The following are three possible mismatched pairs.

1. Guanine–thymine wobble pair

Use the ordinary guanine and thymine structures given in 4.2. Shift the bases sideways relative to a Watson–Crick arrangement so that:

- Guanine N1–H donates a hydrogen bond to thymine O2.
- Thymine N3–H donates a hydrogen bond to guanine O6.

Draw these two dashed hydrogen bonds. Guanine O6 and thymine O2 are the acceptors.

2. Imino-adenine–cytosine pair

Use the rare neutral **imino tautomer of adenine**, N=C1[nH]cnc2[nH]cnc12, together with ordinary cytosine.

Relative to ordinary adenine, this tautomer has a hydrogen transferred from the exocyclic N6 amino group to ring N1, with the accompanying double-bond rearrangement. Consequently, N1–H is a donor and the exocyclic imino N6 is an acceptor.

Place the bases with their corresponding pairing edges facing each other and draw:

- Cytosine N4–H donating to imino-adenine N6.
- Imino-adenine N1–H donating to cytosine N3.

This gives two hydrogen bonds.

3. Guanine–adenine pair

Use the ordinary guanine and adenine structures from 4.2, with their Watson–Crick edges facing each other. Draw:

- Adenine N6–H donating to guanine O6.
- Guanine N1–H donating to adenine N1.

This gives two hydrogen bonds. Because both bases are purines, this arrangement is wider than a normal purine–pyrimidine pair and requires distortion of the local DNA geometry.

4.4 — Minimum precursor requirements

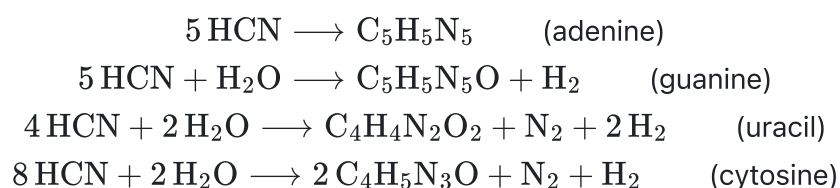
The starting substances are **hydrogen cyanide**, C#N; **ammonia**, N; and **water**, O.

Hydrogen cyanide is the only carbon source, so at least one HCN molecule is required for every carbon atom in the product. Water is the only oxygen source, so at least one H2O molecule is required for every oxygen atom. Ammonia contains neither carbon nor oxygen and cannot reduce these lower bounds.

Adenine, guanine, and cytosine have the structures listed in 4.2. **Uracil** has SMILES O=c1cc[nH]c(=O)[nH]1.

Product	Molecular formula	Minimum HCN	Minimum H ₂ O
Adenine	<chem>C5H5N5</chem>	5	0
Guanine	<chem>C5H5N5O</chem>	5	1
Uracil	<chem>C4H4N2O2</chem>	4	2
Cytosine	<chem>C4H5N3O</chem>	4	1

These minima are compatible with complete atom conservation. For example, the following **formal overall balances** achieve them:



The additional products in these formal balances are **dinitrogen**, $\text{N}\equiv\text{N}$, and **dihydrogen**, $[\text{H}][\text{H}]$. The cytosine equation produces two molecules, so its requirement per molecule is four HCN and one H_2O .

These equations establish stoichiometric consistency; they do not assert particular experimental pathways or byproducts, which the problem does not specify.

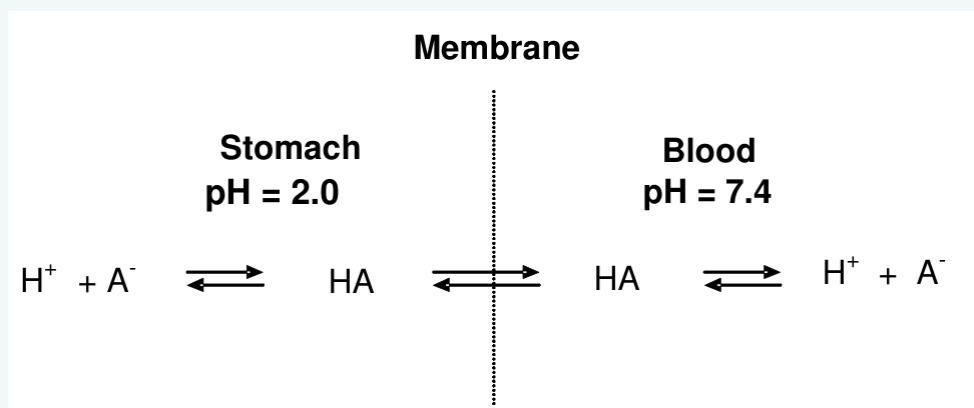
The solution was checked against the official solution.

Problem 5: Acid-Base Chemistry

5.1 Calculate $[\text{H}^+]$, $[\text{OH}^-]$, $[\text{HSO}_4^-]$, and $[\text{SO}_4^{2-}]$ in a 1.0×10^{-7} M solution of sulfuric acid ($K_w = 1.0 \times 10^{-14}$, $K_2 = 1.2 \times 10^{-2}$ at 25°C). In your work you may use mass- and charge-balance equations. Answer with two significant figures.

5.2 Calculate the volume of 0.80 M NaOH solution that should be added to a 250 cm^3 aqueous solution containing 3.48 cm^3 of concentrated phosphoric acid in order to prepare a pH 7.4 buffer. Answer with three significant figures. ($\text{H}_3\text{PO}_4(\text{aq})$, purity = 85 mass %, density = 1.69 g/cm^3 , $M_r = 98.00$) ($pK_1 = 2.15$, $pK_2 = 7.20$, $pK_3 = 12.44$).

5.3 The efficacy of a drug is greatly dependent on its ability to be absorbed into the blood stream. Acid-base chemistry plays an important role in drug absorption.



Assume that the ionic form (A^-) of a weakly acidic drug does not penetrate the membrane, whereas the neutral form (HA) freely crosses the membrane. Also assume that equilibrium is established so that the concentration of HA is the same on both sides. Calculate the ratio of the total concentration ($[\text{HA}] + [\text{A}^-]$) of aspirin (acetylsalicylic acid, $pK = 3.52$) in the blood to that in the stomach.

Official English text of the problem.

Answers

- 5.1:** $[\text{H}^+] = 2.4 \times 10^{-7}\text{ M}$; $[\text{OH}^-] = 4.1 \times 10^{-8}\text{ M}$; $[\text{HSO}_4^-] = 2.0 \times 10^{-12}\text{ M}$; $[\text{SO}_4^{2-}] = 1.0 \times 10^{-7}\text{ M}$.
- 5.2:** $1.03 \times 10^2\text{ cm}^3$ of 0.80 M sodium hydroxide solution.

- 5.3: $\frac{C_{\text{blood}}}{C_{\text{stomach}}} \approx 7.4 \times 10^3$.

Solution

5.1

The chemical species and their SMILES are:

Species	SMILES
Sulfuric acid, H_2SO_4	<chem>O=S(=O)(O)O</chem>
Hydrogen ion (proton), H^+	<chem>[H+]</chem>
Hydroxide ion, OH^-	<chem>[OH-]</chem>
Hydrogen sulfate ion, HSO_4^-	<chem>O=S(=O)(O)[O-]</chem>
Sulfate ion, SO_4^{2-}	<chem>O=S(=O)([O-])[O-]</chem>
Water, H_2O	<chem>O</chem>

The oxyanion SMILES show particular Lewis representations; resonance is not fully conveyed by the localized bond orders and charges.

The first dissociation of sulfuric acid is treated as complete:



The remaining equilibria are

$$\begin{aligned} \text{HSO}_4^- &\rightleftharpoons \text{H}^+ + \text{SO}_4^{2-}, & K_2 &= \frac{[\text{H}^+][\text{SO}_4^{2-}]}{[\text{HSO}_4^-]}, \\ \text{H}_2\text{O} &\rightleftharpoons \text{H}^+ + \text{OH}^-, & K_w &= [\text{H}^+][\text{OH}^-]. \end{aligned}$$

Because the analytical acid concentration is comparable to 10^{-7} M, water's contribution must be included.

Let $C = 1.0 \times 10^{-7}$ M and $h = [\text{H}^+]$. Sulfate mass balance gives

$$[\text{HSO}_4^-] + [\text{SO}_4^{2-}] = C,$$

and charge balance gives

$$h = [\text{OH}^-] + [\text{HSO}_4^-] + 2[\text{SO}_4^{2-}].$$

Combining mass balance with the equilibrium expressions,

$$[\text{HSO}_4^-] = \frac{Ch}{K_2 + h}, \quad [\text{SO}_4^{2-}] = \frac{CK_2}{K_2 + h}, \quad [\text{OH}^-] = \frac{K_w}{h}.$$

Thus,

$$h = \frac{K_w}{h} + C \frac{h + 2K_2}{h + K_2}.$$

Since $h \ll K_2$, an excellent approximation is

$$h = 2C + \frac{K_w}{h},$$

whose positive solution is

$$h = C + \sqrt{C^2 + K_w} \approx 2.4142 \times 10^{-7} \text{ M.}$$

Solving the full balance equation gives $h = 2.4141964 \times 10^{-7} \text{ M}$, confirming the approximation. Substitution gives

$$\begin{aligned} &= 4.14217 \times 10^{-8} \text{ M,} \\ [\text{HSO}_4^-] &= 2.01179 \times 10^{-12} \text{ M,} \\ [\text{SO}_4^{2-}] &= 9.99980 \times 10^{-8} \text{ M.} \end{aligned}$$

Therefore, to two significant figures,

$$\begin{aligned} &= 2.4 \times 10^{-7} \text{ M,} \\ [\text{OH}^-] &= 4.1 \times 10^{-8} \text{ M,} \\ [\text{HSO}_4^-] &= 2.0 \times 10^{-12} \text{ M,} \\ [\text{SO}_4^{2-}] &= 1.0 \times 10^{-7} \text{ M.} \end{aligned}$$

5.2

The additional chemical species are:

Species	SMILES
Sodium hydroxide, NaOH	[Na+] . [OH-]
Phosphoric acid, H ₃ PO ₄	O=P(O)(O)O
Dihydrogen phosphate ion, H ₂ PO ₄ ⁻	O=P(O)(O)[O-]
Hydrogen phosphate ion, HPO ₄ ²⁻	O=P(O)([O-])[O-]
Phosphate ion, PO ₄ ³⁻	O=P([O-])([O-])[O-]

The amount of phosphoric acid is

$$n = \frac{(3.48 \text{ cm}^3)(1.69 \text{ g cm}^{-3})(0.85)}{98.00 \text{ g mol}^{-1}} = 0.0510104 \text{ mol.}$$

At pH 7.4, the principal phosphate species are H₂PO₄⁻ and HPO₄²⁻, because this pH is close to $pK_2 = 7.20$. The other forms are negligible:

$$\begin{aligned} \frac{[\text{H}_3\text{PO}_4]}{[\text{H}_2\text{PO}_4^-]} &= 10^{pK_1 - \text{pH}} = 10^{-5.25}, \\ \frac{[\text{PO}_4^{3-}]}{[\text{HPO}_4^{2-}]} &= 10^{\text{pH} - pK_3} = 10^{-5.04}. \end{aligned}$$

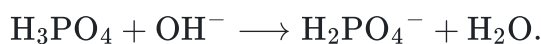
The relevant buffer equilibrium is



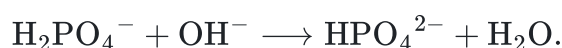
Consequently,

$$\frac{[\text{HPO}_4^{2-}]}{[\text{H}_2\text{PO}_4^-]} = 10^{\text{pH} - pK_2} = 10^{7.40 - 7.20} = 1.584893.$$

Adding hydroxide first neutralizes one proton from each phosphoric acid molecule:



Further hydroxide converts part of the dihydrogen phosphate into hydrogen phosphate:



Let x mol undergo this second neutralization. The final amounts are approximately x mol of HPO_4^{2-} and $n - x$ mol of H_2PO_4^- . Their common final volume cancels:

$$\frac{x}{n - x} = 1.584893.$$

Therefore,

$$x = \frac{1.584893}{1 + 1.584893} n = 0.0312764 \text{ mol.}$$

The total amount of hydroxide required is

$$n_{\text{OH}^-} = n + x = 0.0822868 \text{ mol,}$$

so

$$V_{\text{NaOH}} = \frac{0.0822868 \text{ mol}}{0.80 \text{ mol L}^{-1}} = 0.102858 \text{ L} = 102.858 \text{ cm}^3.$$

Thus, to the requested three significant figures,

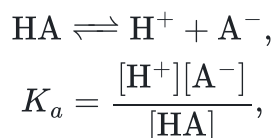
$$\boxed{V_{\text{NaOH}} = 1.03 \times 10^2 \text{ cm}^3}.$$

The initial 250 cm^3 affects the final concentrations but cancels from the buffer ratio. Including all phosphate species and the residual free hydrogen and hydroxide ions does not change the rounded answer.

5.3

Here HA is aspirin (acetylsalicylic acid), $\text{CC}(=\text{O})\text{Oc1ccccc1C}(=\text{O})\text{O}$, and A^- is the acetylsalicylate ion, $\text{CC}(=\text{O})\text{Oc1ccccc1C}(=\text{O})[\text{O}^-]$. Ionization removes the carboxylic acid proton; the ester group remains intact.

For the equilibrium



so

$$\frac{[\text{A}^-]}{[\text{HA}]} = 10^{\text{pH} - \text{p}K_a}.$$

The total drug concentration in either compartment is therefore

$$C = [\text{HA}] + [\text{A}^-] = [\text{HA}] (1 + 10^{\text{pH} - \text{p}K_a}).$$

At membrane equilibrium,

$$[\text{HA}]_{\text{blood}} = [\text{HA}]_{\text{stomach}}.$$

Using the blood pH of 7.4 and stomach pH of 2.0 shown in the figure,

$$\begin{aligned} \frac{C_{\text{blood}}}{C_{\text{stomach}}} &= \frac{1 + 10^{7.4 - 3.52}}{1 + 10^{2.0 - 3.52}} \\ &= \frac{1 + 7585.7758}{1 + 0.0301995} \\ &= 7364.375 \dots \end{aligned}$$

Hence,

$$\frac{C_{\text{blood}}}{C_{\text{stomach}}} \approx 7.4 \times 10^3.$$

The higher blood pH favors the ionized form, which cannot cross the membrane. This produces a much larger total drug concentration in blood even though the neutral-form concentrations are equal.

The solution was checked against the official solution.

Problem 6: Electrochemistry

Water is a very stable molecule, abundant on earth and essential for life. As such, water was long thought to be a chemical element. However, soon after the invention of a voltaic cell in 1800, Nicholson and Carlyle decomposed water into hydrogen and oxygen by electrolysis.

6.1 Water can be thought of as hydrogen oxidized by oxygen. Thus, hydrogen can be recovered by reduction of water, using an aqueous solution of sodium sulfate, at a platinum electrode connected to the negative terminal of a battery. The solution near the electrode becomes basic. Write a balanced half-reaction for the reduction of water.

6.2 Water can also be thought of as oxygen reduced by hydrogen. Thus, oxygen can be recovered by oxidation of water at the Pt electrode connected to the positive terminal. Write a balanced half-reaction for the oxidation of water.

6.3 When copper is used at both electrodes, gas is generated only at one electrode during the initial stage of electrolysis. Write the half-reaction at the electrode that does not generate gas.

Another species in solution that can be reduced is sodium ion. The reduction of sodium ion to metallic sodium does not occur in aqueous solution because water is reduced first. However, as Humphrey Davy discovered in 1807, sodium can be made by electrolysis of fused sodium chloride.

6.4 Based on these observations, connect the half-reactions with the standard reduction potential (in volts).

Reduction of copper ion (Cu^{2+})	+0.340
Reduction of oxygen	-2.710
Reduction of water	-0.830
Reduction of sodium ion (Na^+)	0.000
Reduction of hydrogen ion	+1.230

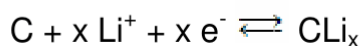
The electrode potential is affected by other reactions taking place around the electrode. The potential of the Cu^{2+}/Cu electrode in a 0.100 M Cu^{2+} solution changes as $\text{Cu}(\text{OH})_2$ precipitates. Answer with 3 significant figures for the following problems. The temperature is 25 °C. Note that $K_w = 1.00 \times 10^{-14}$ at 25 °C.

6.5 Precipitation of $\text{Cu}(\text{OH})_2$ begins at pH = 4.84. Determine the solubility product of $\text{Cu}(\text{OH})_2$.

6.6 Calculate the standard reduction potential for $\text{Cu}(\text{OH})_2(\text{s}) + 2\text{e}^- \longrightarrow \text{Cu}(\text{s}) + 2\text{OH}^-$.

6.7 Calculate the electrode potential at $\text{pH} = 1.00$.

Lithium cobalt oxide and specialty carbon are active ingredients for the positive and negative electrodes, respectively, of a rechargeable lithium battery. During the charge/recharge cycles, the following reversible half-reactions occur.



The total amount of energy a battery can store, is rated in mAh. A battery rated at 1500 mAh can power a device drawing 100 milliamps for 15 hours.

6.8 Graphite has lithium intercalation sites between its layers. Assuming a maximum 6 : 1 carbon-to-lithium intercalation stoichiometry, calculate the theoretical charge capacity of 1.00 gram of graphite to intercalate lithium. Answer in mAh/g with 3 significant figures.

Official English text of the problem.

Answers

- **6.1:** $2 \text{H}_2\text{O}(\text{l}) + 2 \text{e}^- \longrightarrow \text{H}_2(\text{g}) + 2 \text{OH}^-(\text{aq})$.
- **6.2:** $2 \text{H}_2\text{O}(\text{l}) \longrightarrow \text{O}_2(\text{g}) + 4 \text{H}^+(\text{aq}) + 4 \text{e}^-$.
- **6.3:** $\text{Cu}(\text{s}) \longrightarrow \text{Cu}^{2+}(\text{aq}) + 2 \text{e}^-$.
- **6.4:** Copper ion: +0.340 V; oxygen: +1.230 V; water: -0.830 V; sodium ion: -2.710 V; hydrogen ion: 0.000 V.
- **6.5:** $K_{\text{sp}} = 4.79 \times 10^{-20}$.
- **6.6:** $E^\circ = -0.231 \text{ V}$.
- **6.7:** $E = +0.310 \text{ V}$.
- **6.8:** 372 mAh g^{-1} .

All electrode potentials are relative to the standard hydrogen electrode.

Solution

The molecular and ionic species used below have the following names and SMILES:

Species	Name	SMILES
H_2O	Water	O
H_2	Hydrogen	[H][H]
O_2	Oxygen	O=O
H^+	Hydrogen ion, or proton	[H+]
OH^-	Hydroxide ion	[OH-]
Cu^{2+}	Copper(II) ion	[Cu+2]
Na^+	Sodium ion	[Na+]

Species	Name	SMILES
Li^+	Lithium ion	[Li+]

Copper(II) hydroxide, $\text{Cu}(\text{OH})_2$, can be represented compositionally as $[\text{Cu}+2] \cdot [\text{OH}-] \cdot [\text{OH}-]$. This specifies its ionic formula but does not describe its solid-state coordination or crystal structure. Metals, graphite, and lithium-intercalated graphite are extended solids without finite molecular SMILES. The oxygen SMILES specifies connectivity but does not encode its triplet ground state.

For the calculations, use the usual ideal-solution approximation, $a_i \simeq [i]/c^\circ$, where $c^\circ = 1 \text{ mol L}^{-1}$, and unit activities for pure solids and liquid water. Standard constants are

$$R = 8.31446 \text{ J mol}^{-1} \text{ K}^{-1}, \quad F = 96485.3 \text{ C mol}^{-1}, \quad M_{\text{C}} = 12.01 \text{ g mol}^{-1}.$$

At $T = 298.15 \text{ K}$,

$$\frac{RT \ln 10}{F} = 0.0591593 \text{ V}.$$

6.1 — Reduction of water

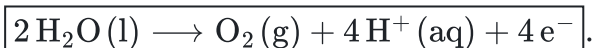
The negative electrode supplies electrons and is the cathode. Hydrogen in water is reduced from oxidation state +1 to 0:



Both atoms and charge are balanced. The production of hydroxide ions explains why the solution near this electrode becomes basic.

6.2 — Oxidation of water

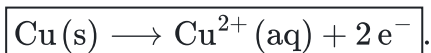
The positive electrode removes electrons and is the anode. Oxygen in water is oxidized from oxidation state −2 to 0:



The production of hydrogen ions makes the solution near this electrode acidic.

6.3 — Copper electrodes

At the copper anode, copper itself is oxidized instead of water:



Thus, the anode dissolves without generating gas. Initially, before copper(II) ions reach the cathode in appreciable amounts, water reduction there produces hydrogen as in part 6.1.

6.4 — Identification of the standard reduction potentials

The correct connections, with the corresponding balanced reduction half-reactions, are:

Reduction	Half-reaction	E°/V
Copper ion	$\text{Cu}^{2+}(\text{aq}) + 2 \text{e}^- \longrightarrow \text{Cu}(\text{s})$	+0.340
Oxygen	$\text{O}_2(\text{g}) + 4 \text{H}^+(\text{aq}) + 4 \text{e}^- \longrightarrow 2 \text{H}_2\text{O}(\text{l})$	+1.230
Water	$2 \text{H}_2\text{O}(\text{l}) + 2 \text{e}^- \longrightarrow \text{H}_2(\text{g}) + 2 \text{OH}^-(\text{aq})$	−0.830
Sodium ion	$\text{Na}^+(\text{aq}) + \text{e}^- \longrightarrow \text{Na}(\text{s})$	−2.710
Hydrogen ion	$2 \text{H}^+(\text{aq}) + 2 \text{e}^- \longrightarrow \text{H}_2(\text{g})$	0.000

The hydrogen-ion reduction potential is zero by definition of the standard hydrogen electrode.

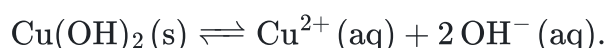
Water is reduced more readily than sodium ions, so its reduction potential is more positive. The two negative values therefore belong to water, -0.830 V , and sodium ions, -2.710 V , respectively.

Copper dissolves at the anode in preference to oxygen evolution. This identifies copper oxidation as the easier of those two oxidations and assigns the lower remaining reduction potential to the copper couple: $+0.340\text{ V}$. Oxygen reduction receives $+1.230\text{ V}$.

The oxygen value refers to the acidic half-reaction shown in the table; the water-reduction value refers to the half-reaction producing hydroxide ions.

6.5 — Solubility product of copper(II) hydroxide

The dissolution equilibrium is



At the onset of precipitation, the copper(II) concentration is still 0.100 mol L^{-1} . Since $K_w = 1.00 \times 10^{-14}$,

$$\text{pOH} = 14.00 - 4.84 = 9.16,$$

so

$$[\text{OH}^{-}] = 10^{-9.16}\text{ mol L}^{-1} = 6.9183 \times 10^{-10}\text{ mol L}^{-1}.$$

Hence,

$$\begin{aligned} K_{\text{sp}} &= a(\text{Cu}^{2+}) a(\text{OH}^{-})^2 \\ &= (0.100)(6.9183 \times 10^{-10})^2 \\ &= 4.7863 \times 10^{-20}. \end{aligned}$$

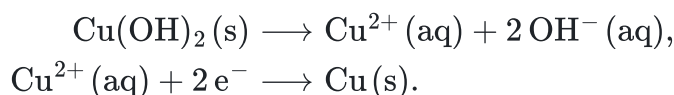
Therefore,

$$\boxed{K_{\text{sp}} = 4.79 \times 10^{-20}}.$$

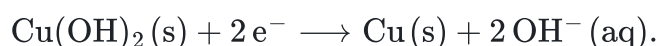
This is the dimensionless equilibrium constant using the stated standard concentration; the corresponding concentration product has units $\text{mol}^3\text{ L}^{-3}$.

6.6 — Standard reduction potential of copper(II) hydroxide

Add the dissolution equilibrium to copper(II) reduction:



The sum is the required half-reaction:



Standard Gibbs energies are additive:

$$\Delta G_{\text{diss}}^{\circ} = -RT \ln K_{\text{sp}}, \quad \Delta G_{\text{Cu}}^{\circ} = -2FE_{\text{Cu}^{2+}/\text{Cu}}^{\circ}.$$

Thus,

$$-2FE^{\circ} = -RT \ln K_{\text{sp}} - 2FE_{\text{Cu}^{2+}/\text{Cu}}^{\circ},$$

giving

$$E^{\circ} = E_{\text{Cu}^{2+}/\text{Cu}}^{\circ} + \frac{RT}{2F} \ln K_{\text{sp}}.$$

Here $\log_{10} K_{\text{sp}} = -19.32$, so

$$\begin{aligned} E^{\circ} &= 0.340 + \frac{0.0591593}{2}(-19.32) \\ &= -0.231479 \text{ V}. \end{aligned}$$

To three significant figures,

$$\boxed{E^{\circ} = -0.231 \text{ V}}.$$

6.7 — Electrode potential at pH 1.00

At pH = 1.00,

$$[\text{H}^{+}] = 0.100 \text{ mol L}^{-1}, \quad [\text{OH}^{-}] = 1.00 \times 10^{-13} \text{ mol L}^{-1}.$$

The ionic activity product is

$$Q_{\text{sp}} = (0.100)(1.00 \times 10^{-13})^2 = 1.00 \times 10^{-27} < K_{\text{sp}}.$$

Consequently, copper(II) hydroxide does not precipitate, and the copper(II) concentration remains 0.100 mol L^{-1} . Use the Nernst equation for

$$\begin{aligned} \text{Cu}^{2+}(\text{aq}) + 2 \text{e}^{-} &\longrightarrow \text{Cu}(\text{s}) : \\ E &= E_{\text{Cu}^{2+}/\text{Cu}}^{\circ} + \frac{RT}{2F} \ln a(\text{Cu}^{2+}) \\ &= 0.340 + \frac{0.0591593}{2} \log_{10}(0.100) \\ &= 0.310420 \text{ V}. \end{aligned}$$

Therefore,

$$\boxed{E = +0.310 \text{ V}}.$$

6.8 — Theoretical charge capacity of graphite

At the maximum carbon-to-lithium ratio of 6 : 1, intercalation can be written as



Each intercalated lithium ion requires one electron. Thus, six moles of carbon correspond to one mole of transferred electrons. Lithium occupies sites between the graphite layers.

For 1.00 g of graphite,

$$n_e = \frac{1.00 \text{ g}}{6(12.01 \text{ g mol}^{-1})} = 0.0138773 \text{ mol}.$$

The charge is

$$Q = n_e F = (0.0138773 \text{ mol})(96485.3 \text{ C mol}^{-1}) = 1338.96 \text{ C}.$$

Since

$$1 \text{ mAh} = (10^{-3} \text{ A})(3600 \text{ s}) = 3.6 \text{ C},$$

the specific capacity is

$$\frac{Q}{m} = \frac{1338.96}{3.6(1.00)} = 371.933 \text{ mAh g}^{-1}.$$

Therefore,

$$\frac{Q}{m} = 372 \text{ mAh g}^{-1}.$$

Although the statement calls the rating an amount of energy, mAh measures electric charge. Calculating stored energy would also require the battery voltage.

The solution was checked against the official solution.

Problem 7: Hydrogen Economy

Hydrogen is more energy-dense than carbon, by mass. Thus, historically there has been a move toward fuel with higher hydrogen content: coal → oil → natural gas → hydrogen. Cost-effective production and safe storage of hydrogen are two major hurdles to the successful inauguration of a hydrogen economy.

7.1 Consider hydrogen in a cylinder of 80 MPa at 25 °C. Using the ideal gas law, estimate the density of hydrogen in the cylinder in kg m^{-3} .

7.2 Calculate the ratio between heat generated when hydrogen is burned and heat generated when the same weight of carbon is burned. The difference comes to a large extent from the fact that the most abundant isotope of hydrogen has no neutron and hydrogen has no inner electron shell. $\Delta H_f^\circ[\text{H}_2\text{O}(\text{l})] = -286 \text{ kJ/mol}$, $\Delta H_f^\circ[\text{CO}_2(\text{g})] = -394 \text{ kJ/mol}$.

7.3 Calculate the theoretical maximum work produced by the combustion of 1 kg hydrogen (a) from the electric motor using hydrogen fuel cell and (b) from the heat engine working between 25 °C and 300 °C. The efficiency (work done/heat absorbed) of an ideal heat engine working between T_{cold} and T_{hot} is given by $[1 - T_{\text{cold}}/T_{\text{hot}}]$.

$$S_{298}^\circ[\text{H}_2(\text{g})] = 131 \text{ J mol}^{-1} \text{ K}^{-1}$$

$$S_{298}^\circ[\text{O}_2(\text{g})] = 205 \text{ J mol}^{-1} \text{ K}^{-1}$$

$$S_{298}^\circ[\text{H}_2\text{O}(\text{l})] = 70 \text{ J mol}^{-1} \text{ K}^{-1}$$

If the fuel cell is working at 1 W and the standard potential difference, how long will the electric motor run at what current?

Official English text of the problem.

Answers

- 7.1:** $\rho \approx 65.1 \text{ kg m}^{-3}$, using the ideal gas law.
- 7.2:** $q_{\text{hydrogen}}/q_{\text{carbon}} \approx 4.32$ for equal fuel masses.
- 7.3(a):** $W_{\text{max}} \approx 1.18 \times 10^8 \text{ J} = 118 \text{ MJ}$.
- 7.3(b):** $W_{\text{max}} \approx 6.81 \times 10^7 \text{ J} = 68.1 \text{ MJ}$.

- **7.3, operation at 1 W:** $t \approx 1.18 \times 10^8 \text{ s} \approx 3.73 \text{ years}$, at $I \approx 0.813 \text{ A}$, with standard cell voltage $E^\circ \approx 1.23 \text{ V}$.

These values use $M(\text{H}_2) = 2.016 \text{ g mol}^{-1}$ and $M(\text{C}) = 12.01 \text{ g mol}^{-1}$.

Solution

Use

$$R = 8.314 \text{ J mol}^{-1} \text{ K}^{-1}, \quad F = 96485 \text{ C mol}^{-1}, \quad T = 298.15 \text{ K}.$$

The molecular species involved are molecular hydrogen, H_2 , $[\text{H}][\text{H}]$; molecular oxygen, O_2 , $\text{O}=\text{O}$; water, H_2O , O ; and carbon dioxide, CO_2 , $\text{O}=\text{C}=\text{O}$. Elemental carbon is taken as graphite, whose extended lattice has no single molecular SMILES.

7.1 — Density of compressed hydrogen

From the ideal gas law,

$$PV = nRT = \frac{m}{M}RT,$$

so

$$\rho = \frac{m}{V} = \frac{PM}{RT}.$$

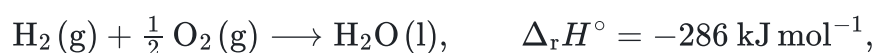
Substituting in SI units,

$$\rho = \frac{(80 \times 10^6 \text{ Pa})(2.016 \times 10^{-3} \text{ kg mol}^{-1})}{(8.314 \text{ Pa m}^3 \text{ mol}^{-1} \text{ K}^{-1})(298.15 \text{ K})} = \boxed{65.1 \text{ kg m}^{-3}}.$$

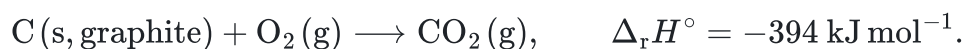
This is the ideal-gas estimate requested.

7.2 — Heat released by equal masses

The balanced combustion reactions are



and



The reaction enthalpies equal the given product formation enthalpies because each reactant is an element in its standard state.

The positive magnitudes of heat released per gram are

$$q_{\text{hydrogen}} = \frac{286}{2.016} = 141.9 \text{ kJ g}^{-1},$$

$$q_{\text{carbon}} = \frac{394}{12.01} = 32.81 \text{ kJ g}^{-1}.$$

Thus, for equal masses,

$$\boxed{\frac{q_{\text{hydrogen}}}{q_{\text{carbon}}} = \frac{286/2.016}{394/12.01} = 4.32}.$$

7.3(a) — Maximum work from the fuel cell and electric motor

At constant temperature and pressure, the maximum electrical work delivered by a reversible fuel cell is the decrease in Gibbs energy:

$$W_{\text{electrical,max}} = -n\Delta_r G^\circ.$$

An ideal electric motor converts all this electrical work into mechanical work.

For the hydrogen combustion reaction,

$$\begin{aligned}\Delta_r S^\circ &= S^\circ(\text{H}_2\text{O}(\text{l})) - S^\circ(\text{H}_2(\text{g})) - \frac{1}{2}S^\circ(\text{O}_2(\text{g})) \\ &= 70 - 131 - \frac{1}{2}(205) \\ &= -163.5 \text{ J mol}^{-1} \text{ K}^{-1}.\end{aligned}$$

Using the supplied 298 K entropy values at 298.15 K,

$$\begin{aligned}\Delta_r G^\circ &= \Delta_r H^\circ - T\Delta_r S^\circ \\ &= -286 - (298.15)(-0.1635) \\ &= -237.252 \text{ kJ mol}^{-1}.\end{aligned}$$

The amount of hydrogen in 1 kg is

$$n = \frac{1000 \text{ g}}{2.016 \text{ g mol}^{-1}} = 496.03 \text{ mol}.$$

Therefore,

$$W_{\text{max}} = (496.03)(237.252) \text{ kJ} = \boxed{1.18 \times 10^8 \text{ J}}.$$

7.3(b) — Maximum work from the heat engine

The temperatures must be expressed in kelvin:

$$T_{\text{cold}} = 298.15 \text{ K}, \quad T_{\text{hot}} = 573.15 \text{ K}.$$

The Carnot efficiency is

$$\eta_{\text{max}} = 1 - \frac{298.15}{573.15} = 0.4798.$$

Using the supplied combustion enthalpy, the heat available from 1 kg of hydrogen is

$$Q = n|\Delta_r H^\circ| = (496.03)(286) = 1.41865 \times 10^5 \text{ kJ}.$$

In the idealized heat-engine model specified by the problem,

$$W_{\text{max}} = \eta_{\text{max}}Q = (0.4798)(1.41865 \times 10^8 \text{ J}) = \boxed{6.81 \times 10^7 \text{ J}}.$$

7.3 — Running time and current at 1 W

Each hydrogen atom changes oxidation state from 0 in H_2 to +1 in water. Consequently, combustion of one molecule of H_2 transfers two electrons through the external circuit.

The standard cell voltage therefore follows from

$$\begin{aligned}\Delta_r G^\circ &= -2FE^\circ : \\ E^\circ &= \frac{237252 \text{ J mol}^{-1}}{2(96485 \text{ C mol}^{-1})} = 1.2295 \text{ V}.\end{aligned}$$

Since electrical power is $P = E^\circ I$,

$$I = \frac{1 \text{ W}}{1.2295 \text{ V}} = \boxed{0.813 \text{ A}}.$$

At a constant power of $1 \text{ W} = 1 \text{ J s}^{-1}$, the maximum running time is

$$t = \frac{W_{\text{electrical,max}}}{P} = \frac{1.17685 \times 10^8 \text{ J}}{1 \text{ J s}^{-1}} = \boxed{1.18 \times 10^8 \text{ s}}.$$

Using 365.25 days per year,

$$\boxed{t \approx 3.73 \text{ years}}.$$

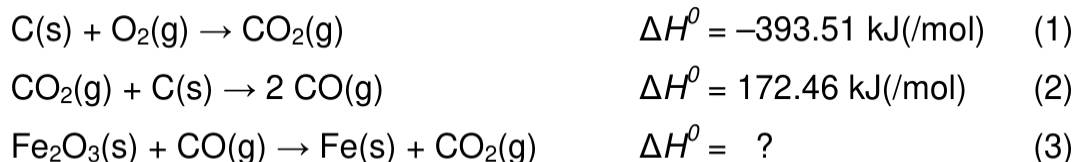
If rounded molar masses $M(\text{H}_2) = 2.00$ and $M(\text{C}) = 12.0 \text{ g mol}^{-1}$ are used instead, the corresponding results are 64.5 kg m^{-3} , 4.36 , 119 MJ , 68.6 MJ , and 3.76 years. The voltage and current are unchanged.

The solution was checked against the official solution.

Problem 8: Chemistry of Iron Oxides

The nucleus of iron is the most stable among all elements and, therefore, iron accumulates at the core of massive red giant stars where nucleosynthesis of many elements essential for life (such as C, N, O, P, S, etc.) takes place. As a result, among heavy elements iron is quite abundant in the universe. Iron is also abundant on Earth.

Development of a technology for reducing iron oxide to iron was a key step in human civilization. Key reactions taking place in the blast furnace are summarized below.



8.1 Indicate the reducing agent in each reaction.

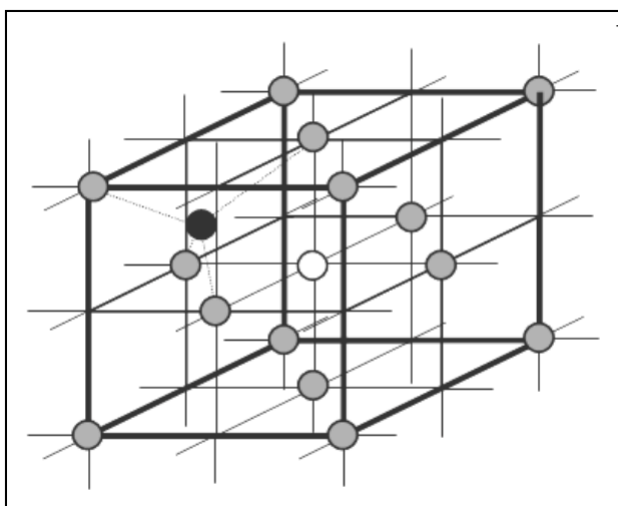
8.2 Balance reaction (3) and calculate the equilibrium constant of reaction (3) at 1200°C .

$$\Delta H_f^\circ(\text{Fe}_2\text{O}_3(\text{s})) = -824.2 \text{ kJ mol}^{-1},$$

$$S^\circ (\text{J mol}^{-1} \text{ K}^{-1}): \text{Fe(s)} = 27.28, \text{Fe}_2\text{O}_3(\text{s}) = 87.40, \text{C(s)} = 5.74, \text{CO(g)} = 197.674, \text{CO}_2(\text{g}) = 213.74$$



In the manufacture of celadon pottery, Fe_2O_3 is partially reduced in a charcoal kiln to mixed oxides of Fe_3O_4 and FeO . The amount of the different oxides seems to be related to the “mystic” color of celadon ceramics. Fe_3O_4 (magnetite) itself is a mixed oxide containing Fe^{2+} and Fe^{3+} ions and belongs to a group of compounds with a general formula of AB_2O_4 . The oxide ions form a face-centered cubic array. The figure shows the array of oxygens (gray circles) and representative sites for divalent A and trivalent B cations. The dark circle represents a tetrahedral site and the white circle an octahedral site.



8.3 How many available octahedral sites for iron ions are there in one AB_2O_4 unit? Certain sites are shared by neighbouring units.

AB_2O_4 can adopt a normal- or an inverse-spinel structure. In normal-spinel structure, two B ions occupy two of the octahedral sites and one A occupies one of the tetrahedral sites. In an inverse-spinel structure, one of the two B ions occupies a tetrahedral site. The other B ion and the one A ion occupy octahedral sites.

8.4 What percentage of available tetrahedral sites is occupied by either Fe^{2+} or Fe^{3+} ion in Fe_3O_4 ?

8.5 Fe_3O_4 has an inverse-spinel structure. Draw the crystal field splitting pattern of Fe^{2+} and fill out the electrons. The electron pairing energy is greater than the octahedral field splitting.

Official English text of the problem.

Answers

- **8.1:** (1) Carbon, $\text{C}(\text{s})$; (2) carbon, $\text{C}(\text{s})$; (3) carbon monoxide, CO , $[\text{C}^-]^\#[\text{O}^+]$.
- **8.2:** $\text{Fe}_2\text{O}_3(\text{s}) + 3\text{CO}(\text{g}) \longrightarrow 2\text{Fe}(\text{s}) + 3\text{CO}_2(\text{g})$. At 1200°C , $[K \approx 47.9]$, dimensionless, using the supplied thermodynamic data without temperature corrections.
- **8.3:** $[4]$ available octahedral sites per AB_2O_4 formula unit.
- **8.4:** $[12.5\%]$ of the available tetrahedral sites are occupied.

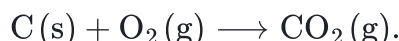
- **8.5:** Iron(II), Fe^{2+} , $[\text{Fe}+2]$, is octahedral and high spin: $t_{2g}^4 e_g^2$. The lower three orbitals contain one pair and two single electrons; the upper two each contain one electron. There are **four unpaired electrons**.

Solution

8.1 — Reducing agents

The reducing agent is the species that is oxidized.

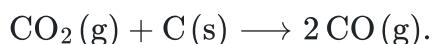
1. Reaction (1) is



Carbon changes from oxidation state 0 to +4, while oxygen changes from 0 to −2. Thus **carbon is the reducing agent**.

The molecular species are dioxygen, O_2 , $\text{O}=\text{O}$, and carbon dioxide, CO_2 , $\text{O}=\text{C}=\text{O}$.

2. Reaction (2) is



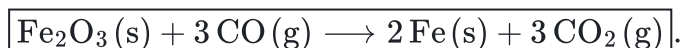
The carbon initially present as $\text{C}(\text{s})$ changes from 0 to +2. The carbon initially present in carbon dioxide changes from +4 to +2. Thus **solid carbon is the reducing agent**.

The product is carbon monoxide, CO , $[\text{C}-]\#[\text{O}+]$.

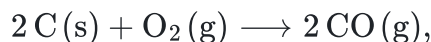
3. In reaction (3), carbon in carbon monoxide changes from +2 to +4, while iron in iron(III) oxide changes from +3 to 0. Thus **carbon monoxide is the reducing agent**.

8.2 — Balanced equation and equilibrium constant

Two iron atoms must be produced per formula unit of iron(III) oxide. Its three oxygen atoms convert three carbon monoxide molecules into carbon dioxide:



First obtain the standard formation enthalpy of carbon monoxide. Adding reactions (1) and (2) gives



with enthalpy

$$-393.51 + 172.46 = -221.05 \text{ kJ mol}^{-1}.$$

Therefore,

$$\Delta_f H^\circ(\text{CO}(\text{g})) = \frac{-221.05}{2} = -110.525 \text{ kJ mol}^{-1}.$$

Reaction (1) also gives

$$\Delta_f H^\circ(\text{CO}_2(\text{g})) = -393.51 \text{ kJ mol}^{-1}.$$

Using zero standard formation enthalpy for elemental iron,

$$\begin{aligned}\Delta_r H^\circ &= [2(0) + 3(-393.51)] - [-824.2 + 3(-110.525)] \\ &= -24.755 \text{ kJ mol}^{-1} \approx -24.8 \text{ kJ mol}^{-1}.\end{aligned}$$

The standard reaction entropy is

$$\begin{aligned}\Delta_r S^\circ &= [2S^\circ(\text{Fe(s)}) + 3S^\circ(\text{CO}_2(\text{g}))] \\ &\quad - [S^\circ(\text{Fe}_2\text{O}_3(\text{s})) + 3S^\circ(\text{CO}(\text{g}))] \\ &= 2(27.28) + 3(213.74) - 87.40 - 3(197.674) \\ &= 15.358 \text{ J mol}^{-1} \text{ K}^{-1}.\end{aligned}$$

No heat capacities or phase-transition data are supplied, so use these enthalpy and entropy values without temperature corrections. At

$$T = 1200 + 273.15 = 1473.15 \text{ K},$$

the standard Gibbs energy change is

$$\begin{aligned}\Delta_r G^\circ &= \Delta_r H^\circ - T\Delta_r S^\circ \\ &= -24.755 - (1473.15)(0.015358) \\ &= -47.3796 \text{ kJ mol}^{-1}.\end{aligned}$$

Since

$$\Delta_r G^\circ = -RT \ln K,$$

using $R = 8.314 \text{ J mol}^{-1} \text{ K}^{-1}$,

$$\ln K = \frac{47379.6}{(8.314)(1473.15)} \approx 3.868,$$

and hence

$$\boxed{K = e^{3.868} \approx 47.9}.$$

For pure solid phases and ideal gases, the dimensionless equilibrium constant is

$$K = \frac{(p_{\text{CO}_2}/p^\circ)^3}{(p_{\text{CO}}/p^\circ)^3} = \left(\frac{p_{\text{CO}_2}}{p_{\text{CO}}} \right)^3.$$

8.3 — Number of available octahedral sites

The oxide ion is O^{2-} , [O-2]. Its SMILES specifies the individual ion; the fcc arrangement is a property of the extended crystal.

A conventional cell of the fcc oxygen array contains

$$N_{\text{O}} = 8 \left(\frac{1}{8} \right) + 6 \left(\frac{1}{2} \right) = 4$$

oxide ions. Thus its oxygen content corresponds to one AB_2O_4 formula unit.

Octahedral sites occur at the body center and at the twelve edge centers. The body-center site belongs entirely to the cell, while each edge-center site is shared by four cells:

$$N_{\text{oct}} = 1 + 12 \left(\frac{1}{4} \right) = \boxed{4}.$$

These are the **available** octahedral sites; only two are occupied per formula unit in either spinel arrangement described.

8.4 — Fraction of tetrahedral sites occupied

The fcc oxygen cell has eight tetrahedral sites, all inside the cell, at positions whose fractional coordinates are independently $1/4$ or $3/4$. Therefore, there are eight available tetrahedral sites per four oxide ions, or per AB_2O_4 formula unit.

Exactly one tetrahedral site is occupied per formula unit:

- In normal spinel, its occupant is iron(II), Fe^{2+} , [Fe+2].
- In inverse spinel, its occupant is iron(III), Fe^{3+} , [Fe+3].

Consequently, the percentage is the same for either arrangement:

$$\frac{1 \text{ occupied tetrahedral site}}{8 \text{ available tetrahedral sites}} \times 100\% = 12.5\%.$$

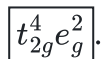
8.5 — Crystal-field splitting and electron occupation

In inverse-spinel magnetite, the divalent iron ion occupies an **octahedral site**. Iron(II), Fe^{2+} , has the configuration $[\text{Ar}] 3d^6$.

An octahedral crystal field splits the five d orbitals into:

- Three lower-energy t_{2g} orbitals: d_{xy} , d_{xz} , and d_{yz} , each at $-\frac{2}{5}\Delta_o$ relative to the barycenter.
- Two higher-energy e_g orbitals: d_{z^2} and $d_{x^2-y^2}$, each at $+\frac{3}{5}\Delta_o$.

Because the pairing energy exceeds Δ_o , the configuration is **high spin**. The first five electrons singly occupy the five orbitals with parallel spins; the sixth pairs in a lower t_{2g} orbital:



The requested drawing should have energy increasing upward, with three equal-height orbital lines below two equal-height orbital lines, separated by Δ_o . Put an up-arrow and a down-arrow in one lower orbital, and one up-arrow in each of the other four orbitals. Any of the three lower orbitals may contain the pair.

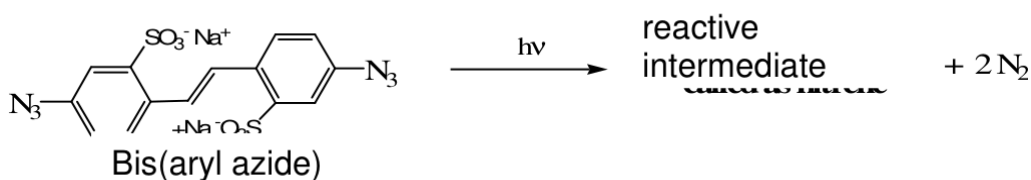
This gives **one electron pair and four unpaired electrons**. The ionic SMILES [Fe+2] does not encode the octahedral coordination geometry or these orbital occupations.

The solution was checked against the official solution.

Problem 9: Photolithographic process

Photolithography is a process used in semiconductor device fabrication to transfer a pattern from a photomask to the surface of a substrate. In a typical photolithography process, light is projected, through a mask that defines a particular circuitry, onto a silicon wafer coated with a thin layer of photoresist.

The earliest photoresists were based on the photochemistry that generates a reactive intermediates from bis(aryl azide). Patterning becomes possible through the cross-linking reaction of the nitrenes generated from the azides.

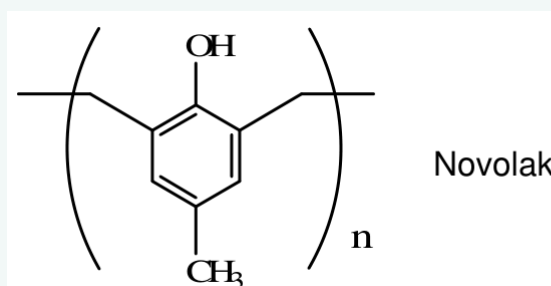


9.1 Draw two possible Lewis structures of CH_3-N_3 , the simplest compound having the same active functional group of bis(aryl azide). Assign formal charges.

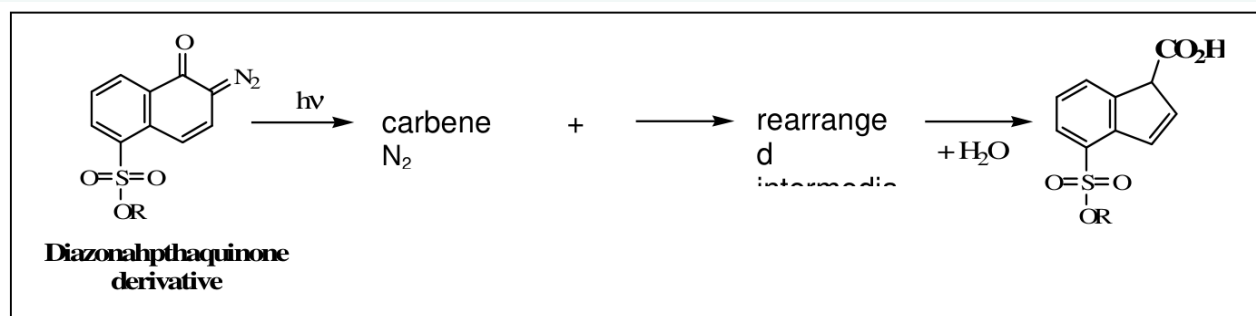
9.2 Draw the Lewis structure of nitrene expected from CH_3-N_3 .

9.3 Draw the structures for two possible products, when this nitrene from CH_3-N_3 reacts with ethylene gas (CH_2CH_2).

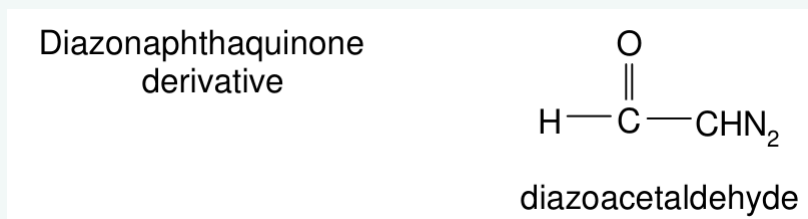
Photoresists consisting of Novolak polymers, utilizes acid to change their solubility. The acid component can be produced photochemically from diazonaphthaquinone. In fact, "Novolaks" have been the representative "positive" photoresists of the modern microelectronic revolution.



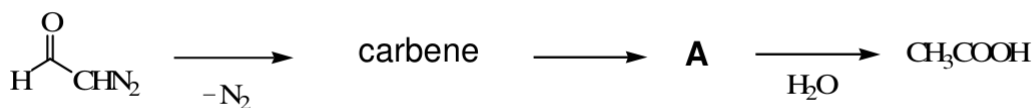
When irradiated, diazonaphthaquinone undergoes photochemical decomposition followed by rearrangement eventually producing a carboxylic acid.



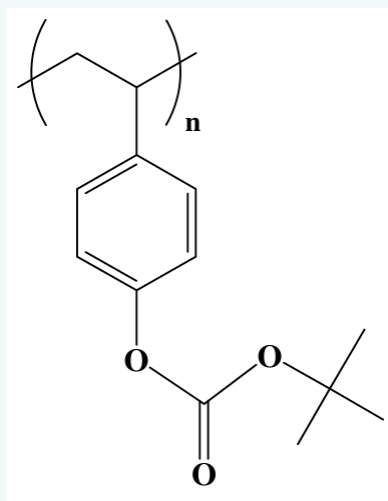
9.4 Draw three Lewis structures of diazoacetaldehyde (see below), the simplest compound having the same active functional group of diazonaphthaquinone. Indicate formal charges.



9.5 Draw a Lewis structure of the rearranged intermediate, **A** (see below), generated from diazoacetaldehyde after losing N_2 . **A** satisfies Lewis' octet rule and reacts with water to form acetic acid, CH_3COOH .

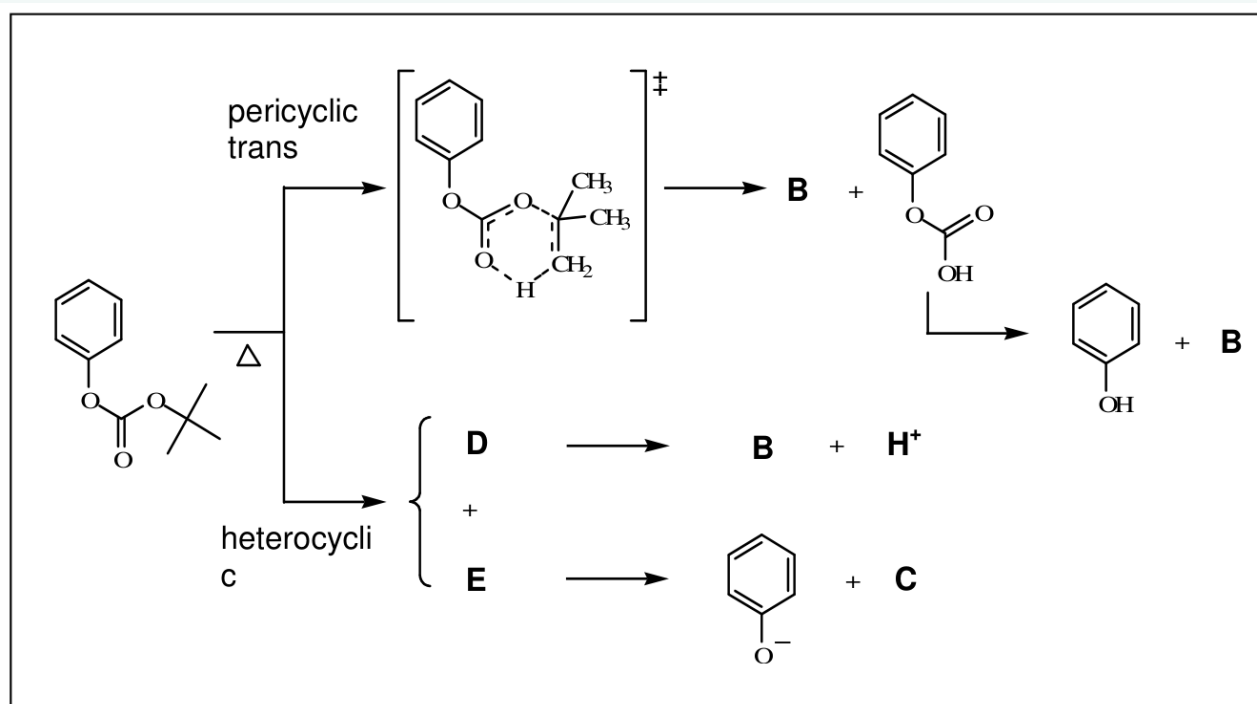


Advanced photoresists were invented in 1982 based on chemical amplification. The most popular chemical amplification for positive-tone involves the acid catalyzed deprotection of poly(*p*-hydroxystyrene) resin protected by various acid-sensitive protecting groups such as *t*-butyloxycarbonyl (*t*-BOC).

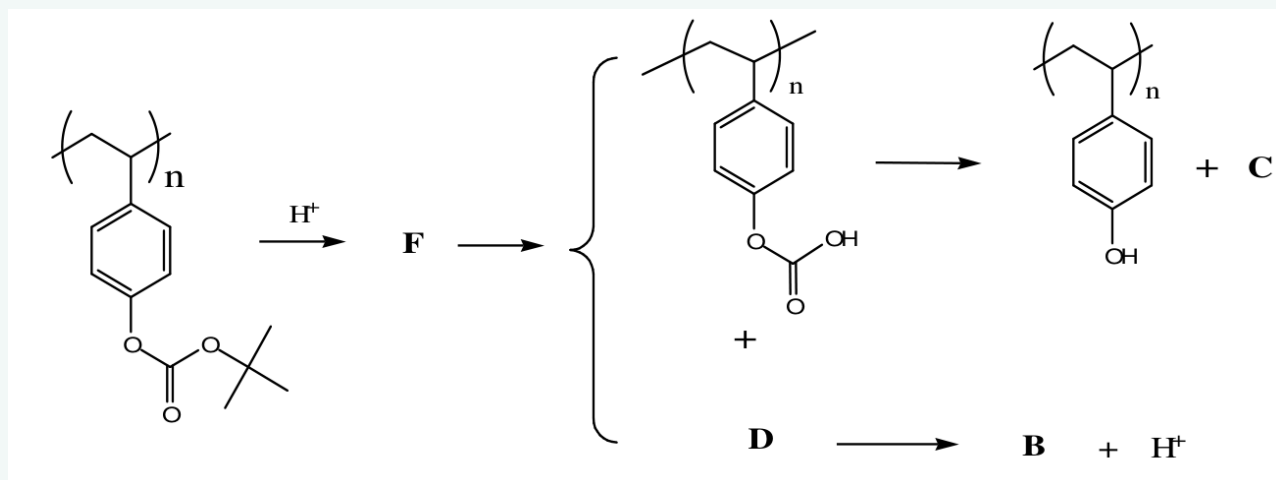


The thermal decomposition of carbonate ester itself normally occurs well above 150 °C.

9.6 Two plausible mechanisms have been suggested for this decomposition reaction having relatively high activation energy. Draw expected intermediates and products from this reaction.



9.7 In the presence of a trace amount of acid, the reaction temperature can be reduced to below 100 °C. Draw expected intermediate F from the following chemical amplification process based on using *t*-BOC.



Official English text of the problem.

Answers

- **9.1.** The two principal resonance contributors of **methyl azide** are $CH_3-N=N^+=N^-$, $CN=[N^+]=[N^-]$, and $CH_3-N^--N^+\equiv N$, $C[N^-][N^+] \# N$. Unmarked atoms have zero formal charge.
- **9.2. Methylnitrene**, CH_3-N , $C[N]$: nitrogen has one single bond and four nonbonding electrons, giving a sextet and zero formal charge. The singlet drawing has two lone pairs; the triplet drawing has one lone pair and two unpaired electrons. SMILES does not specify this spin distinction.
- **9.3. 1-Methylaziridine**, $CN1CC1$, from addition across the double bond, and **N-methylethenamine (N-methylvinylamine)**, $CH_2=CH-NH-CH_3$, $C=CNC$, from insertion into a carbon-hydrogen bond.
- **9.4.** Three resonance contributors of **diazoacetaldehyde** are $H-C(=O)-CH=N^+=N^-$, $O=CC=[N^+]=[N^-]$; $H-C(=O)-CH^--N^+\equiv N$, $O=C[CH^-][N^+] \# N$; and $O^--CH=CH-N^+\equiv N$, $[O^-]C=C[N^+] \# N$.
- **9.5. A is ketene (ethenone)**, $CH_2=C=O$, $c=c=o$. Oxygen has two lone pairs; all formal charges are zero.
- **9.6. B:** 2-methylpropene (isobutene), $CH_2=C(CH_3)_2$, $c=c(c)c$; **C:** carbon dioxide, CO_2 , $o=c=o$; **D:** tert-butyl cation, $(CH_3)_3C^+$, $c[c+](c)c$; **E:** phenyl carbonate anion, $PhO-C(=O)-O^-$, $o=c([O^-])Oc1ccccc1$. The gas shown beside phenol in the upper route must be **C**, despite its printed label **B**.

- **9.7. F is a protonated Boc carbonate**, conventionally drawn with protonation at the carbonyl oxygen: $\text{Ar}-\text{O}-\text{C}(=\text{OH}^+)-\text{O}-\text{C}(\text{CH}_3)_3$. A protonated polymer repeat unit is represented by $[\ast]\text{CC}([\ast])\text{c1ccc}(\text{OC}(=\text{OH}^+)\text{OC}(\text{C})(\text{C})\text{C})\text{cc1}$, where $[\ast]$ marks polymer-chain continuation. The tert-butoxy-oxygen-protonated alternative is discussed below.

Solution

Here, **Ph** denotes phenyl, and **Ar** denotes the polymer-bound, para-substituted phenyl group in 9.7. Small species used below are **dinitrogen**, $\text{N}\equiv\text{N}$; **ethene (ethylene)**, $\text{C}=\text{C}$; **water**, O ; and the **proton**, $[\text{H}^+]$.

9.1

Formal charge is calculated from

$$q_{\text{formal}} = V - n_{\text{nonbonding}} - \frac{1}{2}n_{\text{bonding}},$$

where V is the number of valence electrons of the free atom.

The two principal Lewis structures of methyl azide are resonance contributors:



Number the nitrogen atoms from the methyl end.

Contributor	Formal charges on the three nitrogen atoms	Lone pairs on the three nitrogen atoms
$\text{CH}_3-\text{N}=\text{N}^+=\text{N}^-$	0, +1, -1	1, 0, 2
$\text{CH}_3-\text{N}^--\text{N}^+\equiv\text{N}$	-1, +1, 0	2, 0, 1

Both structures contain 22 valence electrons, satisfy the octet rule, and have zero net charge. They differ only in electron placement.

9.2

Photolysis expels dinitrogen:



The remaining species is methylnitrene, $\text{C}[\text{N}]$. Draw a methyl group joined to nitrogen by a single bond.

Nitrogen retains four nonbonding electrons. In a singlet Lewis drawing these form two lone pairs; in the triplet representation they comprise one lone pair and two unpaired electrons. In either case,

$$q_{\text{N}} = 5 - 4 - \frac{2}{2} = 0.$$

The nitrogen has only six electrons around it: four nonbonding electrons and the two electrons of its carbon–nitrogen bond. This electron deficiency explains its high reactivity. The molecular connectivity alone does not specify its spin state.

9.3

Two standard reactions of the nitrene give the requested products.

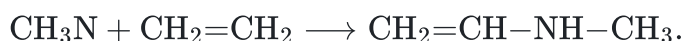
1. Addition across the double bond gives 1-methylaziridine, CN1CC1:



Draw a three-membered triangle with nitrogen at one vertex and a methylene group at each of the other two vertices. Attach a methyl group to nitrogen. Nitrogen has three single bonds, one lone pair, and zero formal charge.

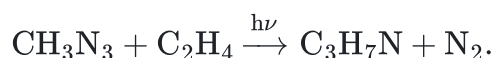
The ethene double bond becomes a single bond, and nitrogen forms a bond to each carbon.

2. Insertion into a vinylic carbon–hydrogen bond gives N-methylethenamine, C=CNC:



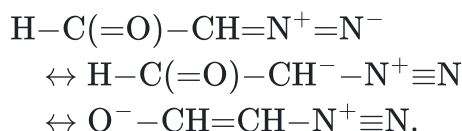
Nitrogen becomes bonded to both atoms of the original carbon–hydrogen bond. The carbon–carbon double bond remains. Draw the open chain $\text{CH}_2=\text{CH}-\text{NH}-\text{CH}_3$, with one lone pair on nitrogen.

For either product, the overall photochemical equation is



9.4

The diazo group is conjugated with the carbonyl group. Consequently, its negative charge can be represented on terminal nitrogen, the adjacent carbon, or oxygen:



These are three resonance contributors of diazoacetaldehyde, rather than three distinct compounds.

Contributor	Nonzero formal charges	Lone pairs to include
$\text{O}=\text{CC}=[\text{N}^+]=[\text{N}^-]$	Central nitrogen +1; terminal nitrogen –1	Two on oxygen; two on terminal nitrogen
$\text{O}=\text{C}[\text{CH}^-][\text{N}^+\#\text{N}]$	Diazo-bearing carbon –1; central nitrogen +1	Two on oxygen; one on the negative carbon; one on terminal nitrogen
$[\text{O}^-]\text{C}=\text{C}[\text{N}^+\#\text{N}]$	Oxygen –1; central nitrogen +1	Three on oxygen; one on terminal nitrogen

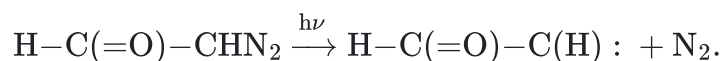
The positively charged nitrogen has no lone pair in any contributor. All unmarked atoms are neutral.

The first-to-second conversion forms a nitrogen–nitrogen triple bond while moving the carbon–nitrogen π -electron pair onto carbon. Donation of that carbon lone pair toward the carbonyl, accompanied by movement of the carbonyl π electrons onto oxygen, gives the third contributor.

Each structure has 26 valence electrons, complete octets, and zero net charge.

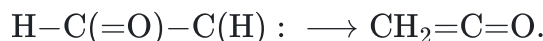
9.5

Loss of dinitrogen initially gives **formylcarbene (2-oxoethylidene)**, $\text{O}=\text{C}[\text{CH}]$:



The colon indicates the carbene electron pair in a singlet Lewis representation; SMILES does not specify spin.

A Wolff rearrangement then transfers the aldehydic hydrogen to the carbene carbon while forming a carbon–carbon double bond:



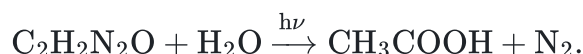
Thus **A is ketene**, $\text{C}=\text{C}=\text{O}$.

Draw the sequence carbon–carbon–oxygen with two consecutive double bonds. The terminal carbon bears two hydrogens, and oxygen bears two lone pairs. Both carbon atoms and oxygen satisfy the octet rule; every formal charge is zero.

Hydration gives **acetic acid (ethanoic acid)**, $\text{CC}(=\text{O})\text{O}$:



Formally, hydrogen adds to the terminal carbon and hydroxyl to the central carbon. The complete reaction is



9.6

The model substrate is **tert-butyl phenyl carbonate**, $\text{CC}(\text{C})(\text{C})\text{OC}(=\text{O})\text{Oc1ccccc1}$.

In the upper pathway, a six-membered cyclic transition state transfers a hydrogen from a tert-butyl methyl group to the carbonyl oxygen. Carbon–carbon double-bond formation, cleavage of the tert-butyl–oxygen bond, and redistribution of the carbonate bonds occur together.

This gives **B, isobutene**, and **phenyl hydrogen carbonate**, $\text{O}=\text{C}(\text{O})\text{Oc1ccccc1}$:

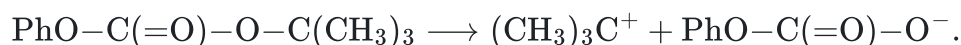


Phenyl hydrogen carbonate subsequently loses **C, carbon dioxide**, giving **phenol**, Oc1ccccc1 :



This identifies the apparent labeling error in the upper scheme: the species released beside phenol is carbon dioxide, **C**.

In the lower pathway, heterolytic cleavage of the tert-butyl–oxygen bond leaves its electron pair on oxygen:



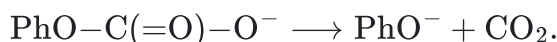
Therefore:

- **D is the tert-butyl cation**, $\text{C}[\text{C}^+](\text{C})\text{C}$. Draw its central, positively charged carbon bonded to three methyl groups.
- **E is the phenyl carbonate anion**, $\text{O}=\text{C}([\text{O}^-])\text{Oc1ccccc1}$. Draw the negative charge on the singly bonded terminal oxygen; it is delocalized over the two non-phenoxy oxygens.

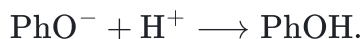
The subsequent steps shown in the problem are



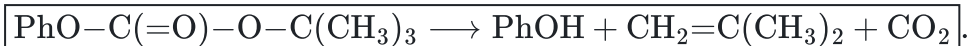
and



The **phenoxide ion**, $[\text{O}^-]\text{c1ccccc1}$, is then protonated:



Both pathways have the same balanced overall reaction:

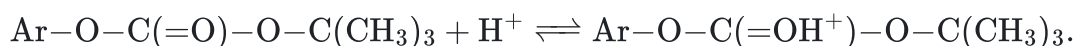


Thus one carbonate group produces one molecule each of phenol, isobutene, and carbon dioxide.

9.7

The starting material is **Boc-protected poly(p-hydroxystyrene)**. One repeat unit can be represented as [*]CC([*])c1ccc(OC(=O)OC(C)(C)C)cc1; the wildcard atoms mark chain continuation, and no polymer stereochemistry is specified in the question.

A conventional first step is protonation of the carbonyl oxygen:



This is **F**, the carbonyl-protonated carbonate, with repeat-unit SMILES [*]CC([*])c1ccc(OC(=[OH+])OC(C)(C)C)cc1.

For the requested drawing, retain the polymer backbone and the para-substituted aromatic ring. Add hydrogen to the carbonate's carbonyl oxygen and place a positive charge on that oxygen. It has one lone pair and a bond-order sum of three.

Cleavage releases the tert-butyl cation:



During this cleavage, the tert-butoxy oxygen can supply the new carbonyl π bond while the original carbonyl π electrons move onto the protonated oxygen. The latter consequently becomes the hydroxyl oxygen of the carbonic-acid monoester.

The **polymer-bound hydrogen carbonate** has repeat-unit SMILES

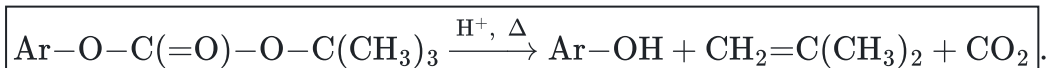
[*]CC([*])c1ccc(OC(=O)O)cc1. It decomposes to the **deprotected poly(p-hydroxystyrene)** repeat, [*]CC([*])c1ccc(O)cc1, and carbon dioxide:



Meanwhile, D loses a proton to give B:

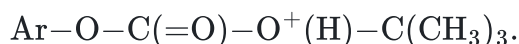


The overall reaction is therefore



The proton is regenerated. A single photogenerated acid molecule can therefore promote removal of many protecting groups: this is the chemical amplification.

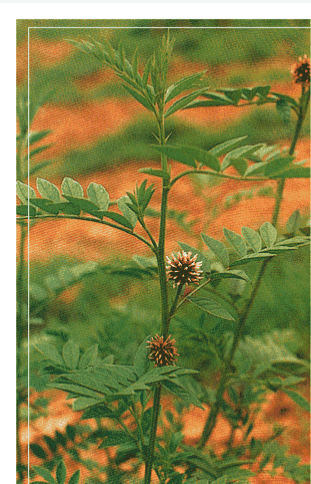
An alternative representation of the acid-activated intermediate protonates the **tert-butoxy oxygen**:



This **tert-butoxy-oxygen-protonated carbonate protomer** has repeat-unit SMILES [*]CC([*])c1ccc(OC(=O)[OH+]C(C)(C)C)cc1. Cleavage of its tert-butyl–oxygen bond directly gives the same hydrogen carbonate and D. The two protonation-site structures are distinct protomers, not resonance contributors.

The solution was checked against the official solution.

Problem 10: Natural Products - Structural Analysis



Licorice (*Glycyrrhiza. Uralensis*)

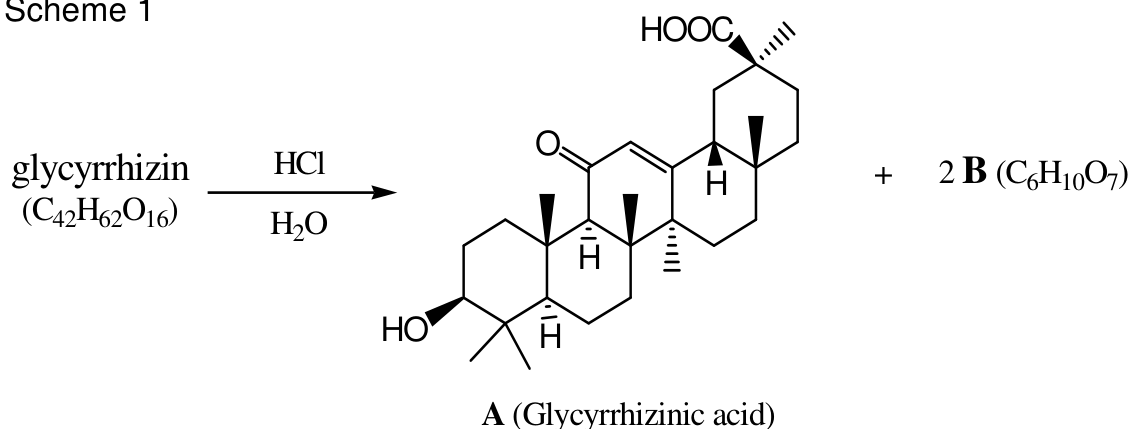


Licorice Root

The flavour extracted from the licorice root is 50 – 150 times sweeter than table sugar. The most important and abundant compound responsible for the sweetness and medicinal effects of licorice is *glycyrrhizin* ($C_{42}H_{62}O_{16}$).

Glycyrrhizin requires three equivalents of NaOH to effect neutralization. When *glycyrrhizin* was subjected to acid hydrolysis, *Glycyrrhizinic acid* (**A** ($C_{30}H_{46}O_4$)) and **B** ($C_6H_{10}O_7$) were obtained in a 1:2 molar ratio (Scheme 1).

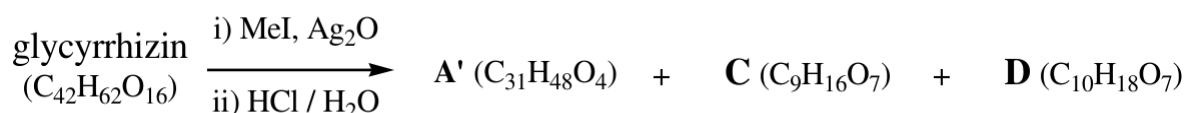
Scheme 1



Scheme 1

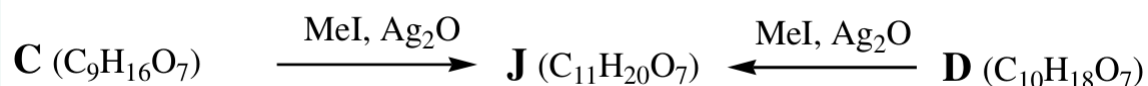
When *glycyrrhizin* was methylated with methyl iodide (MeI) at every possible site before hydrolysis, hydrolysis produced **A'** (methyl glycyrrhizinate), and **C** and **D** (Scheme 2).

B, **C** and **D** exist as mixtures of anomers.



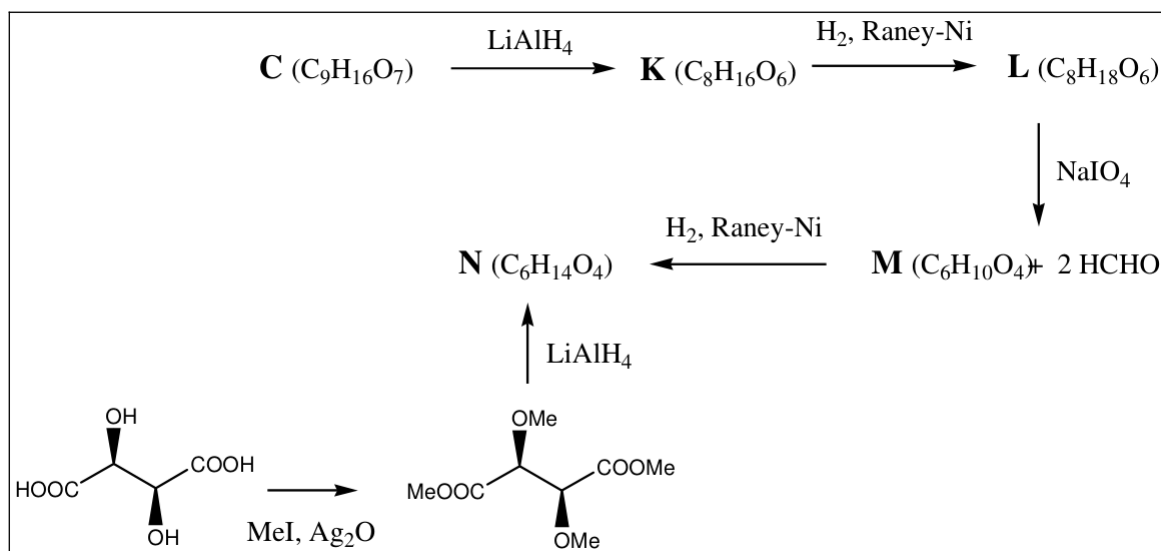
Scheme 2

Methylation of **C** and **D** with MeI produced the same isomeric mixture of compounds, **J** (Scheme 3).



Scheme 3

C was reduced with $LiAlH_4$ to give **K**, and **L** was produced by the reduction of **K**. Oxidative cleavage of vicinal diol of **L** with $NaIO_4$ produced **M** and two equivalents of formaldehyde. Reduction of **M** produced **N**. The structure and stereochemistry of **N** was confirmed by the synthesis of **N** from D-(-)-tartaric acid through methylation followed by reduction (Scheme 4). A ^1H -NMR spectrum of **L** showed two distinct peaks for methyl groups. (There is no symmetry in **L**)



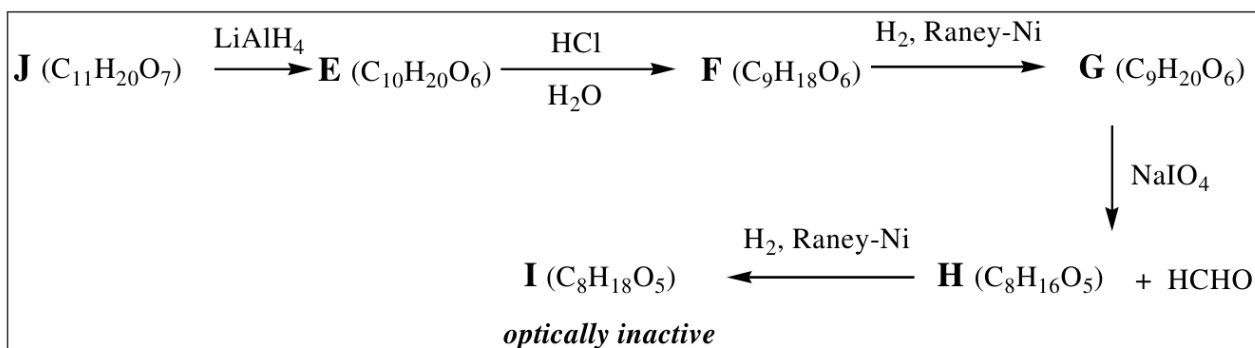
Scheme 4

10.1 Complete structures for **L**, **M**, and **N** in the answer sheet.

10.2 How many structures for **C** are possible? Complete possible structures for **C**.

To determine the correct structure of **C**, following set of reactions were performed.

J was reduced to **E**, and acid hydrolysis of **E** produced **F**. Reduction of **F** generated **G**, and **G** was oxidized with NaIO_4 to **H** with formation of one equivalent of formaldehyde. **I** was obtained from **H** through reduction. Among all compounds from **A** to **I**, only **I** was optically inactive (Scheme 5).



Scheme 5

10.3 Complete structures for **G** and **I**.

10.4 Which one is the correct structure for **C** among ones you have drawn in 10-2?

10.5 Complete structures for **B**, **D**, and **J**.

10.6 Complete the structure for Glycyrrhizin.

Official English text of the problem.

Answers

- **10.1.**

L: 3,4-di-O-methyl-D-glucitol, $C_8H_{18}O_6$.

SMILES: OC[C@H](O)[C@@H](OC)[C@H](OC)[C@H](O)CO

M: (2S,3S)-2,3-dimethoxybutane-1,4-dial, $C_6H_{10}O_4$.

SMILES: O=C[C@@H](OC)[C@H](OC)C=O

N: (2R,3R)-2,3-dimethoxybutane-1,4-diol, $C_6H_{14}O_4$.

SMILES: OC[C@@H](OC)[C@H](OC)CO

- **10.2.** There are **two possible sugar configurations, each occurring as two anomers:** thus **two anomeric pairs, or four individual cyclic stereoisomers.**

Candidate 1: methyl 3,4-di-O-methyl-D-glucopyranuronate.

α : COC(=O)[C@H]1O[C@H](O)[C@H](O)[C@@H](OC)[C@@H]1OC

β : COC(=O)[C@H]1O[C@@H](O)[C@H](O)[C@@H](OC)[C@@H]1OC

Candidate 2: methyl 3,4-di-O-methyl-L-gulopyranuronate.

α : COC(=O)[C@@H]1O[C@@H](O)[C@@H](O)[C@@H](OC)[C@@H]1OC

β : COC(=O)[C@@H]1O[C@H](O)[C@@H](O)[C@@H](OC)[C@@H]1OC

- **10.3.**

G: 2,3,4-tri-O-methyl-D-glucitol, $C_9H_{20}O_6$.

SMILES: OC[C@H](OC)[C@@H](OC)[C@H](OC)[C@H](O)CO

I: meso-2,3,4-tri-O-methylxylitol, $C_8H_{18}O_5$.

SMILES: OC[C@H](OC)[C@@H](OC)[C@H](OC)CO

- **10.4. Candidate 1 is correct:** **C** is methyl 3,4-di-O-methyl-D-glucopyranuronate, as the α/β pair specified in 10.2.
- **10.5.**

B: D-glucopyranuronic acid, $C_6H_{10}O_7$.

α : O=C(O)[C@H]1O[C@H](O)[C@H](O)[C@@H](O)[C@@H]1O

β : O=C(O)[C@H]1O[C@@H](O)[C@H](O)[C@@H](O)[C@@H]1O

D: methyl 2,3,4-tri-O-methyl-D-glucopyranuronate, $C_{10}H_{18}O_7$.

α : COC(=O)[C@H]1O[C@H](O)[C@H](OC)[C@@H](OC)[C@@H]1OC

β : COC(=O)[C@H]1O[C@@H](O)[C@H](OC)[C@@H](OC)[C@@H]1OC

J: methyl 1,2,3,4-tetra-O-methyl-D-glucopyranuronate, $C_{11}H_{20}O_7$; equivalently, the methyl ester bearing a methyl glycoside at C1 and methoxy groups at C2, C3 and C4.

α : COC(=O)[C@H]1O[C@H](OC)[C@H](OC)[C@@H](OC)[C@@H]1OC

β : COC(=O)[C@H]1O[C@@H](OC)[C@H](OC)[C@@H](OC)[C@@H]1OC

- **10.6.** The established connectivity is **A 3-O-[D-glucopyranuronosyl-(1→2)-D-glucopyranuronoside]**, with all three carboxyl groups free.

The conventional **β,β structure of glycyrrhizin**, $C_{42}H_{62}O_{16}$, is:

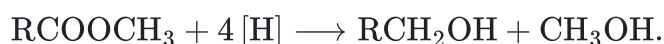
```
CC1(C)[C@@H](O[C@@H]6O[C@H](C(=O)O)[C@@H](O)[C@H](O)[C@H]6O[C@@H]7O[C@H](C(=O)O)[C@@H](O)[C@H](O)[C@H]7O)CC[C@]2(C)[C@H]3C(=O)C=C4[C@@H]5C[C@@](C)(C(=O)O)CC[C@]5(C)CC[C@@]4(C)[C@]3(C)CC[C@H]12
```

Qualification: the supplied degradation experiments determine the connectivity and sugar configurations, but do not independently establish the two original β anomeric configurations.

Solution

In the Fischer projections described below, the carbon chain is vertical, horizontal bonds point toward the viewer, and hydrogen occupies the position opposite the stated oxygen substituent. Sugar positions refer to the original six-carbon chain.

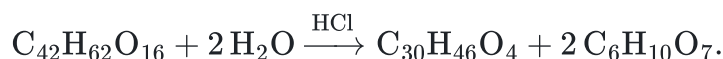
For the reduction balances, $[H]$ denotes a formal reducing hydrogen equivalent. Ester reduction is written as



This expresses the net organic transformation after work-up.

10.1. Structures of L, M and N

Hydrolysis has the balanced stoichiometry

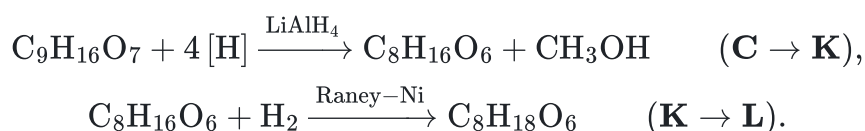


The aglycone contains one carboxyl group. Since glycyrrhizin consumes three equivalents of base and yields two identical molecules of **B**, each **B** supplies one further carboxyl group.

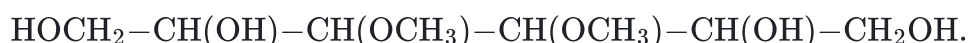
Replacing an O–H hydrogen by methyl adds CH_2 . Relative to **B**, **C** contains three such increments:



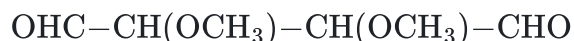
One methyl group forms the carboxylic methyl ester; the other two are methyl ethers. Ester reduction removes the ester methyl carbon from the isolated carbohydrate product as methanol, giving **K**, followed by reduction to the alditol **L**:



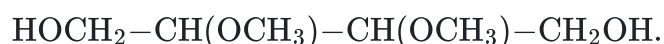
The production of **two equivalents of formaldehyde** requires a terminal vicinal diol at each end of **L**. Its constitution must therefore be



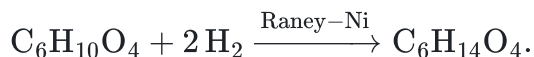
Periodate cleaves the C1–C2 and C5–C6 bonds, leaving



as **M**. Reduction of its two aldehyde groups gives **N**:



The balanced reactions are



The tartaric-acid experiment fixes the absolute configurations of the two central carbons.

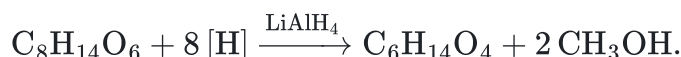
D-(-)-tartaric acid is **(2S,3S)-2,3-dihydroxybutanedioic acid**, SMILES

O=C(O)[C@H](O)[C@H](O)C(=O)O.

Its fully methylated derivative is **dimethyl (2S,3S)-2,3-dimethoxybutanedioate**, SMILES

COC(=O)[C@H](OC)[C@H](OC)C(=O)OC.

The balances are



Neither transformation changes the spatial configuration at the two existing stereocentres. The Fischer projections of **M** and **N**, with identical terminal groups at the top and bottom, consequently have **methoxy left, then methoxy right**.

Thus **M** is (2*S*, 3*S*), whereas **N** is (2*R*, 3*R*). This change of descriptors results from changed CIP priorities upon reduction; it does not indicate inversion.

For **L**, the central methoxy groups likewise lie left at C3 and right at C4. The remaining possibilities concern the hydroxyl groups at C2 and C5:

C2 hydroxyl	C5 hydroxyl	Consequence
Right	Left	End-exchange symmetry makes the methoxy groups equivalent
Left	Right	End-exchange symmetry makes the methoxy groups equivalent
Right	Right	Methoxy groups are inequivalent
Left	Left	Same alditol as the preceding row after rotating the Fischer projection by 180°

The two distinct methyl resonances therefore select the single asymmetric alditol **L** given in the Answers.

To draw it, place CH2OH at both ends and arrange the oxygen substituents from C2 through C5 as:

OH right;\ OMe left;\ OMe right;\ OH right.

10.2. Possible structures of C

Reduction to **L** makes both ends of the original sugar into CH2OH. It therefore erases the distinction between the original reducing end and the original carboxyl end.

Assigning those ends in the two possible ways gives the following Fischer configurations. The top is the original C1 aldehyde position and the bottom is the C6 methyl ester.

Candidate for C	C2-OH	C3-OMe	C4-OMe	C5-OH
D-glucuronic configuration	Right	Left	Right	Right
L-guluronic configuration	Left	Left	Right	Left

In the cyclic structures, the C5 oxygen forms the pyranose ring, and C1 is a hemiacetal bearing a free hydroxyl group. Each configuration therefore gives an α and a β anomer.

Hence there are **two configurational candidates, represented by four individual anomers**.

For a conventional Haworth drawing with the ring oxygen at the upper right:

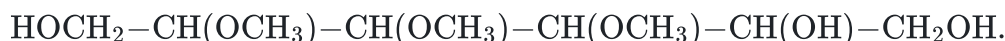
- **D-glucuronic candidate:** C5–COOCH₃ up, C2–OH down, C3–OMe up, C4–OMe down; C1–OH down for α and up for β .
- **L-guluronic candidate:** C5–COOCH₃ down, C2–OH up, C3–OMe up, C4–OMe down; C1–OH up for α and down for β .

These are the structures encoded by the four SMILES in 10.2.

10.3. Structures of G and I

Exhaustive methylation gives **J** with methyl groups at the carboxyl oxygen and at O1, O2, O3 and O4.

Reduction of the ester produces a C6 primary alcohol. Acid hydrolysis then removes the anomeric methyl group, while retaining the ordinary methyl ethers at C2, C3 and C4. Reduction of the reducing sugar consequently gives an alditol of constitution



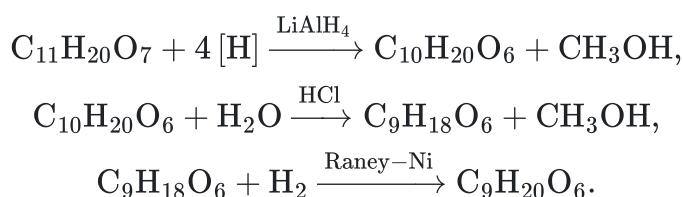
For the D-glucuronic candidate, this is **G**, 2,3,4-tri-O-methyl-D-glucitol. Its Fischer oxygen-substituent sequence is

OMe right;\ OMe left;\ OMe right;\ OH right.

The intermediate structures for this candidate are:

Compound	Identification	Representative β -anomer SMILES
E	Methyl 2,3,4-tri-O-methyl-D-glucopyranoside	<chem>OC[C@H]1O[C@@H](OC)[C@H](OC)[C@@H](OC)[C@@H]1OC</chem>
F	2,3,4-Tri-O-methyl-D-glucopyranose	<chem>OC[C@H]1O[C@@H](O)[C@H](OC)[C@@H](OC)[C@@H]1OC</chem>

The corresponding α forms differ only at C1. The balanced transformations are



Only C5–C6 in **G** is a free vicinal diol. Its cleavage produces one molecule of formaldehyde and the aldehyde **H**:



H is open-chain 2,3,4-tri-O-methyl-L-xylose, SMILES

OC[C@H](OC)[C@@H](OC)[C@H](OC)C=O.

Reduction gives **I**, with CH₂OH at both ends and the Fischer methoxy sequence **right–left–right**:



The balanced reactions are



The two ends of **I** are identical. Its internal mirror symmetry exchanges C2 with C4, making it a **meso compound** and therefore optically inactive. This gives the required structure of **I**.

10.4. Selection of C

The L-guluronic candidate would instead give a pentitol with the Fischer methoxy sequence **left-left-right**.

That alternative is **2,3,4-tri-O-methyl-D-lyxitol**, SMILES

OC[C@H](OC)[C@H](OC)[C@H](OC)CO.

It is chiral and would remain optically active. The stated optical inactivity of **I** therefore selects the **D-glucuronic candidate**:

C = methyl 3,4-di-O-methyl-D-glucopyranuronate.

The terminal aldehyde reduction does not generate a new stereocentre, so the optical inactivity is explained by the meso structure, without invoking racemization.

With this selection, **K** is **3,4-di-O-methyl-D-glucopyranose**; a representative β-anomer SMILES is OC[C@H]1O[C@H](O)[C@H](O)[C@H](OC)[C@@H]1OC.

10.5. Structures of B, D and J

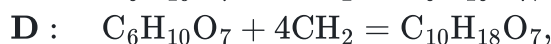
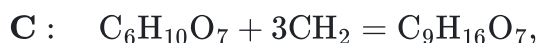
Removing the methyl groups from the identified **C** gives **B**, D-glucuronic acid.

The substitution patterns are:

Compound	C1 substituent	C2 substituent	C3 substituent	C4 substituent	C6 group
B	OH	OH	OH	OH	COOH
C	OH	OH	OCH ₃	OCH ₃	COOCH ₃
D	OH	OCH ₃	OCH ₃	OCH ₃	COOCH ₃
J	OCH ₃	OCH ₃	OCH ₃	OCH ₃	COOCH ₃

All retain the D-glucos configuration at C2–C5.

The formula differences confirm these assignments:



To reach **J**, **C** requires methylation of O1 and O2, whereas **D** requires methylation only of O1:



Thus both give the same pair of methyl-glycoside anomers of **J**, as required.

10.6. Structure of glycyrrhizin

Methylation analysis identifies the original glycosidic attachment positions: hydroxyl groups exposed only by hydrolysis were unavailable for methylation in intact glycyrrhizin.

Attachment to the aglycone. The depicted aglycone **A** is commonly called **glycyrrhetinic acid**, although the problem labels it "Glycyrrhizinic acid." Its stereochemical SMILES is

```
CC1(C)[C@@H](O)CC[C@]2(C)[C@H]3C(=O)C=C4[C@@H]5C[C@@](C)(C(=O)O)CC[C@]5(C)CC[C@@]4(C)[C@]3(C)CC[C@@H]12
```

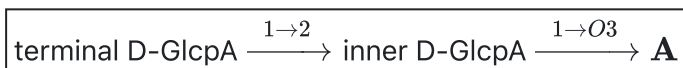
After methylation and hydrolysis, **A'** contains only one added methyl group. It is **methyl glycyrrhetinate**, SMILES

```
CC1(C)[C@@H](O)CC[C@]2(C)[C@H]3C(=O)C=C4[C@@H]5C[C@@](C)(C(=O)OC)CC[C@]5(C)CC[C@@]4(C)[C@]3(C)CC[C@@H]12
```

Its carboxyl group was methylated, but its C3 hydroxyl was protected by a glycosidic linkage during methylation. Hydrolysis restores that hydroxyl. Consequently, the sugar chain is attached through **the aglycone's C3 oxygen**.

Attachment between the sugars. The inner sugar gives **C**, which has an unmethylated hydroxyl at C2 after hydrolysis. Its O2 must therefore have participated in the intersugar glycosidic bond. The terminal sugar gives **D**, methylated at all three non-anomeric hydroxyl positions.

The connectivity is therefore

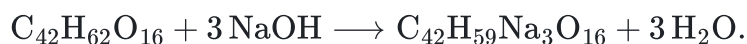


where GlcpA denotes a glucopyranuronic-acid residue.

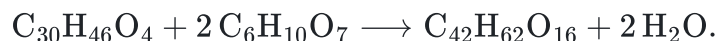
For the drawing, copy the aglycone in Scheme 1 and:

1. Replace the hydrogen of its C3 hydroxyl by the anomeric carbon of the inner D-glucopyranuronic-acid residue.
2. Attach the terminal residue's anomeric carbon through the inner residue's O2.
3. Retain the carboxyl group on the aglycone and the C6 carboxyl group of each sugar as free acids.
4. For the conventional β,β glycyrrhizin structure, draw both anomeric glycosidic substituents on the same side as the corresponding C5 carboxyl substituent.

The three free carboxyl groups explain the neutralization:



The composition also agrees with condensation of **A** and two molecules of **B**:



There are five free alcoholic hydroxyl groups and three free carboxyl groups in glycyrrhizin, giving eight methylations. The combined balance for exhaustive methylation followed by hydrolysis is



whose organic products are **A'**, **C** and **D**, respectively.

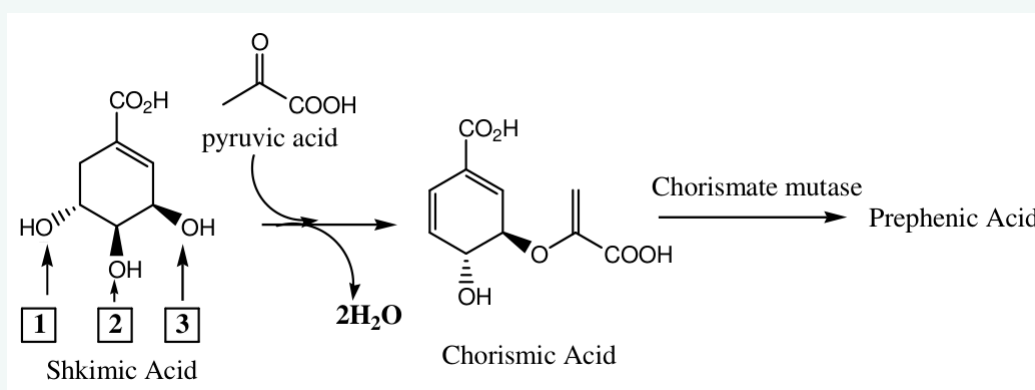
For completeness, the small species used in these balances have the following SMILES: formaldehyde C=O; methanol CO; water O; hydrogen [H][H]; methyl iodide CI; hydrogen chloride Cl; lithium aluminium hydride [Li+].[AlH4-]; silver(I) oxide [Ag+].[Ag+].[O-2]; silver iodide [Ag+].[I-];

sodium periodate $[\text{Na}^+] \cdot [\text{O}-]\text{I}(=\text{O})(=\text{O})=\text{O}$; sodium iodate $[\text{Na}^+] \cdot [\text{O}-]\text{I}(=\text{O})=\text{O}$; sodium hydroxide $[\text{Na}^+] \cdot [\text{OH}-]$. Raney nickel is a porous solid catalyst, for which $[\text{Ni}]$ represents the element but not the catalyst morphology.

The solution was checked against the official solution.

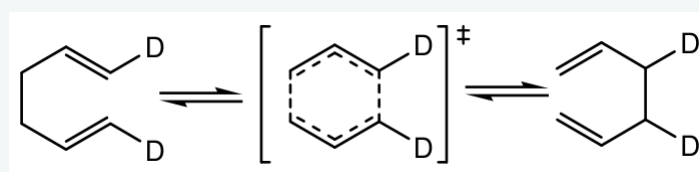
Problem 11: Enzyme Reaction

Shikimic acid biosynthesis is an important pathway for amino acids, alkaloids and heterocyclic natural product production. Nature converts shikimic acid to chorismic acid through a cascade of enzymatic reactions. Then chorismate mutase catalyzes the conversion of chorismic acid to prephenic acid at the branch point for the biosynthesis of aromatic amino acids such as tyrosine and phenylalanine.



11.1 During the transformation of shikimic acid to chorismic acid, dehydration is occurring. Choose the hydroxyl group in shikimic acid that is lost through above dehydration among all possible reactions.

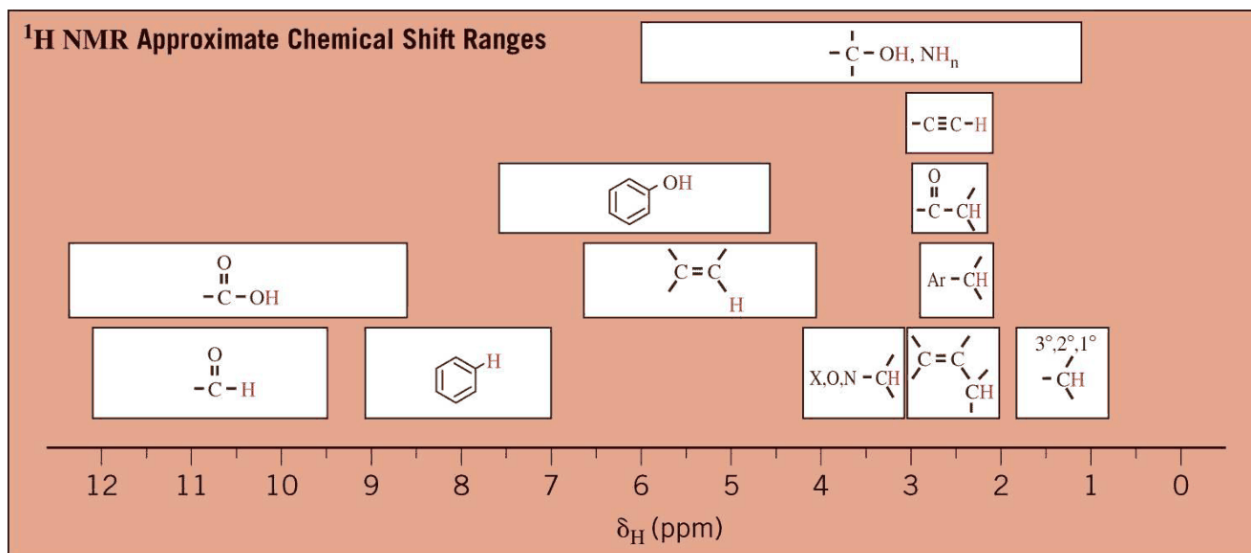
11.2 Chorismate mutase rearranges chorismic acid into prephenic acid without changing the molecular formula. Chorismic acid becomes prephenic acid through the Claisen rearrangement, a concerted pericyclic process like the Cope rearrangement as shown below:



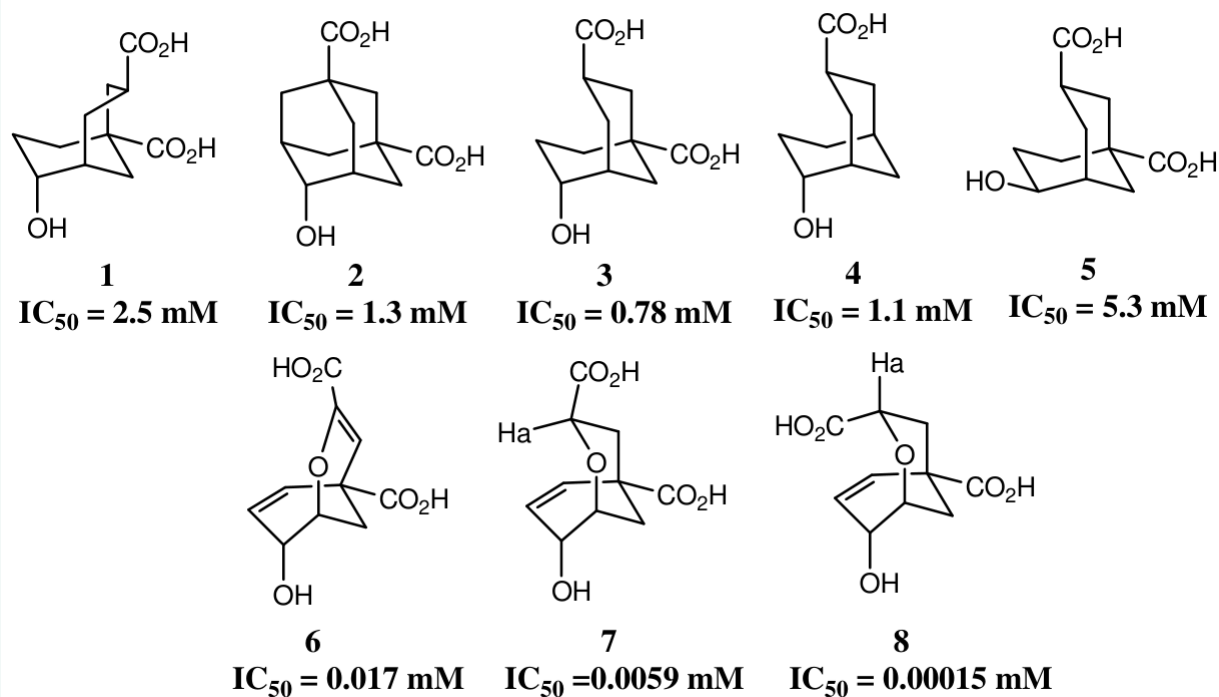
Based on the following spectral data, propose the structure of prephenic acid.

^1H -NMR (D_2O , 250 MHz): δ 6.01 (2H, d, $J = 10.4$ Hz), 5.92 (2H, dd $J = 10.4, 3.1$ Hz), 4.50 (1H, t, $J = 3.1$ Hz), 3.12 (2H, s). Note that there are three protons, which have been exchanged by D_2O very fast, and two protons at δ 3.12, which are exchanged slowly in prephenic acid. ^{13}C -NMR (D_2O , 75 MHz): δ 203, 178, 173, 132 (for two identical carbons), 127 (for two identical carbons), 65, 49, 48.

δ , chemical shift; H, integrals; d, doublet; dd, doublet of doublet; J, coupling constant; t, triplet; s, singlet



Chorismate mutase is believed to stabilize the transition state of Claisen rearrangement. Thus it is an interesting target for inhibitor design. Inhibitors, called transition state analog (TSA)s that resemble the transition state (TS, e.g., the species in brackets "[]" above) of the reaction are designed to occupy the active site. Several inhibitors were designed and synthesized, and among them eight turned out to be potent inhibitors of the enzyme. The lower is the IC_{50} (inhibitor concentration of 50 % of the enzymatic activity) value, the better is the inhibitor.



11.3 Choose all correct statements based on the structures and IC_{50} values of above inhibitors. Increase of factor 5 is considered to be important.

- (a) Configuration of the hydroxyl group plays an important role in the TS and inhibitor design.
- (b) The presence of both carboxylic groups is important in the TS and inhibitor design.
- (c) Transition state of the reaction contains two six-membered rings with one chair and one twist-boat conformation.

(d) **7** and **8** can be distinguished on the basis of the ^1H -NMR of H_a .

11.4 Draw the transition state of the transformation of chorismic acid to prephenic acid based on the TSA structures and their IC_{50} values.

11.5 Compared with the uncatalyzed thermal conversion, chorismate mutase accelerates conversion of chorismic acid to prephenic acid 1.0×10^6 fold at 25°C by lowering the activation energy of the reaction. Calculate the decrease in activation energy of chorismate mutase at 25°C .

$\Delta H_{\text{uncat}}^\ddagger$ is $86,900 \text{ J mol}^{-1}$ for the thermal conversion of chorismic acid to prephenic acid. At what temperature will the rate of the *uncatalyzed* thermal conversion be the same as that of the *enzyme-catalyzed* conversion at 25°C , assuming that $E_a = \Delta H^\ddagger$.

Official English text of the problem.

Answers

- **11.1:** Hydroxyl group **3**.
- **11.2: Prephenic acid**, O=C(O)[C@]1(CC(=O)C(=O)O)C=C[C@H](O)C=C1. Its ring hydroxyl and ring-bound carboxyl group are **cis**.
- **11.3: (a), (c), and (d)**.
- **11.4:** A concerted $[3, 3]$ -Claisen transition state resembling inhibitor **8**, with a **chair-like pericyclic ring** and a **twist-boat carbocyclic ring**. The ring–oxygen bond breaks while a bond forms between the carboxyl-bearing ring carbon and the terminal methylene carbon of the side chain.
- **11.5:** Activation-energy decrease: 34.2 kJ mol^{-1} . Matching uncatalyzed temperature: 492 K , **approximately** 219°C .

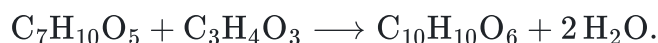
Solution

11.1 — Identifying the hydroxyl group lost

The structures in the overall transformation are:

Name	SMILES
Shikimic acid	<chem>O=C(O)C1=C[C@@H](O)[C@@H](O)[C@H](O)C1</chem>
Pyruvic acid	<chem>CC(=O)C(=O)O</chem>
Chorismic acid	<chem>O=C(O)C1=C[C@@H](OC(=C)C(=O)O)[C@H](O)C=C1</chem>
Water	<chem>O</chem>

The balanced overall equation represented by the supplied scheme is



The decisive information is the **relative stereochemistry**, rather than the positions occupied by groups on the page:

- In shikimic acid, hydroxyl groups **1 and 2 are trans**, whereas **2 and 3 are cis**.

- In chorismic acid, the remaining ring hydroxyl and the oxygen bearing the enolpyruvyl side chain are **trans**.

Thus hydroxyl **2** remains the alcohol, and the oxygen of hydroxyl **1** becomes the ether oxygen. Hydroxyl **3** is lost.

To track the carbon skeleton explicitly, number the original shikimate ring clockwise from its carboxyl-bearing carbon as $S_1, \dots, S_6$. Hydroxyls 3, 2, and 1 then occupy S_3, S_4, S_5 , respectively. The final double bonds are $S_2 = S_3$ and $S_6 = S_1$, and the side chain is attached through the oxygen at S_5 . Reading this product ring in the opposite direction gives the orientation used in the supplied chorismic-acid drawing. No inversion of either retained oxygen-bearing stereocentre is required.

11.2 — Identifying prephenic acid

Chorismic acid has formula $C_{10}H_{10}O_6$, which is retained during rearrangement. Its degree of unsaturation is

$$\text{DBE} = \frac{2(10) + 2 - 10}{2} = 6.$$

The carbon spectrum accounts for these six units as one ring, two carbon–carbon double bonds, and three carbonyl groups:

δ_C , ppm	Assignment
203	Ketone carbonyl
178, 173	Two carboxyl carbonyls
132, 127, each representing two carbons	Four alkene carbons in two equivalent pairs
65	Alcohol-bearing methine carbon
49, 48	Quaternary ring carbon and side-chain methylene carbon

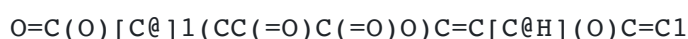
These features require a symmetric cyclohexa-2,5-diene ring carrying both a carboxyl group and a $-\text{CH}_2-\text{C}(=\text{O})-\text{CO}_2\text{H}$ side chain at C1, with an alcohol at C4.

The proton spectrum supports this connectivity:

Signal	Assignment and explanation
$\delta 6.01$, 2H, d, $J = 10.4$ Hz	H2 and H6; each couples principally to the other proton on its double bond. C1 has no hydrogen.
$\delta 5.92$, 2H, dd, $J = 10.4, 3.1$ Hz	H3 and H5; each couples to its alkene neighbour and to H4.
$\delta 4.50$, 1H, t, $J = 3.1$ Hz	H4 on the alcohol-bearing carbon, coupled equally to H3 and H5.
$\delta 3.12$, 2H, s	The side-chain methylene, between a quaternary carbon and a ketone carbonyl; neither adjacent carbon bears a hydrogen.

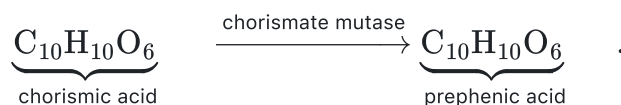
The three rapidly exchanged hydrogens belong to two carboxyl groups and one alcohol. The methylene hydrogens exchange more slowly with heavy water, $[2\text{H}]\text{O}[2\text{H}]$, through enolization next to the ketone.

The product is therefore **prephenic acid**:



Its ring hydroxyl is **cis** to the ring-bound carboxyl group and **trans** to the carbon side chain. The NMR establishes the connectivity and symmetry; this relative configuration follows from the supplied reactant stereochemistry and the concerted rearrangement.

The balanced isomerization is



11.3 — Evaluating the statements

For explicit structural identification, the numbered inhibitors used in the comparisons can be represented as follows. Their chair and twist-boat conformations must be described separately from their SMILES.

Name in the problem	SMILES
Carbocyclic inhibitor 3	<chem>O=C(O)[C@]12C[C@H]([C@H](O)CC1)C[C@@H](C(=O)O)C2</chem>
Monocarboxylic inhibitor 4	<chem>[C@H]12C[C@H]([C@H](O)CC1)C[C@@H](C(=O)O)C2</chem>
Hydroxyl epimer 5	<chem>O=C(O)[C@]12C[C@H]([C@@H](O)CC1)C[C@@H](C(=O)O)C2</chem>
Oxabicyclic inhibitor 7	<chem>O=C(O)[C@]12C[C@H]([C@H](O)C=C1)O[C@@H](C(=O)O)C2</chem>
Oxabicyclic inhibitor 8	<chem>O=C(O)[C@]12C[C@H]([C@H](O)C=C1)O[C@H](C(=O)O)C2</chem>

(a) Correct. Compare hydroxyl epimers **3** and **5**:

$$\frac{\text{IC}_{50}(5)}{\text{IC}_{50}(3)} = \frac{5.3}{0.78} = 6.8.$$

Changing the hydroxyl configuration decreases potency by more than the stipulated factor of five.

(b) Incorrect. Compare dicarboxylic inhibitor **3** with monocarboxylic inhibitor **4**:

$$\frac{\text{IC}_{50}(4)}{\text{IC}_{50}(3)} = \frac{1.1}{0.78} = 1.4.$$

Removing this carboxyl group changes potency by less than fivefold. Thus the data do not support the claim that the presence of **both** carboxyl groups is important under the stated criterion.

(c) Correct. The transition-state assembly contains two distinct six-membered rings. The six-atom ring involved in the Claisen electron redistribution is **chair-like**, while the original carbocyclic ring adopts a **twist-boat** conformation. The geometry represented by the potent bicyclic analogue **8** accommodates both. Describing only the chair-like rearranging ring would omit the second ring.

(d) Correct. Compounds **7** and **8** are diastereomers at the carbon bearing H_a . In the depicted chair framework, H_a is approximately axial in **7** and equatorial in **8**. Consequently, their vicinal coupling patterns differ: the axial proton can have a large approximately antiperiplanar coupling to an adjacent axial methylene hydrogen, whereas the equatorial proton has smaller corresponding couplings. Their H_a resonances can therefore distinguish them.

The correct selection is **(a), (c), and (d)**.

11.4 — Describing the transition-state drawing

Number the chorismic-acid ring clockwise from its carboxyl-bearing carbon:

- C1 bears the ring carboxyl group.
- The initial ring double bonds are C1=C2 and C5=C6.
- C3 bears the ether oxygen O_e .
- C4 bears the alcohol.
- In the side chain, call the substituted alkene carbon C_α and the terminal methylene carbon C_β . Thus the side chain is $O_e - C_\alpha(=C_\beta) - CO_2H$.

The six-atom pericyclic circuit is



Draw this circuit in a **chair-like conformation**, with the original carbocyclic ring in a **twist-boat conformation**, following inhibitor **8**. Its potency relative to **7** is

$$\frac{IC_{50}(7)}{IC_{50}(8)} = \frac{0.0059}{0.00015} \approx 39,$$

supporting the substituent orientation represented by **8**.

The drawing should show these simultaneous bond changes:

Bond	Change during rearrangement
C3- O_e	Breaking
C_β -C1	Forming
C1=C2	Double to single
C2-C3	Single to double
O_e - C_α	Single to carbonyl double bond
$C_\alpha = C_\beta$	Double to single

The three concerted electron-pair movements are:

1. The C1=C2 π electrons form the C2=C3 π bond.
2. The C3- O_e σ electrons form the $O_e = C_\alpha$ carbonyl π bond.
3. The $C_\alpha = C_\beta$ π electrons form the new C_β -C1 σ bond.

Show the forming and breaking bonds as dashed partial bonds, indicate partial π -bond redistribution along the other four edges, and enclose the assembly in brackets with a superscript ‡.

The side chain approaches the ring on the same face as the departing C3-oxygen linkage. The C4 hydroxyl lies on the opposite face. Place the side-chain carboxyl group in the orientation modeled by **8**. This produces the cis relationship between the ring hydroxyl and ring-bound carboxyl group in prephenic acid.

Ordinary SMILES cannot encode fractional transition-state bonds or these conformations; the endpoint SMILES and the specified bond changes define the requested drawing.

11.5 — Activation-energy decrease and equivalent temperature

Use the Arrhenius model

$$k = Ae^{-E_a/(RT)},$$

with the unchanged-prefactor assumption implicit in attributing the acceleration to a decrease in activation energy.

At $T_0 = 298.15 \text{ K}$,

$$\frac{k_{\text{cat}}}{k_{\text{uncat}}} = \exp\left(\frac{E_{a,\text{uncat}} - E_{a,\text{cat}}}{RT_0}\right) = 10^6.$$

Therefore,

$$\begin{aligned}\Delta E_a &= RT_0 \ln(10^6) \\ &= (8.314 \text{ J mol}^{-1}\text{K}^{-1})(298.15 \text{ K})(13.8155) \\ &= 3.4246 \times 10^4 \text{ J mol}^{-1}.\end{aligned}$$

Thus the activation-energy decrease is

$$\boxed{\Delta E_a = 34.2 \text{ kJ mol}^{-1}}.$$

With $E_{a,\text{uncat}} = 86.900 \text{ kJ mol}^{-1}$, the corresponding catalyzed barrier in this model is approximately 52.7 kJ mol^{-1} .

For the uncatalyzed reaction to reach the catalyzed rate at 298.15 K , its rate must increase by 10^6 :

$$\ln(10^6) = \frac{E_{a,\text{uncat}}}{R} \left(\frac{1}{T_0} - \frac{1}{T} \right).$$

Hence

$$\begin{aligned}T &= \left[\frac{1}{298.15 \text{ K}} - \frac{8.314 \text{ J mol}^{-1}\text{K}^{-1}}{86\,900 \text{ J mol}^{-1}} \ln(10^6) \right]^{-1} \\ &= 492.07 \text{ K}.\end{aligned}$$

Therefore,

$$\boxed{T \approx 492 \text{ K} \approx 219^\circ \text{C}}.$$

The solution was checked against the official solution.