Chemistry 2710 Spring 2006 Final Examination

Time: 3 hours

Marks: 103

Aids allowed: Calculator, formula sheet

Instructions: Answer all questions in the booklets provided. You are expected to use your graphing calculator to draw graphs. A reasonable facsimile of your graph with properly labeled axes should be drawn in your exam booklet.

In section 2, you have some choice. Answer *only* the required number of questions. Any extra answers will not be marked. Cross out any work you don't want me to mark.

Useful data:

$$\begin{aligned} h &= 6.626\,068\,8 \times 10^{-34}\,\mathrm{J/Hz} \\ k_B &= 1.380\,650\,3 \times 10^{-23}\,\mathrm{J/K} \\ N_A &= 6.022\,142\,0 \times 10^{23}\,\mathrm{mol^{-1}} \\ R &= 8.314\,472\,\mathrm{J\,K^{-1}mol^{-1}} \\ 1\,\mathrm{m}^3 &= 1000\,\mathrm{L} \end{aligned}$$

To convert degrees Celsius to Kelvin, add 273.15.

1 Answer all questions in this section.

Value of this section: 98

1. Classify each of the following reactions as possibly, probably not or certainly not elementary. Explain your reasoning briefly. [2 marks each]

   (a) $O_{2(g)} + CH_{2(g)} \rightarrow CO_{(g)} + H_2O_{(g)}$

   (b) $2NO_{(g)} + O_{2(g)} \rightarrow 2NO_{2(g)}$

   (c) $OH_{(aq)} + NO_{(aq)} \rightarrow NO^-_{2(aq)} + H^+_{(aq)}$

2. Describe briefly one method for measuring diffusion coefficients. [4 marks]

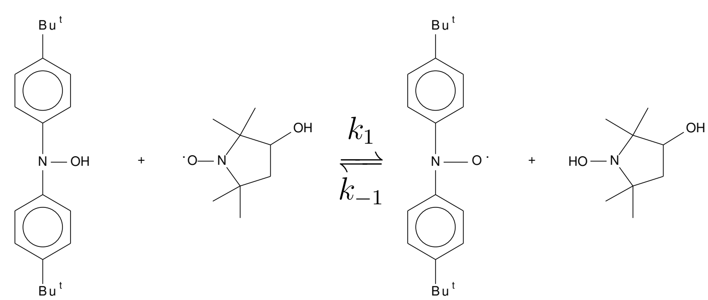
3. The Arrhenius equation applies to a number of physical phenomena in which an energetic barrier must be overcome. For example, diffusion in condensed media (liquids or solids) often obeys an Arrhenius relationship because the diffusing substance must move past the molecules which make up the medium, and there is an energetic cost for this. The following table gives measurements of the diffusion coefficient of *n*-hexane in silicone rubber as a function of temperature:[1]

T/K	368	363	358	353	348
$D/10^{-10}\text{m}^2\text{s}^{-1}$	1.75	1.41	1.11	0.87	0.70

   (a) Show that these data obey the Arrhenius equation and calculate the preexponential factor and activation energy. [12 marks]

   (b) Estimate the diffusion coefficient at 298 K. [2 marks]

4. Sterically hindered hydroxylamines have a number of applications in chemical analysis due to their ability to form stable radicals by transferring a hydrogen atom from their hydroxyl group. The reversible kinetics of the reaction between several hydroxylamines and nitroxyl radicals in aqueous solution have recently been studied.[2] Consider for example the following reaction:



[1]C. Zhao et al., *Eur. Polym. J.* **42**, 615 (2006). The diffusion coefficient depends on a number of details of the preparation of the silicone rubber. One particular data set from this paper is given here.

[2]A. D. Malievskii, S. V. Koroteev and A. B. Shapiro, *Kinet. Catal.* **46**, 812 (2005).

The rate constants are given by

$$k_1 = (5.60 \times 10^5\,\mathrm{L\,mol^{-1}s^{-1}}) \exp\left(\frac{-9205\,\mathrm{J/mol}}{RT}\right),$$

$$\text{and} \quad k_{-1} = (6.90 \times 10^5\,\mathrm{L\,mol^{-1}s^{-1}}) \exp\left(\frac{-753\,\mathrm{J/mol}}{RT}\right).$$

(a) Calculate $\Delta\bar{E}$ for this reaction. [2 marks]

(b) Calculate the equilibrium constant for this reaction at 25°C. [4 marks]

(c) Calculate the entropy of activation of both the forward and reverse reactions at 25°C. Briefly discuss the chemical information about the nature of the transition state contained in the values computed. [7 marks]

5. The rate constant for the elementary reaction

$$\mathrm{Cl} + \mathrm{C_5H_{12}} \rightarrow \mathrm{HCl} + \mathrm{C_5H_{11}}$$

in the solvent carbon tetrachloride has been found to be $7.4 \times 10^9\,\mathrm{L\,mol^{-1}s^{-1}}$ at 25°C.[3]

(a) Use the Stokes-Einstein relationship to estimate the diffusion coefficients of the two reactants at 25°C from the following data:[4]

$$r_{\mathrm{Cl}} = 99\,\mathrm{pm},$$
$$\rho_{\mathrm{C_5H_{12}}} = 0.62\,\mathrm{kg/L},$$
$$M_{\mathrm{C_5H_{12}}} = 72.15\,\mathrm{g/mol},$$
$$\eta_{\mathrm{CCl_4}} = 9.08 \times 10^{-4}\,\mathrm{Pa\,s}$$

Assume that both reactants are approximately spherical. [8 marks]

(b) Estimate the diffusion-limited rate constant for the reaction from these data. Is the reaction diffusion-limited? [5 marks]

6. Triosephosphate isomerase catalyzes the reversible interconversion of glyceraldehyde-3-phosphate and dihydroxyacetone phosphate during glycolysis. In order to function, proteins need to be folded into an appropriate conformation. Mutations which cause misfolding of this protein typically result in haemolytic anaemia coupled with a severe neurodegenerative syndrome. The folding process in normal triosephosphate isomerase has recently been studied.[5] The active form is a dimer, denoted below by $\mathrm{F_D}$ (Folded Dimer). The monomers are initially formed in an unfolded state, $\mathrm{U_M}$ (Unfolded Monomer), which rapidly and reversibly assumes a partially folded conformation, $\mathrm{I_M}$

[3] L. Sheps et al., *J. Phys. Chem. A* **110**, 3087 (2006).

[4] r_{Cl} is the radius of a chlorine atom. $\rho_{\mathrm{C_5H_{12}}}$ is the density and $M_{\mathrm{C_5H_{12}}}$ the molar mass of pentane. $\eta_{\mathrm{CCl_4}}$ is the viscosity of carbon tetrachloride.

[5] H. Pan, A. S. Raza and D. L. Smith, *J. Mol. Biol.* **336**, 1251 (2004).

(Intermediate Monomer). This is then converted more slowly to the Folded Monomer, $\mathrm{F_M}$. Finally, these monomers associate in a fast step into the dimer:

$$\mathrm{U_M} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{I_M} \xrightarrow{k_2} \mathrm{F_M}$$

$$2\mathrm{F_M} \xrightarrow{k_3} \mathrm{F_D}$$

Derive a rate law for the formation of the active dimer. [10 marks]

7. The conversion of testosterone to estradiol is catalyzed by an aromatase enzyme. Methadone, a drug used to treat opiate addicts, has recently been found to inhibit aromatase activity. The following data for the rate of aromatase-catalyzed conversion of testosterone to estradiol were recently obtained using human placental extracts:[6]

[testosterone]/μmol L^{-1}	v/pmol min^{-1}mg^{-1}			
0.05	44	34	23	18
0.1	68	55	43	36
0.2	126	110	76	59
0.4	180	153	126	116
[methadone]/μmol L^{-1}	0	1000	1500	2000

Determine the type of inhibition and the kinetic parameters (e.g. K_S, K_I, $v^0_{\max}$, etc.). [18 marks]

Note: The data are not by any means perfect so some judgement will be required.

8. The incidence of Down's syndrome increases dramatically with maternal age after age 30. The following table gives the probability (P) of Down's syndrome in live births for mothers aged 35 to 49:

Age	35	37	39	40	42	44	46	49
P	$\frac{1}{400}$	$\frac{1}{230}$	$\frac{1}{135}$	$\frac{1}{105}$	$\frac{1}{60}$	$\frac{1}{35}$	$\frac{1}{20}$	$\frac{1}{12}$

One can conceive of at least two general hypotheses to explain these data:

(a) Some toxic substance builds up in the mother's eggs over time.[7]

(b) Some critical component of the mother's eggs breaks down over time.

[6] O. L. Zharikova et al., *Biochem. Pharmacol.* **71**, 1255 (2006). Note that the reaction rate is normalized by the amount of protein in the extract, which explains the units of this quantity in the table.

[7] The father's age has no effect on the incidence of Down's syndrome except for extremely old fathers, so the observed dependence of the incidence on age of the mother is not simply a correlate of the age of the father. We can therefore exclude any hypotheses which involve the sperm.

We can go from these biological hypotheses to kinetic models. If the data are consistent with one model but not the other, then we will know what to look for in a biochemical study of the causes of Down's syndrome. Obviously, a great many kinetic models could be derived from our two biological hypotheses. We will focus on just a few possibilities:

(a) A toxic substance B is produced from a precursor A present at essentially constant levels (perhaps because it is present at very high concentration in the eggs):

$$\mathrm{A} \xrightarrow{k} \mathrm{B},$$

with a constant and $P \propto b$.

(b) A toxic substance B is produced in an autocatalytic process:

$$\mathrm{B} \xrightarrow{k} 2\mathrm{B},$$

where again $P \propto b$.[8]

(c) A critical component B breaks down in, say, a first-order process:

$$\mathrm{B} \xrightarrow{k} \mathrm{X},$$

where X is a harmless product and $1 - P \propto b$. ($1 - P$ is of course the probability of not having a Down's syndrome birth.)

For each of these models,

- Obtain an expression for P as a function of t. This will involve obtaining an integrated rate law for each of the above cases and perhaps doing a little bit of stoichiometry. You'll also have to insert an unknown proportionality constant.
- Devise a graphical method to test the hypothesis implied by the kinetic model. Are all of the models distinguishable based on kinetic evidence alone?
- Apply your test.

Finally, present your conclusions regarding the biochemical basis for Down's syndrome. [20 marks]

[8] If this seems farfetched, note that prion diseases display exactly this kind of kinetics. In prion diseases, B is a misfolded protein which catalyzes the misfolding of other proteins of the same type. The rate constant k is a pseudo-first-order constant which in fact depends on the concentration of the precursor.

2 Answer exactly *one* question in this section.

Value of this section: 5 marks

1. Catalysts are often used in CSTRs by immobilizing them to a solid support. Provided there is plenty of room for fluid to flow around the catalyst, then the CSTR theory we learned in class applies at least approximately to the reactants and products. Suppose that we have immobilized an enzyme in a CSTR. Write down the rate equations for the reactant (substrate), enzyme-substrate complex and product. Assume that the solution pumped into the CSTR during operation contains only the substrate. Note that we can still use enzyme conservation to eliminate the enzyme concentration in this case. [5 marks]

2. Describe the structure of ice cream on a microscopic/chemical level (what it's made of, how these materials are arranged, etc.). [5 marks]

3. Describe briefly the flash photolysis experiment, with a particular emphasis on features which make this experiment suitable for the study of fast reactions. [5 marks]