THE PREPARATORY PROBLEMS FROM THE INTERNATIONAL CHEMISTRY OLYMPIADS

Series 3

33rd – 37th IChOs
2001 – 2005

Edited by Anton Sirota

IChO International and Information Centre

IUVENTA, Bratislava, 2018

34th

PREPARATORY PROBLEMS

Edited by Anton Sirota

23 theoretical problems
6 practical problems

2002

THE PREPARATORY PROBLEMS FROM THE INTERNATIONAL CHEMISTRY OLYMPIADS, Series 3
The Preparatory Problems from the 34th IChO

Edited by Anton Sirota

IChO International Information Centre, Bratislava, Slovakia

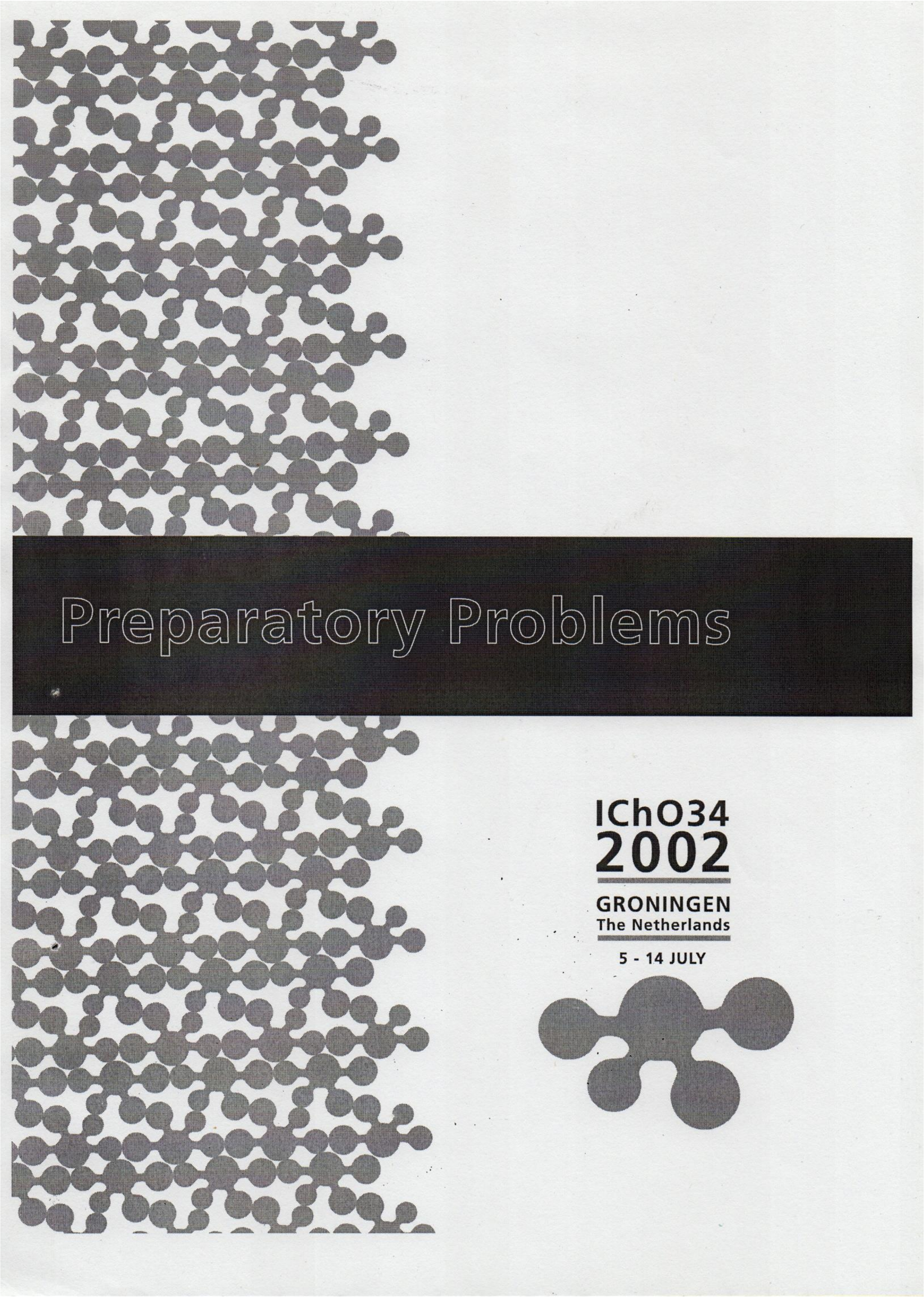
ISBN 978-80-8072-172-5

Issued by IUVENTA in 2018
with the financial support of the Ministry of Education of the Slovak Republic

Number of copies: 200
Not for sale.

:
International Chemistry Olympiad
International Information Centre
IUVENTA
Director: Anton Sirota
Karloveská 64
84258 Bratislava 1, Slovakia
Phone: +421-907-473367
E-mail: anton.sirota@stuba.sk
Web: www.icho.sk

The original title page:



Preparatory Problems

IChO34
2002

GRONINGEN
The Netherlands

5 - 14 JULY

Preface

This booklet contains a series of preparatory problems for the International Chemistry Olympiad in 2002. Most of the problems refer to level 3 mentioned in the Syllabus of the International Chemistry Olympiad. Topics from various areas of chemistry are covered. The scientific committee selected problems which reflect the relevance of modern chemistry and which receive current interest. Of course, problems concerning the understanding of chemistry in qualitative and quantitative terms are included as well.

While working on the problems students will encounter, for example, the chemistry of lactose, which is the by-product of Dutch cheese making, how whales manage to stay under water for a considerable length of time, how the color of Delft blue pottery can be understood, how a bio-compatible polymer can be made from lactic acid, how modern spectroscopy is applied, how the structure of the natural product carvone can be unravelled, how aspects of green chemistry can be treated more quantitatively, how detergents aggregate to give micelles, how a hard coating can be made, and how fuel cells can produce electricity.

In the practical problems microscale equipment will be used. The synthesis of some organic compounds, the use of thin-layer chromatography, the quantitative analysis using spectroscopic methods and the use of enzymes are illustrative for this section.

We recommend that students try to with stand the temptation to look too early at the answers which are included in this booklet. Students will benefit most from these preparatory problems when they try to solve the problems on their own.

It should be emphasized that in answering the questions concise but clear answers must be given. During the Olympiad answer boxes will be provided and the students must give the answers in that box. For two problems such answer boxes have been included in this booklet.

We hope that students and their teachers will consider the problems described in this booklet as a stimulus for the preparation for the competition during the Olympiad in July 2002.

We wish you good luck and hope to welcome you in Groningen.

Acknowledgement
We thank the members of the Scientific Committee for their invaluable contribution in making suitable and relevant problems for the Olympiad in The Netherlands. The contents of this booklet is the result of real teamwork. We owe a special word of thanks to Peter de Groot, Dolf Witte, Ton van Weerd and Wout Davids who served as consulting members of the committee. Their critical comments and constructive remarks were highly appreciated. We also thank Dr. Gordon J.F. Chittenden for proof-reading the manuscript and correcting the English.

Binne Zwanenburg
Chairman

René Ruinaard
Secretary

Scientific Committee of the 34th International Chemistry Olympiad

Chairperson:
Prof.dr. B. Zwanenburg University of Nijmegen

Section Theory:

Prof.dr.ir. H. van Bekkum	Delft University of Technology
Prof.dr. H.P.J. Bloemers	University of Nijmegen
Prof.dr. F.B. van Duijneveldt	University of Utrecht
Prof.dr. J.B.F.N. Engberts	University of Groningen
Dr. GA van der Marel	University of Leiden
Prof.dr. E.w. Meijer	Eindhoven University of Technology
Prof.dr. A Meijerink	University of Utrecht
Prof.dr. A Oskam	University of Amsterdam
Prof.dr. J. Schoonman	Delft University of Technology
Prof.dr. AJ. Schouten	University of Groningen
Ms. Prof.dr. N.H. Velthorst	Free University, Amsterdam
Prof.ir. J.A. Wesselingh	University of Groningen

Section Practical:

Prof:dr. J.F.J. Engbersen	Twente University of Technology
Dr. E. Joling	University of Amsterdam
Dr. A.J.H. Klunder	University of Nijmegen
Dr. AJ. Minnaard	University of Groningen
Dr. JAJ.M. Vekemans	Eindhoven University of Technology
Dr. W.H. de Wolf	Free University, Amsterdam

THE THIRTY-FOURTH INTERNATIONAL CHEMISTRY OLYMPIAD

5 – 14 JULY 2002, GRONINGEN, THE NETHERLANDS

PREPARATORY PROBLEMS

Contents

Theoretical problems

Practical Problems

* * *

PREPARATORY THEORETICAL PROBLEMS

THEORETICAL PROBLEM 1

Production of ammonia

Ammonia is an important commodity chemical used for the manufacture of the fertilizer urea and many other products. The production of ammonia takes place according to the equilibrium reaction:

$$N_2 + 3\ H_2 \leftrightarrows 2\ NH_3$$

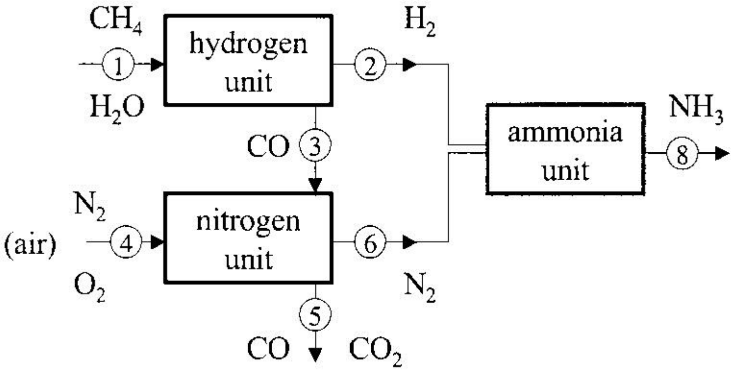
The hydrogen in the ammonia plant is obtained from methane and water by the reaction:

$$CH_4 + H_2O \rightarrow CO + 3\ H_2$$

Nitrogen is taken from the air, whereby oxygen is removed by the reaction with CO as follows:

$$O_2 + 2\ CO \rightarrow 2\ CO_2$$

In the air the nitrogen content is 80%. The reactions are performed in a catalytic reactor, the diagram of which is shown below. The respective flows are numbered in the arrows.



Assume that the reactants are converted completely. Take as flow for ammonia at position ⑧; [n(NH$_3$) ⑧] = 1000 mol s^{-1}.

1.1 Calculate the following flows in the plant in mol s^{-1}

n[H$_2$ ②], for hydrogen at position ②

n[N$_2$ ⑥], for nitrogen at position ⑥

n[CH$_4$ ①], for methane at position ①

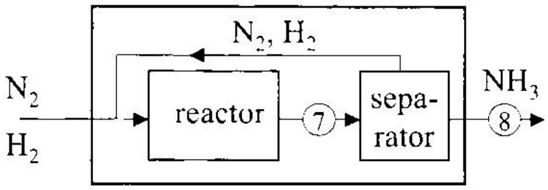
n[H$_2$O ①], for water at position ①

n[CO ③], for CO at position ③

n[O_2 ④], for oxygen at position ④

n[CO ⑤], for CO at position ⑤

In real practice the ammonia formation is an equilibrium reaction, converting only a part of the reactants. The ammonia unit thus must be equipped with a separator and a recycle unit, as shown below.



ammonia unit

Suppose the recycle of N_2 + H_2 that leaves the separator is two times the NH_3 flow.

1.2 Calculate the flow of N_2 at position ⑦ and the flow of H_2 at positions ⑦.

At a temperature $T = 800$ K, the Gibbs energies of the three gases are:

$G(N_2) = -8.3\times10^3$ J mol^{-1}

$G(H_2) = -8.3\times10^3$ J mol^{-1}

$G(NH_3) = 24.4\times10^3$ J mol^{-1}

1.3 Calculate the change in the Gibbs energy (ΔG_f) for the conversion of one mole of N_2.

1.4 Calculate the equilibrium constant K_r, for the NH_3 formation, using ΔGr_f (see 1.3).

The gas constant equals to: $R = 8.314$ J mol^{-1} K^{-1}. Equilibrium constants can also be expressed in partial pressures of the reactants, thus:

$$K_r = \frac{p_{NH_3}^2}{p_{N_2}\, p_{H_2}^3}$$

The partial pressure of ammonia at position ⑦ is a fraction x of the total pressure:

$p_{NH_3} = x\, p_{tot}$ where x is also expressed by the flow ratio n_{NH_3} / n_{tot}.

1.5 Derive the equations for the partial pressures p_{N_2} and p_{H_2} at position ⑦.

1.6 Insert the partial pressures in K_r and simplify the formula thus obtained as much as possible.

1.7 Calculate x when $p_0 = 0.1$ Mpa and $p_{tot} = 30$ MPa. (Hint: K_r has been calculated in 1.4).

SOLUTION OF PREPARATORY PROBLEM 1

1.1 $n(H_2$, ②$)$ = 3 × ½ × 1000 = 1500 mol s^{-1}

$n(N_2$, ⑥$)$ = ½ × 1000 = 500 mol s^{-1}

$n(CH_4$, ①$)$ = ½ × 1000 = 500 mol s^{-1}

$n(H_2O$, ①$)$ = ½ × 1000 = 500 mol s^{-1}

$n(CO$, ③$)$ = ½ × 1000 = 500 mol s^{-1}

$n(O_2$, ④$)$ = ¼ × ½ × 1000 = 125 mol s^{-1}

$n(CO$, ⑤$)$ = $n(CO$, ③$)$ – 2 $n(O_2$, ④$)$ = 250 mol s^{-1}

1.2 $n(N_2$, ⑦$)$ + $n(H_2$, ⑦$)$ = 2 $n(NH_3$, ⑦$)$ = 2 $n(NH_3$, ⑧$)$

$n(N_2$, ⑦$)$ = 500 mol s^{-1} $n(H_2$, ⑦$)$ = 1500 mol s^{-1}

1.3 $\Delta G_r = 2\,G(NH_3) - G(N_2) - 3\,G(H_2)$

$\Delta G_r = (2 \times 24.4 + 8.3 + 3 \times 8.3) \times 10^3 = 82 \times 10^3$ J mol^{-1}

1.4 $\Delta G_r = -\,\mathrm{RT} \ln K_r$ $K_\mathrm{r} = 4.4 \times 10^{-6}$

1.5 $p_{N_2} = 1/4\,(1 - x)\,p_\mathrm{tot}$

$p_{N_2} = 3/4\,(1 - x)\,p_\mathrm{tot}$

1.6
$$K_r = \frac{x^2}{(1-x)^4}\left(\frac{4^4}{3^3}\right)\left(\frac{p_0}{p_\mathrm{tot}}\right)^2$$

1.7
$$\frac{x^2}{(1-x)^4} = K_r\left(\frac{3^3}{4^4}\right)\left(\frac{p_\mathrm{tot}}{p_0}\right)^2 = 0.0418 \;\Rightarrow\; x = (1-x)^2\sqrt{0.0418}$$

$-\,0.204\,x^2 + 1.408\,x - 0.204 = 0 \rightarrow x = 0.148$

THEORETICAL PROBLEM 2

Myoglobin for oxygen storage

Myoglobin (Mb) is a protein containing a hem (iron) group. Myoglobin is an enzyme that allows storage of oxygen. Each myoglobin molecule can reversibly bind one oxygen molecule according to the equation:

$Mb + O_2$ € MbO_2

This oxygen storage is important for diving animals such as whales. We are going to investigate how whales use it.

The fraction of Mb that is bound to oxygen increases with the oxygen concentration as:

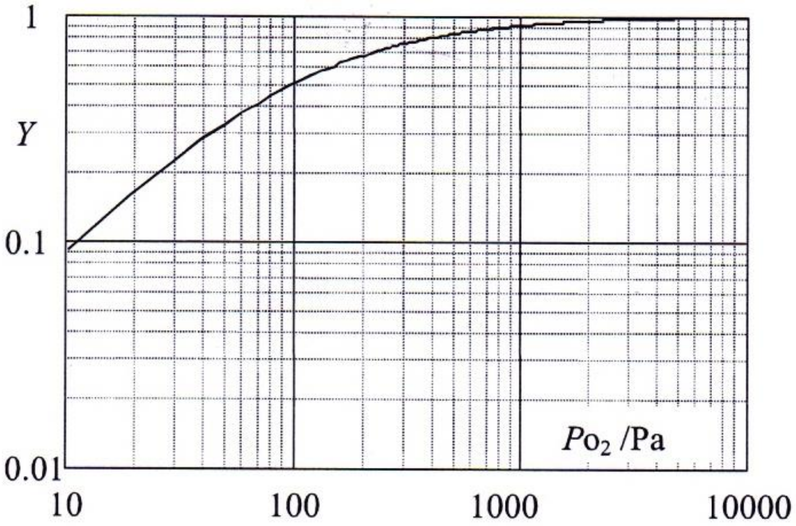
$$Y = \frac{c_{O_2}}{c_{O_2} + K_c}$$, wherein K_c is a constant.

Oxygen is only slightly soluble in water: the amount that dissolves is proportional to the oxygen pressure: $c_{O2} \propto p_{O2}$

The fraction of Mb bound is then related to the oxygen pressure by:

$$Y = \frac{p_{O_2}}{p_{O_2} + K_p}$$ wherein K_p is a constant.

The graph below is showing this relation (the scale of the graph is logarithmic!)



Determine the value and the unit of the constant K_p in the formula above (use the graph).

The Mb molecule has the dimensions of 4.5 × 3.5 × 2.5 nm meaning that Mb fits in a box with these dimensions. Because the molecule is roughly elliptical in shape it will have a volume of about one half of the volume of the box. Proteins have a density of about 1400 kg m^{-3}. The Avogadro number is $N_A = 6.02\times10^{23}$ mol^{-1}.

2.2 Estimate the molar mass of Mb.

Whales obtain their oxygen by breathing air. They can stay under water for a long time using their oxygen storage. Assume that 20 % of the mass of their muscular tissues consists of myoglobin.

2.3 Calculate how many moles of oxygen the whale can store per kilogram of tissue.

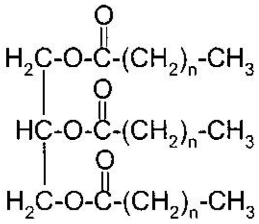
Oxygen is used to produce energy (heat and motion) by burning fat. The overall equation can be approximated by:

$$(CH_2)_n + 1.5\ n\ O_2 \rightarrow n\ CO_2 + n\ H_2O$$

The energy released by this type of reaction is about 400 kJ per mole of oxygen. A large animal, such as a whale, needs to dissipate about 0.5 W per kg of mass of muscle tissue to stay warm and keep moving.

2.4 Calculate how long the whale can stay under water.

2.5 Give the equation for the burning of a real fat molecule:



SOLUTION OF PREPARATORY PROBLEM 2

2.1 Take at the X-axis 100, this corresponds with 0.5 at the Y-axis, thus

$$0.5 = \frac{100}{100 + K_p} \qquad 50 + 0,5\ K_p = 100 \qquad K_p = 100$$

2.2 Volume of myoglobin V_{Mb}:

$V_{\text{Mb}} = 0.5 \times 4.5\ \text{nm} \times 3.5\ \text{nm} \times 2.5\ \text{nm} = 19.7\ \text{nm}^3 = 19.7\times10^{-27}\ \text{m}^3$

Molecular mass of Mb, M_{Mb}:

$M_{\text{Mb}} = V_M \times \rho_{\text{Mb}} \times N_A = 19.7\times10^{-27}\ \text{m}^3 \times 1400\ \text{kg m}^{-3} \times 6.02\times10^{23}\ \text{mol}^{-1} = 16.6\ \text{kg mol}^{-1}$

2.3 1 kg Mb is 1/16 mol: 20 % is 0.2/16.6 = 0.012 mol kg^{-1}

2.4 400 kJ mol^{-1} → 400 000 × 0.012 J kg^{-1} of muscle tissue W = J s^{-1} ⇒ per second per kg of muscle tissue 0.5 J.

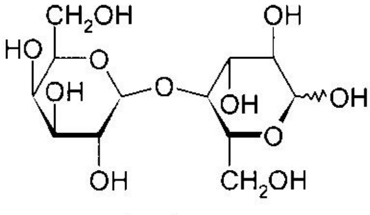
$$\text{Time} = \frac{400000 \times 0.012}{0.5} = 9.600\ \text{s} = 2\ \text{hours and } 40\ \text{minutes}$$

2.5 $(CH_2)_{3n+6}\ (CO_2)_3H_2 + (4.5n + 9.5)\ O_2 \rightarrow (3n + 9)O_2 + (3n + 7)\ H_2O$

THEORETICAL PROBLEM 3

Lactose Chemistry

Lactose (milk sugar) is produced on a fairly large scale in The Netherlands starting from whey (a by- product of cheese manufacture). Lactose is applied in baby food and in pharmaceutical tablets. It is a disaccharide composed of the monosaccharides D-galactose and D-glucose. The structure is shown below (Haworth projection). The left hand monosaccharide unit is D-galactose.



Lactose

3.1 Draw the Fischer projection of D-galactose and D-glucose.

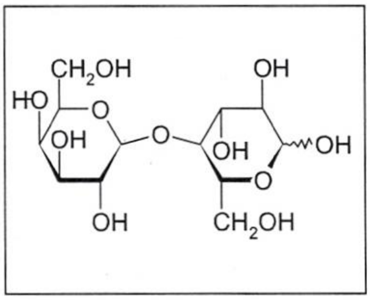
3.2 The acid-catalysed hydrolysis of lactose gives D-galactose and D-glucose.

Indicate with an arrow in the formula of lactose:

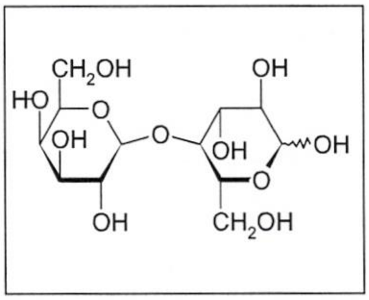
(a) To which oxygen atom a proton will be attached in order to effect hydrolysis.

(b) Which carbon-oxygen bond will be cleaved during the hydrolysis reaction.

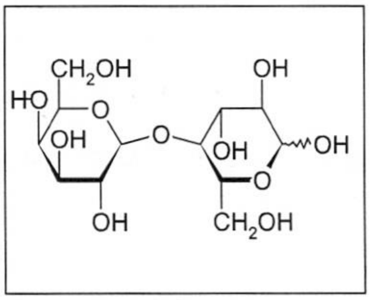
(c) Which carbon atom will be involved in the reaction with Fehling's reagent (this reagent is used to detect reducing sugars).



Answer box (a)



Answer box (b)



Answer box (c)

The hydrolysis of lactose can be coupled with hydrogenation using a metal catalyst which leads to the polyalcohols sorbitol and galactitol, also known as glucitol and dulcitol, respectively.

3.3 Draw Fischer projections of sorbitol and galactitol.

Indicate whether these compounds are optically active or inactive.

Sorbitol: Optically active – Yes / No,

Galactitol. Optically active – Yes / No,

In industrial processes lactose is isomerised to lactulose, which is an intestinal pharmaceutical. Hydrogenation of lactose leads to lactitol, a C_{12}-polyol which is a low-calorific sweetener. Both processes are executed in The Netherlands.

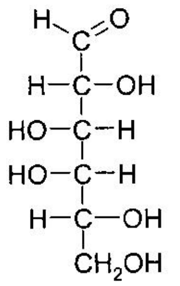
3.4 (a) Draw the Haworth structure of lactulose.

(Hint: The glucose part of lactose has been isomerised to be keto-sugar fructose.)

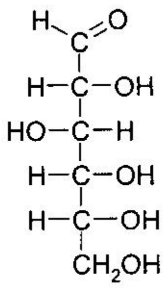
(b) Draw the Haworth structure of lactitol.

SOLUTION OF PREPARATORY PROBLEM 3

3.1

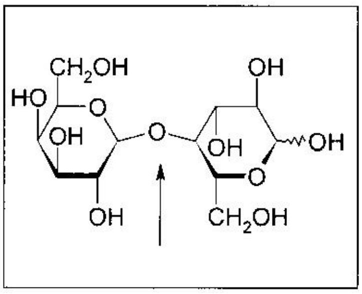


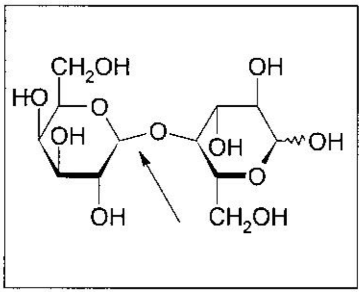
D-galactose

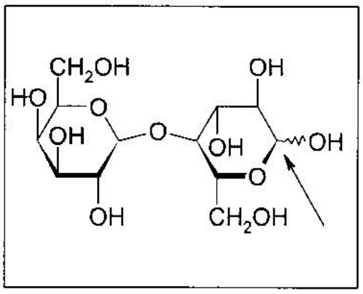


D-glucose

3.2

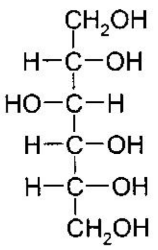






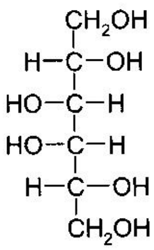
3.3

Sorbitol



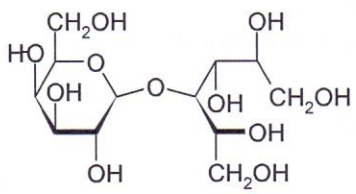
Optically active: [✓ yes] / no

Galactitol

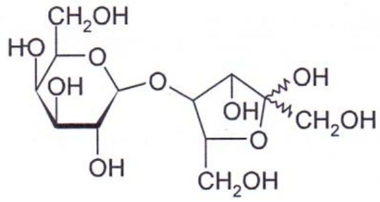


Optically active: yes / [✓ no]

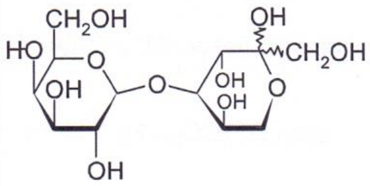
3.4



Lactitol



Lactulose
furanose form



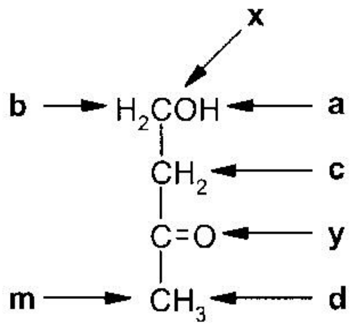
Lactulose
pyranose form

Lactulose is a mixture of the furanose and pyranose form in the ration 4 : 6. When a student gives either the furanose or the pyranose form, he/she will receive full marks.

THEORETICAL PROBLEM 4

Atom Mobility (Dynamics) in Organic Compounds

For the study of reaction mechanism in organic chemistry isotopic labeling, e. g. with ^{2}H or ^{17}O can give valuable information. Modern NMR techniques are able to “see“ deuterium ^{2}H and the oxygen isotope ^{17}O. As an example, the introduction of isotopic labels in 4-hydroxybutan-2-one is considered.



a, **b**, **c**, **d** are hydrogen atoms, **x**, **y** are oxygen atoms and **m** is a carbon atom.

4.1 The substrate is treated with $^{2}H_2O$ at pH = 10. Rank the order the exchange (introduction) of deuterium atoms (^{2}H) from first to last.

First ☐ ☐ ☐ ☐ last.

4.2 Similarly the substrate is treated with $H_2{}^{17}O$ at pH = 10. Rank the order of introduction of ^{17}O from the first to the last.

First ☐ ☐ last.

4.3 Do you consider the exchange method appropriate for the introduction of a ^{13}C at position **m.** Yes or No?

SOLUTION OF PREPARATORY PROBLEM 4

4.1 a >> c, d > b

4.2 y > x

4.3 No

THEORETICAL PROBLEM 5

Towards Green Chemistry: The E-factor

He well being of modern society is unimaginable without a myriad of products of industrial organic synthesis, from pharmaceutical combating diseases or relieving pain, to synthetic dyestuffs for aesthetic appeal. The flip side of the coin is that many of these processes generate substantial amounts of waste. The solution is not less chemistry bur alternative, cleaner technologies that minimize the waste. In order to evaluate the environmental (un)friendliness of a process, the terms “atom utilization” and “the E-factor” were introduced. The atom utilization is obtained by dividing the molar mass of the desired product by the sum of the molar masses of all substances produced according to the reaction equations. The E-factor is the amount (in kg) of by-products per kg of the product.

Methyl methacrylate is an important monomer for transparent materials (Plexiglas).

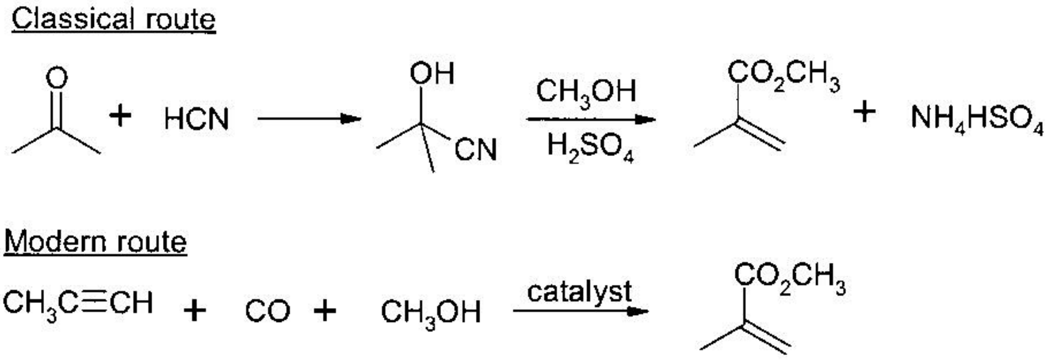


Figure 1: Methyl methacrylate synthesis.

5.1 Calculate the atom utilization and the E-factor for both processes. The classical and a process for methyl methacrylate manufacture are shown in Figure 1.

Another example is the manufacture of ethane oxide (see Figure 2). The classical route produces calcium chloride. Moreover, 10 % of the ethane is converted into 1,2-ethanediol by hydrolysis. In the modern direct route a silver catalyst is applied. Here, 15 % of the ethene is oxidized to carbon dioxide and water.

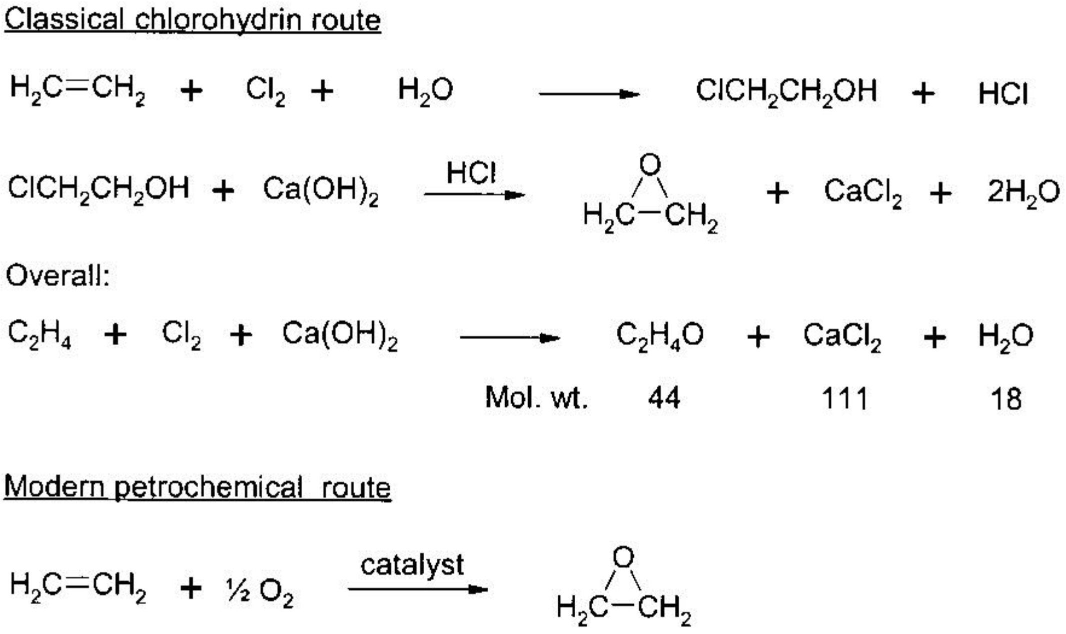


Figure 2: Ethene oxide synthesis.

5.2 Calculate the atom utilization and *E*-factor for both processes.

SOLUTION OF PREPARATORY PROBLEM 5

5.1 The relative molecular mass of methyl methacrylate = 100

The relative molecular mass of NH_4HSO_4 = 115

Classical route: Atom utilization = 100/(100 + 115) = 0.47 or 47 %

E-factor= 115/100 = 1.15

Classical route: Atom utilization = 115/115 = 1 or 100 %

E-factor= 0/100 = 0

5.2 Classical chlorohydrin route: Atom utilization = 44/173 = 0.25 or 25 %

Modern petrochemical route: Atom utilization = 44/44 = 1 or 100 %

Classical route: *E*-factor = 133.4/39.6 = 3.37

product: 44 – (10 % of 44) = 39.6

by-products: 111 + (10 % of 62) + (18 – 10 % of 18) =

= 111 + 6.2 + 16.2 = 133.4

Modern route: *E*-factor = 18.6 / 37.4 = 0.50

product: 44 – (15 % of 44) = 37.4

by-products: 2 CO_2 + 2 H_2O per mole of C_2H_4 (15 %) $\Rightarrow$

2 × 15 % of 18 = 5.4

THEORETICAL PROBLEM 6

Selective solubility

Solubility is an important factor of the measurements of the environmental pollution of salts. The solubility of a substance is defined as the amount that dissolves in a given quantity of solvent to form a saturated solution. The solubility varies greatly with the nature of a solute and the solvent, and the experimental conditions, such as temperature and pressure. The pH and the complex formation also may have influence on the solubility.

An aqueous solution contains $BaCl_2$ and $SrCl_2$ both in a concentration of 0.01 mol dm^{-3}. The question is whether it will be possible to separate this mixture completely by adding a saturated solution of sodium sulphate. The criterion is that at least 99.9 % of the Ba^{2+} has precipitated as $BaSO_4$ and that $SrSO_4$ may be contaminated with no more than 0.1 % $BaSO_4$. The solubility product constants are as follows:
$K_s(BaSO_4) = 1\times10^{-10}$ and $K_s(SrSO_4) = 3\times10^{-7}$.

6.1 (a) Give the relevant equations.
(b) Calculate the residual concentration of Ba^{2+}.
(c) Calculate the percentage of Ba^{2+} and Sr^{2+} in the separated substances.

Complex formation may have a profound effect on the solubility. A complex is a charged species consisting of a central metal ion bonded to one of more ligands. For example $Ag(NH_3)_2^+$ is a complex containing Ag^+ as the central ion and two NH_3 molecules as ligands.

The solubility of AgCl in water is 1.3×10^{-5} mol dm^{-3}.
The solubility product constant of AgCl is 1.7×10^{-10}.
The equilibrium constant K_f for the formation of the complex has a value of 1.5×10^7.

6.2 Show by calculation that the solubility of AgCl in aqueous ammonia (c = 1.0 mol dm^{-3}) is higher than in pure water.

SOLUTION OF PREPARATORY PROBLEM 6

6.1 The relevant equations are:

$Ba^{2+}(aq) + SO_4^{2-}(aq) \leftrightarrows BaSO_4(s)\downarrow$

$Sr^{2+}(aq) + SO_4^{2-}(aq) \leftrightarrows SrSO_4(s)\downarrow$

Precipitation of $BaSO_4$ will start when

$$[SO_4^{2-}] = \frac{K_{sp}(BaSO_4)}{[Ba^{2+}]} = \frac{1\times10^{-10}}{1\times10^{-2}} = 1\times10^{-8} \qquad (1)$$

Precipitation of $SrSO_4$ will start when

$$[SO_4^{2-}] = \frac{K_{sp}(SrSO_4)}{[Sr^{2+}]} = \frac{3\times10^{-7}}{1\times10^{-2}} = 3\times10^{-5} \qquad (2)$$

If there are no kinetic complications (for example when the formation of $BaSO_4$ would be very slow) first $BaSO_4$ will be formed. This results in a decrease of the concentration of Ba^{2+} ions. If the concentration SO_4^{2-} satisfies equation (2), the concentration of Ba^{2+} can be calculated from the formula:

$K_{sp}(BaSO_4) = 1\times10^{-10} = [Ba^{2+}]\ 3\times10^{-5}$

$$[Ba^{2+}] = \frac{1\times10^{-10}}{3\times10^{-5}} = 1/3\times10^{-8}$$

Al the starting point the concentration of Ba^{2+} was 1×10^{-2} mol dm^{-3}. This means that the loss amounts to

$$\frac{1/3\times10^{-5}}{1\times10^{-2}}\times100\ \% = 0.033\ \%$$

The separation meets the criterion. The following equilibrium reactions have to be considered:

$$AgCl(s) \leftrightarrows Ag^+(aq) + Cl^-(aq)$$

$$Ag^+(aq) + 2\,NH_3(aq) \leftrightarrows Ag^+(aq) + Cl^-(aq)$$

$$\text{Total: } AgCl(s) + 2\,NH_3(aq) \leftrightarrows Ag(NH_3)_2^+(aq) + Cl^-(aq)$$

$$\text{overal} = K_{sp}\ K_f = \frac{[Ag(NH_3)^{2+}][Cl^-]}{[NH_3]^2} = 1.7\times10^{-10}\times1.5\times10^{-7} = 2.6\times10^{-3}$$

If x is the molar solubility of AgCl (mol dm^{-3}) then the changes in concentration of AgCl as the result of the formation of the complex ion are:

$$AgCl(s) + 2\,NH_3(aq) \leftrightarrows Ag(NH_3)_2^+(aq) + Cl^-(aq)$$

Concentration			
Starting point:	1.0	0.0	0.0
Change:	$-2x$	$+x$	$+x$
Equilibrium:	$(1.0 - 2x)$	$+x$	$+x$

K_f is quite large so most of the Ag^+ ions exist in the complexed form.

In absence of NH_3 at equilibrium holds $[Ag^+] = [Cl^-]$.

Complex formation leads to: $[Ag(NH_3)_2^+] = [Cl^-]$

$K_{overall}$ can be written as:

$$K_{overal} = \frac{x\,.\,x}{(1.0 - 2x)^2} \qquad 2.6\times10^{-3} = \frac{x^2}{(1.0 - 2\,x)^2} \quad \text{or} \quad 0.051 = \frac{x}{(1.0 - 2x)}$$

and $x = 0.046$ mol dm^{-3}

This result means that 4.6×10^{-2} mol of AgCl dissolves in 1 dm^3 of NH_3 aqueous solution with the concentration of 1.0 mol dm^{-3}. Thus the formation of the complex ion $Ag(NH_3)_2^+$ enhances the solubility of AgCl, because in pure water the solubility of AgCl amounts to only 1.3×10^{-5} mol dm^{-3}.

THEORETICAL PROBLEM 7

UV-spectroscopy as an Analytical Tool

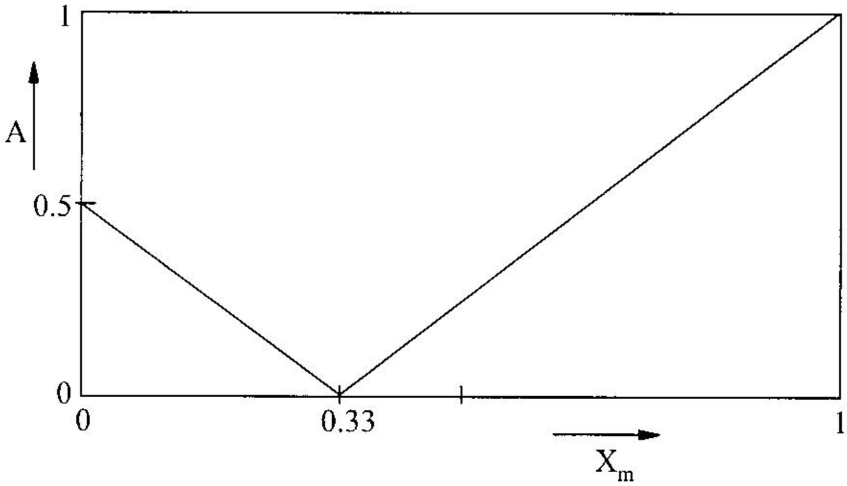
UV-spectrometry is frequently used to determine the concentration of a substance in solution by measuring the UV absorbance at a certain wavelength or either visible or ultraviolet light. The law of Lambert and Beer states that the absorbance is directly proportional to the concentration in moles per dm^3 at a given wavelength: $A = \varepsilon\, c\, l$ (ε is a molar absorptivity or extinction coefficient in dm^3 mol^{-1} cm^{-1}, the path length in cm. $A = \log I_o / I$.

Here the maximal and minimal concentration that can be measured for the redox concentration Fe(II) fenathroline (ferroin) will be considered: (λ_{max} = 512 nm, ε = 10500 dm^3 mol^{-1} cm^{-1}).

7.1 Calculate the lowest concentration of ferroin that can be measured in a 1 cm cuvet at 512 nm. If a 2 % difference of light intensity still can be measured.

7.2 Calculate the highest concentration of ferroin that can be measured in a 1 cm cuvet at 512 nm if at least 2 % of the incident light must reach the detector.

The composition of a complex between a metal M and a ligand L can also be determined spectrometrically using the method of Continuous Variations, also known as Job' s method whereby the sum of molar concentrations of M and L is kept constant as their ration is varied. The following graph of absorbance vs. mol fraction for a complex is given, whereby the mol fraction $x_M = c_M / (c_M + c_L)$ is varied (measurement at 552 nm).



7.3 Determine the composition of the complex and show your calculation.

7.4 Which compounds absorb at x_M = 0?

Which compounds absorb at x_M = 1?

Show how you derive your answer.

7.5 Calculate the ratio of the extinction coefficients of M and L.

7.6 Calculate the percentage of the incident light that has been transmitted through the solutions belonging to $x_M = 0$ and $x_M = 1$, respectively.

SOLUTION OF PREPARATORY PROBLEM 7

7.1 2% decrease in light intensity implies: $I / I_0 = 98/100$ and $A = -\log 98/100 = 0.01$

This absorption corresponds with $0.01 = 10500 \times c_{\min} \times l \Rightarrow c_{min} = 0.95\times10^{-6}$ mol dm^{-3}

7.2 2 % light throughput means that: $I / I_0 = 2/100$ and $A = \log 100/2 = 2 - 0.3010 = 1.6990$

For ferroin this absorption at 512 nm corresponds with:

$1.6990 = 10500 \times c_{\max} \times l \Rightarrow c_{\max} = 1.618\times10^{-4}$ mol dm^{-3}

7.3 Minimum in curve at $x_M = 0.33$: $c_M = 0.33\ c_M + 0.33\ c_L$ or $0.67\ c_M = 0.33\ c_L$

7.4 For $x_M = 0$: $c_M / c_M + c_L = 0$, $c_M = 0$ and $c_L = 1$

For $x_M = 1$: $c_M / c_M + c_L = 1$, $c_M = 1$ and $c_L = 0$

M and L both absorb and have an absorption of $A_M = 1.0$ and $A_L = 0.5$, respectively.

7.5 $x_M = 0$, $c_L = 1$, $A_L = \varepsilon_L\ c_L\ l$

$x_M = 1$, $c_M = 1$, $A_M = \varepsilon_M\ c_M\ l$

l has the same value in booth formulas, just as c_L and c_M, so that

$\varepsilon_L / \varepsilon_M = A_L / A_M = 0.5 / 1$, thus $c_M = 2\ \varepsilon_L$

7.6 For $x_M = 0$ holds $0.5 = -\log I / I_0$ $I / I_0 = 0.32$ thus 32 % has been transmitted

For $x_M = 1$ holds $1 = -\log I / I_0$ $I / I_0 = 0.1$ thus 10 % has been transmitted

THEORETICAL PROBLEM 8

Reaction Kinetics

The study of reaction kinetics provides essential information about details of chemical reactions. Here the formation of NO and its reaction with oxygen is considered. The formation of NO takes place according to the equation:

$2\ NOCl(g) \rightarrow 2\ NO(g) + Cl_2(g)$

The rate constant $k = 2.6\times10^{-8}\ dm^3\ mol^{-1}\ s^{-1}$ at 300 K and $4.9\times10^{-4}\ dm^3\ mol^{-1}\ s^{-1}$ at 400 K. The gas constant $R = 8.314\ J\ mol^{-1}\ K^{-1}$.

8.1 Calculate the activation energy for the NO formation using the Arrhenius equation.

The reaction of NO with oxygen is as follows:

$2\ NO(g) + O_2(g) \rightarrow 2\ NO_2(g)$

8.2 Give the rate equation for the NO_2 formation on basis of this mechanism.

Experimentally, the rate equation reads $s = k\ [NO]^2\ [O_2]$

8.3 Which conclusion do you draw?

☐ The proposed mechanism is incorrect.

☐ The proposed mechanism is correct.

☐ The experiment is non-conclusive.

Mark the correct answer.

SOLUTION OF PREPARATORY PROBLEM 8

8.1 Due to the Arrhenius equation: $\log k = \log A - E_a / 2.3\,RT$

we can substitute the values of k and T:

$\log k_1 = \log A - E_a / 2.3\,RT_1$, $\log k_2 = \log A - E_a / 2.3\,RT_2$

Subtraction gives:

$$\log k_1 - \log k_2 = -\frac{E_a}{2.3\,R}\left(\frac{1}{T_1} + \frac{1}{T_2}\right)$$

$$E_a = 2.3\,R\left(\frac{T_1\,T_2}{T_2 - T_1}\right) = \log\frac{k_2}{k_1} = 2.3 \times 8.314 \times \frac{300 \times 400}{400 - 300}\log\frac{4.9\times 10^{-4}}{2.6\times 10^{-8}}$$

E_a = 98.225 kJ mol^{-1}

8.2 The slow step is the rate determining; this is the second reaction.

The expression for s is: $\frac{d[NO_2]}{dt} = k_2[NO_3][NO]$

The equilibrium gives: $K = \frac{k_1}{k_{-1}} = \frac{[NO_3]}{[NO][O_2]}$

Rewritten this is: $[NO_3] = K\,[NO][O_2]$

Substitution gives for s: $s = k_2\,K\,[NO]^2[O_2]$

8.3 The proposed mechanism is correct.

THEORETICAL PROBLEM 9

Bonding and bond energies

A number of processes with salts and crystals can be understood by estimating the energies involved with a simple ionic model in which the ions have a specific radius and a change equal to an integer number times by elementary charge. This model is used to describe the dissociation of ionic molecules in the gas phase. Such dissociations usually lead directly to neutral atoms, but the dissociation energy can be calculated by assuming a hypothetical reaction path which involves dissociation to free ions, followed by neutralization of the ions. This is the Born-Haber cycle.

The bonding energies, electron affinity and ionization energies of the following diatomic species have been measured:

Bonding energy NaCl = – 464 kJ mol^{-1}
Bonding energy KCl = – 423 kJ mol^{-1}
Bonding energy MgCl = – 406 kJ mol^{-1}
Bonding energy CaCl = – 429 kJ mol^{-1}

Electron affinity Cl = – 360 kJ mol^{-1}
Ionization energy Na = 496 kJ mol^{-1}
1st ionization energy Ca = 592 kJ mol^{-1}
2nd ionization energy Ca = 1148 kJ mol^{-1}

9.1 Design a Born-Haber cycle for the dissociation of NaCl into neutral atoms and calculate the dissociation energy of NaCl. Assume that the bonding is completely (100 %) ionic in nature.

9.2 Design a Born-Haber cycle for the dissociation of $CaCl_2$ into three neutral atoms and calculate the dissociation energy of $CaCl_2$ assuming that the bond length in the triatomic species is 9 % shorter than in the diatomic species.

SOLUTION OF PREPARATORY PROBLEM 9

9.1 Born-Haber cycle for the dissociation of NaCl into Na + Cl:

$NaCl \longrightarrow Na^+ + Cl^-$

$Na^+ + Cl^- \longrightarrow Na + Cl$

The energy loss in the first step is 464 kJ mol^{-1}.

The energy gain in the second step is – (I.E. of Na + E.A. of Cl) = – 136 kJ mol^{-1}

Overall loss = dissociation energy = 328 kJ mol^{-1}

9.2 Born-Haber cycle for the dissociation of $CaCl_2$ into Ca + 2 Cl :

$CaCl_2 \longrightarrow Ca^{2+} + 2\,Cl^-$

$Ca^{2+} + 2\,Cl^- \longrightarrow Ca + 2\,Cl$

The (ionic) bond energy of $Ca^{2+}Cl^-$ = – 429 × 2 / 0.91 = – 943 kJ mol^{-1}

(The measured value for CaCl is – 429, but the change of Ca is now +2 and the bond length has decreased by a factor of 0.91).

The energy loss in the first step = – (bond energy of $CaCl_2$) = 2 × 942 minus the Cl–Cl repulsion.

The Cl–Cl repulsion is (429 / 2) × (1 / 0.91) = 236 kJ mol^{-1}, so the energy loss in the first step = 1650 kJ mol^{-1}.

The energy gain in the second step is:

– (2 × E.A. of Cl + total I.E. of Ca) = –1020 kJ mol^{-1}.

Dissociation energy into atoms = 630 kJ mol^{-1}.

THEORETICAL PROBLEM 10

The Nature of Phosphorus

Phosphorus is an important element in naturally occurring as well as in man-made products. Typical examples are phospholipids, nucleic acids and ligands for efficient catalysis. Furthermore, ^{31}P-NMR spectra can provide valuable information of P containing products. A characteristic feature of ^{31}P-NMR spectra (interaction with protons is removed by decoupling) is the rather large chemical shift differences for structurally related structures. (Note: Optical antipodes = enantiomers do not show a difference in NMR-spectra.)

The dialkyl phosphate **A** is derived from racemic butan-2-oland dialkyl phosphate **B** from enantiomerically (optically) pure (S)-butan-2-ol. The 1H-decoupled ^{31}P-spectrum of **A** is shown in the figure. The spectrum of **B** shows only one peak and that has the same chemical shift as one of tzhe signal of **A**.

Note: A dialkylphosphite has the formula $(RO)_2P\text{-}OH$.

10.1 Draw the spatial structures and the corresponding Fischer projections of the stereoisomers that can account for the spectrum of **A** (Figure 1).

Draw the spatial structures and the Fischer projections of compound **B**.

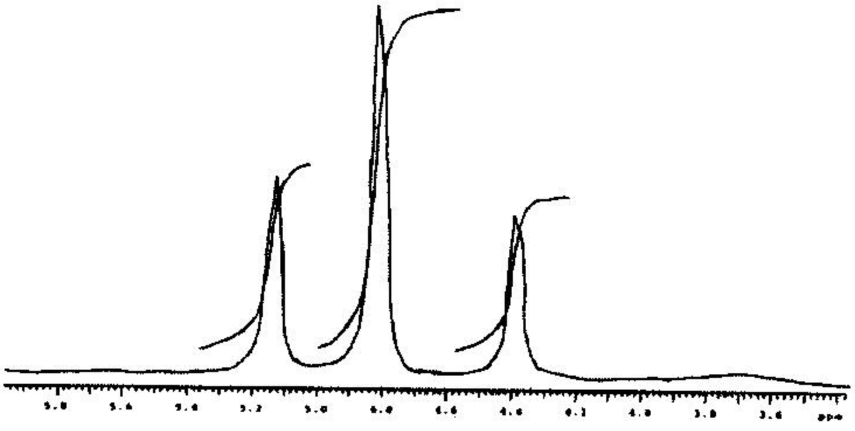


Figure: The ^{31}P-NMR spectrum of **A** (^{1}H-decoupled).

Compound **C** is a dialkyl phosphate derived from methanol.

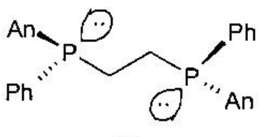
Compound **D** is a dialkyl phosphate derived from propan-2-ol.

Compound **E** is a dialkyl phosphate derived from racemic 1-phenylethanol.

10.2 How many signals are present in the ^{31}P-NMR spectra of the compound **C**, **D** and **E**? If there is more than one signal, then indicate also the relative peak areas.

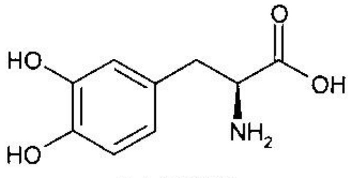
10.3 Sketch the 1H-NMR spectrum of **A** (assume that there is no overlap of signals). Show the relative peak heights also for the splitting pattern of the signals.)

William S. Knowles (Nobel prize 2001) used a rhodium catalyst containing the phosphorus-ligand **F** for the synthesis of L(-) DOPA which is an important anti-Parkinson drug.



F

Ph = C_6H_5
An = *ortho*-CH_3O-C_6H_4
(··) is a lone pair of electrons



L (-) DOPA

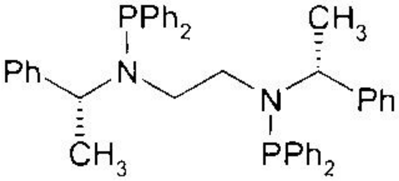
10.4 Draw the spatial structures of all possible steroisomers of compound **F** and indicate which of them would be suitable in an asymmetric synthesis of either L(-) or D(+) DOPA. (Use spatial structures as shown for **F**.)

10.5 In compound F phosphorus is pyramidal. This is:

☐ Absolutely essential for compound **F** to serve as a chiral ligand.
☐ Not essential at all.
☐ Only true when there is no pyramidal inversion.
☐ Only true at very high temperatures.

More than one correct answer is possible.

Later the ligand **G** was developed for the same purpose.



Ph = C_6H_5

G

10.6 Draw he spatial structures of all possible stereoisomers of ligand **G** and indicate which of them would be suitable in an asymmetric synthesis of either L(-) or D(+) DOPA. (Use spatial structures as in the figure above.)

10.7 In ligand **G** phosphorus is pyramidal. This is:

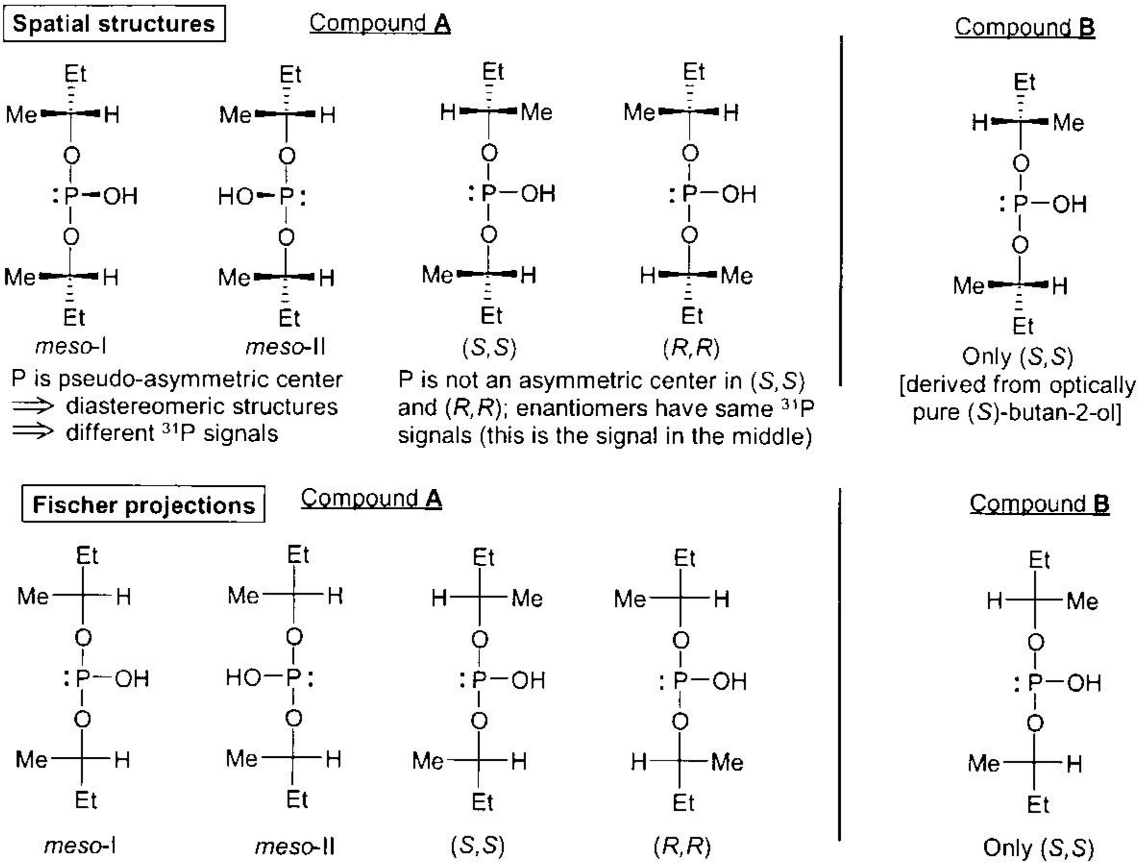
- ☐ Absolutely essential for compound **G** to serve as a chiral ligand.
- ☐ Not essential.
- ☐ Only true when there is a pyramidal inversion.
- ☐ Only true at very high temperature.

More than one correct answer is possible.

10.8 How many signals will be present in the ^{31}P-NMR spectrum of ligand **G**? If there is more than one signal then indicate also the relative peak areas.

SOLUTION OF PREOPARATRY PROBLEM 10

10.1



P is pseudo-asymmetric center ⇒ diastereomeric structures ⇒ different ^{31}P signals

P is not an asymmetric center in (*S,S*) and (*R,R*); enantiomers have same ^{31}P signals (this is the signal in the middle)

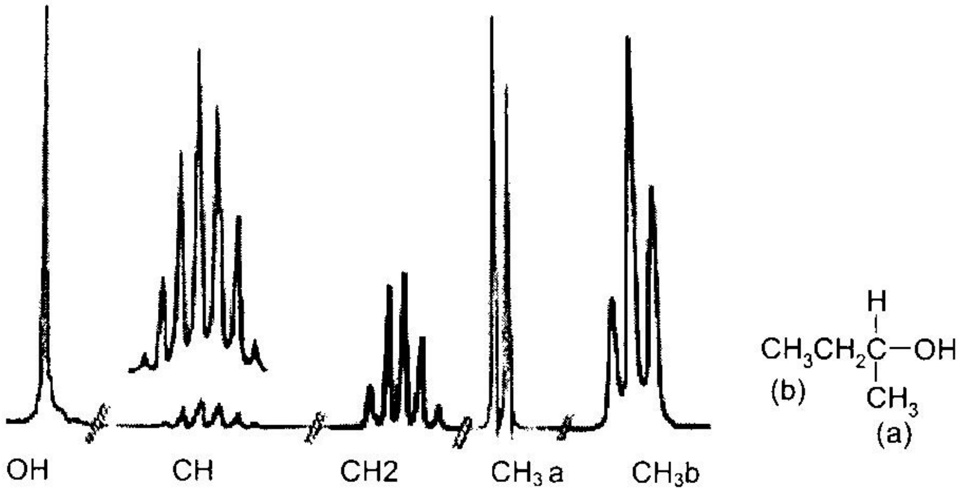
Only (*S,S*) [derived from optically pure (*S*)-butan-2-ol]

(*Hint:* You may wish to compare the 2 *meso* structures of 2,3,4-trihydroxypentane)

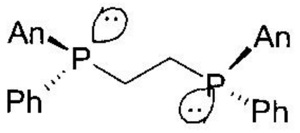
10.2

10.2	**C**:	$(CH_3O)_2P\text{-}OH$	one signal
	D:	$[(CH_3)_2CHO]\text{-}P\text{-}OH$	one signal
	E:	$(Ph\text{-}(CH_3)CH_2O)_2P\text{-}OH$	three signals as in **10-1** ratio 1:2:1 (meso-I : *RR* + *SS* : *meso*-II)

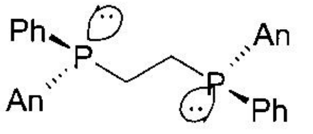
10.3



10.4



meso not chiral
not suitable as catalyst



(R,*R*) will give D(+) DOPA
F is (S,*S*) and gives L(-) DOPA

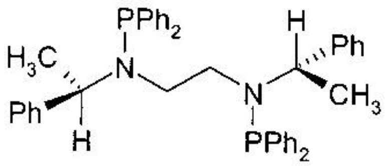
It should be noted that is extra information which was not part of the question.

The essence is that the non-chiral *meso* isomer is recognized.

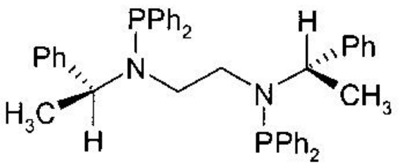
10.5 Option 1 and option 3; P is the asymmetric centre

Phosphorous compounds are pyramidal and they are configurationally very stable (no inversion).

10.6



meso compound
not suitable as
chiral catalyst



(*S*,*S*) will give D(+) DOPA
G is (*R*,*R*) and gives L(-) DOPA

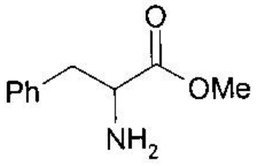
10.7 Option 2.

10.8 One signal, substituents have the same chirality (*R*). No splitting.

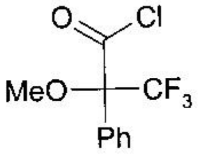
THEORETICAL PROBLEM 11

Optical purity

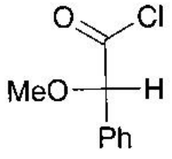
Antipodes (enantiomers) of optically active compounds have different physiological properties e.g. the R-enantiomer of asparagines tastes sweet, whereas the S-enantiomer is bitter. In modern drug design utmost attention is paid to the optical purity of active ingredients. Phenylalanine is an amino acid that is a building block for pharmaceuticals. Enantiomers do not show different signals in the NMR-analysis. However, when suitable derivatives are made, different NMR signals may be possible. For this purpose, phenylalanine methyl ester A which has an optical purity of 75 %, is treated with optically pure Mosher's reagent P and optically pure reagent Q derived from mandelic acid in the presence of triethylamine, $(C_2H_5)_3N$.



A



P
Fischer projection



Q
Fischer projection

Me = CH_3
Ph = C_6H_5

11.1 Draw the formulas of the derivatives which are obtained from compound **A** with reagent **P** and reagent **Q**.

11.2 What is the function of triethylamine in this derivatization reaction? Mark the correct answer.

☐ To prevent racemization nof ester **A**.
☐ To neutralize the hydrogen chloride formed.
☐ The activate ester **A**.
☐ To form a complex with excess reagent **P** or **Q**.

11.3 Sketch the ^{1}H-NMR signals for the following protons in the derivatives made in 11.1. (<u>Note</u>: Compound A has an optical purity of 75 %.)

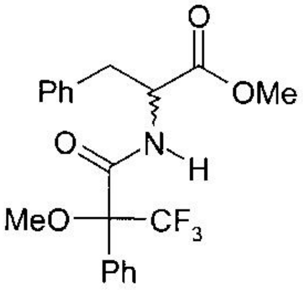
(a) The methoxy protons of the derivative from **P**.
(b) The methoxy protons of the derivative from **Q**.

11.4 Sketch the ^{19}F-NMR signal(s) for the derivative from **P**.

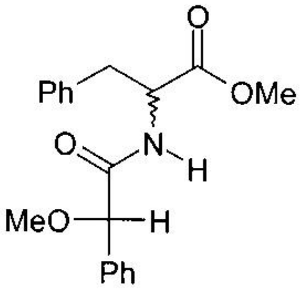
SOLUTION OF PREPARATORY PROBLEM 11

11.1

From P

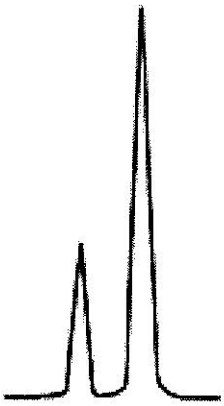


From Q

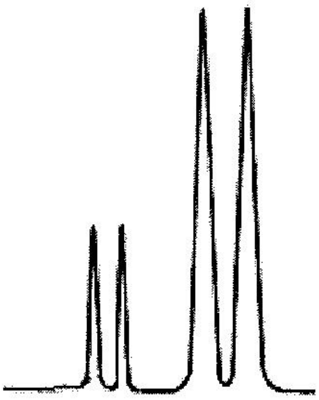


11.2 Option 2

11.3

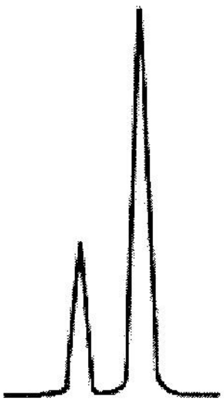


(a) ratio 1:3



(b) ratio 1:1:3:3 Long range coupling of the CH_3O protons with the CH is very small (close to zero). The essence of the question is to indicate the peak ratio's.

11.4

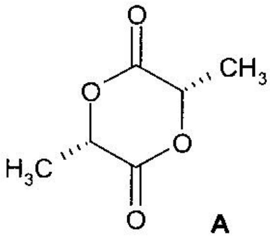


ratio 1:3

THEORETICAL PROBLEM 12

Polylactic Acid

Polylactic acid (PLA) is an important biocompatible polymer. It is produced on a rather large scale in The Netherlands. The building block is (+)-lactic acid which is obtained from sugar by fermentation. An attractive feature of PLA is its biodegradability. PLA is used in medical applications, e.g. medical implants and controlled drug delivery. High-molecular weight PLA can be obtained from either lactic acid or its cyclic dilactone **A**.



A

Cyclic dilactone of (+)-lactic acid

12.1 Give the equation for the formation of the tetramer of PLA starting from lactic acid.

12.2 Give the equation for the formation of the tetramer of PLA starting from cyclic dilactone **A**.

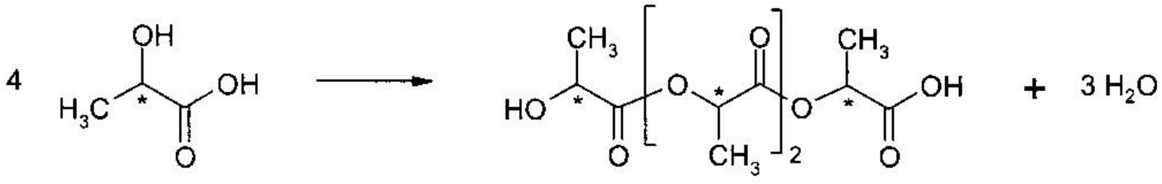
It is assumed that during the polymerisation of lactic acid the reaction volume does not change and that the equilibrium constant K for the ester formation equals 4. The progress of polymerization is p. The average polymer chain length $P = 1/(1 - p)$. The polymerization starts with U mol of lactic acid.

12.3 Calculate the maximal attainable average number of monomer units per chain <u>when no water</u> is removed.

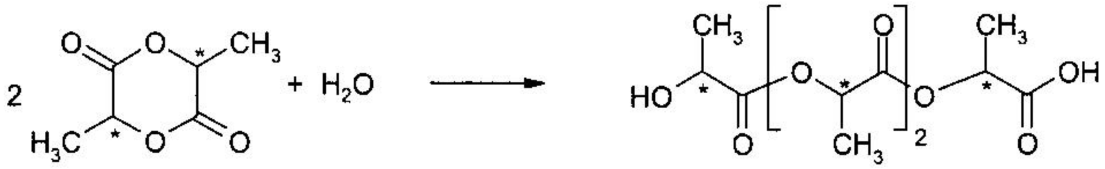
12.4 Calculate how much water has to be removed in the production of PLA from lactic acid to obtain an average number of monomer units per chain of 100, starting from 10 moles of lactic acid.

SOLUTION OF PREPARATORY PROBLEM 12

12.1



12.2



12.3 The aim here is working with reactive groups.

$$K = \frac{\text{[Ester][Water]}}{\text{[-OH][-COOH]}} = \frac{p^2\,\mathrm{U}^2}{(1-\mathrm{p})^2\,\mathrm{U}^2} = 4 \;\Rightarrow\; \frac{p}{1-p} = 2 \;\Rightarrow\; p = 2/3 \;\Rightarrow\; P = \frac{1}{1-p} = 3$$

12.4 First the remaining amount of water at a chain length of 100 units is calculated:

$$\left\{\begin{aligned} &K = 4 = \frac{\text{[Ester][Water]}}{\text{[-OH][-COOH]}} = \frac{p^2\,\mathrm{U}^2 W}{(1-p)^2\,\mathrm{U}^2} \\ &U = 10 \;\text{ and }\; P = 100 = \frac{1}{1-p} \;\Rightarrow\; p = 0.99 \end{aligned}\right\} \Rightarrow W = 0.0040404\ \text{mol}$$

Water formed: pU = 0.99 × 10 = 9.9 mol

Water removed: 9.9 – 0.0040404 = 9.896 mol = 178 g of H_2O

THEORETICAL PROBLEM 13

A chemical puzzle

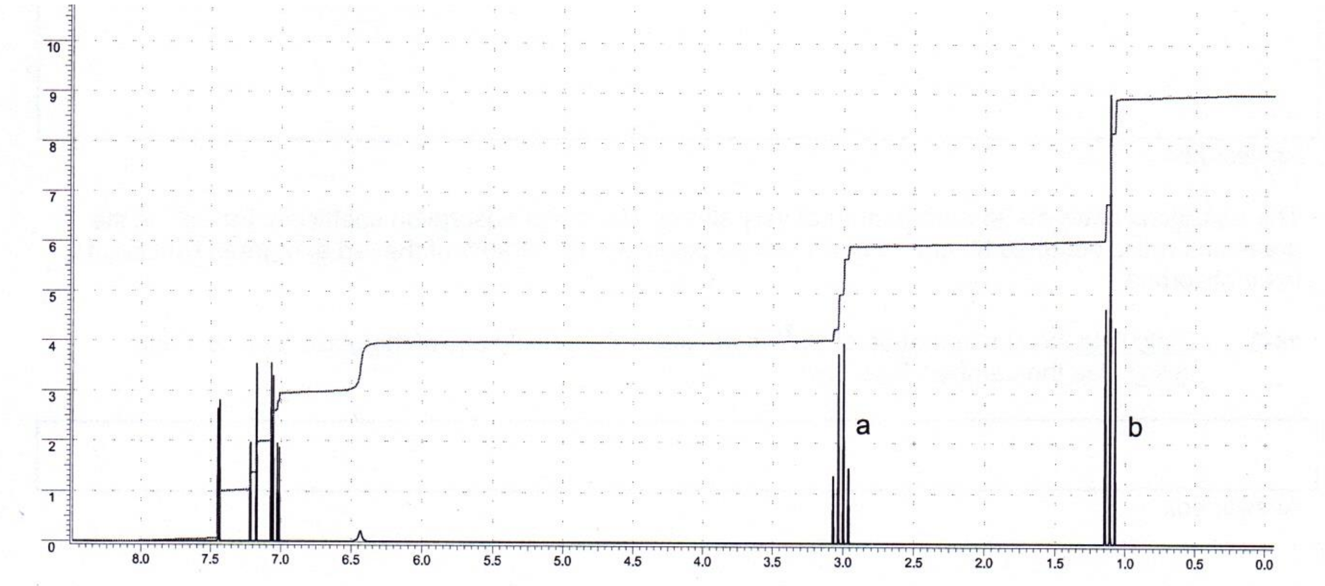
Compound **A** with the formula $C_8H_9N_2O_2Cl$ is insoluble in water and base. Compound A slowly dissolves in a dilute solution of hydrochloric acid.

13.1 Which atom of **A** is involved in the reaction with HCl?

Compound A readily reacts with acetyl chloride yielding a product which is insoluble in acid and base.

13.2 Which functional group(s) in **A** can account for the reaction with acetyl chloride?

The ^{1}H-NMR spectrum of **A** is shown in the figure:



13.3 Which groups can account for the signals **a** and **b**?

13.4 Which functional group is involved in the reaction with Sn/HCl?

13.5 Draw the structure(s) of **A** that can be deduced on the basis of the information given. (Hint: Compound **A** does not react with a solution of silver nitrate, even not on heating.)

SOLUTION OF PREPARATORY PROBLEM 13

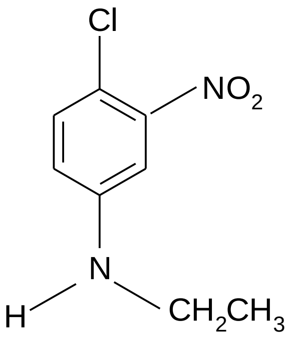
13.1 Nitrogen atom

13.2 $–NH_2$ or $–NHR$

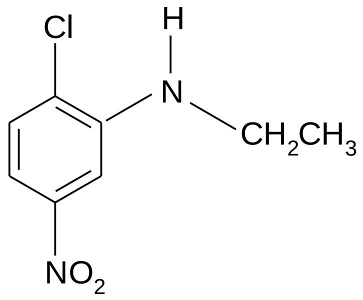
13.3 $–CH_2CH_3$

13.4 $–NO_2$

13.5 No $AgNO_3$ reaction → no aliphatic chlorine substituent

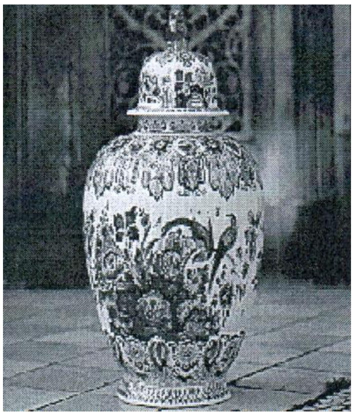


or



THEORETICAL PROBLEM 14

Delft Blue and Vitamin B 12



The typical blue colour of the famous Delft pottery originates from the absorption of red and green light by Co^{2+} ions which are incorporated in the thin layer of glaze on the pottery. The glaze is made by mixing cobalt salt with the glass forming components, e. g. silicate, borate and sodium. Upon heating the thin glass layer is formed which contains Co^{2+} ions. The Co^{2+} ion is a transition metal ion which has a partially filled 3d orbital. The colour of the 3d transition metal ions is caused by electronic transition between lower and higher energy 3 d orbitals which are split by the crystal field.

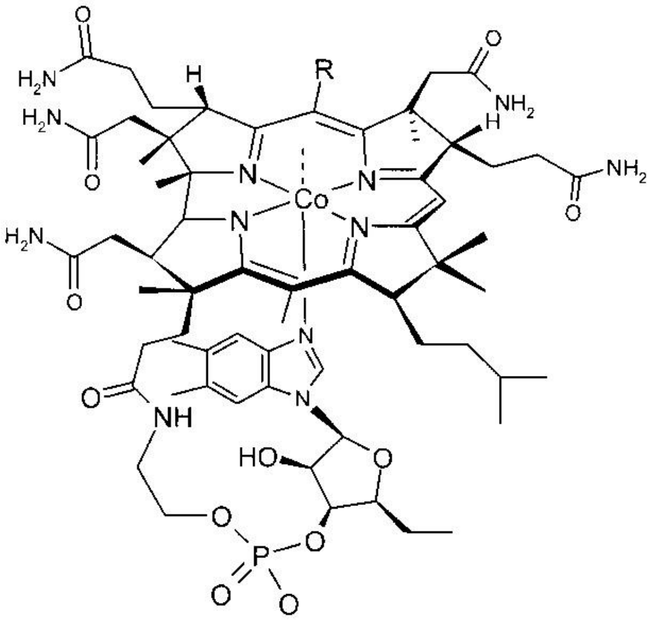
14.1 What is the full electron configuration of Co^{2+}? (Atomic number of cobalt = 27)

14.2 Sketch the shape of the 3d orbitals. Draw also the *x*, *y*, and *z* axes.

The transitions between 3d orbitals are not very strong. The molar absorption coefficient for Co^{2+} in the green and red is about 20 $dm^3\ mol^{-1}\ cm^{-1}$. For an intense blue colour about 99 % of the read and green light needs to be absorbed.

14.3 Calculate the concentration of Co^{2+} in the glaze if the thickness of the glaze layer is 1 mm. (Hint: Use the Lambert-Beer law.)

In the body trace amounts of Co ions are present mainly incorporated in vitamin B_{12}. The total amount of Co in a human body of 70 kg is about 3 mg. In 1964 Dorothy Crowfoot-Hodgkin received the Nobel prize for the structure determination of this vitamin. The structure is shown below. The oxidation state of Co can vary. Common oxidation states are II and III, but in the vitamin B12 also Co^+ is possible.



Vitamine B_{12} (R = adenosyl)

14.4 Arrange the Co ions in order of increasing ionic radii for the three different oxidation states.

14.5 For which oxidation state of Co ions (I, II, III) do expect to see a signal in an EPR spectrum (Electron Paramagnetic Resonance). Assume a high-spin configuration in all oxidation states.

Co^{+} Yes / No

Co^{2+} Yes / No

Co^{3+} Yes / No

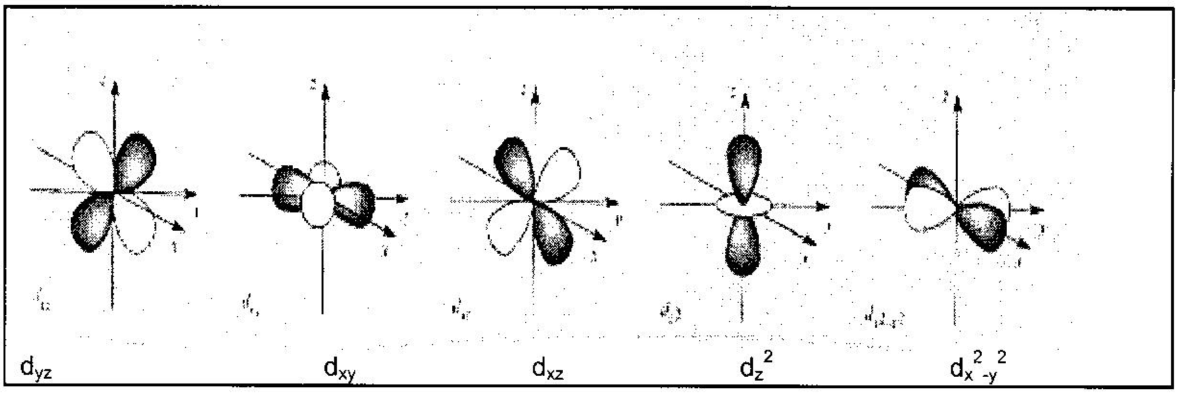
14.6 Calculate how many Co ions are present in a human body of 70 kg. (The relative atomic mass of Co = 58.93.)

14.7 What is the coordination number of cobalt in the vitamin B_{12} complex.

SOLUTION OF PREPARATORY PROBLEM 14

14.1 Electron configuration of Co^{2+}: $1s^2\,2s^2\,2p^6\,3s^2\,3p^6\,3d^7$

14.2



14.3 If 90 % of the light is absorbed, the transmission *T* is 0.1 (10 % transmitted). Fill out:

$A = -\log I / I_0 = \varepsilon\, c\, l \;\Rightarrow -\log 0.1 = 20\, c\, 0.1 \;\Rightarrow c = 1 / (20 \times 0.1) = 0.5$ mol dm^{-3}

14.4 $r(Co^{3+}) < r(Co^{2+}) < r(Co^{+})$

14.5 All three oxidation states have unpaired d-electrons (d^6, d^7 and d^8) in the high spin configuration and thus for all three oxidation states an EPR spectrum can be measured. The correct answer in all cases is „yes“.

14.6 $\dfrac{3\times10^{-3}\ \text{g}}{58.93\ \text{g mol}^{-1}} \times 6.022\times10^{23}\ \text{mol}^{-1} = 3\times10^{19}$ Co ions

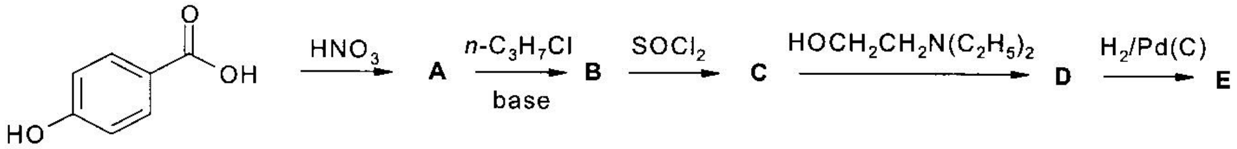
14.7 Six

THEORETICAL PROBLEM 15

Synthesis of a local anaesthetic

The development of new pharmaceutical drugs depends heavily on organic synthesis. Molecular finetuning is often required to obtain the desired properties. Here the synthesis of the local anaesthetic proparacaine (also called proxymetabaine) which is used in treatment of eye problems, is considered.

15.1 Complete the synthetic scheme by drawing the structures **A**, **B**, **C**, **D**, and **E**.



It may be assumed that all products are properly isolated.

15.2 Which nitration product(s) will be obtained when <u>*meta*</u>-hydroxybenzoic acid is taken as starting material? Draw the structure(s).

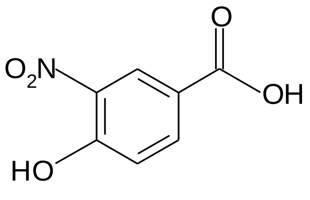
15.3 When tert-C_4H_9Cl is used in the second step istead of n-C_3H_7Cl, this will lead to:

☐ a similar product as **B**. If it is so, give its structure.
☐ no reaction at all.
☐ a decomposition of the tert-C_4H_9Cl.
☐ an aromatic substitution reaction.

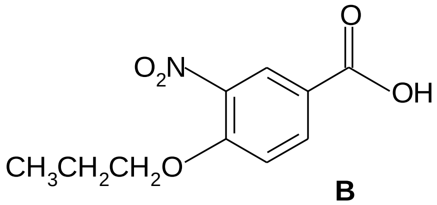
Mark the correct answer.

SOLUTION OF PREPARATORY PROBLEM 15

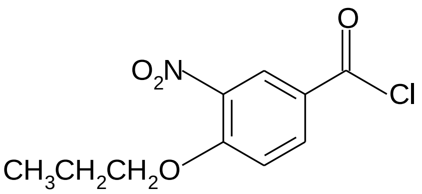
15.1



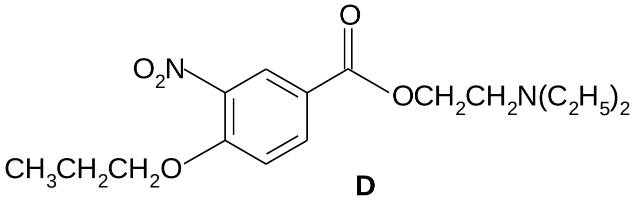
A



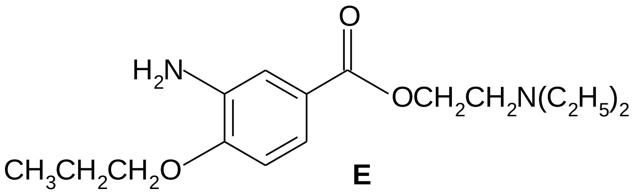
B



C

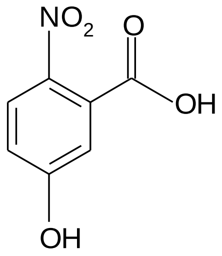


D

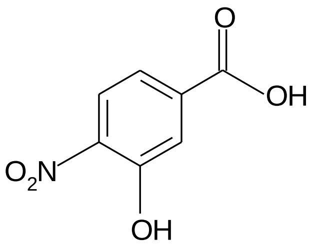


E

15.2



and



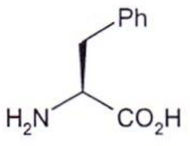
15.3 Decomposition of the tert-C_4H_9Cl.

THEORETICAL PROBLEM 16

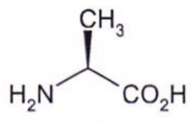
Structure of Peptides

Proteins are present in all living cells and fulfil numerous functions in the chemistry of life. They are composed of α-aminocarboxylic acids. Peptides are ‘small’ proteins with a relative small number of amino acids. The peptide bond is a amide bond formed by interaction of the amino group of an amino acid with the carboxylic acid group of its neighbour.

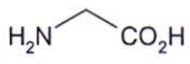
16.1 Which dipeptides can be derived from phenylalanine F and alanine A? Give the structures.



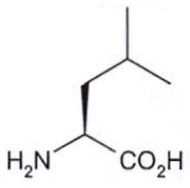
F



A



G



L

In the structure analysis of peptides the N-terminal and C-terminal residues play an important role. Sanger’s method for the determination of the N-terminal residue (this is an amino acid unit in the peptide with the free NH_2 group) involves treatment with 2,4.dinitrofluorobenzene under mid alkaline conditions, followed by a total acid hydrolysis of all peptide linkages. The N-terminal amino acid then has a yellow tag which can readily be spotted in the paper chromatographic analysis. Sanger received the Nobel prize in 1958 and 1980.

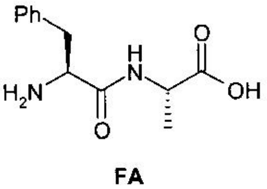
16.2 Which reaction takes place with Sanger’s reagent (for reason of simplicity write the N-terminal side of the peptide as H_2NR). Give the equation.

The C-terminal residue which contains the free COOH group in the peptide, is performed by a selective enzymatic hydrolysis of the C-terminal amino acid unit by carboxypeptidase (from the pancreas). From the tetrapeptide composed of the amino acids F, A, glycine G and Leucine L, the C-terminal residue was identified as F. Sanger’s method indicated that the N-terminal unit is G.

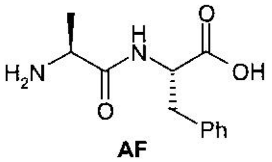
16.3 Deduce the possible structure(s) of this tetrapeptide. Give the structure(s).

SOLUTION OF PREPARATORY PROBLEM 16

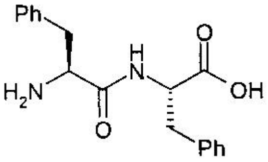
16.1



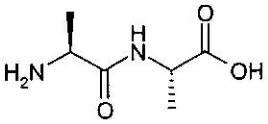
FA



AF



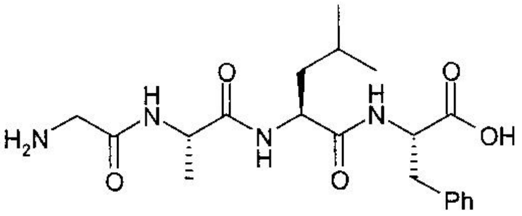
FF



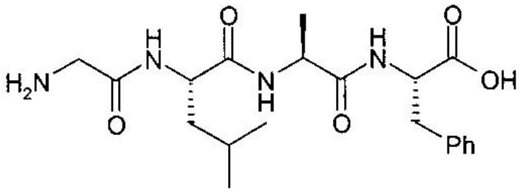
AA

16.2 This is a nucleophilic aromatic substitution.

16.3



GALF



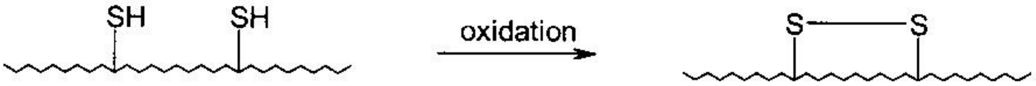
GLAF

Only the positions of G and F are determined, the other two are in the middle, but no information is provided if this is AL or LA.

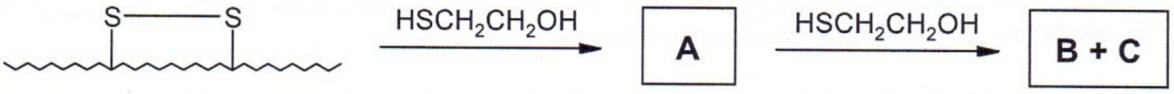
THEORETICAL PROBLEM 17

Ribonuclease

Bovine pancreatic ribonuclease A is an enzyme that digests RNA. It is very stable. It retains its activity after heating in water at 100 °C and pH = 7, while practically all other enzymes are inactivated by that treatment. The stability of ribonuclease A is attributed to an unusually stabile 3D-structure kept together by four S-S bridges between its eight cysteine residues. The S-S bridges are formed by oxidation of the thiol groups present in the cysteine according to the equation.



17.1 Reducing agents such as 2-mercaptoethanol can cleave the S-S bridges. Complete the equation for the cleavage using two equivalents of 2-mercaptoethanol. Draw the structures **A**, **B** and **C**.



17.2 Which other factors are known to determine the 3D structure of a protein?

- ☐ high proline content,
- ☐ atmospheric pressure,
- ☐ electrostatic forces,
- ☐ gravity,
- ☐ hydrogen bonds,
- ☐ magnetic forces,
- ☐ the size of the organism (large animals have more stable proteins),
- ☐ van der Waals forces.

Mark your answer. More than one answer may be correct.

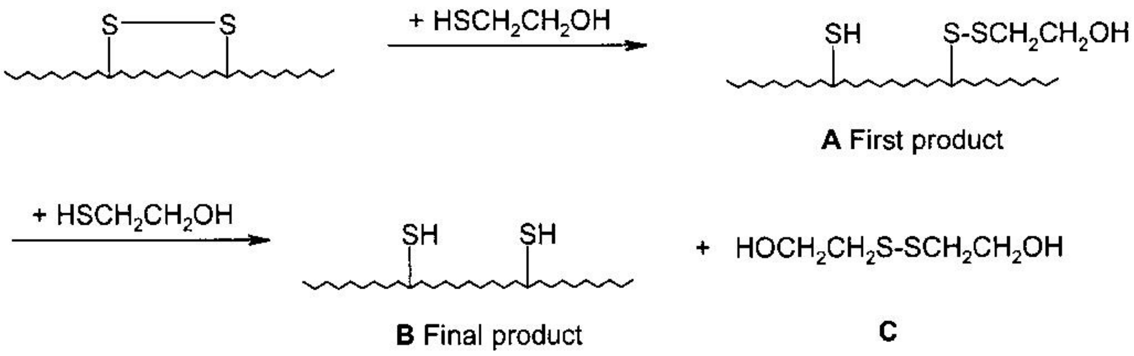
Treatment of ribonuclease A a solution of urea (c = 8 mol dm^{-3}), $H_2N\text{-}CO\text{-}NH_2$, in the presence of 2-mercaptoethanol (c = 0.01 mol dm^{-3}) results in a complete disappearance of the enzymatic activity by disruption of S-S bridges. Slow removal of the urea and 2-mercaptoethanol by means of dialysis together with re-oxidation in the presence of oxygen restores the enzymatic activity. The classical experiment carried out by Christian Anfinsen nearly fifty years ago was interpreted as the proof that proteins spontaneously fold into their native, biologically active 3d-conformation. In a modified experiment Anfinsen only removed the 2-mercaptoethanol and brought it, still in presence of the urea solution, in contact with oxygen. Now S-S bridges were formed at random. Subsequent removal of urea led to the restoration of approximately 1 % of the enzymatic activity.

Assume that only one specific set of S-S bridges out all possible combinations renders the protein enzymatically active. Assume also that every possible combination of S-S bridges gas an equal probability of being formed under experimental conditions described.

17.3 Calculate the resulting fraction of enzymatically active ribonuclease **A**.

SOLUTION OF PREPARATORY PROBLEM 17

17.1



17.2 Electrostatic forces, hydrogen bonds and van der Waals forces.

17.3 There are 8 Cys residues. The probability that any residue is coupled to its correct partner is 1 : 7. Next there remain 6 residues to consider. The chance that any of those is coupled to its correct partner is 1 : 5, etc. Therefore the fraction of active molecules is: 1/7 × 1/5 × 1/3 × 1/1 = 1/105.

THEORETICAL PROBLEM 18

Enzyme Kinetics

Reactions with enzymes play an important role in chemistry. Kinetic analyses of these reactions help to understand the typical behavior of enzymes. An enzymatic reaction of substrates A and B witn an enzyme E can be described by the equations (1) – (5):

(1) E + A € EA equilibrium constant K_A
(2) E + B € EB equilibrium constant K_B
(3) EB + A € EAB equilibrium constant K'_A
(4) EA + B € EAB equilibrium constant K'_B
(5) EAB → products reaction rate $v = k[EAB]$

When the rate constant is small the equilibria (1) – (4) are hardly shifted due to the reaction (5). This leads to expression (6) in which V_{max} is the maximal velocity of the reaction, that is reached when the enzyme is saturated with the substrates (all enzyme is bound to A and B).

$$v = \frac{V_{max}}{1 + K_A/[A] + K_B/[B] + K_A K'_B/[A][B]} \qquad (6)$$

18.1 Give the equilibrium constants K_A, K_A, K_A', K_B' in terms of the respective concentrations.

Consider the enzymatic hydrolysis of maltose by the enzyme α-glucosidase from yeast.

maltose + H_2O → 2 glucose (7)

The substrate maltose is usually present in concentrations ranging from 10^{-4} – 10^{-1} mol dm^{-3}. Water is the solvent, thus its concentration is practically constant at 55.6 mol dm$^{–3}$. Expression (6) can now be simplified by letting [B] approach infinity.

18.2 Give the simplified expression. NB: The simplified expression is the famous Michaelis-Menten equation for an enzymatic reaction with one substrate.

18.3 (a) Simplify the Michaelis-Menten equation further by taking [A] as very small (thus approaching zero).

(b) The order *n* of a reaction is defined by $v = k\,c^n$. Thus, for $n = 1$ the kinetics are first order. What is the *n* of the reaction [A] → 0.

18.4 (a) Simplify the Michaelis-Menten equation by taking [A] as very high, thus [A] $\rightarrow \infty$, which is the case when the enzyme is completely saturated with substrate.

(b) What is the order *n* of the reaction for [A] $\rightarrow \infty$**.**

18.5 The constant K_A is a measure for the affinity of an enzyme for its substrate. Does a high affinity correspond with a high or a low value of K_A? At which velocity is [A] = *K?*

18.6 Draw a graph of *v* versus [A]. (Take [A] at the *x*-axis.) Indicate v_{max} and K_A in this graph.

An enzymatic reaction can be strongly retarded or blocked by an inhibitor I according to the equation:

$$E + I \leftrightarrows EI \qquad (8)$$

with equilibrium constant K_I. For competitive inhibition the inhibitor competes with the substrate at the binding side of tze enzyme, thus the reaction is slowed down but leaving v_{max} unaffected. In the Michaelis-Menten equation K_A is then multiplied by a factor (1 + [I] /K_i), which equals 1 for [I] = 0 and is large when [I] is large. For non-competitive inhibition I does not compete with A: K_A is not affected, v_{max} is lowered. In the Michaelis-Menten equation v_{max} is then divided by a factor (1 + [I] /K_i). Inorder to investigate the hydrolysis by α-glucosidase he model substrate *p*- nitrophenyl-α-D-glucoside (PNPG) is used instead of maltose whereby the release of nthe yellow *p*-nitrofenol is monitored spectrophotometrically. The following experiment is carried out: PNPG is used in the presence of maltose to measure the activity of glucosidase.

18.7 Which situation applies**:**

☐ The maltose does not influence the rate of release of *p*-nitrophenol.

☐ Maltose functions as a competitive inhibitor.

☐ Maltose functions as a non-competitive inhibitor.

Mark the correct answer.

18.8 Draw a graph of *v* versus [A] (take [A] at the *x*-axis) for the release of *p*-nitrophenol in the presence of maltose for [maltose] = $K_{maltose}$. Insert the graph made in question 18.6. Mark the points v_{max} and ½ v_{max}.

SOLUTION OF PREPARATORY PROBLEM 18

18.1 $K_A = [E][A] / [EA]$

$K_B = [E][B] / [EB]$

$K'_A = [EB][A] / [EAB]$

$K'_B = [EA][B] / [EAB]$

18.2 $v = \dfrac{V_{max}}{1 + K_A / [A]}$

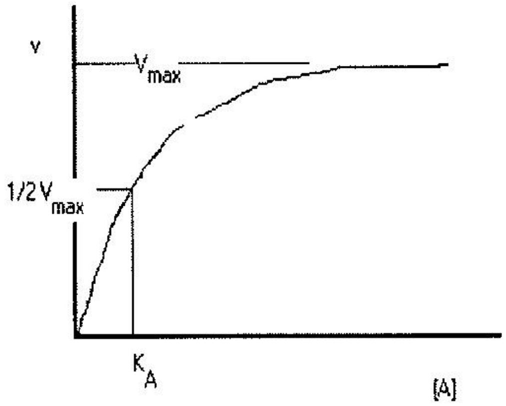
18.3 If $[A] \rightarrow 0$ then $K_A / [A] >> 1$ and $v = V_{max} [A] / K_A$. This corresponds with first order kinetics.

18.4 If $[A] \rightarrow \infty$ then $K_A / [A] << 1$ and $v = V_{max}$. This corresponds with zero order kinetics.

18.5 A high affinity corresponds with a small K_A.

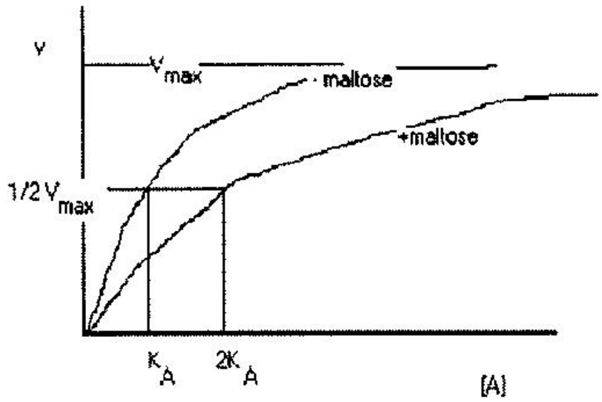
$v = ½ V_{max}$ when $[A] = K_A$.

18.6



18.7 Maltose functions as a competitive inhibitor.

18.8



THEORETICAL PROBLEM 19

Dendrimers: Tree-like Macromolecules

Dendrimers are fascinating highly branched macromolecules with tree-like structures. One method of preparation of these compounds makes use of the Michael addition reaction, a simple example of which is shown below:

$$(C_2H_5)_2NH \quad + \quad H_2C{=}CHCO_2Et \quad \xrightarrow[0\ ^{\circ}C]{\text{inert solvent} \atop \text{+ acetic acid}} \quad (C_2H_5)_2N{-}CH_2CH_2CO_2Et$$

A dendrimer can be obtained by the following sequence of reactions:

(1) NH_3 is treated exhaustively with an excess of acrylonitrile $(H_2C=CH-C\equiv N)$ to give a product that contains 3 cyanide groups.

(2) This product is reduced catalytically with H_2 and a catalyst to produce a molecule with three primary amines.

(3) This primary amine is treated again with an excess of acetonitrile.

(4) The product of step (3) is again hydrogenated with H_2 and a catalyst to give a hexa-amine. This is the beginning of a branched macromolecule.

19.1 (a) Give the equation for the reaction of step (1).

(b) Give the equation for the reaction of step (2).

(c) Give the structure for the product from step (3).

(d) Give the structure of the hydrogenated product from step (4).

The sequence of treatment with acetonitrile and subsequent reduction of the cyanide group can be repeated several times, leading finally to a spherical type of molecule with primary amino groups on the surface.

19.2 Calculate the amount of primary amine end groups that are present in the dendrimer after 5 full cycles. (The first cycle consists of steps 1 + 2.)

19.3 (a) Calculate the amount of hydrogen (in moles per one mole of NH_3) which is needed for 5 cycles.

(b) Calculate the number of moles of acrylonitrile which is needed for 5 cycles.

(c) The dendrimer increases in diameter by about 10 Å per cycle. Calculate the volume of the dendrimer after 5 cycles.

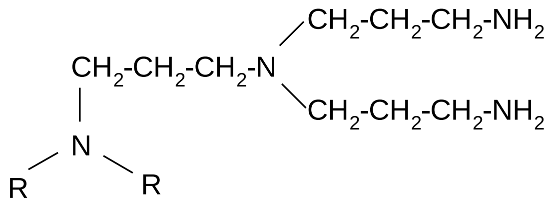
SOLUTION OF PREPARATORY PROBLEM 19

19.1 (a) $NH_3 + H_2C{=}CHCN \longrightarrow N(CH_2CH_2C{\equiv}N)_3$

(b) $\xrightarrow{H_2/Pd} N(CH_2CH_2CH_2NH_2)_3$

(c) $N[CH_2CH_2CH_2N(CH_2CH_2CN)_2]_3$

(d)



R = The same chains at these position

19.2 After the first cycle there are 3 amine groups (see answer). Then the number of amine groups is doubled after each cycle (see answers 19.1 c and 19.1 d). Thus, after 5 full cycles the total number of amine end groups is 48.

19.3 (a) After 5 full cycles 3 + (3 × 2) + (6 × 2) + (12 × 2) + (24 × 2) = 93 mol of H_2 have been used.

(b) Idem for acrylonitril (93 mol).

(c) Radius = diameter / 2 = 50 / 2 = 25 Å. Volume: $4/3\ \pi\ r^3$.

THEORETICAL PROBLEM 20

Carvone

The natural compound *l*-carvone is found in spearmint and gingergrass oil. *l*-Carvone has a negative optical rotation. Its enantiomer *d*-carvone which has a positive optical rotation is present in caraway seeds. Carvone has been analyzed and consists of 80.00 % carbon, 9.33 % hydrogen and 10.67 % oxygen. Mass spectroscopy indicates that the molecular mass of carvone = 150. The NMR and IR spectra of carvone are shown below. In the UV spectrum of carvone there is a strong absorption maximum at 238 nm.

20.1 Calculate the molecular formula of carvone.

20.2 Calculate the number of unsaturation of carvone.

20.3 Which functional group is responsible for the strong absorption at 1680 cm^{-1} in the IR spectrum?

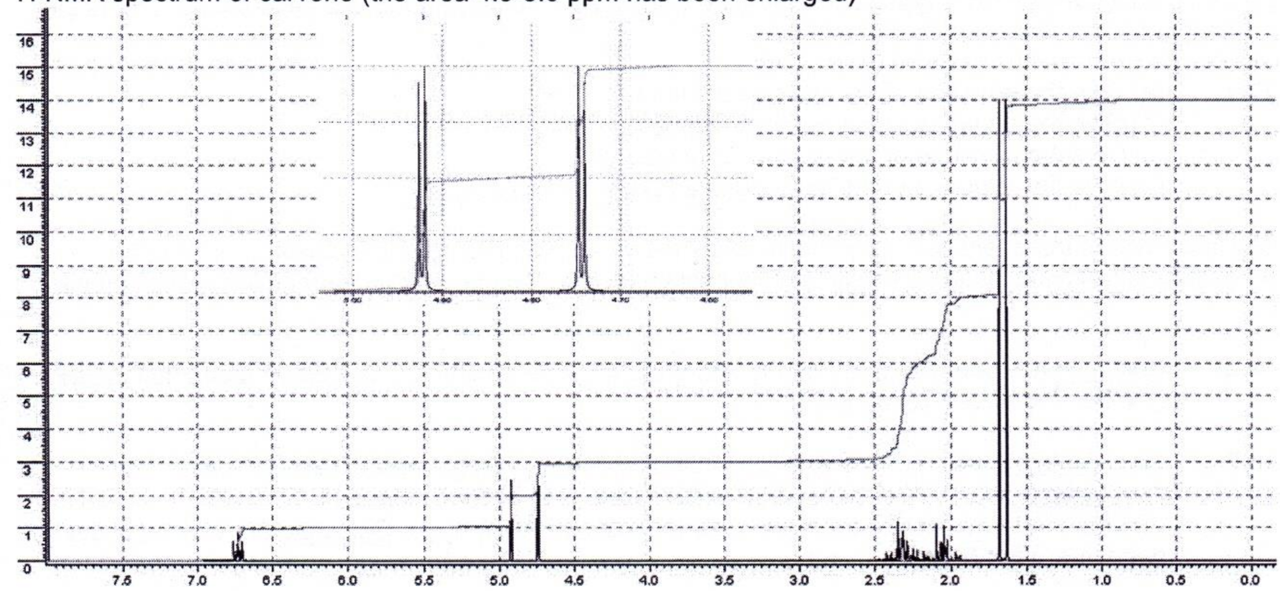
20.4 In the IR spectrum there is no absorption above 3000 cm^{-1}. Indicate which type of functional group is absent in carvone.

In the 200 MHz ^{1}H-NMR spectrum the type of the signals is as follows (we don not consider long range couplings).

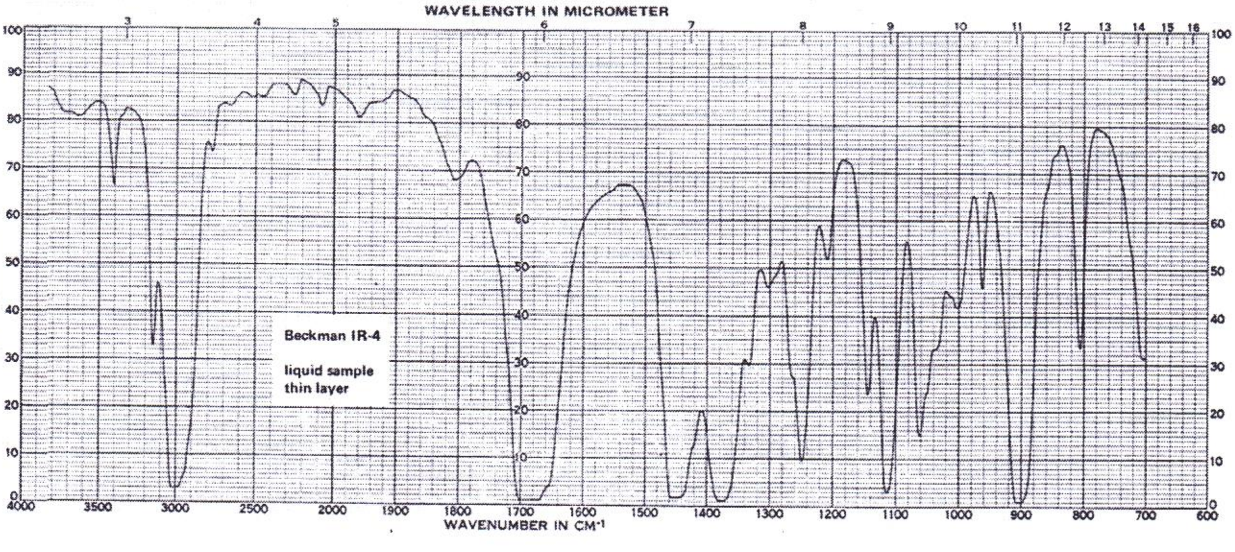
δ (ppm)	Type	Integration
1.63	singlet	3
1.68	singlet	3
1.9 – 2.2	multiplet	2
2.2 – 2.5	overlapping multiplets	3
4.75	doublet	1
4.93	doublet	1
6.73	triplet	1

20.5 Propose the most likely structure for carvone when it is given that it is a 1,2,4-trisubstituted 6-membered ring system. (The overlapping multiplets consist of a CH and a CH$_2$ signal.)

^{1}H-NMR spectrum of carvone (the area 4.5-5.0 ppm has been enlarged)



IR spectrum of carvone:



SOLUTION OF PREPARATORY PROBLEM 20

20.1 Number of C-atoms: $N_C = (M_r, \times \%C) / 12 = (150 \times 0.8) / 12 = 10$

Number of H-atoms: $N_H = (M_r, \times \%H) / 1 = (150 \times 0.0933) / 1 = 14$

Number of O-atoms: $N_O = (M_r, \times \%C) / 16 = (150 \times 0.1067) / 16 = 1$

20.2 A fully saturated hydrocarbon with 10 carbon atoms has the formula $C_{10}H_{22}$. Carvone has the formula $C_{10}H_{14}O$. For calculation of the unsaturation, the O is not relevant. Subtraction gives a shortage of 8H for carvone. This is equivalent to 4 unsaturated sites (either double bonds or rings).

20.3 C═O group.

20.4 –OH (–COOH is not a correct answer. Carvone has one oxygen atom only.) There is no relevant strong absorption above 3000 cm^{-1}. That means that no –OH group is present.

20.5 Carvone contains a 6-membered ring. This leaves three more unsaturated sites. The IR indicates the presence of a C═O group, and this leaves 2 more unsaturated sites and they must C═C bonds.

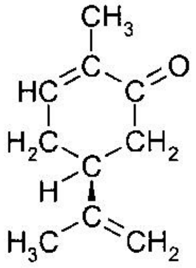
The strong UV-absorption suggests a conjugated system, most likely C═C–C═O.

The singlets at 1.63 and 1.68 ppm in the ^{1}H-NMR are two $–CH_3$ groups with no vicinal coupling.

The multiplet from 1.9 – 2.2 ppm consists of a –CH and a $–CH_2–$ groups (from the question). The multiplet from 2.2 – 2.5 ppm is most likely a $–CH_2–$ group with many neighbouring H-atoms.

The dublets at 4.75 and 4.93 ppm are indicative of two =CH– groups, it might even be $=CH_2$ given the small and identical coupling constants (see the enlarged area).

The triplet at 6.73 ppm is indicative of a =CH– which is situated next to $–CH_2–$ group. Combining all these information with the given 1,2.4 substitution pattern gives the structure below as the most likely structure of carvone.



THEORETICAL PROBLEM 21

Electrochemical Energy Conversion

Mobility is of vital importance for our modern society. Electric cars are under active development to ensure our future needs of transportation. One of the major problems for electrically driven vehicles is a supply of a suitable source of electricity. Batteries have the drawback that they must be recharged, thus the action radius is limited. The in situ generation of electricity in fuel cells is an attractive alternative. A fuel battery, or flow battery, is a galvanic cell for which the reactants are continuously supplied. Fuel cells utilize combustion reactions to produce electricity. The reactants undergo half-reactions at the electrodes, and the electrons are transferred through an external circuit. The electrodes are separated by an ionically conducting liquid or a molten or solid electrolyte. The electrode half-reactions for a hydrogen-oxygen fuel cell with a concentrated potassium hydroxide electrolyte are:

$$O_2(g) + 2\ H_2O + 4\ e^- \rightarrow 4\ OH^-(aq) \qquad (1)$$

$$H_2(g) + 2\ OH^-(aq) \rightarrow 2\ H_2O(l) + 2\ e^- \qquad (2)$$

The fuel-cell reaction, after making electron loss equal to electron gain, is:

$$2\ H_2(g) + O_2(g) \rightarrow 2\ H_2O(l) \qquad (3)$$

The reaction product is water! and the efficiency is about 50 – 60 %.

21.1 Which reaction occurs at the cathode?

21.2 Which reaction occurs at the anode?

21.3 Give the electrode reactions when the electrolyte is phosphoric acid.

The change of Gibbs energy ΔG^0 is a measure of the driving force of a reaction. The change of energy is given by:

$$\Delta G^0 = -\, n\, F\, E$$

where n is the number of electrons transferred in the reaction and F is the Faraday constant (96 487 C mol^{-1}). The standard electrode potential for $O_2(g)$ at 25 °C is +1.23 V.

21.4 Calculate the ΔG^0 of the fuel-cell reaction under acidic conditions (see 21.3).

The production of usable energy by combustion of fuels is an extremely inefficient process. In The Netherlands natural gas is a highly attractive energy source as it is abundantly available. Modern electric power plants are able to furnish only 35-40 % of the energy theoretically available from natural gas. The exothermic reaction of natural gas (methane) with oxygen is:

$CH_4(g) + 2\ O_2(g) \rightarrow CO_2(g) + 2\ H_2O(g) + \text{energy}$

Usually the energy released from this reaction is used indirectly to heat houses or to run machines. However, in a high-temperature ceramic fuel cell based on a solid oxide-ion conducting electrolyte, natural gas can be utilized directly, without a catalyst and with a high efficiency of conversion (75 %). The net fuel-cell reaction is:

$CH_4(g) + 2\ O_2(g) \rightarrow CO_2(g) + 2\ H_2O(g)$

21.5 Give the reactions at the anode and the cathode.

Another high-temperature fuel cell utilizes molten Carbonate as the ionically conducting electrolyte. Hydrogen is used as fuel, oxygen is mixed with CO_2.

21.6 Give the half-reactions at the anode and cathode, and the net fuel-cell reaction.

SOLUTION OF PREPARATORY PROBLEM 21

21.1 At the cathode oxygen is reduced to hydroxide, i.e. half-reaction (1).

21.2 At the anode hydrogen is oxidized to water, i.e. reaction (2).

21.3 Anode: $2\ H_2(g) \rightarrow 4\ H^+ + 4\ e^-$

Cathode: $4\ H^+ + O_2(g) + 4\ e^- \rightarrow 2\ H_2O(g)$

Fuel cell reaction: $2\ H_2(g) + O_2(g) \rightarrow 2\ H_2O(g)$

21.4 The standard electrode potential of the reaction at the anode = 0 V

The standard electrode potential of the reaction at the cathode = + 1.23 V

The total number of electrons transferred in the reaction = 4

$\Delta G^o = -n\,F\,E = -4 \times 96487 \times (1.23\ \text{V} - 0\ \text{V}) = -474.716\ \text{J}$

21.5 $CH_4(g) + 2\ O^{2-}$ (electrolyte) $\rightarrow 2\ H_2O(g) + CO_2 + 4e^-$

$O_2(g) + 4\ e^- \rightarrow 2\ O^{2-}$ (electrolyte)

$CH_4(g) + 2\ O_2(g) \rightarrow 2\ H_2O(g) + CO_2(g)$

21.6 Anode: $2\ H_2(g) + 2\ CO_3^{2-}(l) + 2\ H_2O(g) + 2\ CO_2(g) + 4\ e^-$

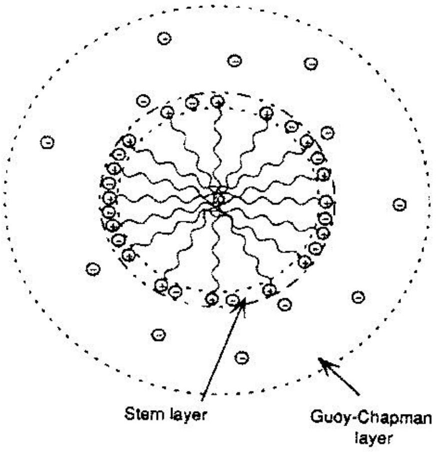
Cathode: $O_2(g) + 2\ CO_2(g) + 4\ e^- \rightarrow 2\ CO_3^{2-}(l)$ (cathode)

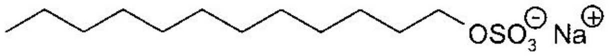
Fuel cell reaction: $2\ H_2(g) + O_2(g) \rightarrow 2\ H_2O(g)$

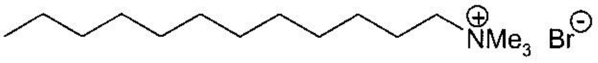
THEORETICAL PROBLEM 22

Micelles

Biomembranes fulfill many important functions in the living cell. Membranes in plant and animal cells contain 40 – 50 % proteins. Phospholipids, which are key constituents in biomembranes, have hydrophobic fatty acid tails and polar hydrophilic head groups. Such structures are commonly called amphiphiles. Knowledge of membranes is obtained from studies of the aggregation behavior of amphiphiles with a simple(r) molecular structure. Typical aggregates are micelles, mono-, and bilayer structures and vesicles (liposomes). Single-tailed surfactant molecules like sodium *n*-dodecylsulfate (*SDS*) and *n*-dodecyltrimethylammonium bromide (*DTAB*) cooperatively form micelles upon dissolution in water above the critical micelle concentration (*CMC*). The structure of micelles is pictured in the figure. In these micelles, a central hydrophobic core can be recognized and a layer containing head groups and some counter ions (Guoy-Chapman layer). For micelles of *SDS* the central core has a radius of 16.6 Å and the Stern layer has a thickness of 4.6 Å.




(*SDS*)


(*DTAB*)

Amphiphile	*CMC* (mmol dm^{-3})	Relative micelle mass (g mol^{-1}×10^3)
SDS	8.1	18.0
DTAB	14.4	15.0

22.1 Calculate the volume of the Stern-layer in this micelle of SDS.

In a simplified model, Micelle formation can be expressed by the equilibrium:

$n\,S + n\,B \leftrightarrows M$

wherein S is the amphiphile, B is counter ion and n is the number of molecules involved. The standard Gibbs energy of micelle formation per S is expressed by:

$$\Delta G_M = -\frac{RT}{n}\ln K_M$$

KM is the equilibrium constant. At the critical micelle concentration [M] = 0. Furthermore, assume that [S] is approximately equal to [B]. R is the gas constant (8.314 J mol^{-1} K^{-1}).

22.2 Calculate ΔG_M for the micelle formation of *SDS* and of *DTAB*.

22.3 Calculate the number of amphiphile molecules in the micelles of *SDS* and that of *DTAB*.

SOLUTION OF PREPARATORY PROBLEM 22

22.1 Volume SDS micelle = 4/3 π (16.6 + 4.6)^3 = 39911.33 Å^3

Volume of the core = 4/3 π 16.6 ^{3} = 19160.77 Å^3

Volume of the Stern layer = volume of the SDS micelle – volume core = 20750.56 Å^3

22.2 The equilibrium constant $K_\mathrm{M} = \dfrac{[\mathrm{M}]}{[\mathrm{S}]^n[\mathrm{B}]^n}$

Substitution in ΔG_M : $\Delta G_M = -\dfrac{RT}{\mathrm{n}}\ln\dfrac{[\mathrm{M}]}{[\mathrm{S}]^n[\mathrm{B}]^n} = -\dfrac{RT}{\mathrm{n}}(\ln[\mathrm{M}] - \mathrm{n}\ln[S] - \mathrm{n}\ln[B])$

At the CMC there aro no micelles: [M] = 0 and [S] = [B], thus: $\Delta G_\mathrm{M} = 2\,RT\ln[\mathrm{S}]$

For SDS: ΔG_M = – 23.86 kJ mol^{-1}

For TDAB: ΔG_M = – 21.01 kJ mol^{-1}

22.3 Average number of amphiphiles per micelle = relative micelle mass / relative amphiphile mass

For SDS (M_r = 288): n = 18×10^3 / 288 = 62.5

For TDAB (M_r = 308): n = 15×10^3 / 308 = 48.7

THEORETICAL PROBLEM 23

A Ceramic Hard Coating

BP (boron phosphide) is a valuable wear-resistant hard coating that is produced by the reaction of boron tribromide and phosphorus tribromide under a hydrogen atmosphere at high temperature (>750 °C). This ceramic material is used as a protecting thin film on metal surfaces. BP crystallizes in a cubic-close-packed structure with tetrahedral surrounding.

23.1 Give the equation for the formation of BP.

23.2 Draw the Lewis structures of boron tribromide and phosphorus tribromide.

23.3 Draw the structure of BP in the crystalline state.

23.4 Give the overall composition of the unit cell corresponding with the formula BP.

23.5 Calculate the density of BP in kg m^{-3} when the lattice parameter of the unit cell is 4.78 Å.

23.6 Calculate the distance between a boron and a phosphorus atom in BP.

The Born-Lande formula given below can be used to calculate the lattice energy:

$$U_{\text{lattice}} = -f\,\frac{Z_+ Z_-\, A\, e^2}{r_+ + r_-}\left(1 - \frac{1}{\text{n}}\right)$$

The factor $f\,e^2$ amounts to 1390 when the ionic radii r_+ an r_- are given in Å. The Madelung constant is 1.638. The Born exponent n is 7. The charges of the ions Z_+ and Z_- are integer numbers.

23.7 Calculate the lattice energy of BP.

The rate (r) of formation of BP depends on the concentration of the reactants as given in the table:

Temperature, °C	[BBr$_3$], mol dm^{-3}	[PBr$_3$], mol dm^{-3}	[H$_2$], mol dm^{-3}	r, mol s^{-1}
800	2.25×10^{-6}	9.00×10^{-6}	0.070	4.60×10^{-8}
800	4.50×10^{-6}	9.00×10^{-6}	0.070	9.20×10^{-8}
800	9.00×10^{-6}	9.00×10^{-6}	0.070	18.4×10^{-8}
800	2.25×10^{-6}	2.25×10^{-6}	0.070	1.15×10^{-8}
800	2.25×10^{-6}	4.50×10^{-6}	0.070	2.30×10^{-8}
800	2.25×10^{-6}	9.00×10^{-6}	0.070	4.60×10^{-8}
800	2.25×10^{-6}	9.00×10^{-6}	0.070	19.6×10^{-8}

23.8 Determine the order of the reaction leading to BP and give the equation.

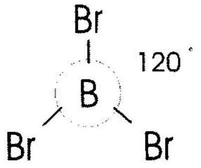
23.9 Calculate the rate constants at 800 and 880 °C.

23.10 Calculate the activation energy for the formation of BP.

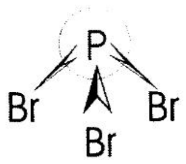
SOLUTION OF PREPARATORY PROBLEM 23

23.1 $BBr_3 + PBr_3 + 3\ H_2 \rightarrow BP + 6\ HBr$

23.2

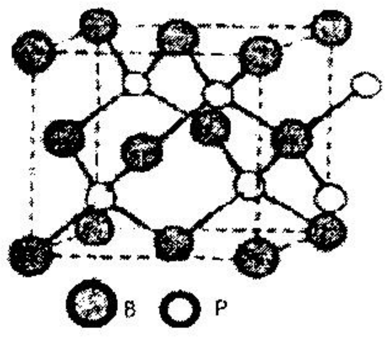


planar and trigonal



trigonal pyramidal

23.3



23.4 A FCC-structure of the B atoms and that gives:

Angular points: 8 × 1/8 = 1

Planes: 6 × 1/2 = 3

Total: 4

In each cell 4 phosphorus atoms are present which are tetrahedrally surrounded by atoms of boron.

23.5 The relative atomic masses of boron and phosphorus are 11 and 31, respectively.

$$R = \frac{m}{V} = \frac{(\mathrm{n}\ M_{\mathrm{bp}})}{N_a\ a^3} = \frac{4 \times 42}{6.022 \times 10^{26}\ \times\ (4.78 \times 10^{-10})^3} = 2554\ \mathrm{kg\,m^{-3}}$$

23.6 Distance B–P is $1/2 \times 3^{1/2} \times 1/3$ a = 2.069 Å.

23.7 Lattice energy of BP:

$$= -\ \frac{1390 \times 3 \times 3 \times 1.638\ Z_+ Z_-\ A\ e^2}{2.069}\ \frac{6}{7} = 8489\ \mathrm{kJ\,mol^{-1}}$$

23.8 The order of the reaction is 2.

$r = k\ [\mathrm{BBr_3}]\ [\mathrm{PBr_3}]$

23.9 $k_{800} = r_{800}\ /\ [\mathrm{BBr_3}]\ [\mathrm{PBr_3}] = 4.60 \times 10^{-8}\ /\ 2.25 \times 10^{-6} \times\ 9 \times 10^{-6}\ \dfrac{\mathrm{mol\ s^{-1}}}{\mathrm{mol^2\ dm^{-6}}} =$

$= 2\ 272\ \mathrm{dm^6\ mol^{-1}\ s^{-1}}$

$k_{880} = r_{880}\ /\ [\mathrm{BBr_3}]\ [\mathrm{PBr_3}] = 19.60 \times 10^{-8}\ /\ 2.25 \times 10^{-6} \times 9 \times 10^{-6}\ \dfrac{\mathrm{mol\ s^{-1}}}{\mathrm{mol^2\ dm^{-6}}} =$

$= 9679\ \mathrm{dm^6\ mol^{-1}\ s^{-1}}$

23.10 $\Delta H = -\ R\ \ln(k_2\,/\,k_1) \times (1/T_2 - 1/T_1)^{-1}$

$T_1 = 800 + 273 = 1073\ \mathrm{K}$

$T_2 = 880 + 273 = 1153\ \mathrm{K}$

$\Delta H = -\ R\ \ln(9679\,/\,2272) \times (1\ /\ 1153 - 1\ /\ 1073)^{-1} = 186\ \mathrm{kJ\ mol^{-1}}$

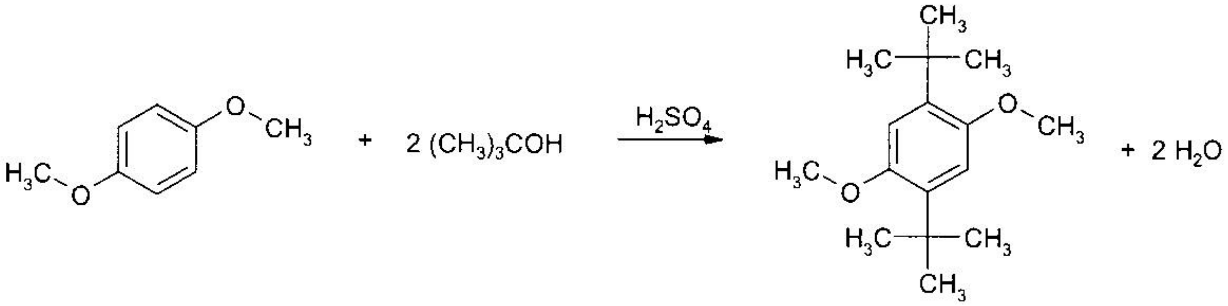
PRACTICAL PROBLEMS

Note: Micro scale equipment was used in the practical exam of the 42nd IChO. Since this equipment was used for the first time in the practical part of the IChO competition the authors of the practical preparatory tasks gave a more detailed description of the micro scale glasswork parts and their use in practice.

PREPARATORY PROBLEM 24 (PRACTICAL)

Preparation of 1,4-di-tert-butyl-2,5-dimethoxybenzene; an example of a Friedel-Crafts alkylation

The equation for the di-tert-butylation of 1,4-dimethyoxybenzene is as follows:



Procedure

A stirred mixture of 1,4-dimethoxybenzene (360 mg) in glacial acetic acid (15 cm^3) contained in an Erlenmeyer flask of 50 cm^3 is heated gently (water bath) until dissolved. *tert*-Butyl alcohol (0.6 cm^3) is then added using the pipette and the mixture is cooled in a crushed ice bath, while stirring is continued, and treated dropwise with concentrated sulphuric acid (45 drops). The addition is achieved using a Pasteur pipette and it must be ensured that each drop is mixed thoroughly with the reaction mixture before the next drop is added. The mixture is then removed from the ice bath, allowed to attain room temperature, and then stirred for a further 25 minutes. The mixture is again cooled in an ice-bath (0 °C) whereon water (3 drops) is added VERY CAREFULLY with slow stirring. Crystallization of the product begins and is accelerated by the slow, careful addition of ice water (7.5 cm^3). After ca. 10 minutes the crystalline material is collected by filtration using a Hirsch funnel. The crystals are washed twice with water and allowed to dry. The product is recrystallized by dissolving in hot methanol (10 cm^3) and cooling in an ice bath and again collected using a Hirsch funnel. The material is allowed to dry on the air. Determine the weight, calculate the yield and determine the melting point. The purity of the product is determined by thin-layer chromatography (silica gel 60 F254) using hexane as the eluent. The starting material is run on the same TLC plate as a reference. Determine the R_f-value of the product, of the starting material and of any contaminant in the product if present.

Record the following data:

1. The mass of the product.
2. The yield of product in percentage of the theoretical yield (show your calculation).
3. The appearance of the crystals and their colour.
4. The melting point
5. Copy your TLC plate on the data sheet + the respective R_f –values.

List of chemicals needed:

1,4-dimethoxybenzene (400 mg)
Acetic acid (2.0 cm^3)
tert-butyl alcohol (1.0 cm^3)
conc. sulfuric acid (0.5 cm^3)
methanol (10 cm^3)
water (20 cm^3)
TLC plates (silica gel 60 F254)

Safety: Concentrated H_2SO_4 must be handled with great care, read the safety rules for working with strong acids. In the event that you spill this acid on your hands and clothes, immediately rinse with running tap water.

Questions:

24.1 Which species is the electrophile in this alkylation?

24.2 Give the structure of the product when 1,3-dimethoxybenzene had been taken as a starting material.

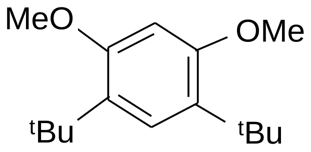
Note: Melting points can be determined in various ways, for instance, by using silicon oil in a round bottomed flask equipped with a magnetic stirrer and a thermometer or using a Kofler block (metal block with holes to fit a thermometer and a capillary tube) or employing a Kofler hot bench (a metal alloy strip with gradient heating).

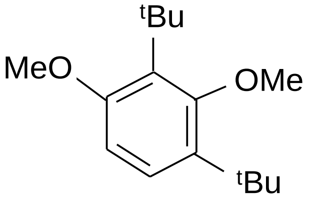
ANSWERS TO QUESTIONS IN PREPARATORY PROBLEM 24

- the field will be ca. 75 %, m. p. 104 – 105 °C

24.1 tert-butyl cation: $(CH_3)_3C^+$

24.2 Methoxy group is strongly activating in electrophilic aromatic substitution reactions and will direct the tert-butyl to ortho-para positions.





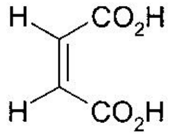
much less likely
due to steric hindrance

PREPARATORY PROBLEM 25 (PRACTICAL)

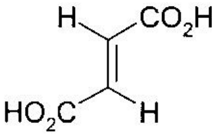
Titration of maleic acid (cis-butenedioic acid)

Introduction

Maleic acid is an unusual compound since the pK_a values for the first and second dissociation are very different, pK_a(1) = 1.8 and pK_a(2) = 6.1. In contrast, fumaric acid which is the corresponding *trans*-diacid, has pK_a values tat differ only slightly: 3.0 and 4.4, respectively. In this experiment the first and second dissociation of maleic acid will be demonstrated by titration using different pH indicators phenolphthalein and methyl orange.



maleic acid



fumaric acid

List of chemicals needed:

maleic acid, 600 mg

NaOH, aqueous solution, c = 1 mol dm^{-3}, 20 cm^3

phenolptphalein, few drops

methyl orange, few drops

Procedure 1

Maleic acid (290 mg) is dissolved in water (5 cm^3), 2 drops of phenolphthalein are added and the solution is titrated with a solution of NaOH (c = 1 mol dm^{-3}) until a clearly visible, permanent change of colour has taken place.

Record the following data:

1. Volume (cm^3) of the NaOH solution used.
2. Calculated amount of maleic acid in mmol.
3. Colour of the solution before titration.
4. Colour of the solution after completion of the titration.

Questions:

25.1 Determine on the basis of the titration results the minimum pK_a value of

i) phenolphthalein

ii) methyl orange

25.2 The difference in the pK_a values of maleic acid can be attributed to:

☐ intramolecular hydrogen bonding,

☐ steric hindrance of the –COOH group,

☐ large dipole moment of the *cis*-acid compared with the *trans*-acid,

☐ intermolecular hydrogen bonding.

Mark the correct answer.

ANSWERS TO QUESTIONS IN PREPARATORY PROBLEM 25

25.1 i) pK_a phenolphthalein pK_a > 6.1

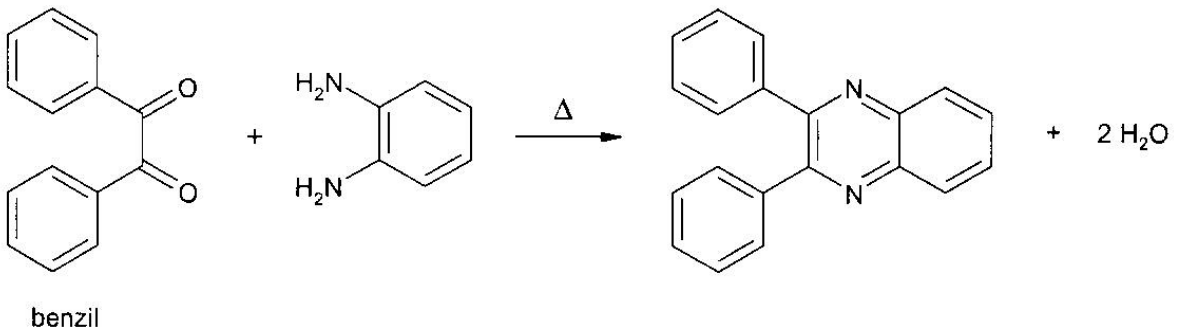
ii) pK_a methylorange pK_a > 1.8

25.2 The correct answer is the intramolecular hydrogen bonding.

PREPARATORY PROBLEM 26 (PRACTICAL)

Preparation of 2,3-diphenylquinoxaline

This preparation is an example of Schiff base formation leading to an aromatic compound. The reaction scheme for the preparation of 2,5-diphenylquinoxaline is as follows:



Chemicals

- Benzyl, 240 mg,
- 1,2-diaminobenzene, 250 mg,
- Methanol,
- Water.

Procedure

Benzil (240 mg) and and 216 mg of 1,2-diaminobenzene (*ortho*-phenylenediamine) are mixed in a regular test tube and the mixture is heated in a hot water bath for 20 minutes. The mixture will first melt and then change into a light tan-coloured solid. The solid is dissolved in hot methanol (ca 10 cm^3) and the solution is left undisturbed until crystallization starts. If crystallization fails to start, reheat the solution and add small amount of water using a Pasteur pipette to the point of turbidity. Crystallization will then begin and will be completed on cooling to ambient temperature. The crystals should be filtered off as soon as they are formed, otherwise brown oxidation by-product may accumulate on standing too long. The product should appear as colourless needles. Weigh the product, calculate the yield and determine the melting point.

Record the following data:

1. The mass of the product.

2. The yield of product as percentage of the theoretical yield. (Show your calculation.)
3. The appearance and colour of your product.
4. The meting point.

Note: The starting material 1,2-diaminobenzeneis often coloured and its purification by sublimation prior to this experiment may be necessary.

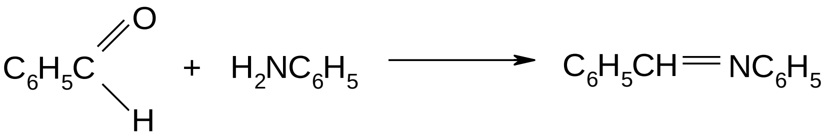
Question:

26.1 Show the equation for the reaction of benzaldehyde (C_6H_5CHO) with aniline (aminobenzene).

ANSWER TO THE QUESTION IN PREPARATORY PROBLEM 26

The yield will be ca 360 mg, and m. p. 125 °C.

26.1

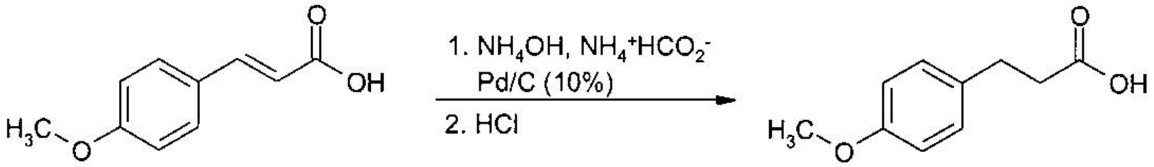


$$C_6H_5C(=O)H + H_2NC_6H_5 \longrightarrow C_6H_5CH{=}NC_6H_5$$

PREPARATORY PROBLEM 27 (PRACTICAL)

Preparation of 3-(4-methoxyphenyl)propanoic acid

This preparation is an example of a catalytic transfer-hydrogenation. The reaction scheme for the hydrogenation is as follows:



This hydrogenation in which ammonium formate serves as hydrogen source, is an alternative for the conventional catalytic hydrogenation using hydrogen gas. In both procedures Pd on charcoal is used as the catalyst.

Procedure

A magnetically stirred suspension of 4-methoxycinnamic acid (IUPAC name: *E*-3-(4-methoxyphenyl)prop-2-enoic acid) (450 mg) in water (7 cm^3) is treated slowly with concentrated aqueous ammonia (25%, 0.5 cm^3). After 5 min. palladium on charcoal catalyst (10%) and ammonium formate are added and the mixture is heated under reflux. The mixture gradually clears and the reaction is stopped after ca. 30 min. The completeness of the reaction is then checked by thin layer chromatography (TLC) plates (silica gel 60 F254) using heptane / ethyl acetate / formic acid in the ratio 99 : 99 : 2 as the eluent. The starting material is used as reference. If starting material is still present, the reaction mixture is heated for another 10 min. Then the reaction mixture is cooled to room temperature and filtered through a Hirsch funnel covered with a small piece of filter paper. The filter is washed four times with water (0.5 cm^3). The clear solution is then acidified with concentrated hydrochloric acid (c = 10 mol dm^{-3}). It is needed ca 0.5 cm^3 of the acid to reach pH 2. (Check with pH paper.) A white precipitate is formed which is filtered off with a Hirsch filter, washed with water (10 cm^3) and partially dried. Whilst still slightly wet the product is taken up in heptane (10 cm^3) and the mixture is heated under reflux for 5 min. The he obtained colorless solution is decanted. The residue is extracted twice with heptane (5 cm^3). The combined decanted fractions are heated to completely dissolve all material. The product is then allowed to crystallize by cooling in the a crushed ice bath.

The crystals are collected by filtration, dried and weighed. The yield is calculated and the melting point is determined.

Note: This experiment can be carried out on a half scale with micro scale equipment described in this

Record the following data:

1. The mass of the product.
2. The yield of the product in the percentage of the theoretical yield (show your calculation).
3. The appearance of the crystals and their color.
4. The melting point of the crystals.
5. Copy your TLC plate on the date sheet and calculate the respective R_f values.

Questions:

27.1 Calculate the quantity of starting material in mmoles.

27.2 Is ammonium formate used in excess? If so, calculate its molar quantity.

27.3 Propose a catalytic cycle for the transfer hydrogenation process.

Hint: CO_2 is formed during the reaction.

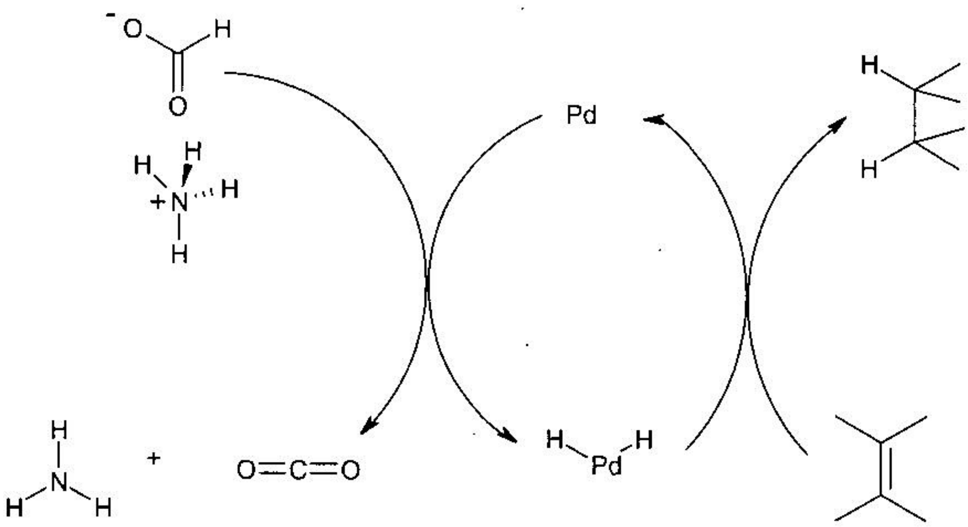
ANSWERS TO QUESTIONS IN PREPARATORY PROBLEM 27

The yield is expected to be ca. 64 %, melting point = 103.5 – 104.5 °C.

27.1 From the experiment.

27.2 From the experiment.

27.3



PREPARATORY PROBLEM 28 (PRACTICAL)

Complexometric titration; an example of metal ion determination using complexometry

This task serves as an example of metal ion determination using complexometry.

Introduction:

The concentration of Ni^{2+} ions can be determined by complexation with EDTA (ethylenediamine tetraacetate). EDTA is a multidentate ligand which forms a 1 : 1 complex with Ni^{2+} ions. The indicator is murexide which also form a complex with Ni^{2+} ions but this complex is less stable than that with EDTA. The aim of this experiment is to determine the amount of crystal water in nickel(II) sulphate.

List of chemical needed:

- hydrate of nickel(II) sulfate, solid, 300 mg
- standard EDTA solution
- murexide, indicator
- ammonium chloride, solid, 3 g
- ammonia solution, concentrated, 20 cm^3
- demineralized water

Procedure:

Hydrate of nickel(II) sulphate (ca. 300 mg) is weighed accurately and dissolved in water. Use a 100 cm^3 volumetric flask. Make a buffer solution by dissolving ammonium chloride (2.7 g) and concentrated ammonia (17.5 cm^3) in water (50 cm^3). Fill the burette with EDTA standard solution (0.01 mol dm^{-3}). Transfer 10.00 cm^3 of nickel(II) sulphate solution with a pipette into an Erlenmeyer flask (200 cm^3) and dilute it with water (ca. 90 cm^3). Add buffer (10 cm^3) while swirling the Erlenmeyer flask. Add a small amount of solid murexide indicator and ensure its complete dissolution. Titrate with EDTA solution until change of color (yellow to purple). When the change of color is slow, add some concentrated ammonia at the end of the titration. This experiment should be carried out in duplicate.

Record the following data:

1. The amount of EDTA solution used in cm^3. Record also the exact titer of this solution.
2. The mass of the hydrate of nickel(II) sulfate used.
3. Calculate the concentration of Ni^{2+} in the solution.
4. Calculate the number of moles of crystal water per one mole of nickel sulfate.

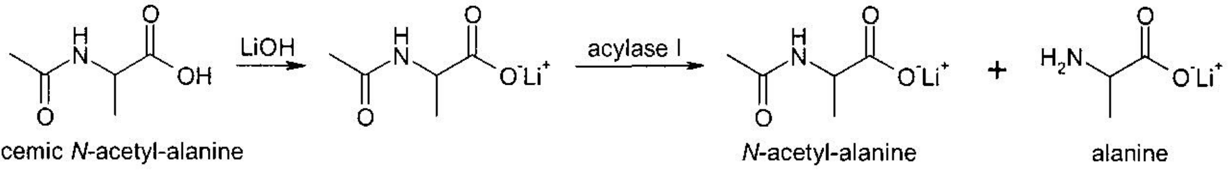
(Show the details of your calculations.)

PREPARATORY PROBLEM 29 (PRACTICAL)

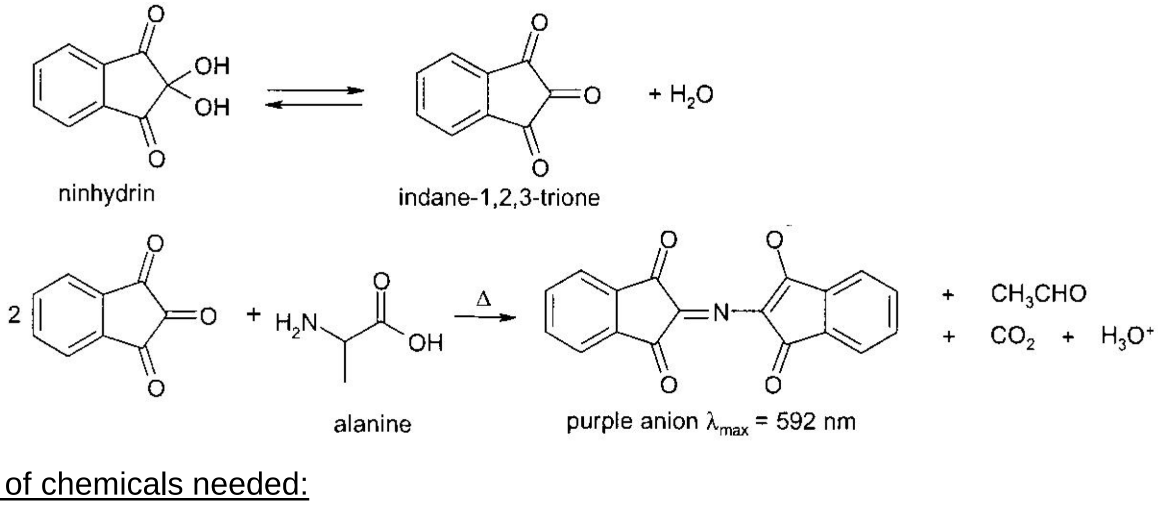
Enzymatic hydrolysis of N-acetyl alanine as an example of an environmentally benign process

Introduction:

Biological reactions are catalyzed by enzymes. Many enzymes show a highly selective behaviour and often are able to selectively catalyze reactions with one enantiomer of a racemate. In modern chemistry enzymes are used for many processes in vitro, especially for the synthesis of enantiomerically pure products. In this experiment the hydrolysis of N-acyl-alanine with the enzyme *acylase I* is investigated.



The process of the reaction can be monitored by following the formation of alanine using the reaction with ninhydrin, as shown below.



List of chemicals needed:

- rac. *N*-acetyl-alanine, 265 mg
- acylase I, 10 mg
- lithium hydroxide, 84 mg
- ninhydrine solution (Sigma N 1632), 2 cm^3
- dimethyl sulfoxide, ca. 70 cm^3
- lithium acetate buffer, pH 5.2.

Procedure:

Racemic N-acetyl-alanine (262 mg, 2.0 mmol) is dissolved in water (10 cm^3). A solution of lithium hydroxide (84 mg, 2.0 mmol) in water (4 cm^3) is then gradually added with gentle stirring. The pH is monitored with pH-paper until pH = 7 is reached. A solution of acylase I (10 mg) in water is added with vigorous stirring for 2 minutes. (The above enzyme solution is prepared by adding the enzyme to 5 cm^3 of water and filtration using a small glass filter covered with diatomaceous earth.) Subsequently, water is added to reach the total volume of exactly 20.0 cm^3. The reaction mixture is kept at a temperature of 37 °C in a water bath for 60 minutes. The an accurate volume of 0.25 cm^3 (use a syringe or a fine measuring pipette) is transferred into a test tube and ninhydrin (Sigma N 1632), (1.25 cm^3) is added. This mixture is heated in boiling water during 20 minutes whereby a deep purple color is developed. After cooling, this mixture is accurately added to buffer solution consisting of 4 M lithium acetate aqueous buffer (pH = 5.2) and dimethyl sulfoxide in the ratio 1 : 3 in a volumetric flask of 250 cm^3. Adjust the volume to 250 cm^3. Then measure the absorbance of the solution at λ = 592 nm using a spectrophotometer. Use as a reference ninhydrin in the same lithium acetate buffer in dimethyl sulfoxide. ε (purple complex) = 13350 dm^3 mol^{-1} cm^{-1}.

Record the following data:

1. The initial concentration of racemic *N.*
2. The absorbance at λ = 592 nm.
3. Calculate the amount of substance (mmol) of alanine formed in the enzymatic reaction. Use the Lambert-Beer's law.
4. Calculate the percentage of conversion.

Questions:

29.1 Will the alanine formed be optically active? (Yes or no.)

29.2 Will the *N*-acetyl-alanine that remains, be optically inactive, optically enriched or optically pure when the conversion is smaller than 50 %?

29.3 Idem when the conversion is 50 % exactly?

29.4 Is the conversion larger than 50 % possible? (Yes or no.)

Special note:

If time permits you may decide to stop the reaction after 10, 25, 40 and 60 minutes and determine the concentration of alanine in each case. Then construct a graph of the concentration of alanine *vs*. time and estimate the optimal reaction time.

ANSWERS TO QUESTIONS IN PREPARATORY PROBLEM 29

29.1 Yes.

29.2 Optically enriched.

29.3 Optically pure.

29.4 When the enzyme is highly selective: no.

When the enzyme is not highly selective: yes. In this case the preferred enantiomer will be hydrolyzed very fast and the other enantiomer will be converted more slowly.