NTNU
Norwegian University of
Science and Technology

Faculty of Natural
Sciences and Technology
Department of chemistry

Page 1 (of 6)

Inquiries concerning the contents of the test to :

Rudolf Schmid,
Phone : 735 96203 (evt. 91375546)
Department of chemistry, 735 50870

Stud nr. :_____

EXAMINATION IN COURSE TKJ 4180 (FORMER SIK 3064)
PHYSICAL ORGANIC CHEMISTRY
(ORDINARY EXAMINATION)

THURSDAY, DESEMBER 9TH 2004,
09:00 - 13:00

Permitted aids:

B1-type calculator with empty memory
(as specified in NTNU's list of calculators approved for use in examinations at NTNU)
Molecular model building sets
No other aids (i.e. printed or handwritten texts or notes) are allowed.

This test consists of six - 6 - pages :
1 front page (p. 1), 4 pages with 7 questions (p. 2-5) and 1 page with appendicies / physical data-tables (p. 6).

Weighting factors for the questions i given in the heading of the question. A maximum of 100 points may be obtained. Alle questions must be answered in order to achieve full score (100 pts.).

Deadline for the results to be anuounced : Friday, January 7th, 2005.

Postadresse	Besoksadresse:	Telefon +47 73 55 08 70	Side 1 av 6
	Realfagbygget,	Telefaks +47 73 55 08 77	4180-04h-norm-eng-end doc
Institutt for kjemi	Høgskoleringen 5		
N-7491 Trondheim	rom D2-136	Org.nr. 974 767 880	

Question 1 :   (2 points for each answer , maximum. 5 av 6 answers: **max. 10 points**)

Define, briefly :

a) Conformational free energy ($-\Delta G°$),

(C/S A4 (2000), ch.3.3. p.139f)

b) Nucleophilic constant , n_{CH3I} ,

(C/S A4 (2000), ch 5 5, p 291)

c) "Super acid"

(C/S A4 (2000), ch.5 7, p 286)

d) "Hofmann rule" and "Saytzeff rule",

(C/S A4 (2000), ch 6 7, p385)

e) Strain energy (*spennings-energi*),

(C/S A4 (2000), ch.3., p.123)

f) "Exploded transition state" (in S$_N$-reactions).

(C/S A4 (2000). ch.5. 3. p273)

Question 2 :   (5 + 10 = **15 points**)

a) What is a "phenonium ion" ? Where and when does it exist ?

(C/S A4 (2000). ch..5.10 , p 314ff)

b) Define the terms "Lewis acid" and "Lewis base". Explain qualitatively the terms "hard" and "soft" acid (or base), and the factors that determine whether a Lewis acid (base) is "hard" or "soft". Present (a) method(s) that quantitatively describe(s) hardness /softness. List 2 examples of hard and of soft Lewis acids and Lewis bases each (i.e., all in all, 8 species).

(C/S A4. ch.1.2.3. s. 20ff. og ch.4.9 235f. c.5.5. p. 293)

Question 3 :   (7 + 8 = **15 points**)

a)   By peroxyformic acid oxidation in aqueous formic acid of cyclohexene one major product $C_6H_{12}O_2$ is obtained. Describe the reaction mechanism and the product (specify the stereochemistry).
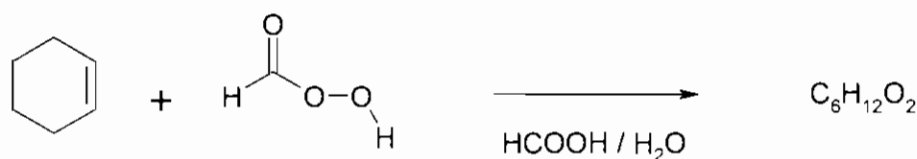
(Question 3 continued on next page)

b) If the same raction is carried out using the medium-sized ring cyclo-octene, then two of the products can be assigned the formula $C_8H_{16}O_2$. Of those two, the minor compund **X** is the one ananloguous to the product of the reaction of cyclohexene with pcroxy-formic acid (*cfr.* 3.a)). The main $C_8H_{16}O_2$ product **Y**, hoewever, has a different structure.
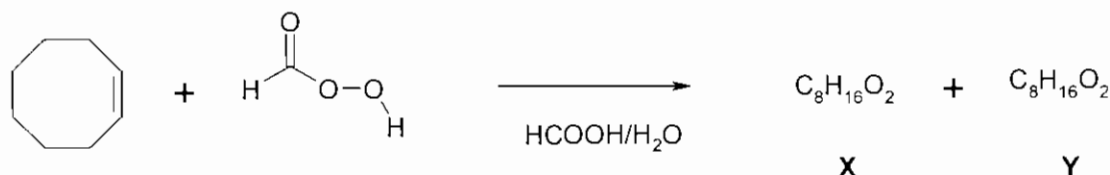

Describe these two products (including their stercochemistry), and suggest a rcaction mechanism for the formation of **Y** (the mechanism for the formation of **X** is assumed to bc analogous to the one described in 3.a))

(Lowry/Richardson, "Mechan. & Theory Org. Chem ", Harper/Row. 1976, p.314ff)

Question 4 : **(7 + 3 + 5 = 15 points)**

(Ref.: G.Solladié & al., J.Org. Chem. <u>60</u>, 4988, (1995))

a) Present your suggestion of a reasonable reaction mechanism for the synthcsis step given below (it is sufficient to illustrate the mechanism for onc of the two equivalent sides of the molecule).

b) For this synthetic step, indicate the configurations at the stercogenic centers in the product applying the *R/S*-convention. also, describe the configuration of the starting sulfoxide compound by means of the *R/S*-convention.

c) In this step, slightly more than 4 quivalents of the sulfoxide and the LDA base are com-bined with onc equivalent of starting ketal: The reaction is teminated by the addition of saturatcd aqueous ammonium chloride solution. Explain why a minimum of 4 equivalents of starting sulfoxide and base arc required to achieve a satisfactory yield
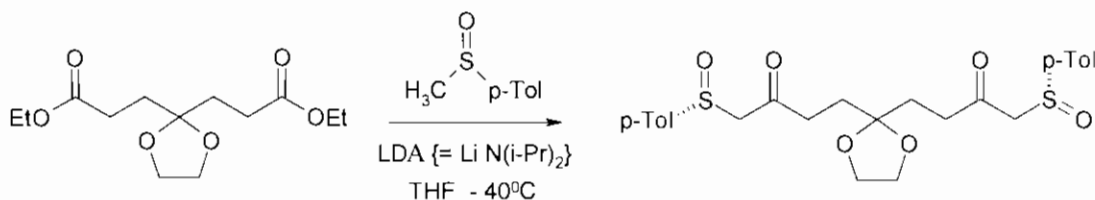
Question 5 :   (10 points)

When phenyl-substituted 1-aryl-2-methyl-propyl chlorides **1** react with sodium methoxide, a mixture of internal (**2**) and terminal (**3**) alkenes is formed.
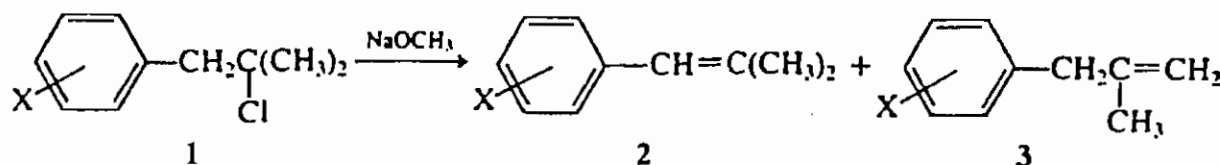
By using the product ratio, the overall reaction rate can be dissected into the individual rates for formation of **2** and **3**. These rates are found to be substituent dependent for the formation of **2** ($\rho = 1,4$) but substituent independent for the formation of **3** ($\rho = -0,1 \pm 0,1$). The reactions are both second-order, first-order in base and first-order in substrate.
Explain the mechanistic basis of these observations and discuss how the observations provide information about the reaction mechanism.

(C/S A4 (2000). ch.6. probl. 10.a, p401)

When $X = NO_2$, does the amount of internal alkene **2** increase, or decrease, as compared to the reaction with $X = H$?

Question 6 :   (8 + 5 + 7 = 20 points)

a) Reactions of substituted cumyl benzoates (2-phenyl-2-propyl benzoates) in 50 : 50 tri-fluoroethanol-water show no effect of sodium azide (NaN_3, between 0 and 0,5 M) on the rate of disappearance of the ester. The product ratio, however, is highly dependent on the cumyl-substituent. Electron-releasing substituents favor formation of azide **K**, whereas electron-withdrawing substituents promote solvent capture and the formation of alcohol **L** and trifluoroethyl ether **M**.
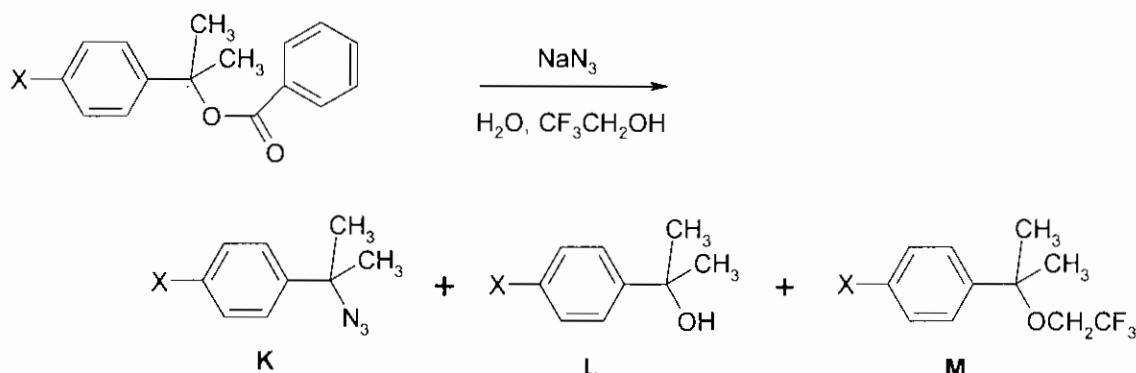
Postulate and explain a detailed reaction mechanism which is consistent with these experimental results.

(C/S A4 (2000). ch.5, probl. 26, p.348)

(Question 6 continued on next page)

b) Assuming that one of the methyl groups in the starting material were substituted with three deuterium atoms instead of protium, would you expect that a kinetic isotope effect $(k_H/k_D \neq 0)$ could be measured, or not. Briefly explain your conclusion, and, in case you would expect an isotope effect, indicate what type, and how large (approximately) an effect you would expect (give a a number, please).

c) If the isotopic composition in the solvent of a reaction is changed, then the reaction rates may change (solvent isotope effects) in many cases. Explain the types of solvent isotope effects there are, and the mechanistic interpretation of these different effects for the reaction under investigation.
Based on the reaction mechanism you proposed in the answer to question 6.a, would you expect a change of reaction rates if the reaction was performed with heavy water (D_2O) instead of ordinary water (H_2O) in the solvent mixture ? Explain your prognosis.

Question 7 :   (5 + 10 = 15 points)

Methylketen dimerises spontaneously, and two alternative dimerisation products could be expected to be formed. Experimentally the product dimers pK_a was determined to be 2.8.
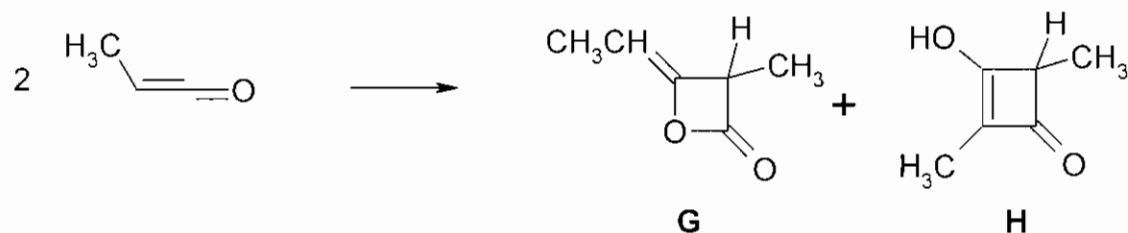
a) Explain which of the two alternative dimer structures, **G** or **H** you would consider most likely to be the one actually formed, using the measured pK_a as the diagnosis tool.

(C/S A4 (2000), ch.7, probl 19, p..446)

b) Racemates of organic acids may often be resolved into the enantiomers by fractional crystallisation after formation av (diastereomeric) salts with chiral organic bases (e.g. 1-phenylethylamine). Assume that there exist suitable organic bases that would yield good quality crystals with the two possible methylketen dimers and could, therefore, make possible racemate resolution.
Explain your expectations, positive or negative, for such a "classical" racemate resolution be successful and yielding the two pure enantiomers of **G** and **H**, respectively (both dimers being (potential) acids).

Universal gas constant .
R = 1,987 cal/K / mol = 8,315 J/K / mol

Hammet σ-parameter values (Tab. 4.5) and selected Hammett ρ-values (Tab. 4.6) (from C/S 4.cd.)

Table 4.5. Substituent Constants[a]

Substituent group		σ_m	σ_p	σ^+	σ^-	σ_I	σ_R^0
Acetamido	CH_3CONH	**0.14**	**0.0**	−0.6	0.47		
Acetoxy	CH_3CO_2	0.39	0.31	0.18			
Acetyl	CH_3CO	0.36	**0.47**		0.82	0.20	0.16
Amino	NH_2	**−0.09**	**−0.30**	−1.3		0.12	−0.50
Bromo	Br	0.37	**0.26**	0.15		0.44	−0.16
t-Butyl	$(CH_3)_3C$	−0.09	**−0.15**	−0.26			
Carbomethoxy	CH_3O_2C	0.35	**0.44**		0.74	0.20	0.16
Carboxy	HO_2C	0.35	**0.44**		0.73		
Chloro	Cl	**0.37**	**0.24**	0.11		0.46	−0.18
Cyano	CN	**0.62**	**0.70**		0.99	0.56	0.08
Ethoxy	C_2H_5O	0.1	−0.14	−0.82			
Ethyl	C_2H_5	**−0.08**	**−0.13**	−0.30			
Fluoro	F	**0.34**	**0.15**	−0.07		0.50	−0.31
Hydrogen	H	**0**	**0**	0	0	0	0
Hydroxy	OH	0.13	−0.38	−0.92			
Methanesulfonyl	CH_3SO_2	**0.64**	**0.73**		1.05	0.60	0.12
Methoxy	CH_3O	**0.10**	−0.12	−0.78		0.27	−0.42
Methyl	CH_3	**−0.06**	**−0.14**	−0.31		−0.04	−0.13
Nitro	NO_2	**0.71**	0.81		1.23	0.65	0.15
Phenyl	C_6H_5	**0.05**	**0.05**	−0.18	0.08		
Trifluoromethyl	CF_3	**0.46**	**0.53**		0.74	0.42	0.08
Trimethylammonio	$(CH_3)_3N^+$	0.99	0.96				
Trimethylsilyl	$(CH_3)_3Si$	−0.04	−0.07				

a. Values of σ_m, σ_p, σ^+, and σ^- from O. Exner, in *Correlation Analysis in Chemistry*, N. B. Chapman and J. Shorter, eds., Plenum Press, New York, 1978, Chapter 10. Values of σ_I and σ_R^0 from J. Bromilow, R. T. C. Brownlee, V. O. Lopez, and R. W. Taft, *J. Org. Chem* **44**:4766 (1979). Values of σ_m and σ_p shown in boldface type are regarded as particularly reliable.

Table 4.6. Reaction Constants[a]

Reaction	ρ
$ArCO_2H \rightleftharpoons ArCO_2^- + H^+$, water	1.00
$ArCO_2H \rightleftharpoons ArCO_2^- + H^+$, EtOH	1.57
$ArCH_2CO_2H \rightleftharpoons ArCH_2CO_2^- + H^+$, water	0.56
$ArCH_2CH_2CO_2H \rightleftharpoons ArCH_2CH_2CO_2^- + H^+$, water	0.24
$ArOH \rightleftharpoons ArO^- + H^+$, water	2.26
$ArNH_3^+ \rightleftharpoons ArNH_2 + H^+$, water	3.19
$ArCH_2NH_3^+ \rightleftharpoons ArCH_2NH_2 + H^+$, water	1.05
$ArCO_2Et + {}^-OH \rightarrow ArCO_2^- + EtOH$	2.61
$ArCH_2CO_2Et + {}^-OH \rightarrow ArCH_2CO_2^- + EtOH$	1.00
$ArCH_2Cl + H_2O \rightarrow ArCH_2OH + HCl$	−1.31
$ArC(Me)_2Cl + H_2O \rightarrow ArC(Me)_2OH + HCl$	−4.48
$ArNH_2 + PhCOCl \rightarrow ArNHCOPh + HCl$	−3.21

a. From P. R. Wells, *Linear Free Energy Relationships*, Academic Press, New York, 1968, pp. 12, 13.