



UNIVERSITI
TEKNOLOGI
PETRONAS

FINAL EXAMINATION MAY 2024 SEMESTER

COURSE : YAB4233/YBB4213 - GREEN PROCESSES AND PRODUCTS
DATE : 30 JULY 2024 (TUESDAY)
TIME : 9:00 AM - 12:00 NOON (3 HOURS)

INSTRUCTIONS TO CANDIDATES

1. Answer **ALL** questions from **Section A** and **B** in the Answer Booklet.
2. Begin **EACH** answer on a new page in the Answer Booklet.
3. Indicate clearly answers that are cancelled, if any.
4. Where applicable, show clearly steps taken in arriving at the solutions and indicate **ALL** assumptions, if any.
5. **DO NOT** open this Question Booklet until instructed.

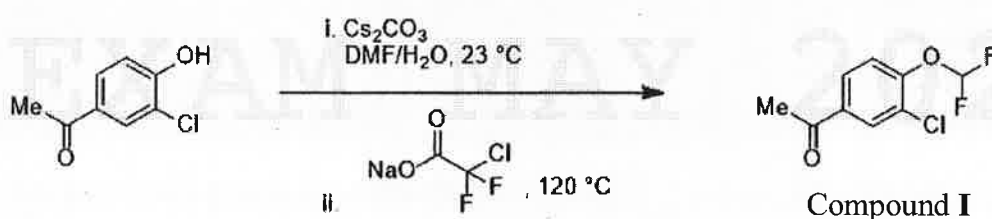
Note :

- i. There are **ELEVEN (11)** pages in this Question Booklet including the cover page .
- ii. **DOUBLE-SIDED** Question Booklet.

Section A

1. Aryl difluoromethyl ethers are found in pharmaceutical products such as pantoprazole. Pantoprazole is used to treat certain stomach and esophagus problems. Despite growing concerns over the environmental impacts of pharmaceuticals, the use of Life Cycle Assessment (LCA) within the pharma-sector remains quite incomplete.

Current syntheses of difluoromethyl ethers require the ozone-depleting compound HCF_2Cl (Freon 22) gas that is difficult to handle. The procedure herein offers quick and facile synthetic access to aryl difluoromethyl ether, Compound I from phenols through a transformation in a series of reactions shown in **SCHEME Q1**.



SCHEME Q1: Synthesis of Compound I

A single-necked 100 mL round-bottomed flask is added sequentially with 1-(3-chloro-4-hydroxyphenyl) ethan-1-one (3.00 g) and cesium carbonate (8.60 g). The flask is then connected to a Schlenk line. Dry dimethyl fluoride, DMF (27 mL) and deionized water (3.2 mL) are added at 23°C to the flask and stirring is initiated. After 1 hour, sodium 2-chloro-2,2-difluoroacetate (7.51 g) is added, then reaction started at 120°C and stirred for 2 hours (500 rpm). The mixture is then rinsed with an additional 60 mL of water. The aqueous layer is extracted with hexane (5 x 100 mL) and the combined organic layers are washed with brine solution (50 mL). The organic phase is dried over anhydrous Na_2SO_4 (30 g), filtered and eluted with hexane (25 mL). The solution is then concentrated which produced Compound I as a yellow oil (3.66 g). This reaction also produced sodium chloride and released carbon dioxide.

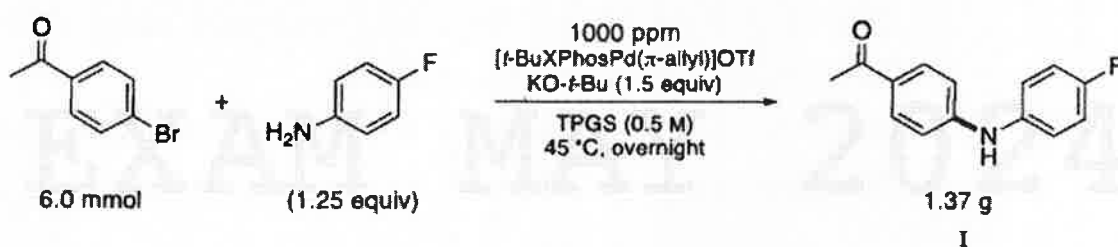
Densities: DMF = 0.944 g/mL; H_2O = 1.000 g/mL; Hexane = 0.6594 g/mL; brine = 1.202 g/mL

- a. As a green chemistry expert, you are required to determine whether the process to synthesis Compound I is 'green'. Propose and determine **FIVE (5)** green matrices/indicators to measure 'greenness' of a chemical process.
[20 marks]
- b. From **TWO (2)** of the green matrixes obtained in **part (a)**, rationalize the 'greenness' of the process and elaborate how to increase the 'greenness' of any matrixes obtained.
[4 marks]
- c. Propose **THREE (3)** methods in which the synthesis steps could be improved in accordance with the Twelve Principles of Green Chemistry.
[6 marks]
- d. Discuss **THREE (3)** life cycle stages in pantoprazole production that you foresee from these processes, anticipate the impacts to **THREE (3)** key environment indicators. Provide **ONE (1)** example for each of them.
[6 marks]
- e. Suggest the best waste management treatment for the excess reagents and byproducts for this reaction. Justify your answer.
[4 marks]

Section B

1. a. Reflux extraction is the most widely used method for the extraction of desired natural products from raw materials. Orientoside, luteolin, and total flavonoids from *C. cajan* leaves are extracted by reflux extraction using ethanol and 2-propanol at different temperatures (20°C, 40°C, and 60°C). After 1 hour, the sample was taken and mixed with petroleum ether (100 ml). Water was added for the separation of phases. After the separation, the petroleum-ether-extract was concentrated at 70°C and 170 mbar in a rotatory evaporator.
- i. Suggest **TWO (2)** drawbacks of the extraction process.
[2 marks]
 - ii. Suggest **TWO (2)** methods which are 'greener' according to Twelve Principles of Green Chemistry.
[2 marks]
 - iii. Discuss the working principle of any of the methods described in **part (a)(ii)**.
[3 marks]

- b. Recently, one of the steps to achieve a 'greener' chemical process is to run organic reactions in water. Pd-catalyzed amination in water was carried out using micellar catalysis route to produce compound I as shown in the reaction below (**SCHEME Q1b**). TPGS as the surfactant was added, and the resulting solution is stirred vigorously at 45°C overnight. Upon reaction completion, ethyl acetate (EtOAc) is added to the vessel. The entire mixture is then filtered through a plug of silica gel to remove the surfactant along with salt impurities. The crude mixture is then concentrated and purified by column chromatography. The reaction yielded compound I in 99 %.

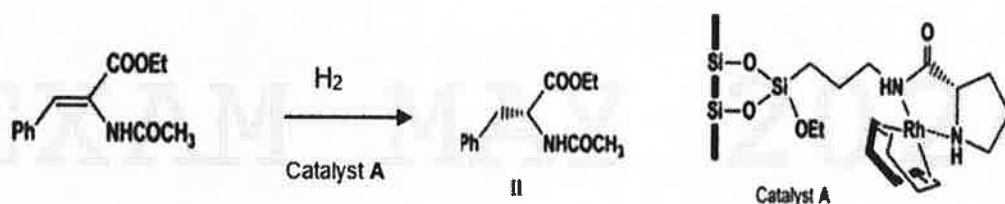


SCHEME Q1b. Pd-catalyzed amination

- Calculate the E-factor for the reaction. Provide comments on the value obtained. [5 marks]
- Discuss how micellar chemistry works with relations to the reaction **SCHEME Q1b**. [3 marks]
- Propose **FOUR (4)** advantages of using this method. [3 marks]
- Propose an alternative technique to make the workup step of compound I more 'greener'. [2 marks]

2. a. Hydrogenation of (*Z*)-*N*-acetamidocinnamic acid derivative using catalyst **A**, which is Rh complexes with proline derived ligand on zeolite yielded compound **II** with 94% ee (**SCHEME 2a**). To a solution of (*Z*)-*N*-acetamidocinnamic acid derivative (3 mmol) in acetonitrile (50 mL), 0.050 mg of catalyst **A** was added. Then hydrogen (3 mmol) was passed to that solution and the resultant mixture were stirred at room temperature for 2 hours. Liquid-liquid separation was carried out with 50 ml of dichloromethane and H₂O, each. The organic layer was separated out, dried with 20 g of MgSO₄. The liquid layer was filtered out and the solvent was removed with rotary evaporator. After removal of solvent, the crude product was purified by flash chromatography using 1000 ml 70:30 hexane:CH₂Cl₂ to give 0.33 g of product.

Note: Densities: acetonitrile = 0.786 g/cm³; hexane = 0.661 g/cm³; dichloromethane = 1.325 g/cm³



SCHEME Q2a. Hydrogenation of (*Z*)-*N*-acetamidocinnamic acid derivative

- i. State the general term catalyst **A** is called and describe the main components in catalyst **A**.
[3 marks]
- ii. Provide **THREE (3)** advantages of using catalyst **A**.
[3 marks]
- iii. Calculate the PMI value for the reaction.
[4 marks]
- iv. Briefly describe how enantioselectivity was obtained for this reaction.
[2 marks]

b. Removal of carbon dioxide, CO₂ a greenhouse gas straight from the atmosphere or direct air capture (DAC), has recently emerged as an important component for addressing climate change. A promising DAC system based on aqueous amine solvents has traditionally been used. However, aqueous amine solvents suffer from high volatility and are corrosive.

i. Provide **TWO (2)** alternative techniques for the CO₂ removal.

[2 marks]

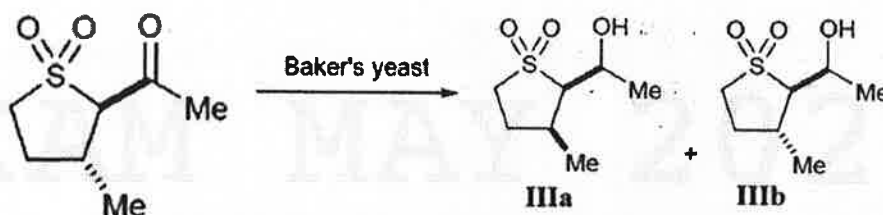
ii. Suggest **TWO (2)** advantages for each of the methods mentioned in **part (b)(i)**.

[3 marks]

iii. Describe the synthesis pathway for **ONE (1)** of the method mentioned in **part (b)(ii)**.

[3 marks]

3. a. *Saccharomyces cerevisiae* (*S. cerevisiae*) or baker's yeast is a species of yeast known since early times for its fermentation properties. The baker's yeast mediated reduction of *trans*-2-acetyl-3-methyl sulfolane in water yielded two diastereomers **IIIa** and **IIIb**, with each of them yielding more than 98% ee, each (**SCHEME 3a**). The diastereomers were isolated in the ratio 40:60.



SCHEME Q3a. Reduction of *trans*-2-acetyl-3-methyl sulfolane

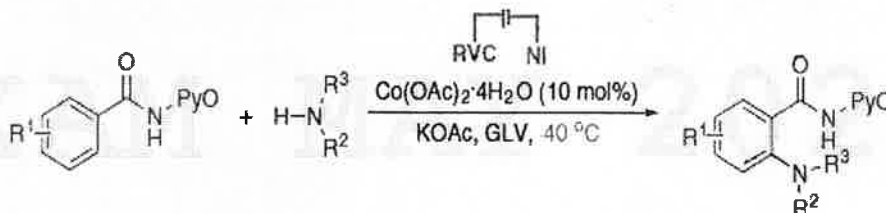
- Identify the categories of enzymes generally used in bio catalysed organic transformations. Give the name for the enzyme capable of catalysing the reaction in **SCHEME Q3a**.

[4 marks]

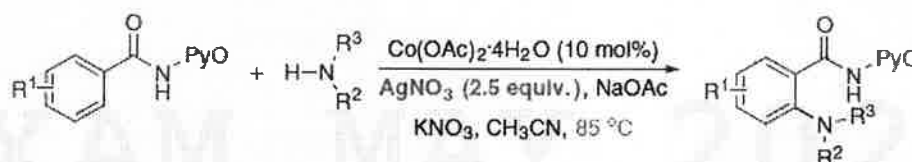
- Describe **THREE (3)** advantages of using biocatalysis in the reaction **SCHEME Q3a** with reference to Twelve Principles of Green Chemistry.

[3 marks]

- b. Electrosynthesis represents a green and advantageous alternative to traditional synthetic methods. C–H amination was carried out using aromatic amides and cyclic secondary amines in renewable solvent, γ -Valerolactone (GVL) with RVC an inert electrode. The traditional method employs 2.5 equiv. of AgNO_3 as the oxidant (**SCHEME 3b(i)** and **(ii)**).



SCHEME 3b(i): Electrochemical C–H amination in renewable solvent



SCHEME 3b(ii): C–H amination using AgNO_3 as oxidant

- i. Describe **THREE (3)** advantages of the electrochemical C–H amination compared to the traditional method.

[3 marks]

- ii. Predict **ONE (1)** limitation of the electrochemical method.

[2 marks]

- iii. Suggest **ONE (1)** way to overcome the limitation mentioned in part (b)(ii).

[3 marks]

- c. Photocatalysis stands out as a promising method for degrading organic pollutants such as dyes in wastewater. With the aid of a diagram, illustrate the working principle of ZnO as the photocatalyst in degrading Eosin Y (FIGURE 3c) as the dye in wastewater.

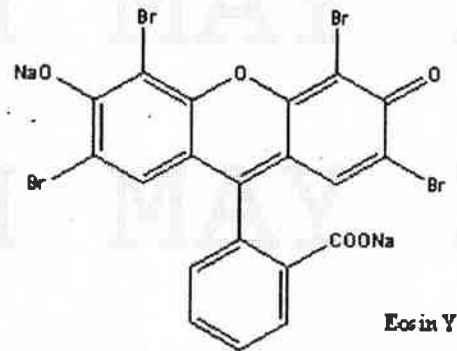


FIGURE 3c Structure of Eosin Y

[5 marks]

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APPENDIX II

LIST OF ELEMENTS

Name	Symbol	Atomic number	Atomic weight	Name	Symbol	Atomic number	Atomic weight
actinium	Ac	89	227.03 ^a	mendelevium	Md	101	258.10 ^a
aluminium	Al	13	26.98	mercury	Hg	80	200.59
americium	Am	95	243.06 ^a	molybdenum	Mo	42	95.94
antimony	Sb	51	121.75	neodymium	Nd	60	144.24
argon	Ar	18	39.95	neon	Ne	10	20.18
arsenic	As	33	74.92	neptunium	Np	93	237.05 ^a
astatine	At	85	209.99 ^a	nickel	Ni	28	58.69
barium	Ba	56	137.33	niobium	Nb	41	92.91
berkelium	Bk	97	247.07 ^a	nitrogen	N	7	14.01
beryllium	Be	4	9.01	nobelium	No	102	259.10 ^a
bismuth	Bi	83	208.98	osmium	Os	76	190.23
bohrium	Bh	107	264.12 ^a	oxygen	O	8	16.00
boron	B	5	10.81	palladium	Pd	46	106.40
bromine	Br	35	79.90	phosphorus	P	15	30.97
cadmium	Cd	48	112.41	platinum	Pt	78	195.08
calcium	Ca	20	40.08	plutonium	Pu	94	244.06 ^a
californium	Cf	98	251.08 ^a	polonium	Po	84	208.98 ^a
carbon	C	6	12.01	potassium	K	19	39.10
cerium	Ce	58	140.12	praseodymium	Pr	59	140.91
cesium	Cs	55	132.91	promethium	Pm	61	145.00 ^a
chlorine	Cl	17	35.45	protactinium	Pa	91	231.04
chromium	Cr	24	52.00	radium	Ra	88	226.03 ^a
cobalt	Co	27	58.93	radon	Rn	86	222.02 ^a
copper	Cu	29	63.55	rhenium	Re	75	186.21
curium	Cm	96	247.07 ^a	rhodium	Rh	45	102.91
dubnium	Db	105	262.11 ^a	rubidium	Rb	37	85.47
dysprosium	Dy	66	162.50	ruthenium	Ru	44	101.07
einsteinium	Es	99	252.08 ^a	rutherfordium	Rf	104	261.11 ^a
erbium	Er	68	167.26	samarium	Sm	62	150.35
europium	Eu	63	151.96	scandium	Sc	21	44.96
fermium	Fm	100	257.10 ^a	seaborgium	Sg	106	266.00 ^a
fluorine	F	9	19.00	selenium	Se	34	78.96
francium	Fr	87	223.02 ^a	silicon	Si	14	28.09
gadolinium	Gd	64	157.25	silver	Ag	47	107.87
gallium	Ga	31	69.72	sodium	Na	11	23.00
germanium	Ge	32	72.61	strontium	Sr	38	87.62
gold	Au	79	196.97	sulfur	S	16	32.07
hafnium	Hf	72	178.49	tantalum	Ta	73	180.95
hassium	Hs	108	269.13 ^a	technetium	Tc	43	98.00 ^a
helium	He	2	4.00	tellurium	Te	52	127.60
holmium	Ho	67	164.93	terbium	Tb	65	158.93
hydrogen	H	1	1.01	thallium	Tl	81	204.37
indium	In	49	114.82	thorium	Th	90	232.04
iodine	I	53	126.90	thulium	Tm	69	168.93
iridium	Ir	77	192.22	tin	Sn	50	118.71
iron	Fe	26	55.85	titanium	Ti	22	47.90
krypton	Kr	36	83.80	tungsten	W	74	183.84
lanthanum	La	57	138.91	uranium	U	92	238.03
lawrencium	Lr	103	262.11 ^a	vanadium	V	23	50.94
lead	Pb	82	207.19	xenon	Xe	54	131.30
lithium	Li	3	6.94	ytterbium	Yb	70	173.04
lutetium	Lu	71	174.97	yttrium	Y	39	88.91
magnesium	Mg	12	24.31	zinc	Zn	30	65.39
manganese	Mn	25	54.94	zirconium	Zr	40	91.22
meitnerium	Mt	109	268.14 ^a				

^aMass of longest-lived or most important isotope

