KINETICS AND MECHANISM OF AMINOLYSIS OF *p*-NITROPHENYL ACETATE IN MIXED WATER-ACETONITRILE SOLVENTS

NOR SALMI BINTI ABDULLAH

SUBMISSION OF DISSERTATION FOR THE FULFILMENT OF THE DEGREE OF MASTER OF SCIENCE

CHEMISTRY DEPARTMENT

FACULTY OF SCIENCE

UNIVERSITY OF MALAYA

KUALA LUMPUR

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ABSTRACT

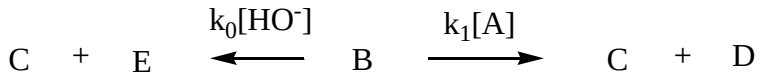
First chapter deals with the literature review of amino alcohols and their derivatives, as well as kinetics and mechanism of aminolysis of esters. The uses of these compounds in biological, pharmacological, synthesis, industries and applied chemistry were discussed briefly. The literature search on some available methods for the synthesis of amine derivatives and esters such as *N*,*N*-(diethylaminomethyl)benzyl alcohol (**35**) and *p*-nitrophenyl acetate (**26**) is described.

Chapter two reports the experimental details on the syntheses and characterization of *N*,*N*-(diethylaminomethyl)benzyl alcohol (**35**), *N*,*N*-diethylphthalamic acid (**34**), 2-((diethylamino)methyl)benzyl acetate (**42**), *N*-benzylacetamide (**44**) and *N*,*N*-diethylacetamide (**45**).

Chapter three provides a brief introduction of chemical kinetics and common methods of carrying out the kinetic studies. General procedures in determining suitable wavelength (λ) for kinetic studies have been discussed. Some experimental details of product characterization using Reverse-phase High Performance Liquid Chromatography have been also described. The results have been divided into four parts according to the types of amines.

Final chapter contains the results of aminolysis of **26**. These results are classified into four major parts, 1) primary amines, 2) secondary amines, 3) tertiary amines and 4) amino alcohols (tertiary amines). The aminolysis of **26** with primary and secondary amines gave an amide and *p*-nitrophenolate ion (**48**), while the hydrolysis of **26** with tertiary amines and amino alcohol gave acetic acid and **48**. The aminolysis of **26** with a series of amines (methylamine, *N*,*N*-dimethylamine, *N*,*N*-diethylamine, benzylamine, *N*,*N*-methylbenzylamine, *N*,*N*-ethylbenzylamine, *N*,*N*-

dimethylbenzylamine and *N,N*-(diethylaminomethyl)benzyl alcohol) have been studied in mixed aqueous solvent containing 50 % v/v acetonitrile. The kinetics of aminolysis of **26** in the presence of amine buffers at 0.3 M or 0.4 M ionic strength have been discussed in terms of the following reaction scheme 1:



Scheme 1

where A = free amine base, B = **26**, C = **48**, D = amide, E = acetic acid. In case of tertiary amine and amino alcohol, the final product gave **48** and acetic acid. In most cases, the plot of k_{obs} versus total amine buffer concentration gave straight line with ~ zero intercepts. The aminolysis of **26** under buffers of primary and secondary amines revealed a bronsted plot of $\beta_{nuc} = 0.91 \pm 0.20$.

ABSTRAK

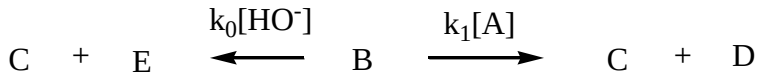
Bab pertama, mengumpulkan maklumat-maklumat daripada rujukan berkenaan dengan sebatian amino alkohol, ester dan terbitannya, disamping kinetik dan mekanisma aminolisis ester. Turut membincangkan berkenaan kegunaan sebatian ini dalam bidang biologi, farmakologi, sintesis, industry dan kimia gunaan. Beberapa kaedah sintesis sebatian *N*-tertukar ganti amino alkohol dan ester seperti *N*,*N*-(dietilaminometil)benzil alkohol dan *p*-nitrophenil acetat dan *N*-tertukar ganti acetat turut dibincangkan.

Bab kedua menjelaskan secara terperinci langkah-langkah eksperimen untuk mensintesis sebatian dan pengenalpastian spektroskopi sebatian berikut: *N*,*N*-(dietilaminometil)benzil alkohol (**35**), *N*,*N*-dietilfthlamic asid (**34**), 2-((dietilamino)metal)benzil acetat (**42**), *N*-benzilacetamida (**44**) dan *N*,*N*-dietilacetamida (**45**).

Bab ketiga mengandungi pengenalan ringkas berkenaan kimia kinetik dan kaedah-kaedah biasa yang digunakan semasa menjalankan kajian kinetik. Membincangkan secara terperinci kaedah eksperimen untuk penentuan panjang gelomgbang (λ). Penjelasan berkenaan eksperimen penentuan hasil tindak balas (produk) mengunakan Fasa-Terbalik Kromatografi Cecair Prestasi Tinggi. Keputusan dibahagikan kepada empat bahagian mengikut jenis-jenis amina.

Bab terakhir mengadungi keputusan hasil daripada aminolisis **26**. Keputusan dibahagikan kepada tiga bahagian iaitu 1) amina primer, 2) amina sekunder, 3) amina tertiar dan 4) amino alkohol. Aminolisis **26** dengan amina primer dan sekunder memberikan amida dan **48** sebagai hasil akhir, manakala hidrolisis **26** dengan amina ketiga dan amino alkohol memberikan asid asetik dan **48.** Aminolisis **26** dengan

beberapa siri amina seperti (metilamina, *N*,*N*-dimetilamina, *N*,*N*-dietilamina, benzilamina, ,*N*,*N*-metilbenzilamina, *N*,*N*-etilbenzilamina, *N*,*N*-dimetilbenzilamina dan *N*,*N*-(dietilaminometil)benzil alkohol) dijalankan didalam campuran pelarut akues yang mengandungi 50 % v/v acetonitril. Kinetik bagi aminolisis **26** dengan kehadiran amina pada kepekatan 0.3 M atau 0.4 M dibincangkan dalam terma seperti skema 1:



Skema 1

dimana A = amina, B = **26**, C = **48**, D = amida dan E = asid asetik. Dalam kebanyakkan kes, plot k_{obs} melawan kepekatan amina memberikan graf garis lurus dengan pintasan menghampiri kosong. Tindak balas aminolisis **26** dalam kehadiran amina primer dan sekunder memberikan plot Bronsted dengan kecerunan $\beta_{nuc} = 0.91 \pm 0.20$.

ACNOWLEDGEMENTS

The work presented in this these would not have been possible the help of a great number of people. Most of all, I want to express my gratitude to my supervisors, Associate Prof. Dr. Azhar Bin Ariffin and Prof. Mohammad Niyaz Khan for their help, encouragement, support and advice over the whole duration of this research. They always available when needed and willing to review my research work and schedule from time to time. I gratefully acknowledgement my indebtedness to my supervisors for many valuable and inspiring ideas as well as comments of the original manuscript of this thesis. A millions thanks to Dr. Azhar, for his kindness, the opportunities and trust he gave to me. Only Allah can pay for their helps.

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Thank you so much

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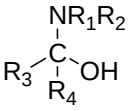
LIST OF SYMBOLS AND ABBREVIATIONS

Abs	absorbance
Ar	aromatic
A_{cald}	calculated absorbance
A_{obs}	observed absorbance
$[Am]_T$	total amine buffer concentrations
A1	k_b/f_b
b.p.	boiling point
$CDCl_3$	deuterated chloroform
CH_3CN	acetonitrile
CH_3NH_2	methylamine
$C_6H_5CH_2NH_2$	benzylamine
(d)	doublet
Eq.	equation
f_b	free base
HPLC	high performance liquid chromatography
HCl	hydrochloric acid
H_2O	water
IGA	intramolecular general acid
IGB	intramolecular general acid
IR	infrared
J	coupling constant
K_a	ionization constant
k_n	second – order rate constant for nucleophlic
$k_{OH'}$	third – order rate constant for specific base – catalyzed
k_b	second – order rate constant
k_o	uncatalyzed catalysis
M	mole per liter

mp.	melting point
m	minute
(m)	multiplet
Mw	molecular weight
NMR	nuclear magnetic resonance
NaOH	sodium hydroxide
NaBr	sodium bromide
(q)	quartet
ref.	reference
R_f	retention rime
rt	room temperature
s	second
(s)	singlet
t	time
(t)	triplet
T	temperature
THF	tetrahydrofuran
TLC	thin layer chromatography
UV	ultraviolet
vis	visible
v/v	volume per volume
λ	wavelength
β_{nuc}	Bronsted slope
μ	ionic strength
%	percentage
[ ]	concentration
$[Am]_T$	total amine buffer concentration
$[Buf]_T$	total buffer concentration

LIST OF COMPOUNDS



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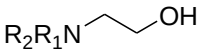

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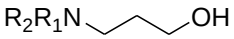

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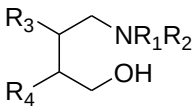

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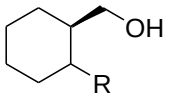

R = **5** = 

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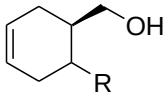

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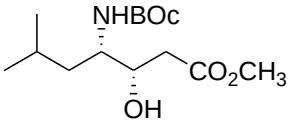

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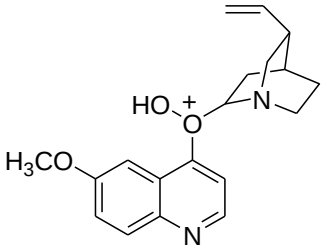

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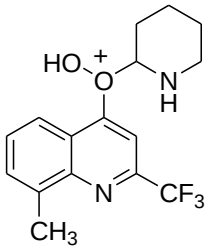

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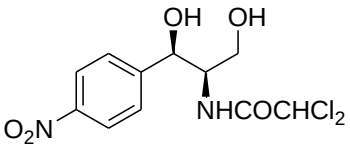

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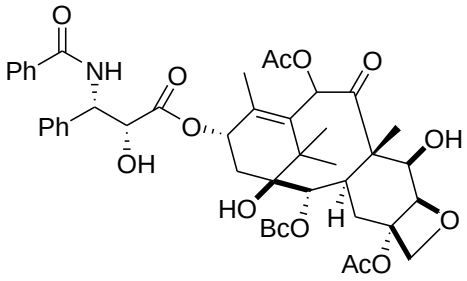

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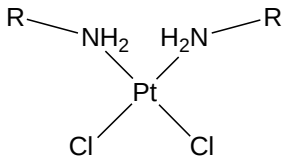

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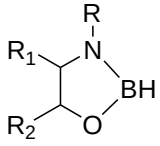
R = -CH_2CH_2OH, -$(CH_2)_2OH$, -$(CH_2)_4OH$



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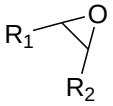

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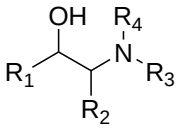

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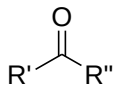

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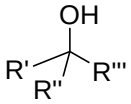

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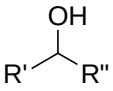

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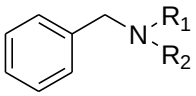

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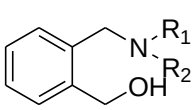

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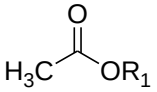

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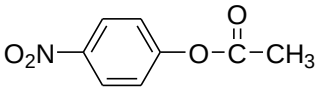

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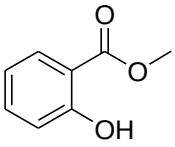

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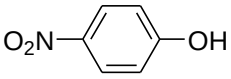

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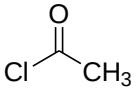

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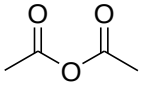

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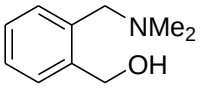

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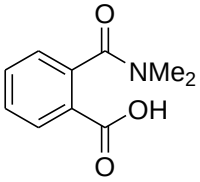

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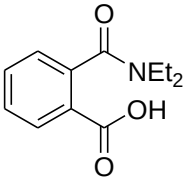

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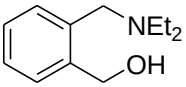

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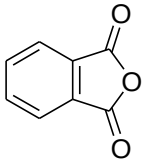

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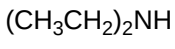

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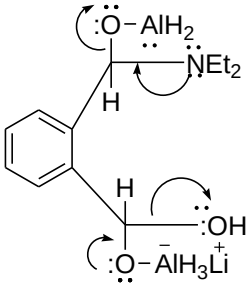

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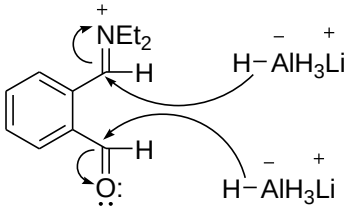

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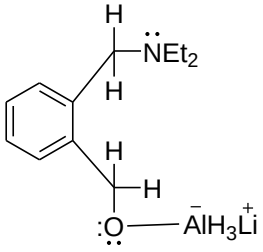

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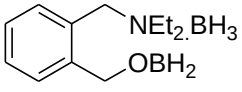

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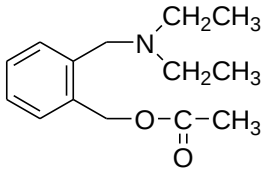

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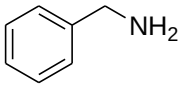

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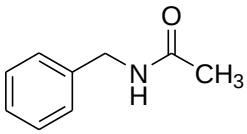

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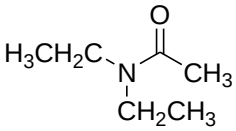

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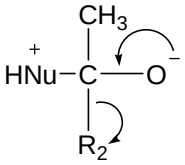

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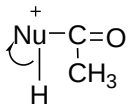

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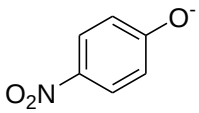


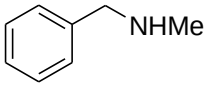
48

$MeNH_2.HCl$

49

$Me_2NH.HCl$

50



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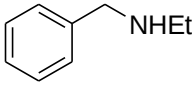

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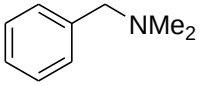

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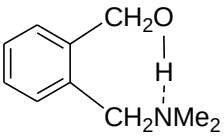

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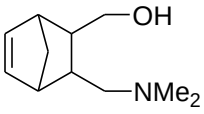

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