شبكة المعلومات الجامعية

بسم الله الرحمن الرحيم

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار

شبكة المعلومات الجامعية

بعض الوثائق الأصلية تالفة

بالرسالة صفحات لم ترد بالأصل

B1747

THE EFFECT OF SOLVENT ON THE KINETICS OF RING OPENING OF ISATIN

THESIS

Submitted to the Faculty of Science,

Alexandria University

In Partial Fulfillment for the Degree of

Master of Science (Chemistry)

By

HANAA HAMMAM ABDEL RAHMAN

(B.Sc. 1989)

Supervised by:

Prof. Dr. A.A. HARFOUSH

Prof. of Physical Chemistry

Dr. A.M. ISMAIL

Lecturer of Physical Chemistry

EGYPT

1994

TO MY FAMILY

NOTE

Beside the work carried out in this thesis, the candidate **Hanaa Hammam Abdel-Rahman** has passed successfully the following courses in partial fulfilment of M.Sc. degree:

1- Inorganic Reaction Mechanisms.

2- Symmetry and Group Theory

3- Instrumental Analysis.

4- Chemical Equilibria.

5- Electrochemistry.

6- Chemical Kinetics and Reaction Mechanism.

7- Thermodynamic in Solutions.

8- Solid State Chemistry.

9- Quantum Chemistry.

10- Polymer Chemistry

11- Organic Chemistry

12- Physical Organic Chemistry

13- German Language

14- Elementary Course in the Basic Language Computer.

15- Seminar and Oral Examination.

M. A. Rahmas

Prof.Dr. M.M. Abd El Rahman

Head of Chemistry Department

ACKNOWLEDGEMENT

The author is gratefully indebted to **Dr. I.M. Sidahmed**, *Prof. of Physical Chemistry, Faculty of Science, Alexandria University; for suggesting the problem and for his interest and helpful discussions.*

The author wishes to express her deep gratitude and thanks to **Dr. A.A. Harfoush**, *Prof. of Physical Chemistry, Faculty of Science, Alex. University for his continuous supervision and guidance, criticism and assistance throughout the duration of this work.*

I am extremely grateful to **Dr. A.M. Ismail**, *Lecturer of Physical Chemistry; for her kind collaboration and endless encouragement which have sustained me during the progress of this work.*

I wish also to extend my thanks to my colleagues in the Chemistry Department, especially those who offered me help during the course of this work.

CONTENTS

Chapter I

INTRODUCTION

CHAPTER I

INTRODUCTION

1) Biological Effects of Isatin

Isatin was found to cause slight fall in blood-sugar level occurs, following by a steady rise which reaches a maximum[1]. A slow decrease then takes place which reaches normal values again. A single dose of isatin does not cause permanent cellular damage. However, the repeated injection of isatin on alternate days causes permanent damage, as evidenced by higher fasting blood sugar levels.

Isatin potentiated the acetyl choline induced contraction of isolated frog rectus abidominis muscle[2]. The compound alone had no effect on the contraction of frog muscle.

Isatin perfusion caused a dose-dependent decrease in the amplitude of ventricular contraction and the cardiac output of *in situ* frog heart[3]. The compound had no effect on guinea pig or dog heart. Also it had little effect on blood pressure of cats or dogs.

Isatin was found to be a satisfactory calorimetric reagent for quantitative determination of proline in

maize and wheat after its separation by paper chromatography[4]. It was found also that isatin has no effect of chick liver acid phosphatase; it inhibits acid phosphatase from sheep and hedgehog and activates rat, goat, and pig acid phosphatase[5]. Inhibition of hedgehog liver acid phosphatase and activation of rat liver acid phosphatase are dependent on isatin concentration. The effect of pH on isatin-hedgehog liver acid phosphatase interaction indicates the existence of acid phosphatase in multimolecular forms. Isatin compound also had an organ-specific effect on rat tissue acid phosphatase[6]. The activation of this compound on the liver enzyme is of mixed type and was concentration and pH dependent. Isatin also inhibited rat testicular alkaline phosphatase uncompetitively[7].

Analysis of human serum albumin binding of 16 isatin derivatives showed that a nitrogen mustrad group on the N-atom of isatin had the greatest substituent effect[8]. Substitution of a diisopropyl group in the same position also increased albumin binding. Morphaline was the only substituent which decrease binding. Also the binding of isatin and its mustard N-Mannich base to human serum albumin was studied by equilibrium dialysis and ultrafiltration[9]. The scatchard plot of isatin binding to albumin shows a biphasic curve which indicates the presence of at least two different binding sites on albumin molecule, one site with higher affinity and the

other site with a lower. The isatin-albumin and isatin-Mannich base-albumin interactions were studied[9] under various experimental conditions in respect to drug and albumin concentration, pH and temperature of the incubation media.

Isatin also reduced the total incidence of audiogenic epileptic seizures in rats highly sensitive to an acoustic epileptogenic stimulus[10].

Purified tribulin, an endogenous monoamine oxidase (MAO) inhibitor, was identified by direct probe insertion mass spectrometry as the indole 2,3 dione isatin[11]. A gas chromatographic-mass spectrometric assay for isatin was used to measure its relatively high concentration in unpurified human urine, and in rat heart and brain. Isatin is a known compound with a broad range of biological activity; and this is the first report by the authors[11] for its presence in the animal body. Isatin is a potent inhibitor of MAO, particularly of MAO β (IC_{50}, 3 μM), and also binds to central benzodiazepine receptors (IC_{50} against clonazepam, 123 μM).

Aryloxotetrahydroindoles I (R, R^1 = H, Me; R^2 = H, Me, Cl; R^3 = 4-Cl, 4-CF_3, 4-Me, 4-F, 4-OMe, H, 3-CF_3, 3-Me, 6-Cl) were prepared by condensation of cyclohexane-dioneacetic esters with anilines[12]. Hydrolysis of (I) gave acids (II). I (R-R^2 = H, R^3 = 4-F) shows anti-inflammatory activity in the carragenin edema test and