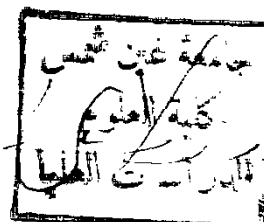


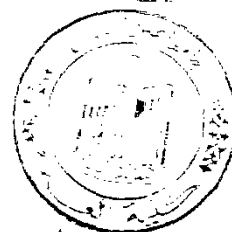
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**THESIS
ON
STUDIES ON SOME METAL-BILIRUBIN
COMPLEXES**

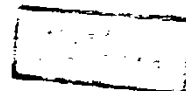
Presented to
Faculty of Science
Ain Shams University
Cairo



By
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M . Sc.



Submitted for the Award
of the Degree of
DOCTOR OF PHILOSOPHY
in
Chemistry



1986

STUDIES ON SOME METAL-BILIRUBIN
COMPLEXES

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ACKNOWLEDGEMENT

I wish to express my deepest gratitude to Prof. Dr. G.R. Choppin Prof. of Inorganic Chemistry, Faculty of Science, ~~Flourida~~ Florida State University and Prof. Dr. E.N. Rizkalla Prof. of Inorganic Chemistry, Faculty of Science, Ain Shams University for suggesting the problem devising the scheme of the work , for their invaluable suggestions and their critical remarks.

I am also greatly indebted to Prof. Dr. N.E. Milad Prof. of Inorganic and Analytical Chemistry, Faculty of Science, Ain Shams University for his contineous help, advice and for his generosity. He offered me a lot of his valuable time.

I would like to take this opportunity to thank Prof. Dr. A.M. Khalil Prof. of Physical Chemistry and A.A.Zahran, Lecturer of Physical Chemistry, Faculty of Science Ain Shams University for their help in carrying out surface area measurements, and Dr. W.G. Hanna Lecturer of Inorganic Chemistry , Faculty of Science Ain Shams University for his help in carrying out spectrophotometric measurements.

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V I T A

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Abbreviations

- 1- Bilirubin : Bil.
- 2- Calcium acid bilirubinate: A- CaBil.
- 3- Neutral calcium bilirubinate: N-CaBil.
- 4- Magnesium bilirubinate : MgBil.
- 5- ethylenediamine N,N, N', N', tetra(methylene phosphonic)
acid: ENTMP
- 6- ethylenediamine tetracetic acid disodium salt: EDTA.2Na
- 7- Sodium salt of urosodeoxycholic acid: URSO
- 8- bovine serum albumin : BSA.

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INTRODUCTION

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CHAPTER I

I N T R O D U C T I O N

I.1 Structure and Nomenclature

True bile pigments, the bilirubinoinds, are linear tetrapyrroles. They are derivatives of the porphyrins which are cyclic tetrapyrroles.

Porphyrins are derived from porphin, they consist of four pyrrole rings attached to each other by four methine bridges; ($-\text{CH}=\text{}$). The four rings are designated I to IV and the bridges α , β , γ and δ . In positions 1 to 8 the H-atoms can be replaced by various radicals. The more common substituents are the methyl (M), vinyl (V), ethyl (E), propionic ($-\text{CH}_2-\text{CH}_2-\text{COOH}$, P) and acetic ($-\text{CH}_2-\text{COOH}$, A).

By substituting the hydrogen in porphin with four methyl and two propionic acid ($-\text{CH}_2-\text{CH}_2-\text{COOH}$) and two vinyl radicals, di-carboxylic prophyrrins are obtained. These porphyrins, containing three different substituents in the porphyrin nucleus, exist in 15 isomeric forms, but only the form known as IX exists when the porphyrin ring is opened by cleavage of a methine bridge, linear tetrapyrroles or bilirubinoids are obtained. Depending on the number of

symmetry planes present in its molecule, a porphyrin can yield two, three or four different linear tetrapyrroles. Thus, bilirubin is called protobilirubin IX- α because it is formed from protoporphyrin IX by opening at the α - bridge, as shown in Figure (1). If the cleavage takes place at the β , γ and δ bridges, the structures shown in figure (2) are obtained.

Fig. (1) Formation of bilirubin IX- α via catabolism of the protoporphyrin IX moiety of hemoglobin.

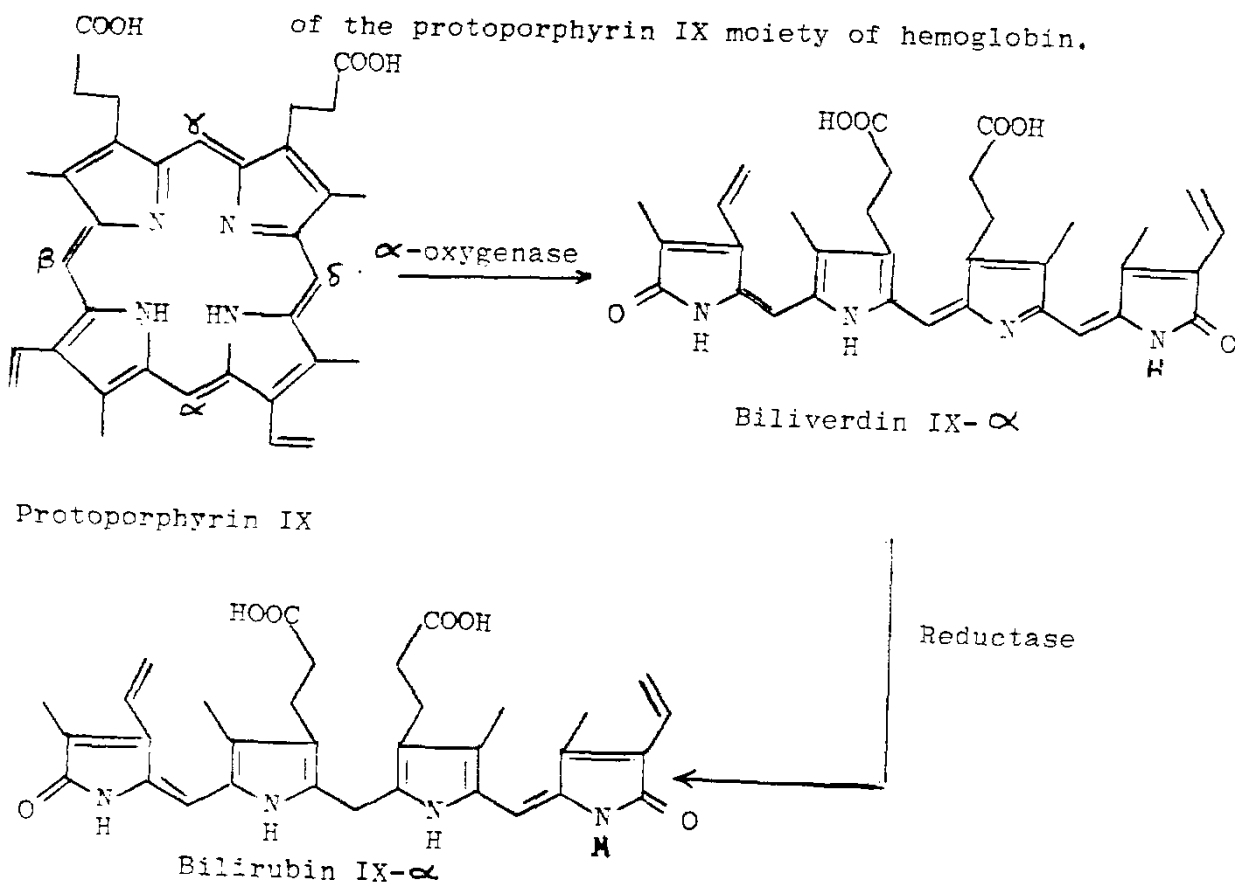
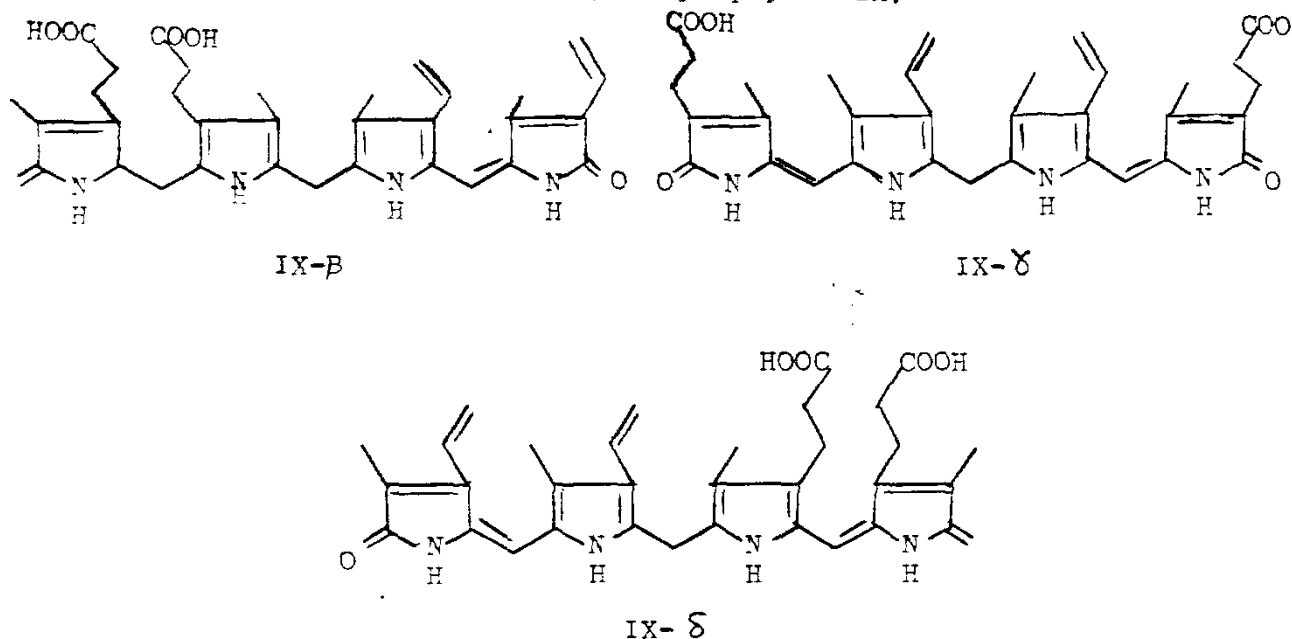
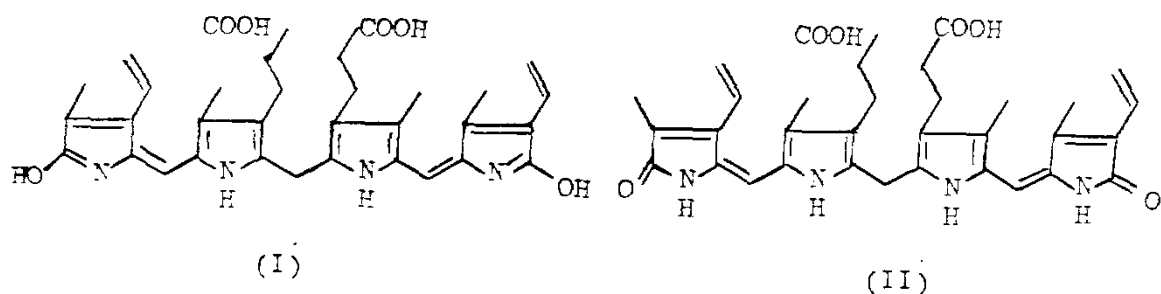


Fig. (2) Structures of bilirubin IX- β , IX- γ and IX- δ

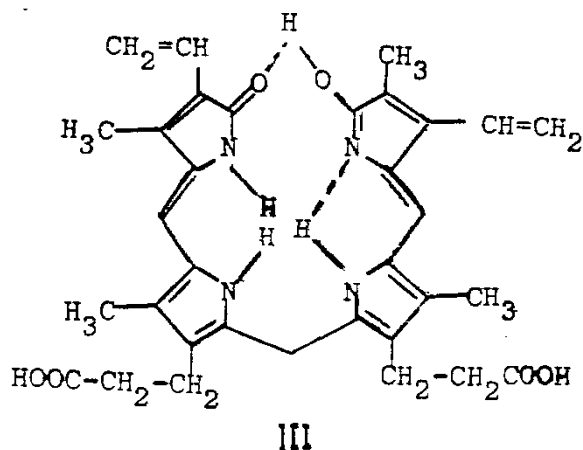
these isomers result from the cleavage of the β , γ or δ bridges of protoporphyrin IX.



Bilirubin can exist in several tautomeric forms, two of which are the bis-lactim(I) and bis-lactam (II), structures⁽¹⁾. Because of its chemical characteristics it was thought that Bil, existed mainly in the bis-lactam form⁽²⁾.



Bilirubin exists in solution as a hydrogen-bound mono-lactam-mono lactim structure (III).



The circular configuration and nucleophilic nitrogen now present are both conducive to complex formation, analogous to the metalloporphyrins⁽³⁾, which in the absence of complexing metal ions may exist partially in solution in the hydrogen bound form (III).

I-2. Stability

Unconjugated bilirubin (bilirubin IX α) is a very unstable compound subject to photooxidation and isomerization. These phenomena are the basis for phototherapy of newborns with serious jaundice, but they are also primary problems in the accurate measurement of the concentration of unconjugated bilirubin.