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ALUMINA IN METHANESULFONIC ACID (AMA) AS A NEW
REAGENT FOR SYNTHESIZING OF XANTHONES AND
BECKMANN REARRANGEMENT

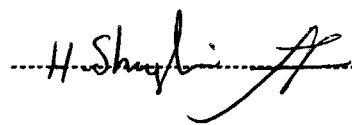
A THESIS BY
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**THIS THESIS IS DEDICATED
TO
MY MOTHER AND FATHER,
THE TEACHERS OF MY LIFE**

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ABSTRACT

Alumina in Methanesulfonic Acid (AMA) as a New Reagent for Synthesizing of Xanthenes and Beckmann Rearrangement

By

Mona Hosseini Sarvary

This thesis is concerned with the synthesis of some xanthone derivatives and Beckmann rearrangement. A comprehensive review of the literature dealing with the properties and synthetic methodologies of xanthenes and the stereochemistry, mechanism and methods for Beckmann rearrangement are discussed in PART A and B, CHAPTER ONE.

Chapter 2 describes the synthesis of some hydroxy xanthenes in high yields. 1,6-Dihydroxyxanthone (10) was also obtained in high yield from condensation of γ -resorcylic acid in AMA. It is found that some hydroxyxanthenes can be obtained by condensation of γ -resorcylic acid and phenols.

Beckmann rearrangement describes in Methanesulfonic acid/Alumina (AMA). Afterwards, we have developed an efficient one-pot method to convert directly ketones and aldehydes to amides by means of AMA and Hydroxylamin hydrochloride.

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ABBREVIATIONS

The following abbreviations are used in this thesis

AMA	Alumina in Methanesulfonic Acid
DDQ	2,3-Dichloro-5,6-dicyclo 1,4-p- benzoquinone
DMSO	Dimethylsulfoxide
Et	Ethyl
Me	Methyl
Ph	Phenyl
PPA	Polyphosphoric acid
PPMA	Polyphosphoric methanesulfonic acid
TFAA	Trifluoroacetic anhydride

CHAPTER 1

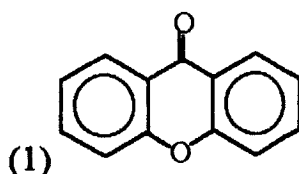
INTRODUCTION AND LITERATURE REVIEW

Part A

Synthesis of Some Xanthenes

1.1 Introduction

Xanthenes are heterocyclic ketones related to γ -pyrone and chromones¹, which are found in nature as glucosides and are produced as metabolic products by certain mold. The parent substance (1) does not occur in nature, but some of its oxygenated derivatives, have been isolated from a variety of natural sources.



1.2 Occurrence and Natural Distribution of Xanthenes

Some of the naturally occurring xanthenes have been isolated and characterized prior to 1960². A number of these xanthenes occur in various parts of flowering plants³⁻²¹ belonging to the Gentianaceae, Guttiferae and Anacardiaceae families; and some of them are metabolic products of members of the lower fungi²²⁻²⁶, and also from Lichen²⁷ origin and one, euthic acid²⁸, which is apparently produced by a detoxication mechanism, is found in the urine of animals which have been fed on Mango leaves.

1.3 Extraction , Purification and Recognition

Xanthones, which are found in various parts of plants or in the mycelia of moulds, are generally obtained by solvent extraction (Soxhelt Method) of the dried and disintegrated material (Pinselic acid and Pinselin are extracted from an aqueous substrate on which the mould has been grown). The crude material may be purified by recrystallization, but a prior purification by chromatography^{22,25} is sometimes desirable.

A significant feature common to all the naturally occurring xanthone is the occurrence of a hydroxyl group in the (1 or equivalent 8) -position. They are yellow in color, the majority of them give a green color with ferric chloride in ethanolic solution. Some hydroxyxanthones (*Gentisin*¹⁰⁻¹¹, *Isogentisin*¹²⁻¹³, *Corymbiferin*³, and created by *Jacareubin*¹⁴⁻¹⁵) give positive reactions in the color test (with magnesium and hydrochloric acid) for flavonoid compounds²⁹.

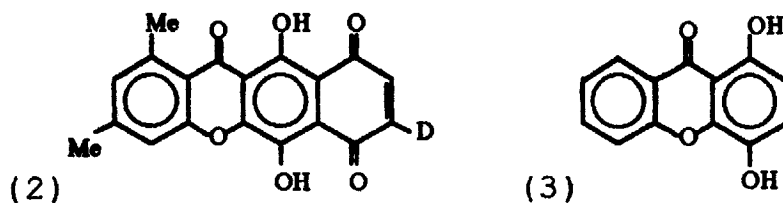
1.4 Biological Properties of Xanthones

Naturally occurring xanthones have unknown function in the metabolism of the living material in which they occur. Therefore, they may be produced merely as metabolic waste products.

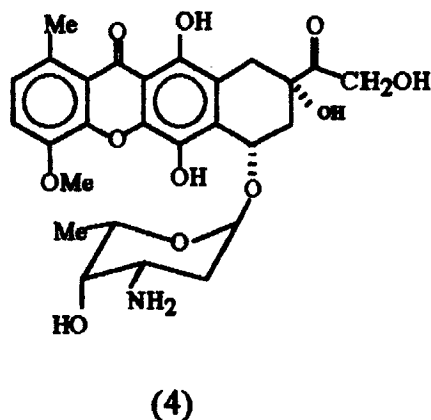
It has been claimed that mangosteen³⁰ hulls have febrifuge properties, and for the treatment of dysentery diseases the hulls and the bark (both of which contain mangostin) have been used .

The bikaverin (2), a red pigment, has high vacuolation³¹ , specific anti protozoal³² , and antitumor³³ activities.

Moreover, 1,4-dihydroxyxanthone (3) is encountered in naturally occurring compounds and constitutes a major part of the bikaverin^{34,35}.



Xanthenes, and specially hydroxyxanthenes, have long been known to produce pharmacological and biological effects³⁶, although few examples of compounds having the general tetracyclic carbon skeleton of compound (4) are known.



Heteroanthracylines, such as, 4-demethoxy-xanthodaunamycin³⁷ (5), and 4-dimethoxy-7-epixanthodaunomycin³⁸ (6) prepared by Wong et al.³⁹, clarified the origin of cardiotoxicity and cytotoxicity of anthracylines.