

# NEW SYNTHETIC PATHWAYS FROM FURFURAL

By

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M.Phil.

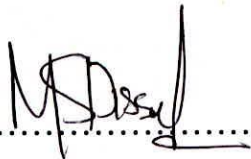
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## DECLARATION

The work describe in this thesis was carried out by me under the supervision of Professor A. M. Abeysekera and Doctor (Mrs.) C. Mahathanthila and a report on this has not been submitted in whole or in part to any University for another Degree / Diploma.

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 .....

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## CERTIFICATION

We certify that the above statement made by the candidate is true and that this thesis is suitable for submission to the University for the purpose of evaluation.

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**NEW SYNTHETIC PATHWAYS**  
**FROM FURFURAL**

**By**

**Jayalath Ranasinghe Dissanayake Mayuri Sajeevani**

Thesis submitted to the University of Sri Jayewardenepura for the award of  
the Degree of Master of Philosophy in Chemistry on June 2004

**I DEDICATE**  
**THIS THESIS**  
**TO**  
**MY DEAR HUSBAND**

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## LIST OF ABBREVIATIONS

<b>MOM</b>	-	Methoxy Methyl
<b>2,4-DNP</b>	-	2,4-dinitrophenyl hydrazine
<b>4,7-DOCA</b>	-	4,7-dioxocarboxylic acid (s)
<b>4-GL</b>	-	four substituted gamma ( $\gamma$ ) lactone (s)
<b>7-GL</b>	-	7-hydroxy gamma ( $\gamma$ ) lactone (s)
<b><i>p</i>-TOSOH</b>	-	Para toluene sulfonic acid
<b>ind.</b>	-	Industrial
<b>Fig.</b>	-	Figure (s)

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## **ABSTRACT**

### **NEW SYNTHETIC PATHWAYS FROM FURFURAL**

**BY**

**JAYALATH RANASINGHE DISSANAYAKE MAYURI SAJEEVANI**

Furfural is a readily available, versatile and cheap starting material suitable for use in the synthesis of higher valued fine chemicals. Furfural can be generated from a variety of waste agricultural biomass such as rice hull and bagasse, and it is therefore particularly appropriate for a predominantly agricultural country such as Sri Lanka which does not produce petrochemicals, to develop syntheses based on furfural.

This thesis describes it self mainly with the synthesis of new  $\gamma$ -lactones, developing new pathways using fufural as one of the starting materials. Overall, the thesis describes the synthesis and spectra of 33 compounds including 23 new compounds.

Furfural was condensed with a series of methyl ketones to obtain furfurylidene ketones, which were subjected to acid catalysed hydrolytic ring cleavage to provide 4,7-dioxocarboxylic acids.

For all methyl ketones other than acetone, the initial product isolated from the condensation with furfural was a mixture, consisting of

- (i) The desired furfurylidene ketone i.e. the one arising from the reaction of the aldehyde group with the methyl group.
- (ii) A mixture of hydroxy ketones – the major compound being that arising from the reaction of the aldehyde group with the longer alkyl group.

This mixture was converted totally to the desired furfurylidene ketone by heating with excess alkali. The regioselectivity in this reaction attributed to the reversibility of the aldol condensation steps, and the steric hindrance to achieving an E<sub>2</sub> transition state for the elimination of water, by the initially formed major hydroxy ketone.

4,7-Dioxocarboxylic acids are useful intermediates in the synthesis of compounds with potential olfactory properties such as  $\gamma$ -lactones. It is to be noted that the ring opening reaction is in competition with polymerization, and the yields in this step were found to be heavily dependent on the substrate and the reaction conditions.

$\gamma$ - lactones are an important class of flavour and perfumery compound. The reduction of the 4,7-dioxocarboxylic acids with sodium borohydride followed by acidification gave in good yields, a new type of  $\gamma$ - lactone i. e. one bearing a hydroxyl group in the 7<sup>th</sup> position. The 4,7-dioxoethanoates were synthesised from the corresponding 4,7-dioxocarboxylic acids and were also reduced and cyclised to obtain the corresponding 7-hydroxy- $\gamma$ -lactones. However, the yields of 7-hydroxy- $\gamma$ -lactones were much higher with the 4,7-dioxocarboxylic acids than their ethyl esters.

The properties of the lactones are dependent on the features of the side chain. The 7-hydroxyl group provides a convenient handle for side chain manipulation. Thus, the 7-hydroxyl group was easily acetylated and also oxidized to a keto group.

The oxo lactones obtained by oxidation can be further condensed with nitrogen nucleophiles, to provide a  $\gamma$ -lactone having a N substituent in the 7<sup>th</sup> position. Dehydration of 7-hydroxy- $\gamma$ -lactones would not be achieved, but the reaction with  $\text{SOCl}_2$  / pyridine provided the corresponding 7-chloro compounds, opening the pathway to 7-halo lactones.

The reaction of 4,7-dioxododecanoid acid with methyl magnesium bromide did not produce the expected angular substituted  $\gamma$ -lactone, but gave a 1,1',4,4'-tetrasubstituted tetrahydrofuran compound.

The 7-hydroxy, -oxo, -acetoxy, -chloro, -2,4-dinitrophenyl hydrazine  $\gamma$ -lactones and the 1,1',4,4'-tetrasubstituted tetrahydrofuran were all new compounds. Their structures were established by using IR, GCMS and NMR ( $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, DEPT, HETERO COSY, COSY, HMBC and HMQC). The 7-substituted  $\gamma$ -lactones represent a new class of  $\gamma$ -lactone not found in nature. Of the new compounds synthesized, strong olfactory properties were observed only in the 7-chloro- $\gamma$ -lactone and the 1,1',4,4'-tetrasubstituted tetrahydrofuran.

The 7-hydroxy, -acetoxy and -chloro lactones are formed as two racemic mixtures of two diastereomeric compounds. This was reflected in the fact that most of the  $^{13}\text{C}$  signals were found as finely separated pairs, which transform in to single peaks in the 7-oxo compounds expected for a single racemic compound. The other interesting feature of the  $^1\text{H}$  NMR spectrum was that the C-5 protons which are diastereotopic in the 4-alkyl substituted- $\gamma$ -lactones (asymmetric centre at C-4), were found to be well differentiated in the 7-oxo series, but not in the 7-hydroxy, -chloro and -acetoxy series despite the presence of a second asymmetric centre at the 7<sup>th</sup> (C-7) position.