SUMMARY (RG/98/C4)

Project Title : Synthesis of potential perfumery and flavour components from furfural.

Institute Where Research was carried out : University of Sri Jayewardenepura

Chief Investigator : Prof. A.M.Abeysekera

Pls check ✓

Period of Contract : 15/01/98 to 01/06/2001

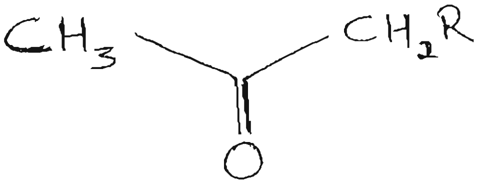
Background and Scope/Objectives :

As an agricultural country without petrochemical reserves, industrial utilization of renewable biomass is an important area of research for Sri Lanka. Sri Lanka produces approximately 5 x 10^5 metric tons of rice hull annually. Rice hull is a convenient source of furfural (~12%). Furfural has expanding fields of applications including that of a starting material for organic synthesis. A limited number of examples of the use of furfural to synthesis two groups of compounds, γ- substituted γ-lactones, and cyclopentenones, both of which are of importance as fragrance and flavour compounds have been reported. Some of these compounds are found as fungal metabolites and insect pheromones. A study of the literature suggests that the biological activities of the γ-susbstituted γ-lactone would depend on the following features of the γ-substituent.

1. Chain length
2. Unsaturation- position and stereochemistry
3. Stereochemistry at point of attachment and at asymmetric centers along the chain
4. Chain branching
5. Nature of functional groups attached to the chain.

Objectives : This project explores some synthesis pathways starting from furfural, to novel γ-substituted γ-lactones, in which there is a functionality in the γ-substituted side chain, with a view to developing new perfumery and flavour compounds.

Experimental Methods : The synthetic pathways that were designed to be explored in this study are given in scheme 1. The reactions in scheme I were realized with five different methyl ketones (Ia – Ie).



I

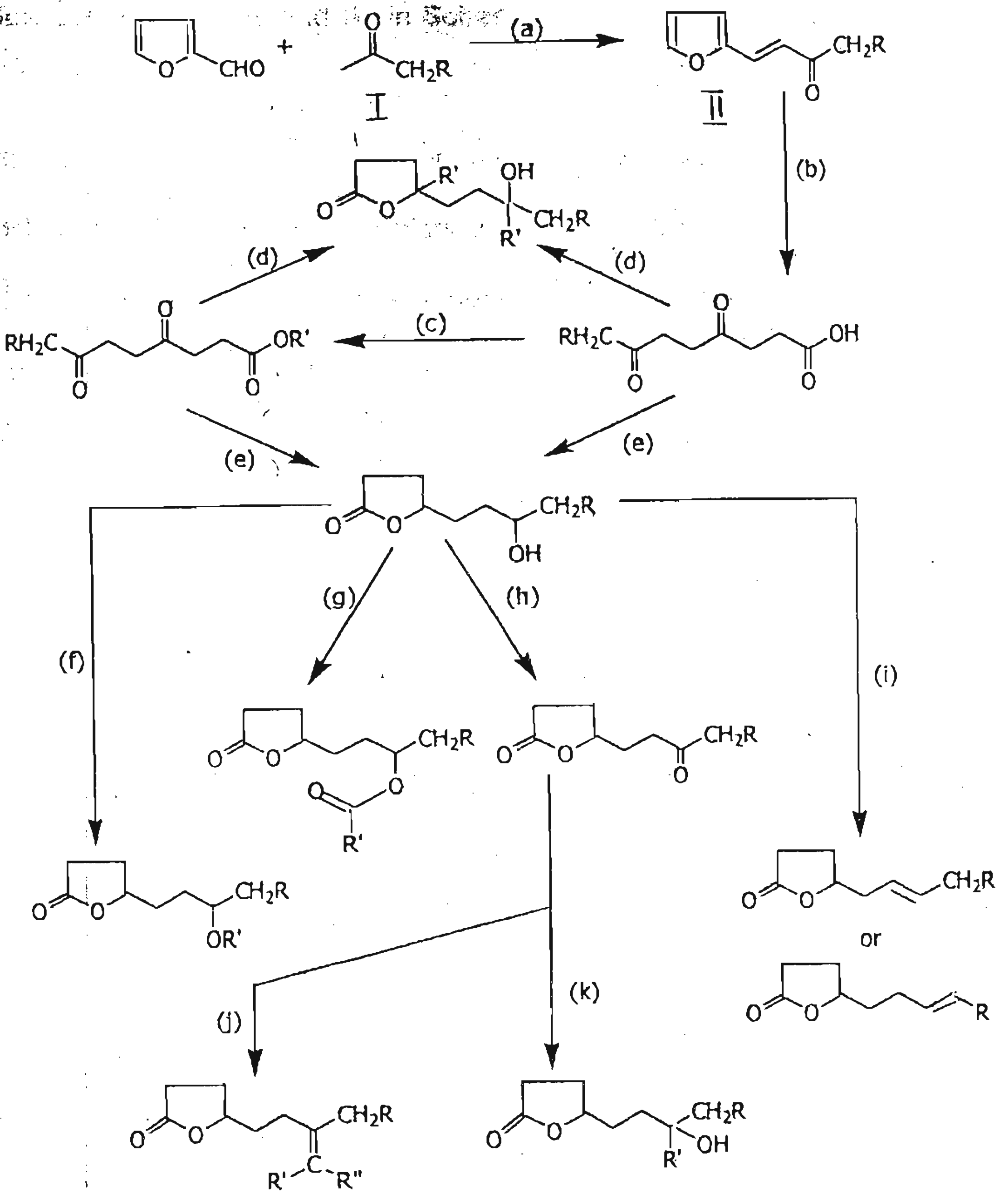
Ia, $R = H$

Ib, $R = CH_3$

Ic, $R = CH_2CH_3$

Id, $R = (CH_2)_2CH_3$

Ie, $R = (CH_2)_3CH_3$



R = H or alkyl

R', R" = alkyl

(a)	aldol condensation
(b)	hydrolytic ring cleavage
(c)	esterification
(d), (k)	reaction with Grignard reagent
(e)	lactonization
(f)	methylation
(g)	acetylation
(h)	oxidation
(i)	dehydration
(j)	Wittig reaction

Scheme I : Synthetic Strategy for 7-functionalized γ-lactones.

The reagents and experimental conditions used in the different steps of the scheme are given below.

(a) Aldol condensation : 3%NaOH/H_2O/10°C.

(b) Hydrolytic ring cleavage :

(i) for furfurylidene ketone from Ia, a two phase system was used. Cyclohexane/aqueous hydrochloric acid at reflux co-solvents-methanol and acetic acid.

(ii) For all other furfurylidene ketones a single phase reactions was used.

Methanol/aqueous hydrochloric acid/at reflux slow addition (30h) of substrate.

(c) Esterification : EtOH/H_2SO_4/reflux

(d) Reaction with Grignard Reagent

MeMgI/Anisole/40°.

(e) Reductive cyclization

(i) $NaBH_4$/EtOH/RT°

(ii) H^+

(f) Etherifications :

MeI/BaO/DMF

(g) Acetylation :

CH_3COCl/Pyridine

(h) Oxidation :

$Na_2Cr_2O_7/H^+$

(i) Dehydration – $SOCl_2$/pyridine

(j) and (k) – were not studied due to lack of time.

Results and Discussion :

(a) Aldol condensation - This reaction proceeded in high yields ($>70^{0}$) for all the methyl ketones. The products are not stable and tend to polymerize.

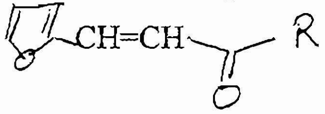
(b) Hydrolytic ring-cleavage – The two phase system developed for furfurylidene methyl ketone, gave very low yields for the ketones with a longer alkyl group. They were therefore hydrolysed by the slow addition of the substrate to the hydrolytic medium in a single phase reaction according to Birch. The yields are given in table I.

Table I - Yield (%) of 4,7-dioxocarboxylic acid from single-phase reaction.

Substrate	Yield (%)		Unreacted enone	Polymer
	Crude	Recrystallised		
II a *	8.2	5.1	32	34
II b	17.1	10.3	16	30
II c	6.7	2.2	21	25
II d	21	17.5	18	16
II e	37.6	32.7	11.3	10.3

* Recrystallised yield from two phase reaction 15%

II a – II c =



II a, R = Me; II b, R = C_2H_5 ; II c, R = C_3H_7

II d , = R = C_4H_9; II e, R = C_5H_{11}.

The yields increased and the amount of polymeric by products decreased with increasing chain length of the alkyl group. The yield obtained for II c, is anomalous, and is probably due to human error. This result is being reinvestigated.

(c) Esterification – This reaction proceeded in good yield (60% - 80%).

(d) Reaction with Grignard Reagent
This reaction proceeds smoothly to give a new product which is being analysed at present. It was noted that the solvent anisole undergoes partial demethylation to give phenol as a by product of the reaction.

(e) Reductive cyclization – This reaction proceeded to give 7-hydroxy-γ-lactones in good yields. (45 – 75%).

(f) Etherification – No reaction took place under the reaction conditions.

(g) Acetylation – The 7-hydroxy lactones did not react with acetic anhydride, but reacted smoothly with acetyl chloride to give the 7-acetoxy compounds in moderate yields (33-45%).

(h) Oxidation – This reaction took place smoothly in moderate yields (32-41%).

(i) Dehydration of the 7-hydroxy lactone was attempted under several conditions. Treatment with $SOCl_2$/pyridine gave a product with a sweet odour, as a single spot on tlc. However, the nmr spectra were complex and indicated a mixture of compounds. There was no evidence in the spectra for the formation of a double bond.

All compounds were analysed and assigned structures based on their ^{1}H and ^{13}C NMR, Mass and IR spectra.

Conclusion and Recommendations :

Fifteen new 7-functinalized γ - alkyl substituted γ - lactones bearing hydroxy, acetoxy and oxo groups, were synthesized and characterized.

None of them possessed a strong odour. It is possible that the polar substituents reduce the volatility of the compounds.

However, the 7-Keto lactones offer a pathway to branched chain lactones using Grignard and Wittig reactions. These may possess novel olfactory properties and should be pursued.

Publications :

1. Chemistry in Sri Lanka, 17:2, 39
2. Chemistry in Sri Lanka, 18:2, 22
3. JNSF – Manuscript in preparation.

AMAbeysekera

Prof. A.M.Abeysekera.