



CHAPTER I

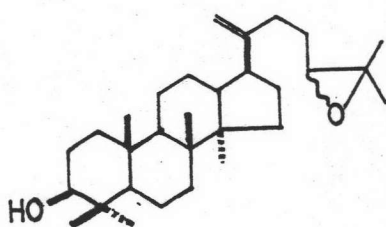
INTRODUCTION

1.1 Chemical Constituents of Aglaia odorata Lour.

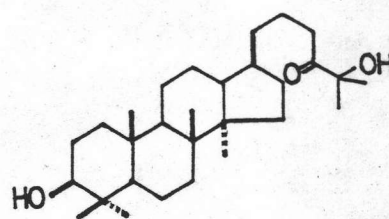
Aglaia odorata Lour. (generally listed as a genus of the family Meliaceae)[1] is a small tree found in Thailand, Malaysia, China and The Philippines. In Thailand, it is commonly known as Pra-yong or Hom-glai. Its dried flowers were used as herbal medicine in the old day[2].

The chemical constituents of Aglaia odorata Lour. have been studied since 1964. Many new compounds were isolated from the light petroleum and ether extracts of the leaves such as tetracyclic triterpenes and nitrogenous compounds. Tetracyclic triterpenes found are aglaiol(1)[3], aglaiondiols(2), and two isomers of aglatriol(3)[4], and nitrogenous compounds are odorine(4) and odorinol(5)[5]. The stereochemistry of odorine was established by synthesis of (-)-odorine and (+)-dihydroodorine from L-proline[6].

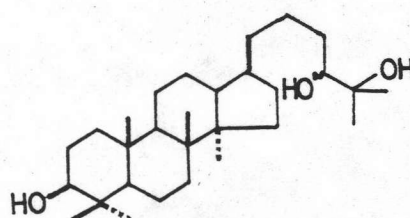
Some known compounds were also isolated and identified such as a lignan: (-)-eudesmin(6)[7] and a long chain alcohol: 1-triacontanol[7]. Furthermore, a mixture of enantiomers of lupinifolin(7) were isolated from the crude ether extract of ground dried stems[8].



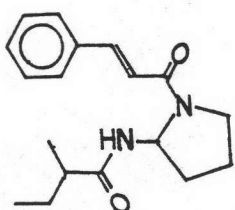
aglatol (1)



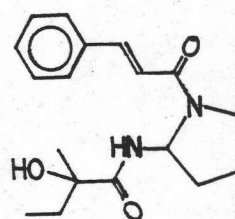
aglaiolol (2)



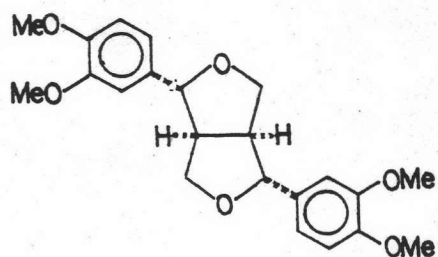
aglatriol (3)



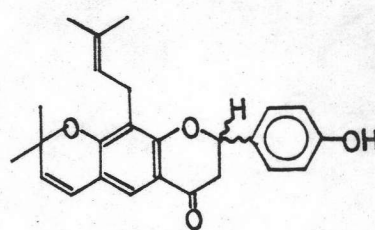
odorine (4)



odorinol (5)

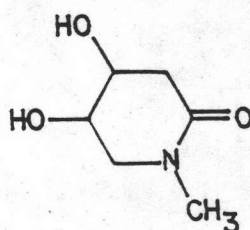


(-)-eudesmin (6)



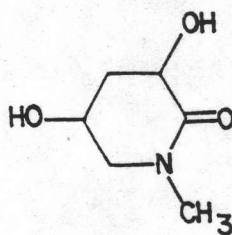
lupinifolin (7)

Several compounds were isolated from the crude hexane extract of dried flowers of *Aglaia odorata* Lour.[9], i.e. tritriacontane, ceryl alcohol, and β -sitosterol. A novel one from the methanol extract was named "odoram"(8). The odoram, white needle crystal, m.p. 236-238°C, is a six-membered ring lactam. The possible structure of odoram was assigned to be 4,5-dihydroxy-1-methyl-2-piperidone(8) as shown below:



odoram (8)

However, additional spectroscopic data exhibited that odoram should be 3,5-dihydroxy-1-methyl-2-piperidone(9) so we would like to confirm this structure by synthesis of 3,5-dihydroxy-1-methyl-2-piperidone(9) and/or its derivatives.



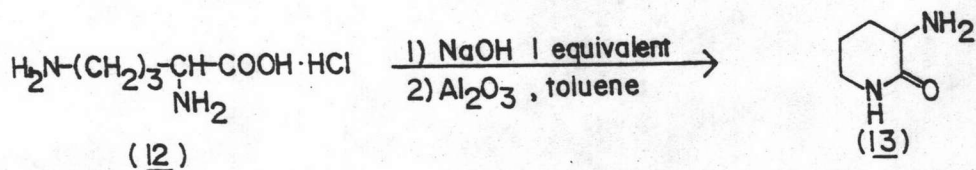
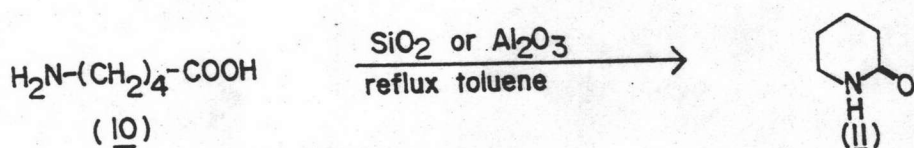
3,5-dihydroxy-1-methyl-2-piperidone (9)

1.2 Preparation of Lactams

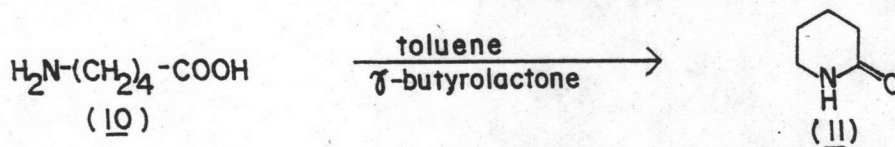
Many methods have been used and developed for the synthesis of lactams[10]. Some approaches which have been employed are:

1.2.1 Cyclization of ω -amino acids

Cyclodehydration of γ -, δ -, and ϵ -amino acids with alumina or silica gel in refluxing toluene yielded corresponding lactams[11].

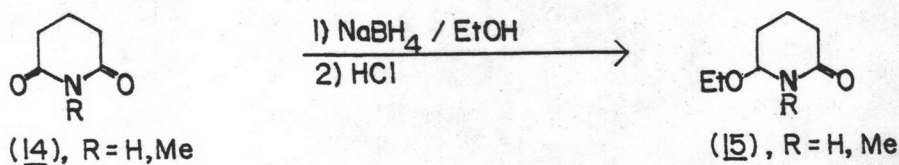


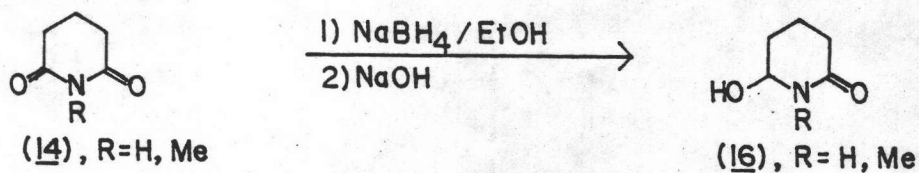
The $\text{H}_2\text{N}-(\text{CH}_2)_n-\text{COOH}$ ($n=3,4,5$) were cyclized in boiling toluene in the presence of γ -butyrolactone to give corresponding lactams[12]. Depsipeptides $\text{HO}(\text{CH}_2)_3\text{CONH}(\text{CH}_2)_n\text{COOH}$ were formed as intermediates.



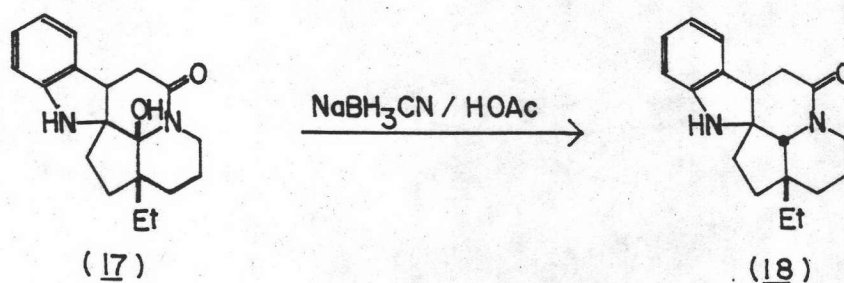
1.2.2 Reduction of imides

The sodium borohydride reduction of imide(14) in ethanol, followed by acidic work-up gave ethoxy compound(15), while by basic work-up the hydroxy compound(16) were formed[13].

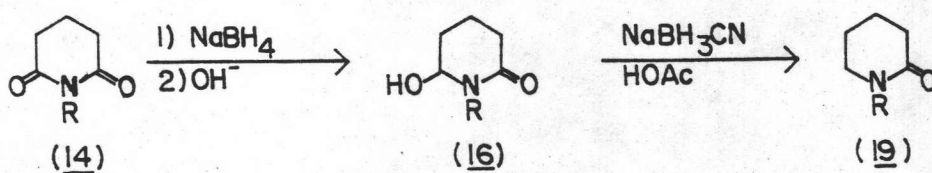




The reduction of hydroxy lactam (17) with excess sodium cyanoborohydride in aqueous acetic acid at 50°C for 2 hours yielded lactam (18) [14].

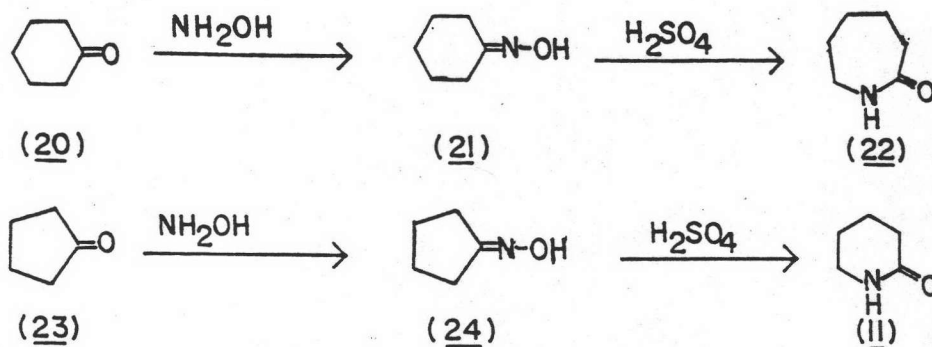


Therefore, imides could also be reduced to lactams by sodium borohydride and sodium cyanoborohydride as following:

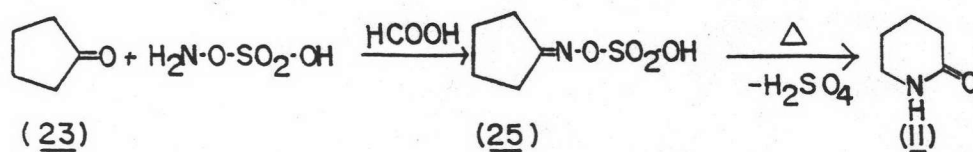


1.2.3 Beckmann rearrangement [10]

Oximes of ketones undergo rearrangement to amides under the influence of a variety of acidic reagents, in the same way, oximes of cyclic ketones undergo rearrangement to cyclic amides, lactams. The oximes of cyclic ketones give the ring enlargement.

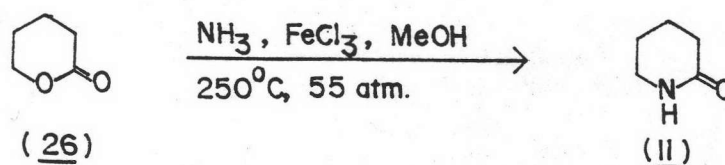


G.A. Olah and A.P. Fung reported a significantly improved one-step mild conversion of alicyclic ketones into their corresponding lactams, generally in high yields, by simply refluxing a mixture of the alicyclic ketone and hydroxylamine-*o*-sulfonic acid[15].



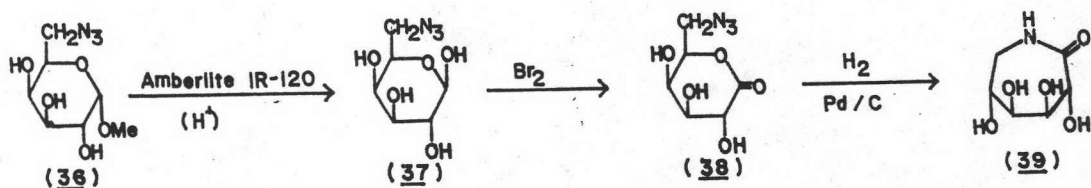
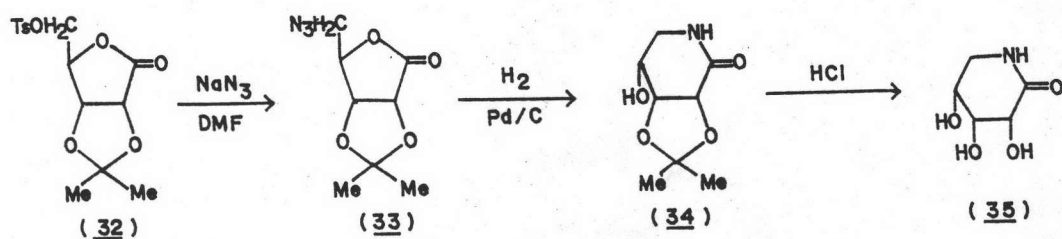
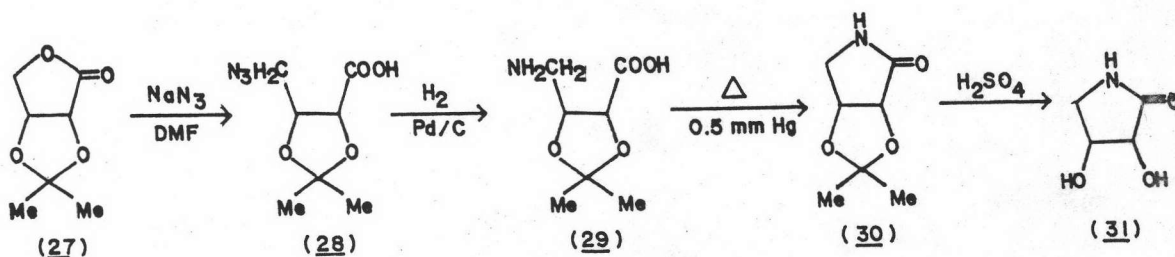
1.2.4 Reaction between lactones and ammonia or amines

Lactones, when treated with ammonia or primary amines, gave lactams[10,16].

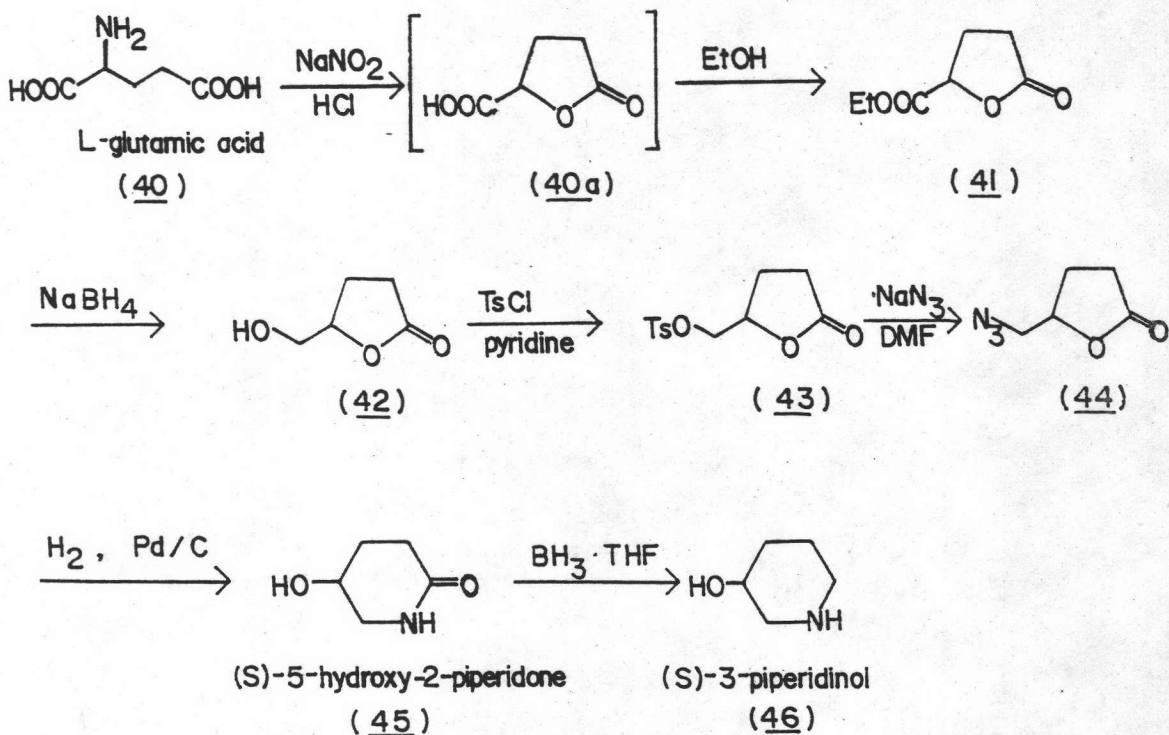


1.2.5 Reductive cyclization of azido lactones

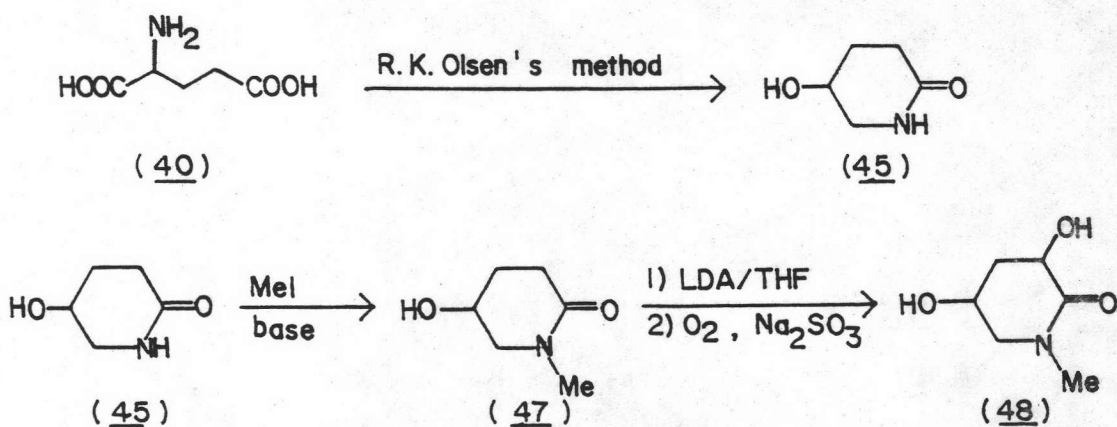
Sugar lactams having five-, six-, and seven-membered ring, e.g. (31), (35), and (39), respectively, were prepared by the hydrogenation of appropriate azido lactones or carboxylic acids [17-19].



R.K. Olsen et al. have synthesized (S)-3-piperidinol via a compound whose structure is similar to odoram using L-glutamic acid as the starting material[20-22]:



So the synthesis of odoram can be proposed using the above approach by synthesizing (s)-5-hydroxy-2-piperidone(45) from L-glutamic acid(40), and then N-methylation[23-26] and α -hydroxylation[27,28].



An alternative route to synthesize odoram is shown below.

