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SYNTHEIS, CHARACTERIZATION AND EVALUATION OF SEMISYNTHETIC DERIVATIVES OF LAWSONE

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ABSTARCT

Quinones are widely distributed in nature, and several of their synthetic and natural products are very important in many diverse areas of chemistry and biochemistry. They play a fundamental role in several living cells as electron carriers in the respiratory chain, as well as in blood coagulation and carboxylation of glutamates. Due to the intimate relationship between quinones and the biochemical processes of cells, these compounds have been extensively explored in the synthesis 2 of several bioactive compounds with antitumor,[3–5] molluscicidal,[6,7] antiparasitic,[8–10] leishmanicidal,[11] antiinflammatory,[12] antifungal,[13] antimicrobial[14] and trypanocidal[15–17] activities. In the present work we have synthesised semisynthetic derivatives of lawsone 2(a-d) by Mannich base reaction. Four derivatives of Lawson were synthesized. All the compounds synthesized were obtained in good yields. Purity of compounds was confirmed by TLC and melting points and compounds were characterized by preliminary laboratory techniques like chemical tests, melting point, Rf. The synthesized compounds were screened for wound healing activity

KEYWORDS: Quinones, Lawson, Wound healing activity, Mannich base reaction.

INTRODUCTION TO LAWSONE IN ORGANIC SYNTHESIS

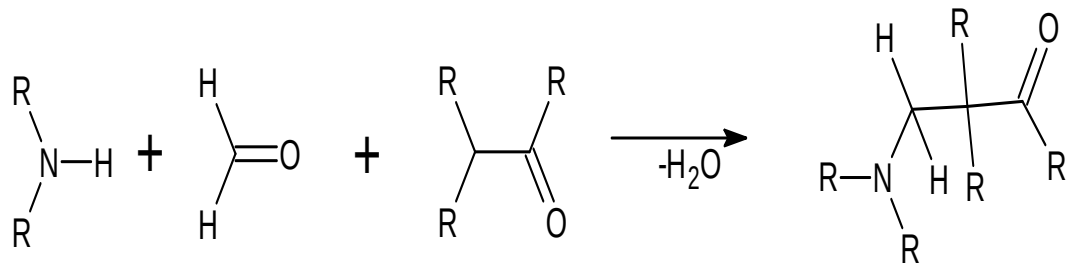
Quinones are widely distributed in nature, and several of their synthetic and natural products are very important in many diverse areas of chemistry and biochemistry. . Due to the intimate relationship between quinones and the biochemical processes of cells, these compounds have been extensively explored in the synthesis of several bioactive compounds The quinine class includes several important synthetic and natural compounds bearing a hydroxy group on the

quinine ring. Specifically, the lawsone motif and that of its isomeric form 4-hydroxy-1, 2-naphthoquinone are common subunits of compounds with a number of valuable biological activities, examples of which are 1: lapachol (2), atovaquone (3), parvaquone (4), NQ1 (5), β-lapachone (6) α-apachone (7). Research work on acute wounds in an animal model shows that wounds heal in four phases. It is believed that chronic wounds must also go through the same basic phases.[9]

INTRODUCTION TO MANNICH BASE REACTION

The Mannich reaction is an organic reaction which consists of an amino alkylation of an acidic proton placed next to a carbonyl functional group by formaldehyde and a primary or secondary amine or ammonia. The final product is a β-amino-carbonyl compound also known as a Mannich base Reactions between aldimines andα-methylene carbonyls are also considered Mannich reactions because these imines form between amines and aldehydes. The reaction is named after chemist Carl Mannich.

Scheme 1: Ammonia or an amine reacts with formaldehyde and an alpha acidic proton of a carbonyl compound to a beta amino carbonyl compound.



The Mannich reaction is also considered a condensation reaction. In the Mannich reaction, primary or secondary amines or ammonia, are employed for the activation of formaldehyde. Tertiary amines lack an N–H protons form the intermediate enamine. α-CH-acidic compounds (nucleophiles) include carbonyl compounds, nitriles, acetylenes, aliphatic nitro compounds, α-alkyl pyridines or imines.

Experimental procedures

Methods

Step-1: Synthesis of 4-phenyl 1,3-thiazole 2-amine[189] (1 a,b): A Finely powdered thiourea (15.2g, 0.2 mol) and iodine (24.4g, 0.1 mol) mixed with acetophenone/4-chloroaceto phenone (0.1mmol) in an 250 ml round bottom flask was refluxed on water bath for 6hrs. The obtained

solid was triturated with diethyl ether to remove unreacted acetophenone, washed with aqueous sodium thiosulpha teto remove excess of iodine and then with water. The crude product was dissolved in hot water, filtered to remove the sulphones 2-amino 4-phenyl thiazole /2-amino 4-(3-chloro phenyl) thiazole was precipitated by addition of ammonia. Solid separated was filtered, washed with water and recrystallized from benzene.

Step-2: Synthesis of Semi synthetic derivatives of Lawsone: 0.1 mole of Lawsone, 4-phenyl 1,3-thiazole and aldehydes- derivatives are taken in a beaker and add Ethanol to it and stir the products. Kept them on a magnetic stirrer for 30 mins up to the formation of a precipitate. Solid separated was filtered, washed with water and finally the products are collected. All the five chemical compounds are synthesized and characterized by the below test:

Test for compound 1A:

Test	Observation	Inference
Hinsberg test	Water soluble ppt	Confirms the 1^o amine
Nitrous acid test	Nitrogen gas evolve	Confirms the 1^o amine
Carbyl amine test	Offensive ordour	Confirms the 1^o amine

Test for compound 2A,2B,2C,2D: Test for compound 2A,2B,2C,2D:

Test	Observation	Inference
Hinsberg test	Water insoluble ppt	Confirms the 2^o amine
Nitrous acid test	Yellow oil is formed	Confirms the 2^o amine
Carbyl amine test	No smell	Confirms the 2^o amine
Libermann nitroso test	Blue colour is formed	Confirms the 2^o amine

RESULTS AND DISCUSSION

Four different semi synthetic derivatives of lawsone (2A,2B,2C,2D)were synthesized and compounds were characterized by preliminary laboratory techniques like chemical tests, melting point, R_f values and further evaluated for wound healing activity. The synthesized derivatives of lawsone and standard were screened for Wound healing activity .The test and standard compounds are prepared with suitable ointment base and it was applied twice per day. Two of the synthesized lawsone derivatives (2A&2B) demonstrated Wound healing activity and percentage of wound contraction are 28&32 respectively. The synthesised lawsone derivatives are not showed significant activity compared with standard.

Wound healing activity: The synthesized compounds were screened for wound healing activity. The percentage Healing of all compounds was calculated.

Sl. No.	Group of Animals	Length in mm of the wound (days)														Reduction of the wound (mm)	Percentage of wound contraction (%)
		1st	2nd	3rd day	4th day	5th day	6th day	7th day	8th day	9th day	10th day	11th day	12th day	13th day	14th day	15th day	
1	Standard	5 mm	5 mm	4.8 mm	4.7 mm	4.6 mm	4.6 mm	4.5 mm	4.3 mm	4.2 mm	3.8 mm	3.6 mm	3.2 mm	3.0 mm	2.0 mm	1.0 mm	4 mm	80
2	Test-1	5 mm	5 mm	5 mm	5 mm	5 mm	5 mm	5 mm	5 mm	5 mm	5 mm	4.9 mm	4.7 mm	4.7 mm	4.0 mm	3.6 mm	1.4 mm	28
3	Test-2	5 mm	5 mm	5 mm	5 mm	5 mm	5 mm	5 mm	5 mm	5 mm	4.9 mm	4.7 mm	4.6 mm	4.5 mm	3.7 mm	3.4 mm	1.6mm	32
4	Test-3	5 mm	5 mm	5 mm	5 mm	5 mm	5 mm	5 mm	5 mm	5 mm	4.9 mm	4.7 mm	4.6 mm	4.4 mm	4.0 mm	3.1 mm	1.9mm	38
5	Test-4	5 mm	5 mm	5 mm	5 mm	5 mm	5 mm	5 mm	5 mm	5 mm	4.9 mm	4.8 mm	4.7 mm	3.9 mm	3.7 mm	3.6 mm	1.4mm	28
6	Normal	5 mm	5 mm	4.9 mm	4.9 mm	4.8 mm	4.8 mm	4.7 mm	4.6 mm	4.5 mm	4.3 mm	4.0 mm	3.9 mm	3.9 mm	3.8 mm	3.7 mm	1.3 mm	26

CONCLUSION

In the present work we have synthesised SEMISYNTHETIC DERIVATIVES OF LAWSONE 2(a-d) by Mannich base reaction. Four derivatives of Lawson were synthesized. All the compounds synthesized were obtained in good yields. Purity of compounds was confirmed by TLC and melting points and compounds were characterized by preliminary laboratory techniques like chemical tests, melting point, Rf. The synthesized compounds were screened for wound healing activity and no significant activity was observed.

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