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Multi component, one-pot synthesis of (1-(4-(*1H*-imidazol-1-yl) phenyl)-1, 2-dihydronaptho[1, 2-e] [1, 3]-3-thione and 3-one derivatives under microwave-assisted conditions

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ABSTRACT

1-(4-(1H-imidazol-1-yl) phenyl)-1, 2-dihydronaptho [1, 2-e] [1, 3]-3-thione and 3-one Derivatives Were moderate high yields using a novel, facile, and one synthesized in pot condensation of β- Napthol, 4-(1H-imidazol-1-yl) benzaldehyde and urea (or) thio urea derivatives under Microwave conditions

Key words: 4-(1H-imidazol-1-yl) benzaldehyde, β- napthol, multi-component, Micro wave assisted Conditions

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INTRODUCTION

The construction of new analogs of bioactive heterocyclic compounds represents a Major challenge in synthetic organic and medicinal chemistry [1]. Imidazoles are an important class of heterocyclic's and include many substances of both biological and chemical interest. They are part of a large number of highly significant biomolecules such as the essential amino acid histidine and related compounds, biotin, and the imidazole alkaloids. Insertion of the imidazole nucleus is an important synthetic strategy in drug discovery. Imidazole drugs have broad applications in many areas of clinical medicine. Due to their broad spectrum of biological activities naphthalene-condensed 1, 3-oxazin-3-ones have been reported to act as antibacterial agents, such as HIV-1 reverse transcriptase inhibitors [2]. They have been used as precursors in the preparation of phosphinic ligands for asymmetric catalysis [3]. Recently, a few methods for the synthesis of 1, 2-dihydro-1-arylnaphtho [1, 2-e] [1, 3] oxazine-3-ones have been reported.

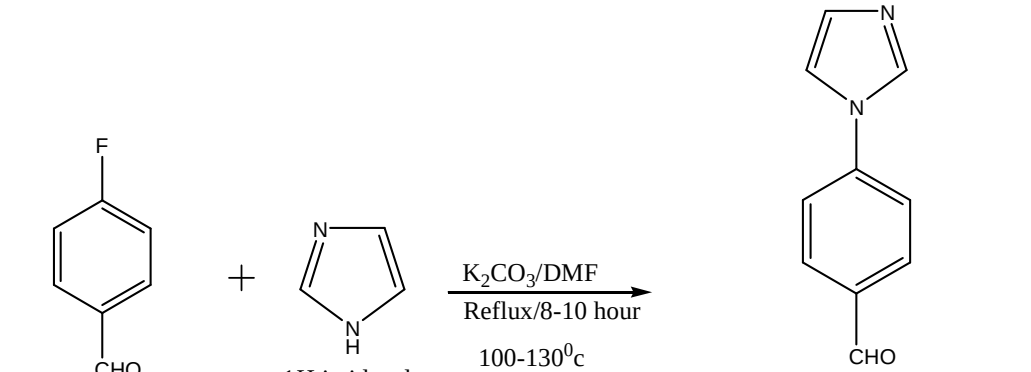
Generally they are synthesized by three component condensation of urea or thiourea with an aldehyde and β-naphthol, which entails the use of pTSA [4], perchloric acid supported on silica [5], montmorillonite K10 [6], phosphomolybdic acid [7], Iodine [8], and nano copper in PEG-400 [9]. However, in spite of their potential utility, some difficulties still exist, such as expensive or toxic reagents. Therefore, the development of new, simple methods for the synthesis of 1-(4-(1H-imidazol-1-yl) phenyl)-1, 2-dihydronaptho [1, 2-e] [1, 3]-3-thione and 3-one derivatives are of main Importance and these compounds show their biological activities

MATERIALS AND METHODS

Starting materials and reagents were commercially available, purchased from Sisco Research Laboratory (SRL).Reactions were monitored by TLC, performed on silica gel aluminum plates And Visualization on TLC was achieved by UV light or iodine indicator. For micro wave radiation used Micro-Wave Oven (KORYO). Multi component-one pot synthesis of 1-(4-(1H-imidazol-1-yl) Phenyl)-1, 2-dihydronaptho [1, 2-e] [1, 3]-3-thione (and 3-one) s were obtained easily in two Steps by using β-napthol, urea (or) thiourea , 4-(1H-imidazol-1-yl) benzaldehyde and few drops of ethanol under microwave conditions. The first step (Scheme 1) consists synthesis of 4-(1H-imidazol-1-yl) benzaldehyde[ ] and the second step consists cyclisation of (Scheme 2) aldehyde ,β-napthol and urea(or) thio urea derivatives under microwave radiation.

A.Synthesis of 4-(1H-imidazol-1-yl) benzaldehyde: (Scheme 1)

A mixture of flouro benzaldehyde(1 mmol),imidazole(1 mmol),potassaium carbonate(K_2CO_3) (1.2 mmol) and Dimethyl formamide(DMF) were taken in 250ml Round Bottam flask was magnetically stirred and reflux in oil bath at 100-130^{0}c for 8-10 hours. The reaction mixture after being cooled to room temperature forms wine yellow colour solid than washed with ethyl acetate (Et-OAc) and water(H_2O).The two layers are separated by separating funnel and ethyl acetate solvent evaporated than light yellow colour solid formed. It is recrystalised with methanol(Me-OH) than dark yellow colored solid ,4-(1H-imidazol-1-yl) benzaldehyde was (3)formed



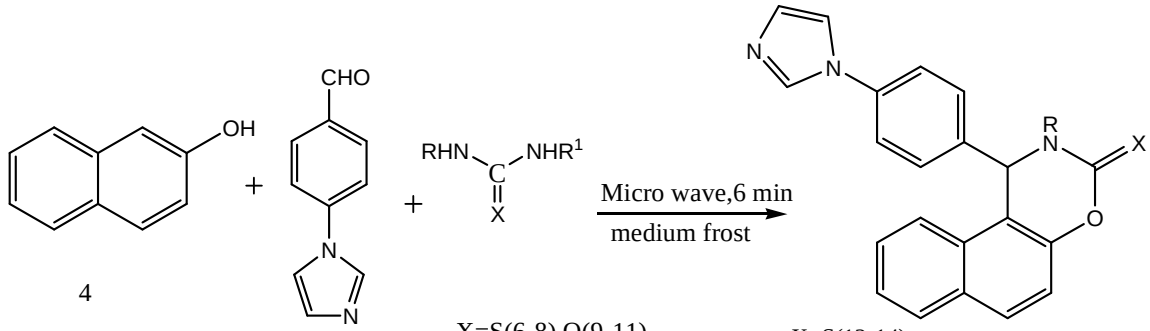
4-fluorobenzaldehyde (1) + 1*H*-imidazole (2) → 4-(1*H*-imidazol-1-yl)benzaldehyde (3)

Scheme 1

B. Synthesis of 1-(4-(1H-imidazol-1-yl) phenyl)-1, 2-dihydronaptho [1, 2-e] [1, 3]-3-thione.
(Scheme 2)

A mixture of β-napthol (1 m mol), 4-(1H-imidazol-1-yl) benzaldehyde (1 mmol), thio urea (or) Urea and few drops of methanol (Me-OH) were finely mixed together. The reaction mixture was Placed in Screw capped bowl and microwave radiation irradiated for 6 min with a power of Medium frost Range. After cooling the reaction mixture was washed with water and than Recrystalised from Ethyl acetate-Hexane (EtOAc and Hexane) (1:3) to afford the pure product as Dark white color powder.

According to these results, the reaction can be mechanistically considered to proceed through The acylimine intermediate (formed insitu by reaction of the aldehyde with urea (or) thio Urea derivatives) [10-13].The subsequent addition of β-napthol to the acylimine intermediate, Followed by cyclization affords corresponding products (12 to 17) and ammonia (scheme-3).The Structures were characterized by IR, H^1NMR, C^{13}NMR and MS Spectra.



4

naphthalen-2-ol

5

4-(1*H*-imidazol-1-yl)benzaldehyde

X=S(6-8),O(9-11)

X=S(12-14)

1-(4-(1*H*-imidazol-1-yl)phenyl)-1,2-dihydronaphtho[1,2-*e*][1,3]oxazine-3-thione derivatives

X=O(15-17)

1-(4-(1*H*-imidazol-1-yl)phenyl)-1,2-dihydronaphtho[1,2-*e*][1,3]oxazine-3-one derivatives

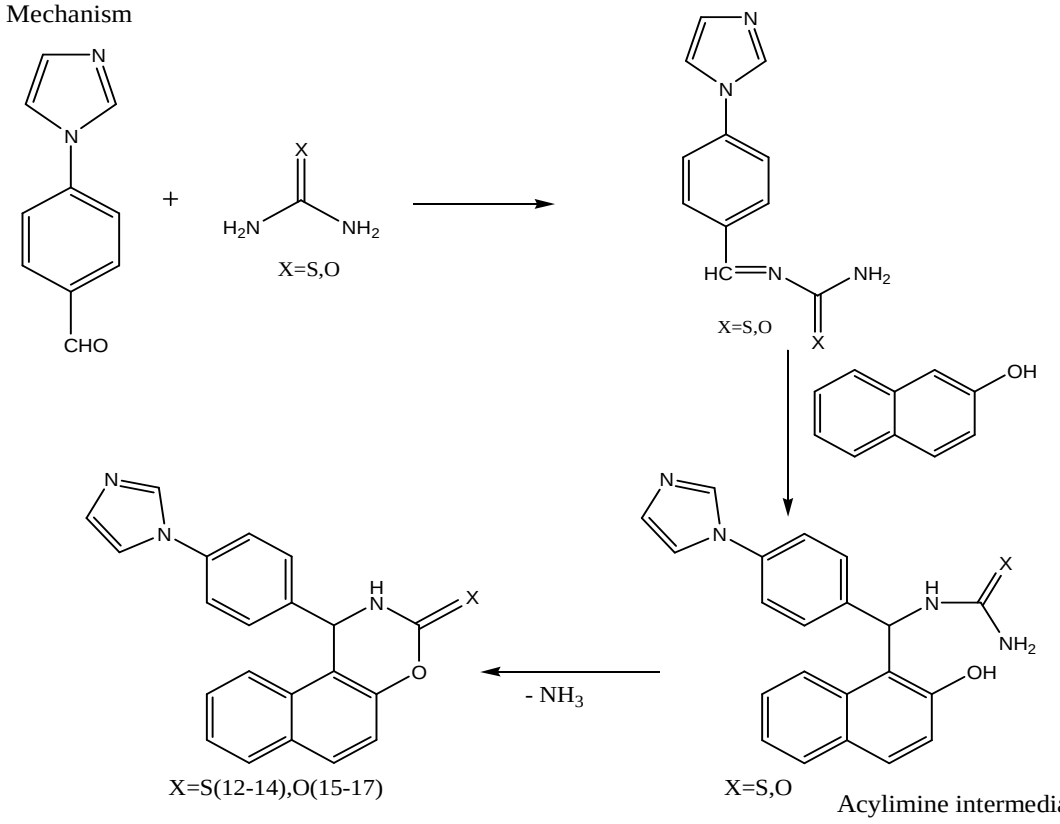
12,15 (R,R^1=H)

13,16 (R=CH_3,R^1=H)

14,17 (R=CH_3,R^1=CH_3)

Scheme 2

Mechanism



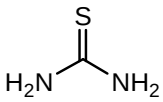
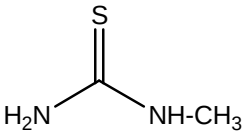
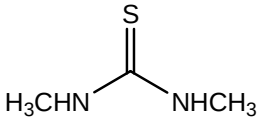
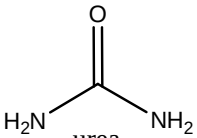
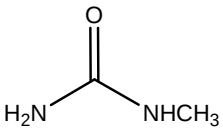
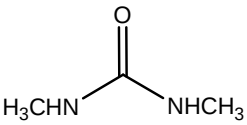
Plausible mechanism

Scheme 3

RESULTS AND DISCUSSION

Encouraged by this success, we attempted the reaction of β-napthol, with a range of urea (or) thio urea derivatives and 4-(1H-imidazol-1-yl) benzaldehyde, under similar micro-wave Conditions, furnishing the respective 1-(4-(1H-imidazol-1-yl) phenyl)-1, 2-dihydronaptho [1, 2-e] [1, 3]-3-thione (or) 3-one derivatives (12-17) in good yields. The optimized results are Summarized in table 1

Table: 1 Reaction of β-napthol with urea or thio urea derivatives and 4-(1H-imidazol-1-yl) benzaldehyde under microwave –Assisted conditions

Product number	Urea derivatives	Time (min)	Yield (%)
12	 thiourea	6	81
13	 1Methyl-thio urea	6	74
14	 1,3-dimethylthiourea	6	No Reaction
15	 urea	6	78
16	 1-methylurea	6	71
17	 1,3-dimethylurea	6	No Reaction

The spectral (IR, 1H NMR, 13C NMR) and analytical data for:

1-(4-(1H-imidazol-1-yl) phenyl)-1, 2-dihydronaptho [1, 2-e] [1, 3]-3-thione (12)
M.P:179–182°C.^{1}HNMR (300MHZ):8.05(s,1H), 6.84-7.68(m,6H),7.46(d,1H),7.27(d,1H), 7.1(d,4H) , 5.19(d,1H), 2.01(d,1H). C^{13}NMR:151.9, 145.0,141.3,135.5,134.9,133.5,130.2,129.2,128.8,128.3, 126.3, 122.9, 122.5, 118.9, 115.7, 115.4, 49.1; M.F: $C_{21}H_{15}N_3OS$

1-(4-(1H-imidazol-1-yl) phenyl)-2-methyl-1, 2-dihydronaptho [1, 2-e] [1, 3]-3-thione (13)
M.P:182-185^{0}C.H^{1}NMR(300MHZ): 8.03(s,1H), 6.91-7.73(m,6H), 7.46(d,1H),7.27(d,1H),7.01(d,4H), 5.19(s,1H), 2.47(s,3H). C^{13}NMR: 151.9, 145.4, 142.3, 135.5,134.1,133.5,130.2 ,129.2,128.8, 128.3, 126.3, 122.9, 122.5, 118.9, 115.7, 115.4, 54.6, 32.9; M.F:$C_{22}H_{17}N_3OS$

1-(4-(1H-imidazol-1-yl) phenyl)-1, 2-dihydronaptho [1, 2-e] [1, 3]-3-one (15)
M.P:167-169^{0}C. H^{1}NMR(300MHZ): 8.06(s ,1H),8.0(s,1H),6.99-7.63(m,6H), 7.56(d,1H), 7.27(d,1H), 7.11(d,4H), 5.19(s,1H). C^{13}NMR:157.8, 150.9, 142.3,135.5, 134.3,133.5,130.2,128.8,128.3,125.3, 123.2, 122.9, 121.5, 118.9, 115.7, 115.4, 49.3; M.F:$C_{21}H_{15}N_3O_2$

1-(4-(1H-imidazol-1-yl) phenyl)-2-methyl-1, 2-dihydronaptho [1, 2-e] [1, 3]-3-one (16)
M.P:170-173^{0}C. H^{1}NMR(300MHZ):8.03(s,1H),6.94-7.63(m,6H),7.46(d,1H),7.37(d,1H), 7.01(d,4H), 5.19(s,1H), 2.90(s,3H). C^{13}NMR:151.9, 149.7, 141.3, 135.5, 134.2,133.5,130.2,129.2,128.8,127.3,126.3, 123.2, 122.9, 118.9, 115.7, 114.4, 54.8, 33.1; M.F:$C_{22}H_{17}N_3O_2$

CONCLUSION

In conclusion, we have described a novel, efficient and one pot synthesis for the preparation of 1-(4-(1H-imidazol-1-yl) phenyl)-1, 2-dihydronaptho [1, 2-e] [1, 3]-3-thione (or) 3-one Derivatives in three-component cyclo-condensation reactions of β-Napthol, 4-(1H-imidazol-1-yl) benzaldehyde and urea (or) thio urea derivatives under Micro wave Assisted Conditions .The Novelty and synthetic utility of this methodology was demonstrated in the efficient synthesis of 1-(4-(1H-imidazol-1-yl) phenyl)-1, 2-dihydronaptho [1, 2-e] [1, 3]-3-thione (or) 3-one derivatives

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