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Research Article

SYNTHESIS OF NOVEL NAPHTHO [2,1-b] FURAN DERIVATIVES AND INVESTIGATION OF ANTIMICROBIAL ACTIVITY FOR THE SUPPRESSION OF PIMPLES

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ABSTRACT
The title compounds 3-nitro-2-acetylnaphtho[2,1-b]furan,3-nitroacetylnaphtho [2,1-b]furanhydrazone,Ethyl-3-aminonaphtho[2,1-b]furan-carboxylate,ethyl (2,5-dimethylpyrrole)naphtho[2,1-b]furan-2-carboxylate, 3-(2,5 dimethylpyrrolenaphtho [2,1-b] furan-2 carboxyhydrazide were synthesized from 2-hydroxy-1-naphthaldehyde which was thought of to be a good starting material, which was prepared from 2-naphthol by Reimer Tiemann reaction. The synthesized compounds were characterized by analytical and spectral studies and were screened for antibacterial activity against gram +ve Staphylococcus *aureus, B. subtilis* and gram–ve *Escherchia coli, Pseudomonas aureus* and antifungal activity against *Candida albicans*, *Aspergillus niger* by cup plate method

KEY WORDS: antibacterial, antifungal, Procaine penicillin, Streptomycin, Griseofulvin Naphtho [2,1- b] furan.

INTRODUCTION

Naphthofuran derivatives have been explored for their wide spectrum of pharmacological profile[1-3]. Hence, we examine the feasibility and efficiency approach to synthesize naphthofuran derivatives which turn to exhibit significant antimicrobial activities [4-9]. The major objective of the present work is to investigate new drugs for the safe and effective treatment of acne. People suffering from acne will feel embarrassed for their look which may also lead to psychological disorders. Acne is a common human skin disease characterized by areas of skin with pimples, pinheads, scaly red skin and large papules. It is associated with microorganisms which lead to inflammation, wound and pain. Hence the synthesized compounds were subjected to antimicrobial activity for the suppression of pimples.

MATERIALS AND METHODS

Melting point was determined by open capillary tube method and is uncorrected.I.R. Spectra were recorded on Shimadzu FTIR Spectrophotometer. NMR on Bruker DRX-300 (300MHz-FT-NMR with low and high temperature facility -90^0 to +80^0). Standard chemical shifts are given in δ ppm valuesAll the reactions were monitored by Thinlayer chromatographic method. TLC was run on silica gel using ethyl acetate and petroleum ether (10:90) as eluent. The newly synthesized products are separated and purified by column chromatography using silica gel (60-120 mesh).

Experiment

Synthesis of 3-nitro-2-acetylnaphtho[2,1-b] furan. [1]

A cooled nitrating mixture of concentrated nitric acid and concentrated sulphuric acid in the ratio 1:2(6.5ml: 13ml) was added very slowly to a cooled solution of 2-acetylnaphtho [2,1-b] furan (2.1g.0.01mol) in glacial acetic acid(4ml) and the mixture was stirred for about 30 min at 0-5 C. The stirring was continued for 3hrs at the same temperature and the reaction mixture was poured on to crushed ice. The product which was separated as solid was collected and dried. Recrystallised from aqueous ethanol. The structure of the compound was confirmed by recording its IR, ^{1}H NMR and ^{13}C NMR and comparing it with an authentic sample.

Synthesis of 3-nitro-2-acetylnaphtho [2,1-b] furanhydrazone. [2]

A mixture of 3-nitro-2-acetylnaphtho[2,1-b]furan (2.5g,0.01mol),hydrazenehydrate (1ml,0.01mol),concentrated hydrochloric acid (3-4drops) in ethanol(30ml) was refluxed on water bath for 6hrs.The reaction mixture was poured in to ice water and neutralized with aqueous sodium hydroxide (5%) Solid thus separated was collected by filtration, dried and recrystallised from ethanol. The structure of the compound was confirmed by recording IR and ^{1}H NMR spectra.

Synthesis of ethyl-3-aminonaphtho [2,1-b]furan-2-carboxylate. [3]

A mixture of 2-hydroxy-1-naphthald oxime(0.93g,0.05mol),ethylchloro acetate(6.13g,0,05 mol) and anhydrous potassium carbonate(4.9g ,0.05mol)was heated under reflux in anhydrous dimethyl formamide(60ml) for 12hrs.The reaction mixture was cooled ,potassium salts were filtered off and the filtrate was poured on to crushed ice to obtain the product as light brown coloured solid. It was collected by filtration and recrystallized from aqueous ethanol.The structure of the compound was established by recording its IR ^{1}HNMR

Synthesis of ethyl 3-(2,5-dimethylpyrrole)naphtho[2,1-b]furan-2-carboxylate. [4]

A mixture of ethyl 3-aminonaphtho[2,1-b]furan-2-carboxylate(25.5g,0.1mol) and acetonyl acetone(13.69g,0.12mol) in glacial acetic acid(100ml) was heated under reflux for 30mins.After removal of the solvent the product was filtered and recrystallized from ethanol. Acid catalyzed reaction of amino ester with acetonyl acetone resulted in the formation of ethyl 3-(2, 5 – dimethylpyrrolenaphtho [2,1-b]furan-2-carboxylate. The structure of the compound was confirmed by recording IR and ^{1}H NMR spectra.

Synthesis of 3-(2,5-dimethylpyrrole)naphtho[2,1-b]furan-2-carboxamide. [5]

A mixture of ethyl 3-(2,5-dimethylpyrrole)naphtho[2,1-b]furan-2-carboxylate(3.33g,0.01mol) and hydrazine hydrate(2.5ml,99%) in ethanol(10ml) was heated under reflux for 5hr,cooled to room temperature and the solid thus separated was filtered, washed with ethanol and recrystallized from aqueous DMF to obtain the product as solid. The structure of the compound was confirmed by recording IR and ^{1}H NMR spectra.

Biological and Pharmacological profile

All the compounds synthesized were screened for antibacterial and antifungal activities[10-14] at two different concentrations (50µg/ml, 100µg/ml) against both gram +ve *Staphylococcus aureus*, , *B. subtilis* and gram–ve *Escherchia coli, Pseudomonas* and antifungal activity against *Candida albicans*, *Aspergillus niger* by cup plate method using Procaine Penicillin, Streptomycin and Griseoflavin respectively as standards. The compounds showed considerable activity against all species tested at 50µg/ml, 100µg/ml. The

synthesized Naphtho [2,1-b]furan derivatives were tested for antimicrobial activity and the results are presented in the tables 1, 2, and 3.

RESULTS AND DISCUSSION

The structures of the synthesised compounds were established by recording its IR, ^{1}HNMR and mass spectral data. The IR spectrum of 3-nitro-2 acetylnaphtho [2,1-b] furan[1] exhibited characteristic absorbtion band at 1681 cm^{-1} due to C=O group and at 1548 cm^{-1} and 1353 cm^{-1} due to NO_2 group. The ^{1}H NMR spectrum showed a singlet at ∂ 2.6 integrating for three protons of CH_3 group and multiplet between ∂7.5 to8.2 for aromatic protons. Mass spectrum showed molecular ion peak at m/Z 255, consistent with the molecular weight. . The IR spectrum of 3-nitro-2-acetylnaphtho [2,1-b]_furanhydrazone[2] exhibited the absorption band at 1621cm^{-1}due to C=N group and at 3450 cm^{-1} due to NH_2 group. In the NMR spectrum singlet at ∂ 2.3,5.6 and multiplet at 7.2-8.0 due to CH_3, NH2 and aromatic protons. The IR spectrum of ethyl -3-aminonaphtho[2,1-b]furan-2-carboxylate[3]exhibited characteristic absorption band at 1724 cm^{-1} due to ester carboxyl group. The ^{1}H NMR spectrum of ethyl 3-(2,5-dimethylpyrrole)naphtho[2,1-b]furan-2-carboxylate[4] exhibited a triplet at ∂ 1.47 (J=7.02 Hz) due to $–CH_2$,A singlet at ∂ 2.08 due to methyl protons, a quartet at ∂ 4.49 (J=7.43 Hz) due to $–CH_3$ ester protons and a multiplet at∂ 7.2-8.2 due to aromatic protons of signal due to $–NH_2$ The IR spectrum exhibited characteristic absorption band at 1720 cm^{-1} due to ester carboxyl group. The structure of ethyl 2,5 dimethylpyrrolenaphtho[2,1-b]furan-2-carboxamide[5] was established by its IR and ^{1}H NMR spectrum. The IR spectrum showed absorption band at 3335 $cm^{-1}$and 3278 cm^{-1} due to amine/amide NH group and strong stretching band at 1650 cm^{-1} due to amide carbonyl. ^{1}H NMR spectrum showed a singlet at ∂ 4.51 and ∂ 9.81 (D_2O exchangeable), which were accounted for NH_2 and NH protons. In addition it also exhibited a singlet at ∂ 2.01 and multiplet at ∂ 7.2 – 8.2 which were attributed to methyl and aromatic protons respectively.

Antibacterial activity

Among the tested compounds 3 and 4 showed better antibacterial activity against *Streptococci aureus* (gram +ve) at lower and higher concentrations. 1, 2 and 4 showed promising antibacterial activity againsty *Pseudomonas aureus* at higher and lower concentration. Compounds 1, 2 and 3 showed promising antibacterial activity against *B.substillis* (gram +ve*)*. Compounds 1 and 5 showed moderate antibacterial activity compared to Procaine penicillin (gram +ve) and streptomycin against *E. coli* (gram –ve).

Anti-fungal activity

Among the screened compounds, 1 and 2 showed moderately significant antifungal activity against *Aspergellus niger* at both concentrations compared to standard Griseofulvin. Compounds 2 and 5 showed fairly promising antifungal activity against *Candida albicans* at both concentrations compared to standard Griseofulvin.

CONCLUSION

The present study has evaluated the effect of five synthetic heterocyclic compounds on antibacterial activity against *S. aureus* (gram +ve*)*, *B.substillis*(gram +ve*)* and *E. coli (gram –ve) Pseudomonas (gram –ve)*.The synthesized compounds were screened for antifungal activity against *P. azadirachtae* ,*Candida albicans* and *Aspergillus niger*. The information obtained in the present study suggests that synthesised compounds containing naphtho [2,1-b]furan moiety shows promising results as antimicrobial agents in controlling the acne.

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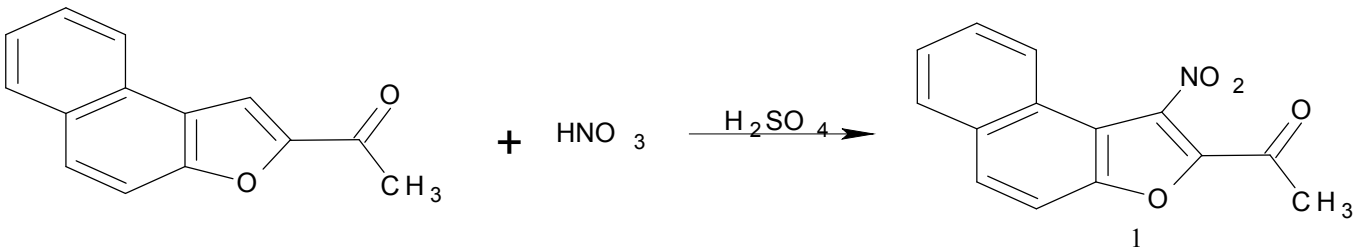
SCHEME



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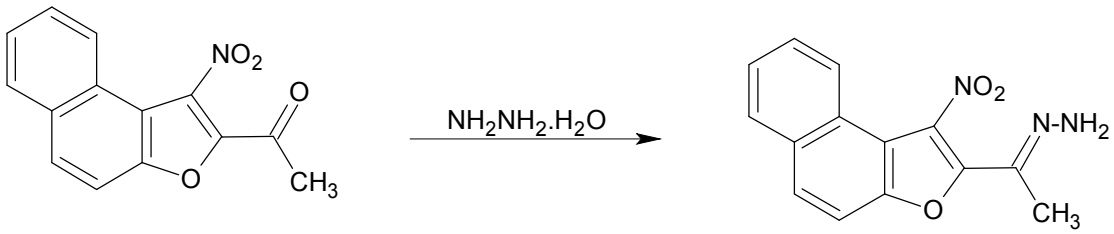

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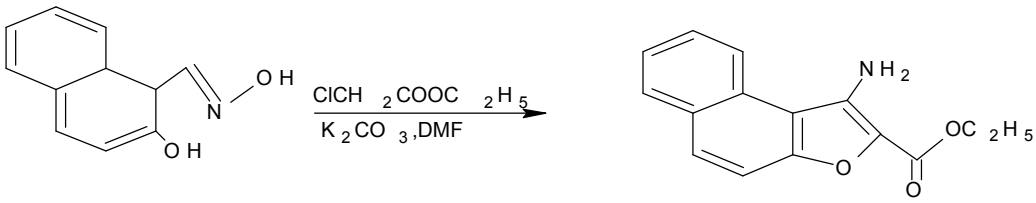

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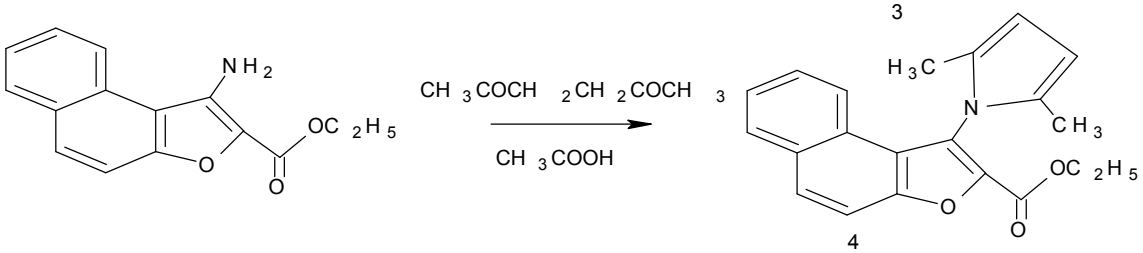

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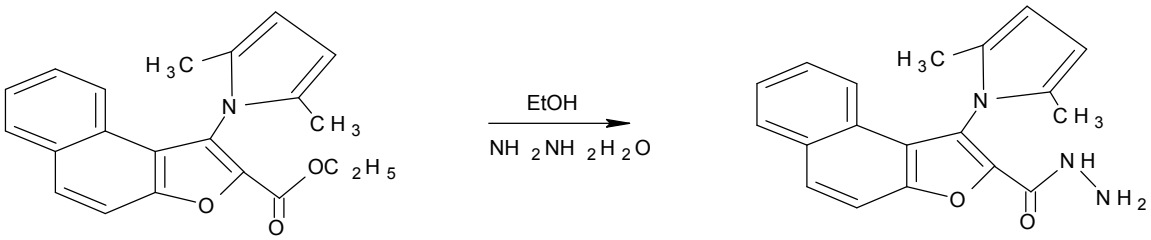

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Table 1: Antibacterial activity of naphtho [2,1- b] furan derivatives

Sl. No	Name of the compounds	*Mean zone of inhibition (in mm)*			
		Staphylococcus aureus		*Escherichia coli*	
		50µg	**100µg**	**50µg**	**100µg**
01	Procaine penicillin (standard)	20	25	-	-
02	Streptomycin (standard)	-	-	20	23
03	1	14 (0.7)	18 (0.72)	14 (0.7)	17 (0.73)
04	2	14 (0.7)	18 (0.72)	13 (0.65)	17 (0.73)
05	3	15 (0.75)	19 (0.76)	13 (0.65)	16 (0.69)
06	4	15 (0.75)	18 (0.72)	13 (0.65)	16 (0.69)
07	5	14 (0.7)	19 (0.76)	14 (0.7)	18 (0.78)

Table 2: Antibacterial activity of naphtho [2,1- b] furan derivatives

Sl. No	Name of the compounds	*Mean zone of inhibition (in mm)*			
		Bacillus subtillis		*Pseudomonas aureus*	
		50µg	**100µg**	**50µg**	**100µg**
01	Procaine penicillin	21	25	-	-
02	Streptomycin	-	-	20	23
03	1	15 (0.71)	19 (0.76)	15 (0.75)	19 (0.82)
04	2	15 (0.71)	18 (0.72)	16 (0.80)	21 (0.91)
05	3	16 (0.76)	17 (0.68)	14 (0.7)	17 (0.73)
06	4	13 (0.61)	16 (0.64)	15 (0.75)	19 (0.82)
07	5	14 (0.66)	17 (0.68)	14 (0.7)	18 (0.78)

Table 3: Antifungal activity of naphtho [2,1- b] furan derivatives

Sl. No	Name of the compounds	**Mean zone of inhibition (in mm)**			
		Candida albicans		*Aspergillus niger*	
		50µg	**100µg**	**50µg**	**100µg**
01	Griseofulvin (standard)	21	25	21	25
02	1	11 (0.51)	15 (0.60)	14 (0.66)	19 (0.76)
03	2	13 (0.61)	16 (0.64)	14 (0.66)	18 (0.72)
04	3	12 (0.56)	16 (0.64)	13 (0.61)	18 (0.72)
05	4	12 (0.56)	16 (0.64)	12 (0.57)	15 (0.6)
06	5	13 (0.61)	18 (0.72)	13 (0.61)	18 (0.72)

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