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Amalgamation and Characterization of unused heterocyclic compounds determined from 5-Bromo-2,3-DI(Furan-2-yl)-1H-Indole

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Abstract

Heterocyclic moietyserve as culminate system on which pharmacophores can be successfully joined to deliver novel drugs. Among different heterocyclic compounds, nitrogen-based heterocycles have been broadly explored as they constitute the center structures of various naturally significant atoms and have been found to be dynamic against distinctive sorts of cancers. Due to the flexibility of indole, it has been a profoundly "privileged motif" for the target-based plan and advancement of anticancer specialists.. In addition, it has been utilized as a synthon for the arrangement of huge number of bioactive heterocycles and cleared a way to create successful targets. This survey article presents comprehensive diagram of anticancer possibility of differently substituted indole subsidiaries counting 1H-indole-2,3-dione subsidiaries.Acid-catalyzed, three-component reaction (Biginelli synthesis) between 5-bromo-2,3-di(furan-2-yl)1H-indole ,acetylacetone and semicarbazide, thiosemicarbazide, urea, thiourea, guanidine constitutes a rapid and facile synthesis of corresponding tetrahydropyrimidines, which are interesting compounds with a potential for pharmaceutical application.

Keywords: Heterocyclic compounds, Biginelli synthesis, indole derivatives and tetrahydropyrimidines

Introduction

Heterocyclic compounds have paid hugely to the society within the shape of expansive number of drugs for the treatment of different afflictions and have involved a unmistakable put in restorativechemistry due to their varied biological activities [1]. Indole center has been ceaselessly pulling in the consideration of analysts and has gotten to be a energetic region of inquire about due to its exceptional pharmacological properties [2]. It is assigned as "privileged scaffolds" which tie to different receptors with tall liking, driving to the advancement of novel bioactive drugs[3]. It is used for the target-based design and development of anticancer agents[4]. In this context, therapeutic effect of multi-target directed indole based hybrid molecules in cancer therapy is recently reviewed by[5]. Indole subsidiaries have been broadly utilized as synthons for the planning of huge number of organically significant heterocycles [6].

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In addition, indoles are found in vital manufactured sedate atoms with curiously pharmacological properties like SARS coronavirus 3CL protease inhibitors[7], anti-HIV movement[8], antituberculosis activity [9], anticonvulsant[10] and HIV-TB coinfection [11] including anti-cancer[12]. Indoles are too related with the hindrance of NFkB/mTOR/PI3K/AkT and control of estrogen-mediated action [13]. A few 3-substituted indole subordinates have been found to display surprising antineoplastic properties viz.. inhibition of cell proliferation of human colon carcinoma (HT-29), human ovarian adenocarcinoma (SK-OV-3), and c-Src kinase activity [14]. together, 3-pyranyl indoles have appeared great anticancer action against MCF-7 breast cancer cell lines in comparison with measures drugs [15]. Biginelli In 1893, the synthesis of functionalized 3,4-dihydropyrimidin-2(1H)-ones (DHPMs) scheme I via three-component condensation reaction of an aromatic aldehyde, urea and acetyl acetone was reported for the first time by P. Biginelli. Within the past decades, such Biginelli-type dihydropyrimidones have gotten a impressive sum of consideration due to the curiously pharmacological properties related with this heterocyclic platform.. one - pot synthesis may be a methodology to progress the productivity of a chemical response whereby a reactant is subjected to progressive chemical responses in fair one reactor.his is often much wanted by chemists since maintaining a strategic distance from a long partition handle and refinement of the middle of the road chemical compounds would spare timeand assets whereas expanding chemical abdicate .Numerousdihydropyrimidinones and their derivatives are pharmacologically[16] important as calcium channel blockers, antihypertensive agents, and biological activities [17] also contain the dihydropyrimidinone-5-carboxylate core. Therefore, many synthetic methods for preparing such compounds have been developed [18].

Material and Methods

All the chemicals and reagents were purchased from MERCK and Himedia fine chemical companies and are used without further purification. Melting points of the synthesized compounds are determined in open capillaries and are uncorrected. Reactions are monitored by thin-layer chromatography (TLC) on silica gel 60 F254 aluminium sheets (MERCK). The mobile phase was chloroform and benzene . IR spectra are recorded in KBr on Perkin-Elmer and FTIR Spectrophotometer (cm-1) and 1H NMR spectra on BRUKER AVENE II 400 MHz NMR Spectrometer (Chemical shift in δ ppm down field from TMS as an internal reference).

Typical procedure of 1,2-di(furan-2-yl)-2-hydroxyethanone (2)

A solution of sodium cyanide (2 mmol, 0.098 g) in H_2O (2 ml), was added to a stirred solution of a furfuraldehyde (10 mmol) in EtOH (10 ml). The mixture was then refluxed. The progress of reaction was monitored by TLC using hexane/ethyleacetate (80:20) as eluent. The solvent was then removed by evaporation under reduced pressure. The residue was washed with water and diethyl ether. Yellow crystals, Yield: 56%, mp: 125-126 0C; FT-IR (KBr, Cm-1):
3420 (OH), 1646 (C=O), 1025(C- O); 1H NMR (DMSO-d6, ppm): δ 5.78 (d, 1H, OH), 5.89 (d, 1H, CH), 6.83 (d, 2H ,furyl), 7.52 (d, 1H, furyl), 7.63 (d, 1H, furyl), 7.99 (d, 1H, furyl), 8.24 (d, 1H, furyl).

5-bromo-2,3-di(furan-2-yl)1H-indole (3)

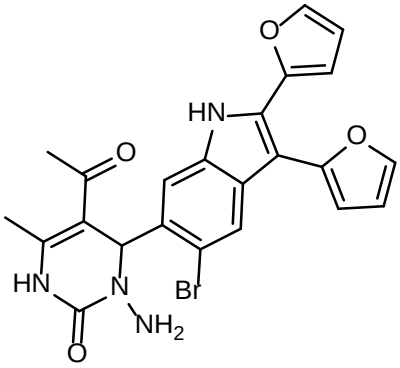
This product was obtained as a brown crystal, The product was purified by recrystalization (EtOH). IR γ [cm−1] = 3410, 1605, 1516, 1486; 1 H NMR δ = 8.2 (br s, 1H, NH), 7.83 (d, 1H), 7.28–7.68 (m, 13H)

5-bromo-2,3-di(furan-2-yl)-1H-indole-6-carbaldehyde (4)

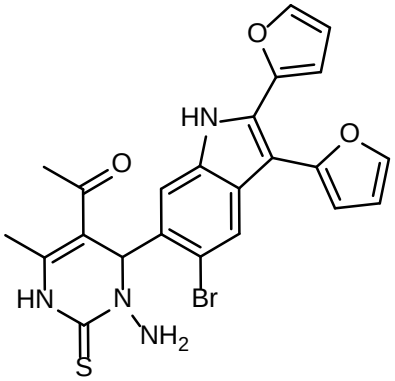
To a cold solution of (3) (20 mmole) in dimethyl formamide (4.2ml,0.0542mole) phosphorus oxychloride(3.5ml,0.038 mole) was added .The reaction mixture was heated on boiling water bath for 2 hrs left to cool to room temperature, the reaction mixture was poured into ice-cold. water and neutralized with sodium acetate tri hydrate (100gm /175ml H2O)solution the solid so obtained was crystalized from ethanol as yellowish crystals.

The new heterocyclic compound 5,6,7,8 prepared by The original Biginelli synthesis was reported by P. Biginelli (Bigenilli , 1983) which involves refluxing of compound (4) as aldehyde, acetyl acetone as diketone and / semecarbazide, thiosemicarbazide/urea/thiourea or guanidine HCl

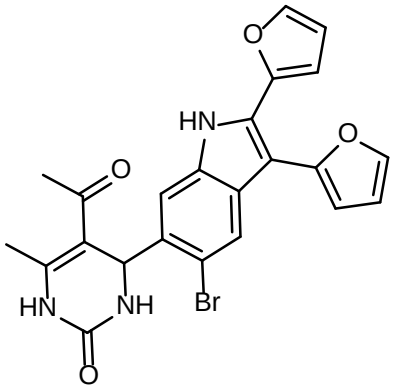
in ethanolic HCl. To give the corresponding compounds (5), (6),(7),(8) and (9)



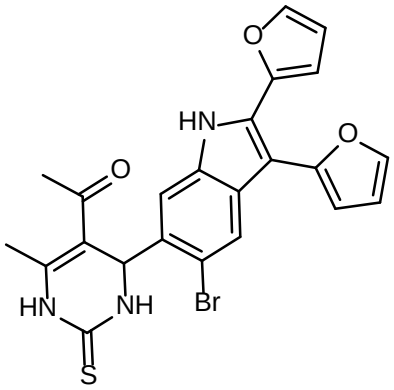
5-acetyl-3-amino-4-(5-bromo-2,3-di(furan-2-yl)-1H-indol-6-yl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one (5)



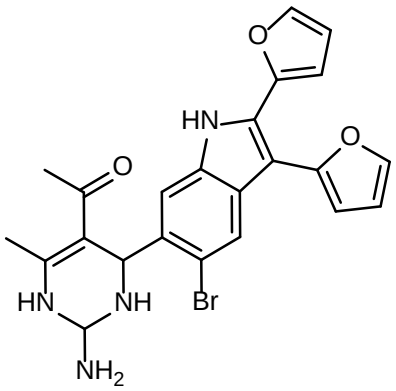
1-(3-amino-4-(5-bromo-2,3-di(furan-2-yl)-1H-indol-6-yl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone (6)



5-acetyl-4-(5-bromo-2,3-di(furan-2-yl)-1H-indol-6-yl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one (7)



1-(4-(5-bromo-2,3-di(furan-2-yl)-1H-indol-6-yl)-c6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone (8)

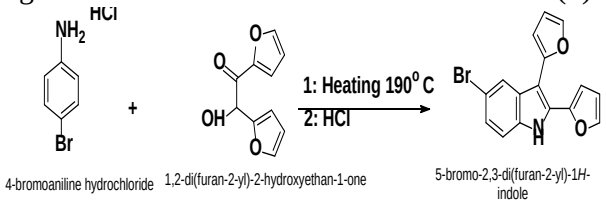


1-(2-amino-4-(5-bromo-2,3-di(furan-2-yl)-1H-indol-6-yl)-6-methyl-1,2,3,4-tetrahydropyrimidin-5-yl)ethanone (9)

Results and Discussion

Avoiding organic solvents during the reactions in organic synthesis leads to a clean, efficient and economical technology (green chemistry). There is an increasing interest in the use of a highly expedient methodology for the synthesis of fine chemicals and heterocyclic compounds of biological importance, we herein report a facile, rapid one pot synthesis of 1,2-di(furan-2-yl)-2-hydroxyethan-1-one (2) with 4-bromoaniline (1) derivatives to afford 5-bromo-2,3-di(furan-2-yl) -1H-indole (3) scheme (I). derivatives were

obtained in good yields .the IR spectrum of compound (2) showed an absorption bond at 1672cm-1,3399cm-1 characteristic for the carbonyl function and hydroxyl Figure (1). The IR spectrum of compound (3) don't showed an absorption for the carbonyl function and hydroxyl figure (2).



Scheme I synthesis of 5-bromo-2,3-di(furan-2-yl)1H-indole

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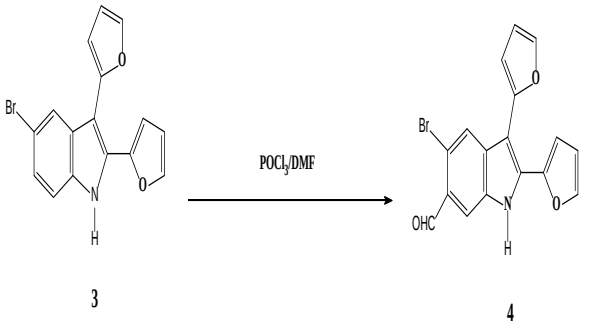
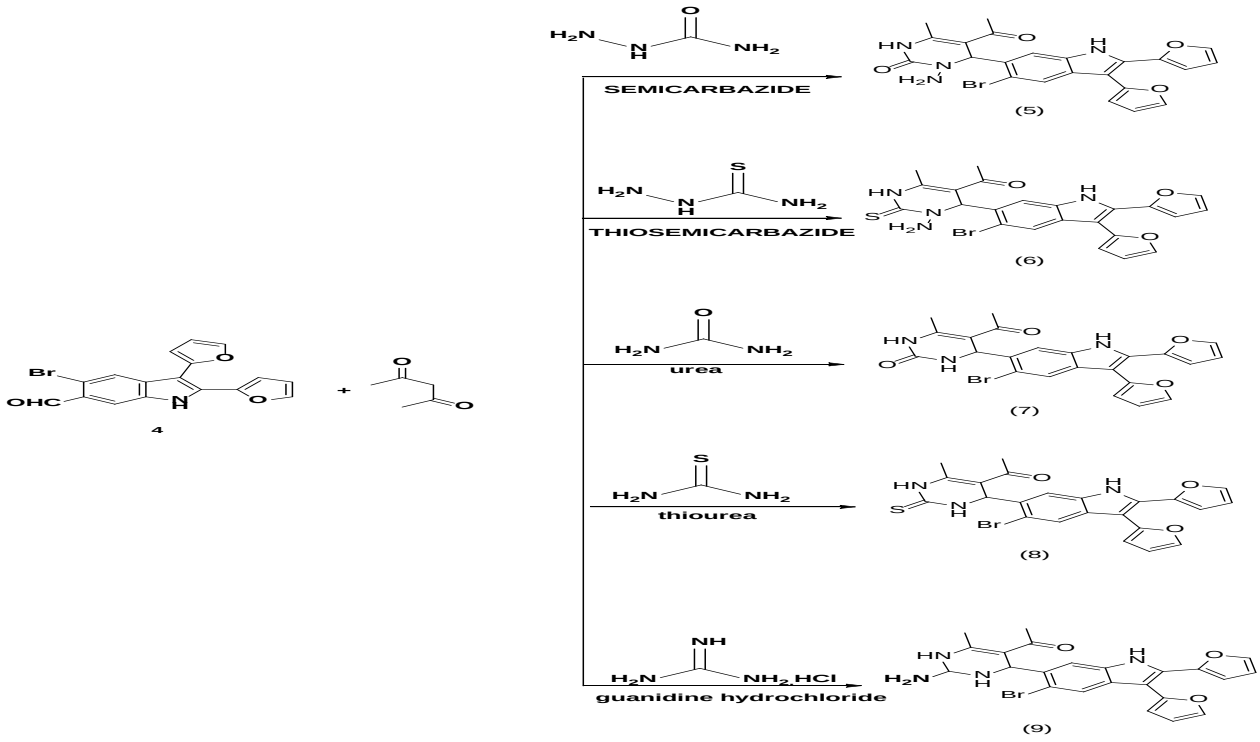


Scheme II synthesis of 5-bromo-2,3-di(furan-2-yl)-1H-indole-6-carbaldehyde

Vilsmeier-Haack formylation of compound (3) with dimethylformamide and phosphorus oxychloride gave 5-bromo- 2,3-di(furan-2-yl)-1H-indole-7-carbaldehyde (4). The IR spectrum of compound (4) showed an absorption band at 1730 cm -1 figure (3) characteristic for the carbonyl function of the formyl group.

1H NMR spectrum (400 MHz, DMSO) revealed signals at 10.2 (s, 1H, CHO group), 8.21 (s, 1H, = NH indole) figure(4). The formylation is directed to position 6 not to any other position since position 6 of compound (3) is the most reactive centre [19].



Scheme III synthesis of tetrahydropyrimidines 5-9

Conclusions

The synthesis of novel, potentially active dihydropyrimidine derivatives. These derivatives were prepared through biginelli reaction.

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