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Barbituric Acid As A Core For Some New Heterocyclic Substituted Derivatives

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ABSTRACT

Different N-heterocyclic substituted derivatives of barbituric acid have been synthesized. The nitrogen atoms have been alkylated first to form N-carboxymethyl followed by cyclization reaction to form heterocyclic/substituted aryl groups. All the synthesized compounds have been identified using I.R, ^{1}H NMR.

Keywords: 5,5-substituted Barbituric acid; Hiburic acid, 1,3-Oxazole, Imidazol, 1,2,4-Triazole, 1,3,4-thiadiazol.

INTRODUCTION

Heterocycles have been studded commonly as pharmaceutical and agricultural active compounds [1]. As a result the development of methodologies useful for the meeting of molecules containing heterocyclic templates continues to be a focus for the attention of both the educational and manufacturing communities. Along with aromatic heterocycles, the 1,3-Oxazole and Imidazol units constitutes an useful biological active compounds [2,3]. Similarly, the 1,3,4-Triazole and 1,3,4-oxadiazol rings is also associated with wide ranging physiological activity [4-11]. Literature survey revealed that when one biodynamic heterocyclic system was coupled with another, a molecule with improved biological activity [12,13] was produced. The chemistry of these linked biheterocycles has been the attractive field of research in medicinal chemistry as they have been found to exhibit enhanced biological profile [14]. Taken these observations in our considerations and in continuation of our interest in the synthesis of substituted biheterocycles, it was thought worthwhile to synthesize and investigate the activity of the compounds in which 1,3-Oxazole, Imidazol, 1,3,4-Triazole and 1,3,4-oxadiazol moiety has been linked with 5-substituted Barbituric acid group. We report in this paper, Synthesis of some N-heterocyclic substituted derivatives of barbituric acid.

MATERIALS AND METHODS

Instruments: Melting point determinations were performed by the open capillary method using a Gallenkamp melting point apparatus and are reported uncorrected. The IR spectra (KBr-discs) were recorded with a pye-Unicam Sp-300 spectrometer. ^{1}H NMR spectra were recorded on a Bruker AV500

spectrometer operating at 500 MHz for ^{1}H measurements. Chemical shifts are reported relative to TMS and coupling constants *J* are in Hz and have been rounded to the nearest whole number. Assignments of signals are based on coupling patterns and expected chemical shift values and have not been rigorously confirmed. Signals with similar characteristics might be interchanged.

Materials: Chemicals were obtained from Aldrich Chemical Company and used without further purification.

Methods:

Synthesis of 2,2'-((2,2'-(5,5-diethyl-2,4,6-trioxodihydropyrimidine-1,3(2H,4H)-diyl)bis(acetyl)) bis(azanediyl))diacetic acid(S2): Compound 1 (0.01mol) in (5ml) dioxane was added to a stirring solution of glycine (1.4g , 0.02mol) and sodium hydroxide (20ml , 10%solution). Then, the reaction mixture was stirring over night and a few grams of crushed ice were added with stirring . After that, the solution was acidified with conc. HCl and the combined solution was concentrated in vacuo and the residual precipitate dissolved in ethanol .The inorganic salts were filtered .the remaining solution concentrated in vacuo. The remainded crude oily. Yield: 71%; m.p. Oily; IR (v, cm^{-1}): 2,974- 3,392 brod ($OH_{carboxyl}$), 1,735 ($C=O_{carboxyl}$), 1,687 ($C=O_{amid}$), 3,392 (NH); ^{1}H NMR (400 MHz, DMSO-d_6) δ(ppm): 1.05 (t , 6H, -CH_3), 1.90 (q, 4H, -CH_2-), 4.48 (S, 4H, N-CH_2-CO), 8.58 (t, 2H, -CO-NH), 3.45 (d, 4H, -CH_2-CO); $C_{16}H_{22}N_4O_9$ (m.w. 414).

Synthesis of 1,3-bis(((E)-4-(4-arylidene)-5-oxo-4,5-dihydrooxazol-2-yl)methyl)-5,5-diethyl pyrimidine -2,4,6(1H,3H,5H)-trione (S3-5): Aromatic aldehyde (0.02 mol) was added to a stirring mixture of compound2 (0.01 mol)acetic acid (10 ml) and acetic anhydride (40 ml) and the refluxing was continued for (7hrs),then the mixture was poured into crushed ice and stirred (30 min).the product was collected.

5,5-diethyl-1-(((E)-4-(2-methylbenzylidene)-5-oxo-4,5-dihydrooxazol-2-yl)methyl)-3-(((E)-4-(2-nitro benzylidene)-5-oxo-4,5-dihydrooxazol-2-yl)methyl)pyrimidine-2,4,6(1H,3H,5H)-trione (S3): Yield: 53%; m.p 158-162 °C; IR (v, cm-1): 3,080 (C-Har), 2,978 – 2,883 (C-Haliph), 1.813 (C=Ooxazole), 1.699 (C=Calkene), 1,220 (C-O); ^{1}H NMR (500 MHz, Chloroform-d) δ (ppm) 0.98 (t , 6H, -CH_3), 2.29 (q, 4H, -CH_2-), 4.74 (S, 4H, N-CH_2-), 7.72 (S, 2H, =CH-), 7.80 (d, 4H, CH)ar, 8.11 (dd, 4H, =CH-)ar, 8.41 (d, 2H,-CH=); $C_{30}H_{24}N_6O_{11}$ (m.w 645).

5,5-diethyl-1,3-bis(((E)-4-(3-nitrobenzylidene)-5-oxo-4,5-dihydrooxazol-2-yl)methyl)pyrimidine-2,4,6 (1H,3H,5H)-trione (S4): Yield: 63%; m.p Oily; IR (v, cm-1): 3,086 (C-Har), 2,970 – 2,858 (C-Haliph), 1.759 (C=Ooxazole), 1.689 (C=Calkene), 1,205 (C-O); ^{1}H NMR (400 MHz, DMSO-d6) δ (ppm) 0.92 (t , 6H, -CH_3), 2.00 (q, 4H, -CH_2-), 4.63 (S, 4H, N-CH_2-), 7.31 (S, 2H, =CH-), 7.82 (d, 2H, C-CH=)ar, 8.21 (dd, 2H, =CH-)ar, 8.51 (S, 2H, =CH-C)ar, 8.71 (d, 2H, -CH=C)ar, $C_{30}H_{24}N_6O_{11}$ (m.w. 645).

5,5-diethyl-1,3-bis(((E)-4-(4-nitrobenzylidene)-5-oxo-4,5-dihydrooxazol-2-yl)methyl)pyrimidine-2,4,6 (1H,3H,5H)-trione (S5): Yield: 55%; m.p 165-167 °C; IR (v, cm-1): 3,012 (C-Har),2,941 – 2,885 (C-Haliph), 1.786 (C=Ooxazole), 1.695 (C=Calkene), 1,230 (C-O); ^{1}H NMR (500 MHz, DMSO-d6) δ (ppm) 0.86 (t , 6H, -CH_3), 2.10 (q, 4H, -CH_2-), 3.34 (S, 4H, N-CH_2-), 7.24 (S, 2H, =CH-), 8.19 (d, 4H, CH=C-CH)ar, 8.31 (d, 4H, CH=CNO_2-CH)ar . $C_{30}H_{26}N_6O_{11}$ (m.w. 645).

Synthesis of 1,3-bis(((E)-1-amino-4-(argiomethylene)-5-oxo-4,5-dihydro-1H-imidazol-2-yl)methyl)-5,5-diethylpyrimidine-2,4,6(1H,3H,5H)-trione(S6-8): Hydrazine hydrate (20 ml) was added to a mixture of compound (3-5) (0.01 mole) in dry benzene (10 ml) ,The reaction mixture was refluxed for (25 hrs).Then, the mixture was allowed to cool to room temperature and benzene was removed.

1,3-bis(((E)-1-amino-4-(2-nitrobenzylidene)-5-oxo-4,5-dihydro-1H-imidazol-2-yl)methyl)-5,5-diethyl pyrimidine-2,4,6(1H,3H,5H)-trione(S6): Yield: 80%; m.p oily; IR (v, cm-1): 3,441 – 3,331 (NH_2), 3,059 (C-Har), 2,966-2,883 (C-Haliph), 1,678 (C=O), 1,558-1,458 (C=Car);); ^{1}H NMR (500 MHz, DMSO-d6) δ

(ppm) 0.77 (t , 6H, -CH_3), 1.76 (q, 4H, -CH_2-), 3.60-3.90 (S, 4H, N-CH_2-), 6.69 (S, 2H, =CH-), 6.85-7.40 (dd, 8H, CHar), 8.80 (S, 4H,N-NH_2); $C_{30}H_{28}N_{10}O_9$ (m.w. 673).

1,3-bis(((E)-1-amino-4-(3-nitrobenzylidene)-5-oxo-4,5-dihydro-1H-imidazol-2-yl)methyl)-5,5-diethyl pyrimidine-2,4,6(1H,3H,5H)-trione(S7): Yield: 85%; m.p oily; IR (v, cm-1): 3338 – 3254 (NH2), 3,057 (C-Har), 2,966-2,879 (C-Haliph.), 1,672 (C=O), 1,558-1,458 (C=Car); ^{1}H NMR (500 MHz, DMSO-d6) δ (ppm) 0.70 (t , 6H, -CH_3), 1.80 (q, 4H, -CH_2-), 3.61 (S, 4H, N-CH_2-), 6.75 (S, 2H, =CH-), 6.30-6.70 (dd, 8H, CHar), 7.60 (S, 4H, N-NH_2). $C_{30}H_{28}N_{10}O_9$ (m. w 673).

1,3-bis(((E)-1-amino-4-(4-nitrobenzylidene)-5-oxo-4,5-dihydro-1H-imidazol-2-yl)methyl)-5,5-diethyl pyrimidine-2,4,6(1H,3H,5H)-trione(S8): Yield: 94%; m.p oily; IR (v, cm-1): 3344 – 3234 (NH2), 3,032 (C-Har), 2,943-2,852 (C-Haliph.), 1,649 (C=O), 1,61,554-1,442 (C=Car); ^{1}H NMR (500 MHz, DMSO-d6) δ (ppm) 0.77 (t , 6H, -CH_3), 1.77 (q, 4H, -CH_2-), 3.62 (S, 4H, N-CH_2-), 7.20 (S, 2H, =CH-), 6.30-6.90 (dd, 8H, CHar), 7.60 (S, 4H, N-NH_2); $C_{30}H_{28}N_{10}O_9$ (m. w 673).

Synthesis of diethyl 2,2'-(((4E,4'E)-2,2'-((5,5-diethyl-2,4,6-trioxodihydropyrimidine-1,3(2H,4H)-diyl) bis(methylene))bis(4-(argiomethylene)-5-oxo-4,5-dihydro-1H-imidazole-2,1-diyl))bis(azanediyl))diacetate(S9-11) : The corresponding compound (6-8) (0.01 mol) was refluxed with (0.02 mol) of sodium in absolute ethanol for (2hrs). Then, ethyle bromoacetate (3.62g, 0.02 mol) was added and refluxed for an additional (5hrs).After evaporating the solvent under reduced pressure.

Diethyl 2,2'-(((4E,4'E)-2,2'-((5,5-diethyl-2,4,6-trioxodihydropyrimidine-1,3(2H,4H)-diyl)bis (methy lene))bis(4-(2-nitrobenzylidene)-5-oxo-4,5-dihydro-1H-imidazole-2,1-diyl))bis(azanediyl))diacetate (S9) : Yield:87%; m.p. Gamy; IR: (v, cm-1) 3,421 (NH), 3,047 (C-Har.), 2,985- 2852 (C-Haliph), 1,735 (C=Oester), 1,668 (C=Oimidazole), 1,558-1,489 (C=Car), 1,294 (C-O); ^{1}H NMR (500 MHz, DMSO-d6) δ (ppm) 0.78 (t , 6H, -CH_3), 1.80 (q, 4H, -CH_2-), 4.10 (S, 4H, N-CH_2-), 6.85 (S, 2H, =CH-), 7.10-7.45 (dd, 8H, CHar), 1.05 (t, 6H, -CH_3), 3.41 (d, 4H, -CH_2-CO), 4.40 (q, 4H, O-CH_2-), 2.25 (t, 2H, N-NH); $C_{38}H_{40}N_{10}O_{13}$ (m.w 845).

Diethyl 2,2'-(((4E,4'E)-2,2'-((5,5-diethyl-2,4,6-trioxodihydropyrimidine-1,3(2H,4H)-diyl)bis (methy lene))bis(4-(3-nitrobenzylidene)-5-oxo-4,5-dihydro-1H-imidazole-2,1-diyl))bis(azanediyl))diacetate (S10) : Yield:75%; m.p. Gamy; IR: (v, cm-1) 3,311 (NH), 3,047 (C-Har.), 2,974- 2864 (C-Haliph), 1,730 (C=Oester), 1,670 (C=Oimidazole), 1,521-1,458 (C=Car), 1,300 (C-O); ^{1}H NMR (500 MHz, DMSO-d6) δ (ppm) 0.75 (t , 6H, -CH_3), 1.76 (q, 4H, -CH_2-), 3.69 (S, 4H, N-CH_2-), 7.59 (S, 2H, =CH-), 6.20-6.80 (dd, 8H, CHar), 1.54 (t, 6H, -CH_3), 3.23 (d, 4H, -CH_2-CO), 3.42 (q, 4H, O-CH_2-), 3.19 (t, 2H, N-NH); $C_{38}H_{40}N_{10}O_{13}$ (m.w 845).

Diethyl 2,2'-(((4E,4'E)-2,2'-((5,5-diethyl-2,4,6-trioxodihydropyrimidine-1,3(2H,4H)-diyl)bis(methy lene))bis(4-(4-nitrobenzylidene)-5-oxo-4,5-dihydro-1H-imidazole-2,1-diyl))bis(azanediyl))diacetate (S11) : Yield:86%; m.p. oily; IR: (v, cm-1) 3,234 (NH), 3,007 (C-Har.), 2,939-2,837(C-Haliph), 1,735 (C=Oester), 1,670 (C=Oimidazole), 1,558-1,489 (C=Car), 1,294 (C-O); ^{1}H NMR (500 MHz, Chloroform-d) δ (ppm) 0.90 (t, 6H, -CH_3), 1.82 (q, 4H, -CH_2-), 4.30 (S, 4H, N-CH_2-), 7.70 (S, 2H, =CH-), 6.50-6.80 (dd, 8H, CHar), 1.30 (t, 6H, -CH_3), 3.70 (d, 4H, -CH_2-CO), 4.22 (q, 4H, O-CH_2-), 2.30 (t, 2H, N-NH); $C_{38}H_{40}N_{10}O_{13}$ (m.w 845).

Synthesis of 2,2'- (((4E,4'E)-2,2'-((5,5-diethyl-2,4,6-trioxodihydropyrimidine-1,3(2H,4H)-diyl)bis (methylene))bis(4-(argiomethylene)-5-oxo-4,5-dihydro-1H-imidazole-2,1-diyl))bis (azanediyl)) di (acetohydrazide) (S12-14) : A mixture of compound 9-11 (0.01, mole) and thiosemicarbazide (1.82 g, 0.02 mole) in ethanol (25 ml) was refluxed for 8 hrs. Upon cooling the solution a solid appeared. This was recrystallized from ethanol to afford the desired compound.

2,2'-(((4E,4'E)-2,2'-((5,5-diethyl-2,4,6-trioxodihydropyrimidine-1,3(2H,4H)-diyl)bis (methylene)) bis(4-(2-nitrobenzylidene)-5-oxo-4,5-dihydro-1H-imidazole-2,1-diyl))bis(azanediyl)) di(aceto hydra zide) (S12): Yield:86%; m.p. Oily; IR: (v, cm-1) 3,371-3,263 (NH2), 3,180 (NH), 3,080 (C-Har.), 2,972-2,858 (C-Haliph), 1,670 (C=Oamide), 1,286 (C=S); ^{1}H NMR (500 MHz, DMSO-d6) δ (ppm) 0.77 (t , 6H, -CH_3), 1.75 (q, 4H, -CH_2-), 4.50 (S, 4H, N-CH_2-), 6.84 (S, 2H, =CH-), 7.10-7.60 (dd, 8H, CHar), 2.51 (d, 2H, NH-CS), 3.54 (t, 2H, N-NH), 4.10 (d, 4H, -CH_2-CO), 8.20 (d, 2H, CO-NH-), 8.61 (S, 4H,CS-NH_2); $C_{36}H_{38}N_{16}O_{11}S_2$ (m.w 935).

2,2'- (((4E,4'E)-2,2'-((5,5-diethyl-2,4,6-trioxodihydropyrimidine-1,3(2H,4H)-diyl)bis(methylene)) bis(4-(3-nitrobenzylidene)-5-oxo-4,5-dihydro-1H-imidazole-2,1-diyl))bis(azanediyl)) di(acetohydra zide) (S13): Yield:64%; m.p. Oily; IR: (v, cm-1) 3,373-3,284 (NH_2), 3,180 (NH), 3,007 (C-Har), 2,955-2,808 (C-Haliph), 1,645 (C=Oamide), 1,286 (C=S); ^{1}H NMR (500 MHz, DMSO-d6) δ (ppm) 0.78 (t , 6H, -CH_3), 1.75 (q, 4H, -CH_2-), 4.10 (S, 4H, N-CH_2-), 7.92 (S, 2H, =CH-), 7.10-7.60 (dd, 8H, CHar), 2.27 (d, 2H, NH-CS), 3.48 (t, 2H, N-NH), 3.60 (d, 4H, -CH_2-CO), 7.70 (d, 2H, CO-NH-), 8.61 (S, 4H, CS-NH_2); $C_{36}H_{38}N_{16}O_{11}S_2$ (m.w 935).

2,2'- (((4E,4'E)-2,2'-((5,5-diethyl-2,4,6-trioxodihydropyrimidine-1,3(2H,4H)-diyl)bis(methylene)) bis(4-(4-nitrobenzylidene)-5-oxo-4,5-dihydro-1H-imidazole-2,1-diyl))bis(azanediyl))di(acetohydra zide) (S14): Yield: 65%; m.p. Oily; IR: (v, cm-1) 3,375-3,265(NH_2), 3,180 (NH), 3,001 (C-Har.), 2,926-2,883 (C-Haliph), 1,645 (C=Oamide), 1,284 (C=S); ^{1}H NMR (500 MHz, DMSO-d6) δ (ppm) 1.19 (t , 6H, -CH_3), 1.75 (q, 4H, -CH_2-),4.50 (S, 4H, -CH_2-N), 6.55 (S, 2H, =CH-), 7.00-7.70 (dd, 8H, CHar), 2.51 (d, 2H, NH-CS), 4.10 (d, 4H, -CH_2-CO), 7.87 (d, 2H, CO-NH-), 8.62 (S, 4H, CS-NH_2); $C_{36}H_{38}N_{16}O_{11}S_2$ (m.w 935).

Synthesis of 5,5-diethyl-1,3-bis(((E)-1-(((5-mercapto-4H-1,2,4-triazol-3-yl)methyl)amino)-4-(subs titutebenzylidene)-5-oxo-4,5-dihydro-1H-imidazol-2-yl)methyl)pyrimidine-2,4,6(1H,3H,5H)-trione (S15-17) : A mixture of compound 12-14 (0.01 mole) and sodium hydroxide (0.02 mole, 4% solution) was stirred for 4 hrs. After cooling, the solution was acidified with conc. HCl and the precipitate was filtered and recrystallized from ethanol to afford the desired compound.

5,5-diethyl-1,3-bis(((E)-1-(((5-mercapto-4H-1,2,4-triazol-3-yl)methyl)amino)-4-(2-nitrobenzylidene)-5-oxo-4,5-dihydro-1H-imidazol-2-yl)methyl)pyrimidine-2,4,6(1H,3H,5H)-trione (S15) : Yield: 85%; m.p. 122-125 °C; IR: (v, cm^{-1}) 3,437 (NHtriazole),3,279 (NHimidazol), 3,070 (C-Har.), 2,970 – 2,852 (C-$H_{aliph.}$), 2,450 (SH), 1,683 (C=$O_{imidazole}$), 1,282 (C=S), ^{1}H NMR (500 MHz, DMSO-d6) δ (ppm) 0.79 (t, 6H, -CH_3), 1.84(q, 4H, -CH_2), 8.20 (S, 2H, =CH-), 7.11-7.65 (dd, 8H, CHar), 11.74 (S, 2H, -SH); $C_{36}H_{34}N_{16}O_9S_2$ (m.w 899).

5,5-diethyl-1,3-bis(((E)-1-(((5-mercapto-4H-1,2,4-triazol-3-yl)methyl)amino)-4-(3-nitrobenzylidene)-5-oxo-4,5-dihydro-1H-imidazol-2-yl)methyl)pyrimidine-2,4,6(1H,3H,5H)-trione (S16) : Yield: 86%; m.p. 250 °C deco; IR: (v, cm^{-1}) 3,443 ($NH_{triazole}$), 3,279 ($NH_{imidazol}$), 3,093 (C-$H_{ar.}$), 2,972 – 2,837 (C-$H_{aliph.}$), 2,500 (SH), 1,687 (C=$O_{imidazole}$), 1,249 (C=S); $C_{36}H_{34}N_{16}O_9S_2$ (m.w 899).

5,5-diethyl-1,3-bis(((E)-1-(((5-mercapto-4H-1,2,4-triazol-3-yl)methyl)amino)-4-(4-nitrobenzylidene)-5-oxo-4,5-dihydro-1H-imidazol-2-yl)methyl)pyrimidine-2,4,6(1H,3H,5H)-trione (S17) : Yield: 83%; m.p. 194-196 °C; IR: (v, cm^{-1}) 3,419 ($NH_{triazole}$), 3,296 ($NH_{imidazol}$), 3,036 (C-$H_{ar.}$), 2,928 – 2,831 (C-$H_{aliph.}$), 2,360 (SH), 1,662 (C=$O_{imidazole}$), 1,242 (C=S); $C_{36}H_{34}N_{16}O_9S_2$ (m.w 899).

Synthesis of 1,3-bis(((E)-1-(((5-amino-1,3,4-thiadiazol-2-yl)methyl)amino)-4-(substitutebenzylidene)-5-oxo-4,5-dihydro-1H-imidazol-2-yl)methyl)-5,5-diethylpyrimidine-2,4,6(1H,3H,5H)-trione (S18-20) : The corresponding compounds (12-14) (0.01 mole) was dissolved in cold conc. Sulfuric acid (20 ml) and stirred at room temperature for 24 hrs. Then, the reaction mixture was poured into crushed ice and diluted

with water; the precipitate was filtered, washed with water and recrystallized from ethanol to afford the desired compound.

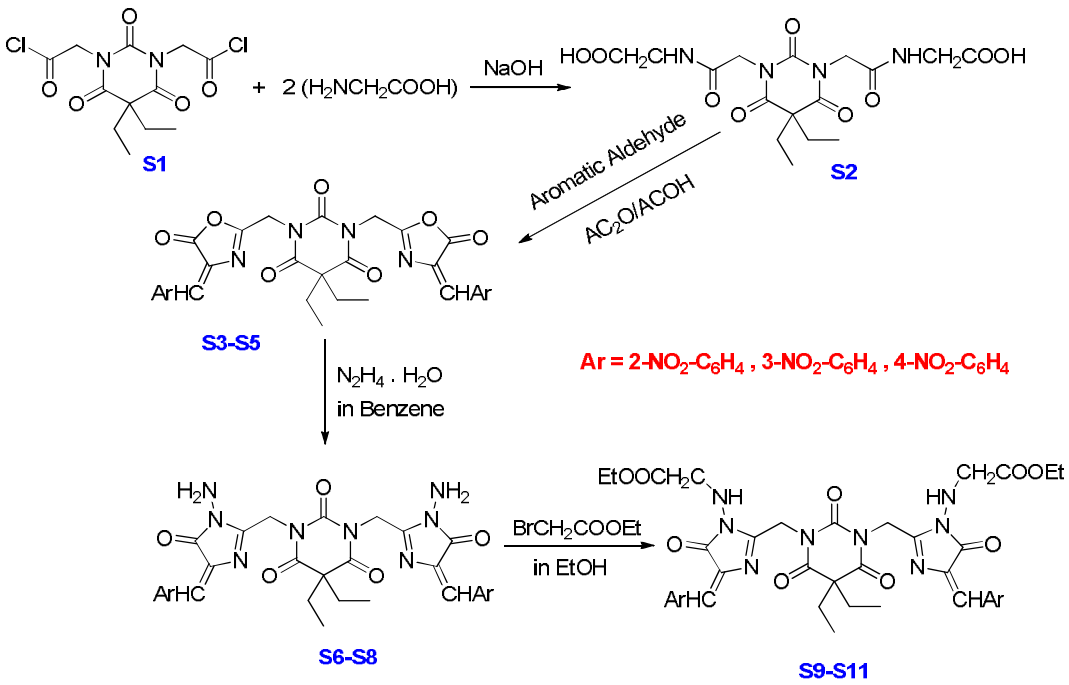
1,3-bis(((E)-1-(((5-amino-1,3,4-thiadiazol-2-yl)methyl)amino)-4-(2-nitrobenzylidene)-5-oxo-4,5-di hydro-1H-imidazol-2-yl)methyl)-5,5-diethylpyrimidine-2,4,6(1H,3H,5H)-trione (S18) : Yield: 65%; m.p. Oily; IR: (v, cm^{-1}) 3,416-3,273 (NH_2), 3,171 (NH), 3053 (C-$H_{ar.}$), 2,928-2,804 (C-$H_{aliph.}$), 1,641 (C=$O_{imidazole}$); ^{1}H NMR (400 MHz, DMSO-d6) δ (ppm) 1.24 (t , 6H, -CH3), 2.11(q, 4H, -CH_2-), 7.00 (S, 2H, =CH-), 7.60-7.72 (dd, 8H, CHar), 3.00 (t, 2H, N-NH), 3.56 (d, 4H, -CH_2-), 4.36 (S, 4H, N-CH_2-), 7.23 (S, 4H, -NH_2); $C_{36}H_{34}N_{16}O_9S_2$ (m.w 899).

1,3-bis(((E)-1-(((5-amino-1,3,4-thiadiazol-2-yl)methyl)amino)-4-(3-nitrobenzylidene)-5-oxo-4,5-di hydro-1H-imidazol-2-yl)methyl)-5,5-diethylpyrimidine-2,4,6(1H,3H,5H)-trione (S19) : Yield: 79%; m.p. 257-260 °C; IR: (v, cm^{-1}) 3,412-3,246 (NH_2), 3,155 (NH), 3047 (C-$H_{ar.}$), 2,931-2,818 (C-$H_{aliph.}$), 1,672 (C=$O_{imidazole}$); $C_{36}H_{34}N_{16}O_9S_2$ (m.w 899).

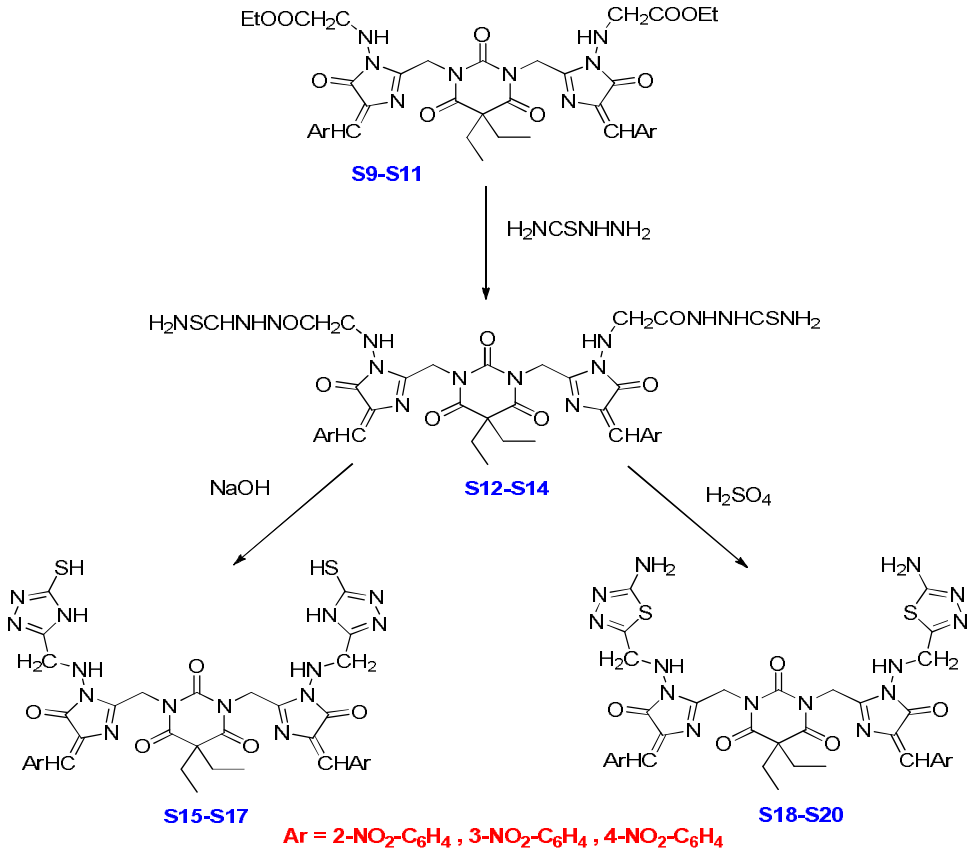
1,3-bis(((E)-1-(((5-amino-1,3,4-thiadiazol-2-yl)methyl)amino)-4-(4-nitrobenzylidene)-5-oxo-4,5-di hydro-1H-imidazol-2-yl)methyl)-5,5-diethylpyrimidine-2,4,6(1H,3H,5H)-trione (S20) : Yield: 77%; m.p. 268-270 °C; IR: (v, cm^{-1}) 3,363-3,246 (NH_2), 3,169 (NH), 3059 (C-$H_{ar.}$), 2,922-2,875 (C-$H_{aliph.}$), 1,647 (C=$O_{imidazole}$); $C_{36}H_{34}N_{16}O_9S_2$ (m.w 899).

RESULTS AND DISCUSSION

The designated compounds were synthesized according to Scheme 1 and 2.



Scheme 1. The synthesis of compounds S1-S11.



Scheme 2. The synthesis of compounds S12-S20.

Reaction of 2,2'-(5,5-diethyl-2,4,6-trioxodihydropyrimidine-1,3(2H,4H)-diyl)diacetyl chloride (S1) with amino acid (Glycine) afforded (2,2'-((2,2'-(5,5-diethyl-2,4,6-trioxodihydropyrimidine-1,3(2H,4H)-diyl)bis(acetyl))bis(azanediyl))diacetic acid (S2) [15]. The IR spectrum of the product indicated the absence of absorption bands due to CO-Cl at 1,805 cm^{-1} and the presence of a OH absorption band at 3,270-2,650 cm^{-1} and showed two sharp absorption band, the first appears at 1,720 cm^{-1} and is attributed to carbonyl function of the carboxylic acid and other, observed at 1,690cm^{-1}, was assigned to a C=O stretching frequency corresponding to the amide carbonyl .In the ^{1}H-NMR spectrum, the proton signals due to (-CO-NH) resonated at 8.58 ppm, integrating for two protons, .Compound S3-S5 1,3-bis(((E)-4-(4-substitutedbenzylidene)-5-oxo-4,5-dihydrooxazol-2-yl)methyl)-5,5-diethylpyrimidine-2,4,6(1H,3H,5H)-trione [16] prepared by oxidative cyclization of compound S2 with aromatic aldehydes. The structures of compounds S3-5 were indicated by the absence of the characteristic OH stretching at 3,270-2,650 cm-1 in addition to the absorption bands for the NH at 3,170 cm^{-1}, also an increase in the absorption band for the carbonyl group have been made to be 1,813 cm^{-1} due to the cyclization reaction. The ^{1}H-NMR spectra of compounds S3-5 showed new signals at 7.80-8.71 ppm integrated for four protons assigned to aryl group, also a single peak at 7.42 ppm appeared suitable to (C=CHAr) group. The key intermediate 1,3-bis(((E)-1-amino-4-(4-substitutedbenzylidene)-5-oxo-4,5-dihydro-1H-imidazol-2-yl)methyl)-5,5-diethylpyrimidine-2,4,6(1H,3H,5H)-trione S6-8 [17] were prepared from the reaction of hydrazine 80% with compounds S3-5. The spectra exhibited a NH_2 stretching vibration at 3,441-3,234 cm^{-1} and decrease C=O stretching vibrations at 1,649 cm^{-1}. The appearance of single peak at 8.00 ppm in the ^{1}H-NMR spectra of compound S3-5 could be a good prove for the substitution of oxygen atom by N-NH_2 group. Alkylation of compound S6-8 with ethyl bromoacetate (Scheme 1) gave diethyl 2,2'-(((4E,4'E)-2,2'-((5,5-diethyl-2,4,6-trioxodihydropyrimidine-1,3(2H,4H)-diyl)bis(methylene)) bis(4-(4-substitutedbenzylidene)-5-oxo-4,5-dihydro-1H-imidazole-2,1-diyl))bis(azanediyl))diacetate S9-11 [18]. The formation of compounds S9-11

was confirmed by the presence of a sharp absorption near 1,735-1730 $cm^{-1}$for the ester C=O and the disappearance of asymmetrical absorption band at 3,441-3,234 cm^{-1} for the NH_2 group. The ^{1}H-NMR spectra of compounds S9-11 has shown the disappearance of singlet peak of NH2 group at 8.00 ppm and the appearance of triplet peak at 2.58 ppm due to NH group, also the appearance of multiplet peak at 4.01 ppm and the triplet peak at 1.29 ppm due to ethyl CH_2 and CH_3 groups respectively could be a good indication for the formation of S9-11 compounds. The treatment of compounds S9-11 with thiosemicarbazide gave compounds 2,2'-(2,2'-(((4E,4'E)-2,2'-((5,5diethyl-2,4,6-trioxodihydropyrimidine-1,3(2H,4H)-diyl)bis(methylene))bis(4-(argiomethylene)-5-oxo-4,5-dihydro-1H-imidazole-2,1-diyl))bis (azanediyl))bis(acetyl)) bis(hydrazinecarbothioamide) S12-14 [19]. The IR spectra of the prepared compounds has shown. The appearance of asymmetrical absorption band at 3,375-3,263 cm^{-1} related to NH_2 group and the stretching band at 3,180 cm^{-1} related to NH group. A significant decrease in the absorption band of the carbonyl group appeared to become 1,645 cm^{-1} was a good indication for the formation of amides carbonyl group. In the ^{1}H-NMR spectra, the proton signals due to ethyl group of ester O-CH_2-CH_3 near 4.01, 1.29 were disappeared. The proton signals due to NH2 group recorded at 8.61 ppm. Compounds S12-14 are useful intermediates leading to the formation of some heterocyclic rings such as 1,2,4- triazoles and 1,3,4-thidiazoles oxidative cyclization of compounds S12-14 with aqueous sodium hydroxide (scheme 2) afforded 5,5-diethyl-1,3-bis(((E)-1-(((5-mercapto-4H-1,2,4-triazol-3-yl) methyl) amino)-4-(substitutebenzylidene)-5-oxo-4,5-dihydro-1H-imidazol-2-yl)methyl)pyrimidine-2,4,6 (1H,3H, 5H) -trione (S15-17) [20]. The IR spectra confirmed by the presence of weak absorptions near 2,500-2,360 cm^{-1} for SH and 3,437 cm^{-1} due to $NH_{triazol}$ and 3,279 cm^{-1} due to $NH_{imidazol}$. The ^{1}H-NMR spectra has revealed the SH protons resonated at 11.74 ppm as a broad singlet integrated for two protons**.** Moreover, $CSNH_2$ signals disappeared from the ^{1}H-NMR spectra. Finally, the treatment of the same compounds S12-14 with conc. H_2SO_4 afforded 1,3-bis(((E)-1-(((5-amino-1,3,4-thiadiazol-2-yl)methyl)amino)-4-(substitutebenzylidene)-5-oxo-4,5-dihydro-1H-imidazol-2-yl)methyl)-5,5-diethylpyrimidine-2,4,6(1H,3H, 5H)-trione S18-20 [21]. The IR spectra of the prepared compounds has shown. The presence of asymmetrical absorption band at 3,416-3,246 cm^{-1} related to $(NH_2)_{thidiazole}$.

APPLICATIONS

In the present study new derivatives of barbituric acid were synthesized. In future we will study their pharmaceutical activity.

CONCLUSIONS

In conclusion, the PPG has been employed as a novel, mild and highly efficient solvent system for the convenient preparation of benzimidazoles in excellent yields from o-phenyldiamine and a wide variety of aryl aldehydes using $ZnCl_2$ as catalyst. In addition low cost, recyclable solvent system and ready availability of catalyst, an environmentally benign procedure makes this methodology a useful contribution to the existing procedures available for the synthesis of benzimidazole derivatives.

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