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The Simple and Efficient Synthesis of Fused Hydroxy Pyrimido Pyrimidine Dinitrile Heterocycles and Its Derivatives.

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Abstract
In the present communication a simple and efficient synthesis of amino pyrimidine have been synthesized by using double Michael addition reaction, in first reaction Michael acceptor is ethyl cyanoacetate, and Michael donor is guanidine nitrate obtain 2,6 diamino 4-hydroxy pyrimidine which act as Michael donor for further reaction with Michael acceptor ethyl 2-cyano-3,3-bis(methylthio)acrylate in the presence of catalytic amount of K_2CO_3 in DMF under reflux condition that offered 4,11-dioxo-2,9-bis(methylthio)-6- hydroxy -7,11-dihydro-4H,6H-dipyrimido[1,2-a:1',2'-c]pyrimidine-3,10-dinitrile and this synthesized compounds are used for derivatization. All synthesized compounds characterized by spectral method.
Keywords: *Michael reaction,ethyl 2-cyano-3,3-bis(methylthio)acrylate, guanidine nitrate.*

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I. Introduction:

Imidazopyridines have displayed a broad spectrum of pharmacological and biological activities.[1] Among the diverse derivatives of imidazopyridine, the imidazo[1,2-*a*]pyridine skeleton is probably the most important structure due to its vital role as a key construction in drugs and biologically active compounds with properties such as anti-inflammatory,[2,3]Pyridopyrimidine derivatives are also known as antidepressant,[4] Quinazolines are considered to be important chemical synthons of various physiological significances and pharmaceutical utilities. They possess a variety of biological effects, including antihypertensive,[5,6] antimicrobial,[7,8] antihyperlipidemic,[9,10] antiinflammatory,[11,12] and anticonvulsant[13–17] activities.

II. Methods:

Melting point were determined in open capillary tubes and are uncorrected. The silica gel F_{254}plates were used for thin layer chromatography (TLC); the spot were examined under UV light and then developed in an iodine vapour. Column chromatography was performed with silica gel (BDH 100-200 mesh). Solvents were purified according to standard procedure. The spectra were recorded as follows; IR KBR pellets, a perkin-Elmer RX1 FT-IR spectrophotometer ; ^{1}H NMR, $CDCL_3$, 200 MHz, a variant Gemini 200 instrument. Elemental analysis was performed on a various CHN-O rapid analyzer.

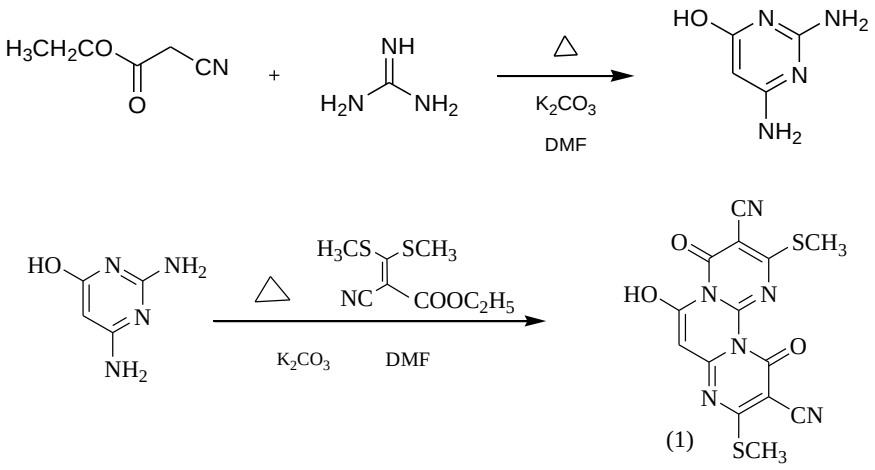
III. Experimental:

3.1 Material:

All solvent and reagent were obtained commercially and used as recived, guanidine nitrate($CH_6N_4O_3$), Malenonitrile($C_3H_2N_2$), Ethyl cyanoacetate($C_5H_7NO_2$), DMF, K_2CO_3, Carbon disulphide(CS_2), Dimethyl sulphate($C_2H_4O_4S$), KOH.

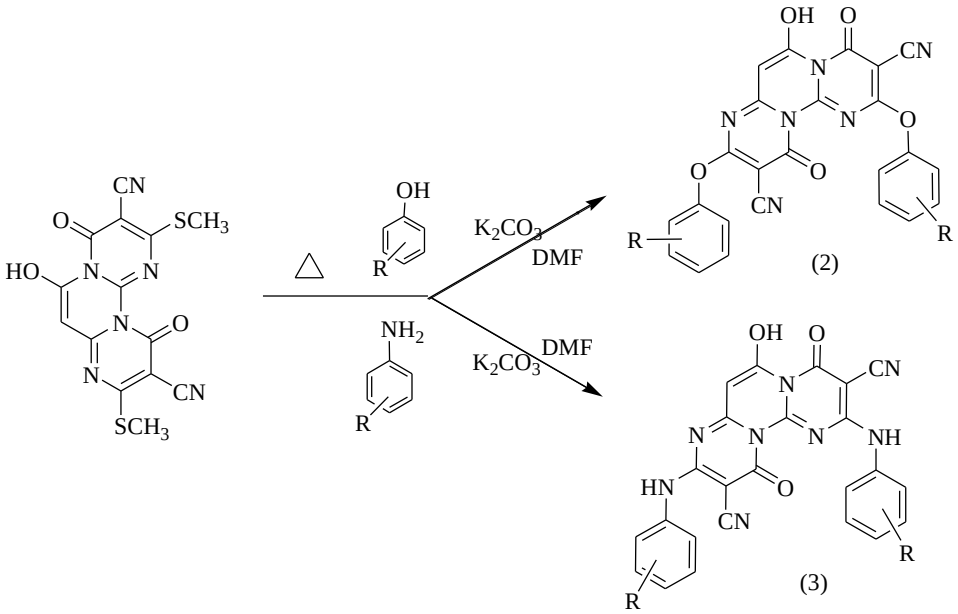
Scheme :

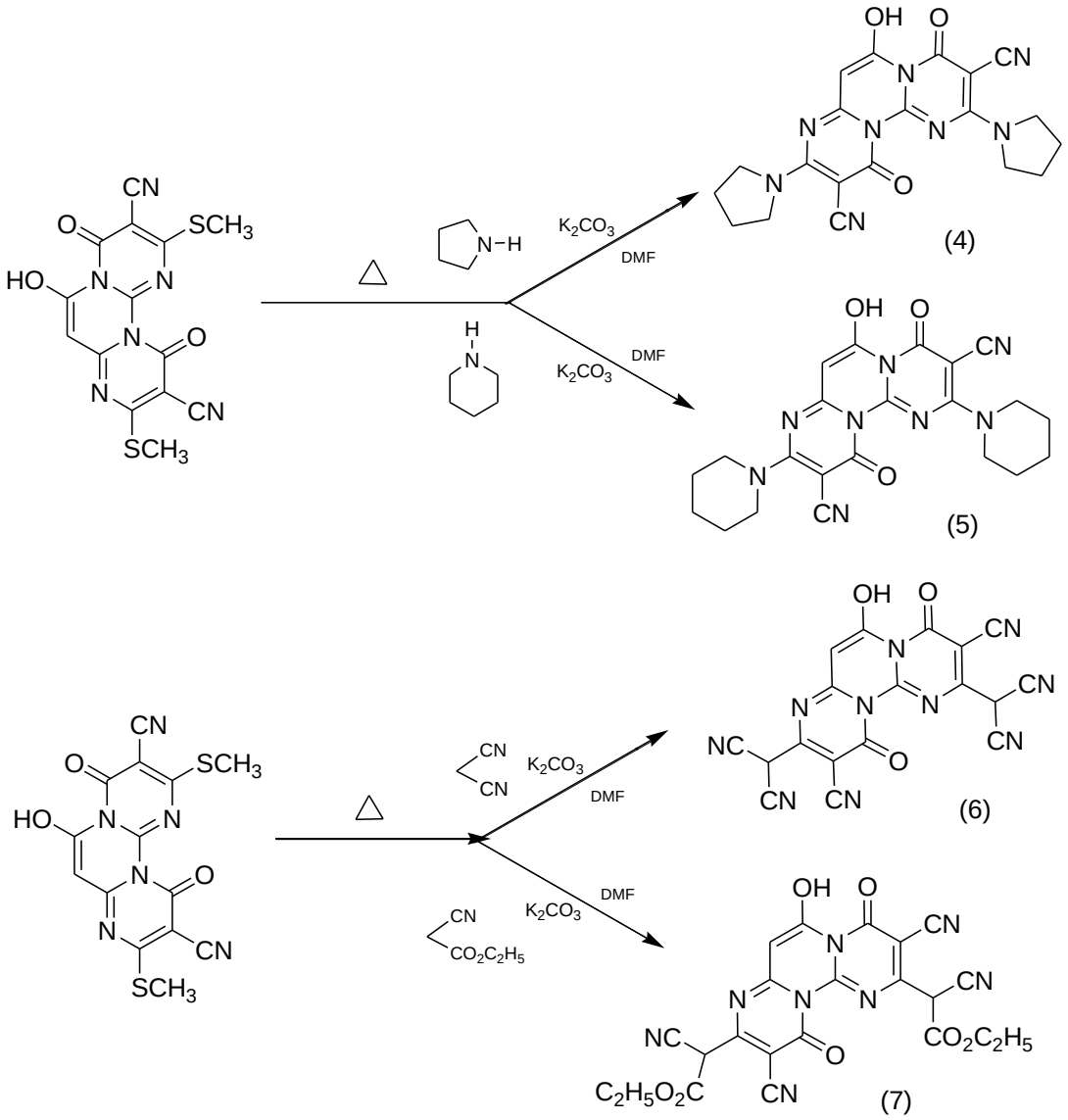
The guanidine nitrate (0.01 mole.) in RBF containing DMF solvent put catalytic amount of K_2CO_3 to heat and stir, reflux half hour, please drop ethyl cyanoacetate to reflux for 4 hour. After reaction complete then diluted with cold water and acidified. The precipitate is separated by filtration and dried under vacuum. They are recrystallised by ethanol. The resulting compound 2,6 diamino 4-hydroxy pyrimidine was further reacted with ethyl 2-cyano-3,3-bis(methylthio)acrylatein the presence of catalytic amount of K_2CO_3 in DMF refluxed for 4hour that offered 6-hydroxy-2,9-bis(methylthio)-4,11-dioxo-4H,11H-dipyrimido[1,2-a:1',2'-c]pyrimidine-3,10-dicarbonitrile (1). The compound (1) confirmed by IR, 1H and C^{13} NMR and MS analytical data.



Synthesis of Derivatives

A mixture of (1) and independently, various substituted aromatic amines, aromatic phenols, heteryl amines and active methylene compounds in DMF (10 ml) and anhydrous potassium carbonate (10 mg) was reflux for 4 to 6 hrs. The reaction mixture cooled to room temperature and poured into ice cold water. The separated solid product was filtered, washed with water and recrystallised using ethyl alcohol.





IV. Conclusion:

A Novel 6-hydroxy-2,9-bis(methylthio)-4,11-dioxo-4H,11H-dipyrimido[1,2-a:1',2'-c]pyrimidine-3,10-dicarbonitrile (1) and derivatives are synthesized by using simple and efficient chemistry and this synthesized compounds act as an electrophilic species and reacting with various nucleophiles. In compounds cyano and thiomethyl groups are at adjecent position it also undergo cyclization to give polycyclic heterocyclic compound.

1) 6-hydroxy-2,9-bis(methylthio)-4,11-dioxo-4H,11H-dipyrimido[1,2-a:1',2'-c]pyrimidine-3,10-dicarbonitrile.

IR: 3340, 3430, 1580, 2250,1645, 1660,1655.

^{1}H NMR: δ 2.25 (S, 3H, SCH_3), δ 2.5 (S, 2H, CH_2), δ 2.52 (S, 3H,SCH_3), 3.4(S, 1H, OH).

ESI-MS : 372.38.

Anal.Calcd for: $C_{14}H_8N_6S_2O_3$.

Mol. Formula: $C_{14}H_8N_6S_2O_3$.

Mol. Wt. 372.38.

2) 6-hydroxy-4,11-dioxo-2,9-diphenoxy-4H,11H-dipyrimido[1,2-a:1',2'-c]pyrimidine-3,10-dicarbonitrile.

IR :3345, 3420, 1585, 2230, 1635, 1650,1640.

^{1}H NMR : δ 2.4 (S, 2H, CH_2), δ 6.73 (d, 2H, Ar-H), δ 7.04 (d, 2H, Ar-H), 3.5(S, 1H, OH).

ESI-MS : . 462.37.

Anal.Calcd for: $C_{24}H_{10}N_6O_5$.

Mol. Formula: $C_{24}H_{10}N_6O_5$.

Mol. Wt. 462.37.

3) 6-hydroxy-4,11-dioxo-2,9-bis(phenylamino)-4H,11H-dipyrimido[1,2-a:1',2'-c]pyrimidine-3,10-dicarbonitrile.

IR :3360, 3425, 1570, 2240, 1640, 1665,1660.

^{1}H NMR : δ 2.22 (S, 2H, CH_2), δ 6.46 (d, 2H, Ar-H), δ 7.01 (dd, 2H, Ar-H).

ESI-MS : . 460.40 .

Anal.Calcd for: $C_{24}H_{12}N_8O_3$.

Mol. Formula: $C_{24}H_{12}N_8O_3$.

Mol. Wt. 460.40 .

4) 6-hydroxy-4,11-dioxo-2,9-di(pyrrolidin-1-yl)-4H,11H-dipyrimido[1,2-a:1',2'-c]pyrimidine-3,10-dicarbonitrile.

IR :3335, 3445, 1550, 2260, 1650, 1645,1665.

^{1}H NMR : δ 2.42 (S, 2H, CH_2), δ 2.8 (t, 4H, C-H), δ 1.59 (m, 4H, C-H), 3.3(S, 1H, OH).

ESI-MS : 418.40.

Anal.Calcd for: $C_{20}H_{18}N_8O_3$.

Mol. Formula: $C_{20}H_{18}N_8O_3$.

Mol. Wt. 418.40.

5) 6-hydroxy-4,11-dioxo-2,9-di(piperidin-1-yl)-4H,11H-dipyrimido[1,2-a:1',2'-c]pyrimidine-3,10-dicarbonitrile.

IR :3345, 3455, 1540, 2250, 1635, 1660,1655.

^{1}H NMR : δ 2.25 (S, 2H, CH_2), δ 2.7 (t, 4H, C-H), δ 1.5 (m, 6H, C-H), 3.2(S, 1H, OH).

.

ESI-MS : . 446.46.

Anal.Calcd for: $C_{22}H_{22}N_8O_3$.

Mol. Formula: $C_{22}H_{22}N_8O_3$.

Mol. Wt. 446.46 .

6) 2,2'-(3,10-dicyano-6-hydroxy-4,11-dioxo-4H,11H-dipyrimido[1,2-a:1',2'-c]pyrimidine-2,9-diyl)dimalononitrile.

IR :3365, 3450, 1575, 2240, 1640, 1665,1650.

^{1}H NMR : δ 2.35 (S, 2H, CH_2), 3.5(S, 1H, OH).

ESI-MS : 406.27.

Anal.Calcd for: $C_{18}H_2N_{10}O_3$.

Mol. Formula: $C_{18}H_2N_{10}O_3$.

Mol. Wt. 406.27.

7) Diethyl2,2'-(3,10-dicyano-6-hydroxy-4,11-dioxo-4H,11H-dipyrimido[1,2-a:1',2'-c]pyrimidine-2,9-diyl)bis(2-cyanoacetate).

IR :3340, 3460, 1565, 2245, 1645, 1650,1635.

^{1}H NMR : δ 2.23 (S, 2H, C-H), δ 3.12 (q, 2H, C-H), 1.30(t, 3H, C-H), δ 3.22 (q, 2H, C-H), 1.60(t, 3H, C-H), 3.3(S, 1H, OH).

ESI-MS : 500.37.

Anal.Calcd for: $C_{22}H_{12}N_8O_7$.

Mol. Formula: $C_{22}H_{12}N_8O_7$.

Mol. Wt. 500.37 .

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