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Research Article

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Synthesis and Characterization of Pyrimidine Derivatives of 1,3,4-Oxadiazole and 1,3,4-Thiadiazole

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ABSTRACT

*In the present work new and simple synthetic methods of 4-aryl-6-methyl-2-oxo-1,2,3,4 tetrahydropyrimidine-(5)-1,3,4-thiadiazole-2-amine **(3)** and 4-aryl-6-methyl-2-oxo-1,2,3,4 tetrahydropyrimidine-(5)-1,3,4-oxadiazole-2-amine **(3a)** are described. Compound **1** is converted to Carbothiamide **2** by the reaction with ethyl ester followed by thiosemicarbazide. Compound **2** has acted as key intermediate for both the final compounds. In one pathway, **2** is converted to corresponding thiadiazloe **3** by treatment with conc.H_2SO_4 and NH_3, and compound **3a** by treatment with I_2 followed by KI and NaOH to furnish the final compound. Structural elucidation is accomplished by IR, ^{1}H-NMR and Mass spectral data of the synthesized compounds.*

Key words : pyrimidine, thiadiazole, oxadiazole, carbothiamide, thiosemicarbazide.

INTRODUCTION

Pyrimidine derivatives have been found to be associated with diverse biological activities and numerous reports have appeared in the literature [1-5]. This highlighted their chemistry and use. The pyrimidine derivatives have remarkable pharmacological activity [6-7] and widely used in the field of anti-microbial, antiviral, etc. Oxadiazole and thiadiazole derivatives were shown to possess many biological activities including anti-inflammatory [8-9].

Such medicinal utilities of the pyrimidine derivatives prompted to synthesize the new pyrimidine thiosemicarbazide, 1,3,4-oxadiazole and 1,3,4-thiadiazole compounds. In this paper we have focused on the incorporation of pyrimidine [10-14], thiosemicarbazide [15-18], oxadiazole [19-20] and thiadiazole [21] in one frame work and we have an intention to scrutinize about the anti-bacterial activities in future.

EXPERIMENTAL SECTION

Melting points (mp) of all synthesized compounds were taken in open capillaries and are uncorrected. IR spectra (KBr) were recorded on a Perkin – Elmer 1300 FT IR spectrometer and ^{1}H-NMR were recorded on a Bruker WM-500 (500 MHz FT NMR) spectrometer using TMS as internal standard, Mass spectra were recorded on GCMS Spectrometer-Jeol GC mate spectrometer. All compounds gave satisfactory micro analytical results.

Purity of the synthesized compound was checked by TLC using Silica gel-G Plates using water-benzene as a solvent. Pyrimidine **1** was prepared by reported method.

Synthesis of 4-aryl-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-(5)-3-carbothioamide 2.
An equimolar mixture of compound **1** (0.01 mole) and thiosemicarbazide (0.01 mole) in acetone were refluxed for 8-10 hrs and allow to cool to form a yellow solid and it was recrystallized from alcohol. Melting point of the compound is 146^0C, yield 75%.

IR (KBr, cm^{-1}): 3242, 3115 cm^{-1}(N-H Str.), 2978 (C-H Str, Ar-H), 1724(C=O Str, CONH), 1647 (C=N Str.), 1313 (C-N Str.), 1090 (C=S Str.).
^{1}H-NMR (Acetone, δ): 8.34 (1H, br, s), 7.82-7.80(1H,m), 6.92(1H,br,s), 5.38(5H, d), 2.10 -1.99(3H, m), 1.17-1.15 3H,s).
GCMS: (m/z) = 305 m^+

Synthesis of 4-aryl-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-(5)-1,3,4-thiadiazole-2-amine 3.
Carbothioamide **2**. (0.01 mole) was dissolved in 5 ml conc.H_2SO_4. This solution was stirred at room temperature and left overnight. It was then poured into crushed ice. The resulting suspension was kept in ammonical water for 2 hrs, filtered and recrystallized from alcohol as white crystals. Melting point 125^0C, Yield 82%.

IR (KBr, cm^{-1}): 3328, 3173 (N-H Str.), 3105 (C-H Str. Ar-H), 2979 (C-H Str.), 1669 (C=O Str. CONH), 1574 (C=N Str.), 1118 (C-S Str.).
^{1}H-NMR(Acetone, δ): 9.24 (1H, s), 8.69 (1H, s), 7.30–7.27 (1H, m), 5.43 (1H, d, J = 3.0 Hz), 4.11-4.01 (2H, m), 2.45 (3H, s).
GCMS : (m/z) = 287 m^+

Synthesis of 4-aryl-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-(5)-1,3,4-oxadiazole-2-amine 3a.
Compound **2**. (0.01 mole) was added into 10 ml of 10% NaOH with cooling and shaking Iodine solution in KI (10%) was added gradually and shaking until the Iodine colour persisted. Heating was continued for 5 hrs and cooled and poured into ice-cold water. The solution was filtered and washed with cold water and little amount of carbon disulphide was added. The product was recrystallized from alcohol. Melting point 168^0C, Yield 85%.

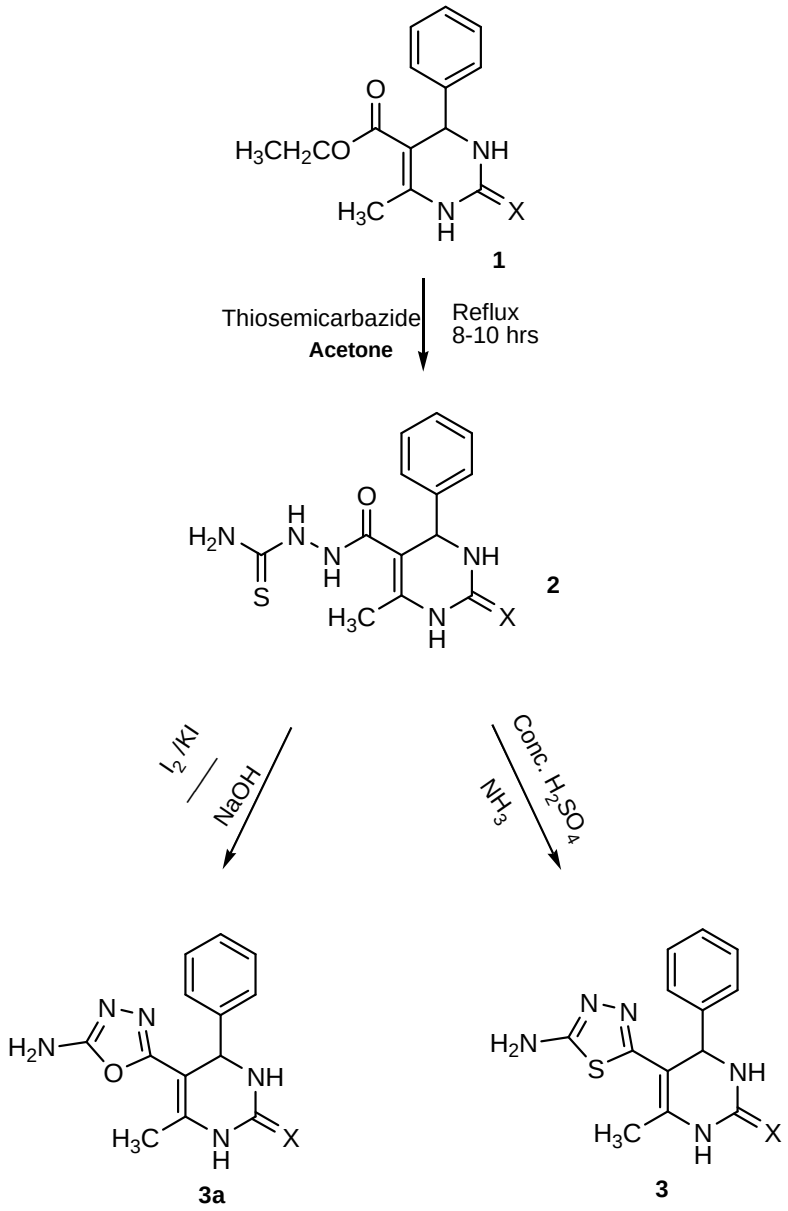
IR (KBr, cm^{-1}): 3245, 3117 (N-H Str.), 3060 (C-H Str. Ar-H), 2979 (C-H Str, CH_2), 1649 (C=N Str.), 1420 (C-O-C Str.), 1699 (C=O Str.).
^{1}H-NMR (Acetone, δ): 8.40 (1H, br), 7.42 – 7.3 (5H, m), 7.32 – 7.40 (1H, m), 6.95 (1H, br), 5.39 (1H, d, J= 3.5 Hz), 2.40 (3H, s).
GCMS: (m/z) = 271 m^+

RESULTS AND DISCUSSION

Compounds were synthesized as per the **scheme,** where 4-aryl-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-(5)-1,3,4-thiadiazole-2-amine (**3)** was synthesized by reacting 4-aryl-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-(5)-thiosemicarbazide with conc.H_2SO_4 and NH_3 by condensation reaction. 4-aryl-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-(5)-1,3,4-oxadiazole-2-amine (**3a)** was synthesized by reacting 4-aryl-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-(5)-thiosemicarbazide with I_2 followed by KI with NaOH. So the compound **(2)** (4-aryl-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-(5)-thiosemicarbazide) has acted as key intermediate for the synthesis of both the final compounds **3** and **3a**.

The intermediate compound **2** was synthesized by reacting 4-aryl-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine carboxylic ethyl ester **1** with thiosemicarbazide by condensation reaction. The structures of all synthesized compounds were confirmed by IR, NMR and Mass analysis (Table-1).

Scheme



X = O, S *R= C_6H_5*

Table – 1: Physical and analytical data of compounds, 2, 3 and 3a

Compounds	Mol. Formula	M.Wt.	R	Yield %	M.P ^{0}C	(Calcd)% C	(Calcd)% N
2	$C_{13}H_{15}N_5O_2S_1$	305	C_6H_5	75	146	51.35	23.03
3	$C_{13}H_{13}N_5O_1S_1$	287	C_6H_5	82	125	54.59	24.48
3a	$C_{13}H_{13}N_5O_2$	271	C_6H_5	85	168	57.82	25.93

CONCLUSION

In conclusion, compound **2** is used for the synthesis of 1,3,4-oxadiazole tetrahydropyrimidine **3** using I_2 / KI and NaOH, similarly 1,3,4-thiadiazole tetrahydropyrimidine using H_2SO_4 / NH_3 for the first time and yields are excellent. This method can be extended largely for the synthesis of more substituted compounds. This condition will tolerate the presences of different constituents of aromatic ring.

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