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Research Article

SYNTHESIS AND CHARACTERISATION OF 8-HYDROXY -3-(4-HYDROXY PHENYL)-8-METHYL-7-(SUBSTITUTED PHENYL HYDRAZONO)-7, 8-DIHYDRO [1, 2, 4] TRIAZOLO [3, 4-b] [1, 3, 4] THIADIAZEPIN-6 (5H) –ONE

S. S. RAJPUT

Department of Chemistry, S.V.S's Dadasaheb Rawal College Dondaicha, Dhule, India. Email: rajputss65@gmail.com

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ABSTRACT

The primary amines were converted ethyl -2- aryl hydrazono -3 oxo – butyrates $_{1a\text{-}e}$. 4- Hydroxyl benzhydrazine was converted to 4 amino -3- (4-hydroxyl phenyl) -5- mercapto -1, 3, 4 triazole 2. This 1,2,4 triazole on condensation with ethyl -2- aryl hydrazono-3 oxo- butyrate's in acetic acid formed 1,3,4 – thiadiazepines **3**$_{a\text{-}e}$.

Keywords: Oxobutyrates, Mercapto 1, 2, 4 - triazole, 1, 3, 4 - thiadiazepines.

INTRODUCTION

The progress achieved in the synthesis of heterocyclic compounds with biological potential is due to improvement of methodological study of tested substances too. Thiazepinones, benzothiazepines and other thiazepine derivatives are moieties whose biological activity has received much attention [1-5]. However [1, 3, 4,] thiadiazepine are relatively unknown heterocycles and may be due to absence of adequate method of synthesis no pharmacological tests have been published.

MATERIALS AND METHODS

All the melting points were determined by open capillary method and are uncorrected. The purity of compound was monitored by TLC on silica gel coating aluminium plate using U.V. light as visualizing agent. The I.R. spectra (KBr in cm^{-1}) were recorded on Perkin-Elmer Spectrophotometer in the range of 4000-400 cm^{-1}. The ^1H NMR Spectra were recorded on Varion 500 MHz NMR Spectrophotometer using DMSO-d^6 as a solvent and TMS as an internal standard (chemical shift in δ ppm). C, H, N determinations were run on CarloErba 1108 (CHNS) Elemental analyzer.

General procedure for the preparation of Ethyl-2-substituted phenyl hydrazono-3-oxobutyrates (1a-e):

Substituted aniline (0.01mol) was dissolved in mixture of con.HCl (5ml) and water (8ml) and cooled to 0 ^0C in an ice bath. To it a cold aqueous solution of sodium nitrate (1gm) was added. The diazonium salt solution was filtered in to cooled solution of ethyl aceto- acetate (0.01mol) and sodium acetate (0.12mol) in 25ml of ethanol and the resulting yellow solid washed with water and then recrystallised from alcohol to furnished **1**$_{a\text{-}e}$. 1_a - M.P. 88 ^0C (86%), 1_b- M.P. 68 ^0C (87%), 1_c - M.P. 118 ^0C (76%), 1_d -M.P. 64 ^0C (84%), 1e-M.P.85^0C (76%).

General procedure for the preparation of 1-amino- 2-mercapto -5-(4-hydroxy phenyl) -1, 2, 4- triazole (2):

The 4- hydroxybenhydrazide (0.01 mol) was added to absolute alcohol (50ml) containing KOH (1.9gm) at room temperature. Carbon disulfide was added (2.3gm, 0.013mol) and the mixture stirred at room temperature for 10 hrs.The mixture was diluted with ether (30ml) and stirred for further 1 hr. The potassium salt was used for the next stage without further purification. Hydrazine hydrate (99%, 0.02mol) was gradually added to above potassium salt (0.01mol) dissolved in water (20ml) with stirring and the mixture changed to deep green. It was then cooled at 5 ^0C and acidified with con.HCl to PH 1.00. A white solid separated out which was filtered, wash with water and purified by recrystallization from ethanol to afford the triazole, **2**.Yield- 72% M.P. 264-266 ^0C. I.R (KBr): 3306 (OH), 3120 (NH), 2591 (SH), 1614(C=N),1515-1442(Ar).^1H-NMR(DMSO-d^6)δ-5.7(2H,S,NH_2),13.7(1H,S,SH),9.9 (1H,S,OH),7.8-7.6 (4H,M,Ar). MS: M/Z (M^+): 209.0 Anal. Calculated for $C_8H_8N_4OS$: C, 46.14; H,3.87; N,26.90; found : C,46.16; H,3.65; N,26.78.

General procedure for the preparation of 1, 3, 4- thiadiazepine (3$_{a\text{-}e}$**):**

To Compound $1_{a\text{-}e}$ (0.001mole) dissolved in glacial acetic acid (20ml), mercapto 1, 2, 4-triazole 2 (0.001mole) in acetic acid was added and the mixture was refluxed for 6 hrs. The reaction mixture on cooling was filtered and purified by recrystalliszation from ethanol to give **3**$_{a\text{-}e}$.

8-hydroxy -3-(4-hydroxyphenyl)-8-methyl -7-(2-(2- nitrophenyl hydrazono)-7,8-dihydro-[1,2,4] triazolo[3,4-b] [1,3,4]thiadiazepin -6(5H)-one(3$_a$**):**Yield – 72% M.P. 90-92 ^0C IR(KBr) Cm^{-1} - 1692(C=0), 3160 (-N-H), 2857 (-CH_3), 2600 (-OH); 1506 (C=N), 745 (C-S-C), 840 (C-N, triazine) ^1H- NMR(DMSO- d^6): δ, 1.3 (S,CH_3), 3.3 (S, OH) 5.7(S, OH), 7.3-6.8(m, 4H,Ar) 8.2-7.8 (m,4H,Ar), 13.7 (S,1H,NH),13.3(S,1H,NH); Anal. Calculated for $C_{18}H_{15}N_7O_5S$: C, 48.98; H, 3.43; N, 22.21 Found: C, 48.83; H, 3.40; N, 22.13.

7-[2-(2-chlorophenyl)hydrazono]-8-hydroxy-3-(4-hydroxyphenyl) 8-methyl-7,8-dihydro-[1,2,4] triazolo[3,4-b][1,3,4]thiadiazepin-6(5H)-one(3$_b$**):** Yield – 70% M.P. 120-122 ^0C IR(KBr) Cm^{-1} - 1666(C=0), 3221 (-N-H), 2823 (-CH_3), 2638 (-OH); 1521 (C=N), 760 (C-S-C), 847 (C-N, triazine); ^1H- NMR(DMSO- d^6): δ, 1.2 (S,CH_3), 3.3 (S, OH) 5.7(S, OH), 7.1-6.6(m, 4H,Ar) 7.8-7.4 (m,4H,Ar), 11.2 (S,1H,NH),12. 5 (S, 1H, NH)**; Anal**. Calculated for $C_{18}H_{15}ClN_6O_3S$: C, 50.18; H, 3.51; N, 19.50 Found: C, 50.13; H, 3.42; N, 19.52.

7-[2-(4-chlorophenyl)hydrazono]-8-hydroxy-3-(4-hydroxyphenyl) 8-methyl-7,8-dihydro-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazepin-6(5H)-one(3$_c$**):**Yield–67%M.P.210-212^0C; IR(KBr) Cm^{-1} - 1666(C=0), 3171 (-N-H), 2850(-CH_3), 2600 (-OH); 1506 (C=N), 747 (C-S-C), 837 (C-N, triazine); ^1H- NMR(DMSO- d^6): δ, 1.2 (S,CH_3), 3.3 (S, OH) 5.7(S, OH), 7.8-7.6(m, 4H,Ar),7.4-6.8(m,4H,Ar),13.7 (S,1H,NH),11.5(S,1H,NH);Anal. Calculated for $_{18}H_{15}ClN_6O_3S$: C,50.18; H,3.51; N,19.50 Found: C,50.10; H,3.53 N,19.50.

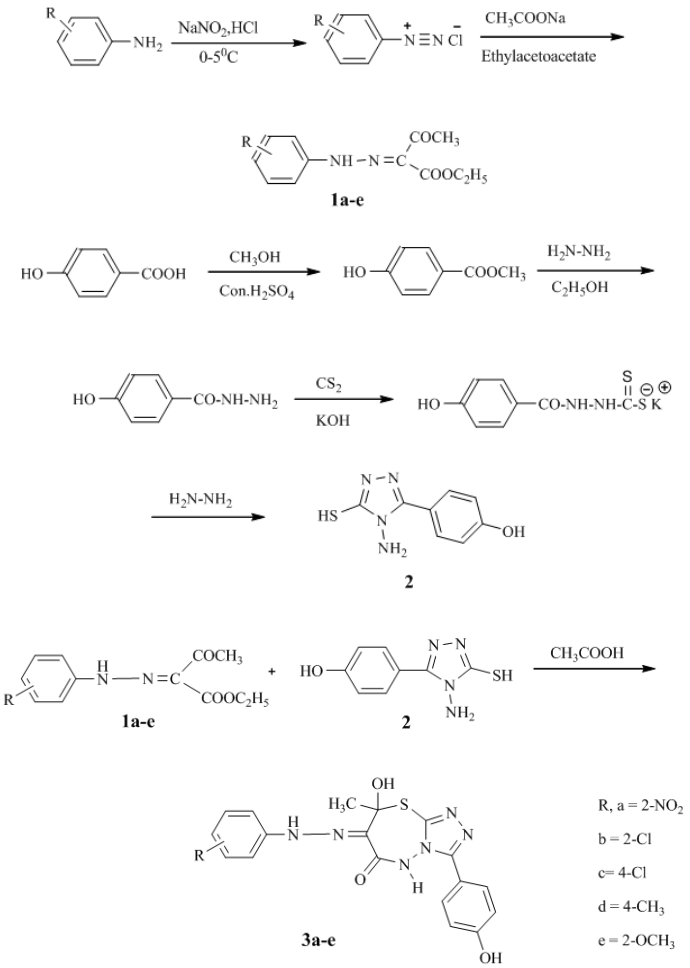
8-hydroxy-3-(4-hydroxyphenyl)-8-methyl-7-(2-(2-O-tolyl hyrozono)-7,8-dihydro-[1,2,4] triazolo[3,4-b] [1,3,4] thiadiazepin-6(5H)-one(3$_d$**):** Yield – 68% M.P. 103-105 ^0C IR(KBr) Cm^{-1} - 1665(C=0), 3129 (-N-H), 2980 (-CH_3), 2513 (-OH); 1521 (C=N), 797 (C-S-C), 821 (C-N, triazine);^1H-NMR(DMSO-d^6):δ,1.8(S,CH_3), 2.4(S,CH_3),3.3(S,OH),5.7(S,OH),7.3-6.8(m,4H,Ar),7.8-7.4(m,4H,Ar), 11.8(S,1H,NH),11.3(S,1H,NH) .Anal. Calculated for $C_{19}H_{18}N_6O_3$: C, 55.60; H, 4.42; N, 20.48 Found: C, 55.54; H, 4.38; N, 20.69.

8-hydroxy-3-(4-hydroxyphenyl)-7-[2-(2-methylphenyl) hydrazono]-8-methyl-7,8-ihydro-[1,2,4] triazolo[3,4-b][1,3,4] thiadiazepin-6(5H)-one(3e): Yield – 72% M.P. 115-117 ^0C IR(KBr) Cm^{-1} - 1664(C=0), 3153(-N-H), 2838 (-CH_3), 2624 (-OH); 1521 (C=N),

745 (C-S-C), 842 (C-N, triazine) ^{1}H- NMR(DMSO- d^6): δ, 1.2 (S,CH_3), 3.9 (S, OCH_3);3.3(S,OH) 4.3(S, OH), 7.7-7.5(m, 4H,Ar); 7.1-6.8 (m,4H,Ar), 12.5(S,1H,NH),10.3(S,1H,NH) .Anal. Calculated for $C_{19}H_{18}N_6O_4S$: C, 53.51; H, 4.25; N, 19.71 Found: C, 53.42; H, 4.21; N, 19.73.

RESULTS AND DISCUSSIONS

The synthesis involves treatment of ethylacetoacetate (EAA) with different diazonium salts in presence of sodium acetate to yield ethyl -2- aryl hydrazono-3 oxo- butyrate's [6]. The mercaptotriazoles are important class of compounds due to presence of functional group at C_1 and C_2 serve as intermediates for large number of heterocyclic compounds having wide range of biological properties. 1-amino-2-mercapto-5-[4-hydroxy phenyl] -1, 2, 4- triazole was prepared from 4-hydroxy methyl benzoates [7] by the treatment with hydrazine hydrate to get 4-hydroxylphenylhydrazide, which was then converted to potassium salt by stirring with carbon disulfide and potassium hydroxide at room temperature, finally 1-amino-2-mercapto-5-(4-hydroxy phenyl) was obtained by refluxing potassium salt with hydrazine hydrate in ethanol for 6 hours. The condensation of ethyl-2- aryl hydrazono-3- oxo-butyrate's with 4-amino-3-(4-hydroxy phenyl)-5-mercapto 1, 2, 4 triazole in acetic acid furnished 1, 3, 4- thiadiazepines **3$_{a-e}$.Scheme –I.**



SCHEME-I

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