International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Impact Factor 2024: 7.101

Microwave Assisted Synthesis and Characterization of 2,7-(substitutedphenyl)-3-phenyl-2,3,7,7a-tetrahydrothiazolo[4,5-d]pyrimidin-5(6H)- One Derivatives

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Abstract: ***Microwave assisted synthesis of thiazolopyrimidine derivatives is economic, convenient and environment friendly method of synthesis. In Scientific microwave oven the rate of reaction enhance due to polarization of molecules. In this reaction, 2,3-substitutedphenylthiazolodin-4-one(0.01M), aromatic aldehyde (0.015M) and urea(0.01M) in presence of pyridine catalyst and DMSO solvent undergo condensation reaction on microwave irradiation for 2-2.5 minutes, synthesized 2,7-(substitutedphenyl)3-phenyl-2,3,7,7a-tetrahydrothiazolo[4,5-d]pyrimidin-5(6H)-one. -The targeted compounds were analysed by IR, NMR, CMR Spectrum and CHNS elemental detection. Melting point are uncorrected and carried out on Thieles apparatus.***

Keywords: Thiazolidin-4-one-, 2,7-(substitutedphenyl)3-phenyl-2,3,7,7a-tetrahydrothiazolo[4,5-d]pyrimidin-5(6H)-one, microwave irradiation.

1. Introduction

Heterocyclic compounds have important medicinal properties. The most commonly present heterocyclic compounds in drugsare five or six membered. It contains one or more heteroatom in the structure like nitrogen, oxygen, sulfur. Heterocyclic systems have widely observed in natural products such as nucleic acids, plant alkaloids, anthocyanins, flavones, haemoglobin and chlorophylls. From many years, It has been noticed that interesting biological activities[1,2]are associated with thiazole derivatives. Thiazoles derivatives were found in drug for the treatment of allergies[3], hypertension[4], inflammation[5], schizophrenia[6], bacterial[7], HIV infections[8], hypnotics[9]. Similarly, Thiazolopyrimidine derivatives are also show distinguishable anti- inflammatory activity to that of some standard drugs in vivo, with no or minimal ulcerogenic effects[10,11]. They have been also useful as analgesic and antiparkinsonian agents[12], modulators of Transient Receptor Potential Vanilloid–receptor 1 (TRPV1)[13], anticancer agents[14-16], pesticides[17], phosphate inhibitors[18-19], acetylcholinesterase inhibitors[20] and antimicrobial susbtances[21-23].

Microwave assisted synthesis of heterocyclic compounds require less time, produce high yield and consume less energy[24]. It is one of the environmental benign methods of synthesis of heterocyclic compounds as compared to conventional method. Conventional method consumes more time, fuel and reduces yield of compounds. Therefore, microwave synthesis is superior method than conventional one.

2. Results and Discussion

All the reactions have carried out in scientific microwave oven (Scientific microwave system model RG311L1, 700w, 2450MHz). Melting points of synthesized compounds has determined by open capillary method and are uncorrected. IR spectra have recorded on instrument Perkin Elmer – Spectrum RX- FTIR spectrometer. 1H NMR and 13C NMR spectra have recorded on Advance II 400 NMR spectrometer in DMSOusing TMS as internal standard. The elemental analysis has carried out using Themofinnigan CHNS analyzer. The purity of compound has determined by TLC on silica gel using an eluent acetone and alcohol. The migrated compounds have visualized by iodine vapours. The physical data of all these compounds are summarized in table.

Scheme 1.Experimental method of preparation of 2,7-(substitutedphenyl)-3-phenyl-2,3,7,7a-tetrahydrothiazolo[4,5- d]pyrimidine-5(6H)-one:-the Target compound have been synthesized by microwave irradiation of 2- (substitutedphenyl)-3-phenylthiazolidin-4-one (0.01M), aldehyde (0.015M), and urea (0.01M) in presence of pyridine catalyst and DMSO solvent on medium power for 2.0 minutes. After completion, reaction mixture has cooled to room temperature and poured over crushed ice, filter out and crystallize inethanol as a solid with maximum yield and appropriate melting point.

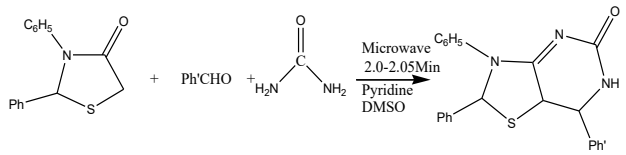

Figure 1: Chemical Reaction

Table 1: Molecular formulae, melting point and percentage yield of compound Ia- Ij

S. No.	COMPOUND	% Yield	Melting Point (^{0}C)	Molecular Formula
Ia	2,3,7-triphenyl-2,3,7,7a-tetrahydrothiazolo[4,5-d]pyrimidin-5(6H)-one	82.4	250	C23H19N3OS
Ib	7-(4-nitrophenyl)-2,3-diphenyl-2,3,7,7a-tetrahydrothiazolo[4,5-d]pyrimidin-5(6H)-one	77.5	280	C23H18N4O3S
Ic	7-(2-chlorophenyl)-2,3-diphenyl-2,3,7,7a-tetrahydrothiazolo[4,5-d]pyrimidin-5(6H)-one	84.8	272	C23H18N3OSCl
Id	7-(2,4-dichlorophenyl)-2,3-diphenyl-2,3,7,7a-tetrahydrothiazolo[4,5-d]pyrimidin-5(6H)-one	87	295	C23H17N3SOCl2
Ie	7(2-hydroxyphenyl)-2,3-diphenyl-2,3-7,7a-tetrahydrothiazolo[4,5-d]pyrimidin-5(6H)-one	72.1	261	C23H19N3O2S
If	2-(4-nitrophenyl)-3,7-diphenyl-2,3,7,7a-tetrahydrothiazolo[4,5-d]pyrimidin-one	79.5	280	C23H18N4O3S
Ig	2,7-bis(4-nitrophenyl)-3-phenyl-2,3,7,7a-tetrahydrothiazolo[4,5-d]pyrimidin-5(6H)one	75.2	300	C23H17N4O5S
Ih	7-(2-chlorophenyl)-2-(4-nitrophenyl)-3-phenyl-2,3,7,7a-tetrahydrothiazolo[4,5-d]pyrimidin-5(6H)-one.	82.3	301	C23H17N4O3SCl
Ii	7-(2,4-dichlorophenyl)-2-(4-nitrophenyl)-3-phenyl-2,3,7,7a-tetrahydrothiazolo[4,5-d]pyrimidin-5(6H)-one	85.2	318	C23H16N4O3SCl2
Ij	7-(2-hydroxyphenyl)-2-(4-nitrophenyl)-3-phenyl-2,3,7,7a-tetrahydrothiazolo[4,5-d)pyrimidin-5(6H)-one	70	290	C23H18N4O4S

3. Conclusion

The ten novel 2,7-(substitutedphenyl)-3-phenyl-2,3,7,7a-tetrahydrothiazolo[4,5- d]pyrimidine-5(6H)-one derivatives containing thiazolidinone and pyrimidine ring of high biological application have been synthesized under microwave with green protocol in maximum yield. The structures of newly synthesized compounds have been confirmed by spectral data (IR, H^1NMR, C^{13} NMR and CHNS analyzer)

4. Experimental Section

Preparation of 2,3,7-triphenyl-2,3,7,7a-tetrahydrothiazolo[4,5-d]pyrimidin-5(6H)-one(Ia) (Ph&Ph' – C_6H_5): A mixture of 2,3-diphenylthiazolidin-4-one (0.01M), benzaldehyde (0.015M), and urea (0.01M) irradiated in microwave oven on medium power for 90 second in presence of pyridine and DMSO (5ml) solvent. After completion, reaction mixture have been cooled to room temperature and poured on crushed ice, filtered out and crystalized in ethanol as a crystalline solid with 81% yield and 250^{0}C melting point. IR(KBr) (Umax in cm-1) 3434 (Broad N-H strching), 3030 (C-H aromatic stretching), 2916 (C-H aliphatic), 1951 (monosubstituted aromatic streching), 1670 (C=O stretching), 1593 (C=N streching) 691-747 (monosubstituted aromatic bending vibration); 1H NMR 400 MHz, DMSO-d6 (∂ value in PPM) 3.8 (d, J3=16,1H), 4.0 (d, J3=16, 1H), 6.5 (S, 1H) 7.11-7.38 (m, 15H aromatic); C13 NMR DMSO d6 (∂ value in PPM) : 63.33 (C2,C7), 32.59 (C7a), 139.95 (C3a), 170.39 (C5), 137.54 (C8, C20), 125.38 (C9, C13,C21, C25), 128.56 (C10, C12,C22, C24), 126.25(C11, C17,C23), 126.87 (C15, C19), 128.31 (C16, C18) , 128.51 (C14). Elemental analysis:- Carbon 67.65%, Hydrogen 5.08%, Nitrogen 5.04%, Sulphur 10.49%;

Preparation of 2-(4-nitrophenyl)-3,7-diphenyl-2,3,7,7a-tetrahydrothiazolo[4,5-d]pyrimidin-5(6H)-one (If)(Ph-C_6H_5& Ph'-$C_6H_4NO_2$) :- A mixture of 2-(4-nitrophenyl)-3-diphenylthiazolidin-4-one(0.01M), benzaldehyde(0.015M), and urea (0.01M) irradiated in microwave oven on medium power for 120 second in presence of pyridine and DMSO (5ml) solvent. After completion, reaction mixture have been cooled to room temperature and poured on crushed ice, filtered out and crystalized in ethanol as a pale yellow crystalline solid with 83% yield and 280oC melting point. IR(KBr) (Umax in cm-1) 3320 (N-H streching), 3074 (C-H aromatic stretching), 2981 (C-H aliphatic), 1875-1933 (P-disubstituted aromatic streching), 1689 (C=O stretching), 1598 (C=N streching) 837-901 (disubstituted aromatic bending vibration); 1H NMR 400 MHz, DMSO-d6 (∂ value in PPM) 3.87 (d, J3=15.6,1H), 4.01 (d, J3=15.6, 1H), 6.56 (S, 1H) 7.45 (d, J3=4.92, 2H), 8.08 (d, J3=4.92, 2H), 7.05-7.45 (m, 10Ar-H, N-H); C13 NMR DMSO d6 (∂ value in PPM) : 64.42 (C2,C7), 33.4 (C7a), 147.92 (C3a), 171.24 (C5), 136.88 (C8, C20), 128.02 (C9, C13), 125.51 (C10, C12), 128.02 (C11), 146.68 (C14), 124.44 (C15, C19,C21, C25), 129.41 (C16, C18, C22, C24), 129 (C17, C23). Elemental analysis:- Carbon 57.71%, Hydrogen 4.34%, Nitrogen 8.6%, Sulphur 10.85%;

Similarly compound Ia- Ij have been prepared. Molecular formulae, melting point and percentage yield are reported in table 1.

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