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NOVEL ONE POT SYNTHESIS OF 3, 5-(SUBSTITUTED PHENYL)-6 -PHENYL-3, 3A, 5, TRIHYDRO-2H-PYRAZOLO[3, 4-D] THIAZOLES BY GREEN METHOD

Sonal S. Mundhada
Department of Chemistry, Brijlal Biyani Science College, Sant Gadgebaba Amravati University Amravati, Maharashtra, 444602, India.
*E-mail: sonal.mundhada@gmail.com

ABSTRACT
Organic reactions on solid phase support represent eligibility and convenient way of traditional synthetic processes. Aluminates used in surface chemistry play an important role in their performance as catalyst and catalyst supporter. The one-pot solid-phase synthesis of novel 3,5-(substituted phenyl)-6- phenyl-3,3a,5,-trihydro-2H-pyrazolo[3,4-d]thiazoles(IIa-IIh) by condensation of 2-(substituted phenyl)-3-phenylthiazolidin-4-one(Ia-Ih) (0.01M) with hydrazinehydrate(0.015M)and aromatic aldehyde (0.02M) in presence of solid-phase catalyst alumina under microwave irradiation, then it was cooled at room temperature and poured into dilute hydrochloric acid, the product thus obtained was filtered, washed with water and recrystallized from ethanol to get the compounds (IIa-IIh).
Keywords: Aromatic Aldehyde, Hydrazine Hydrate, 1, 3-Thiazolidin-4-ones.

INTRODUCTION

To reduce the environmental threat there is a need for clean chemical processes including monitoring analysis, synthetic procedures, catalysts and reaction conditions. To achieve these goals, green chemistry is being developed that based on innovative and unconventional synthetic procedures including reactions carried out in water[1-2](normal[3] and superheated under high pressure[4]), in supercritical fluids[5-6], in ionic liquids[7], in micro emulsions[8], in solvent-free conditions[9], by ultrasounds[10] and microwaves[11-12] Pyrazoline derivatives have been found to possess considerable biological activities, which stimulate research activity in this field.[13-17] Their prominent effects are antimicrobial[18], stimulation of central nervous system[19], immunosuppressive[20], anti-inflammatory[21], anti-fertility[22], anti-implantation[23], insecticidal[24], antiproteolytic[25] activities. Pyrazolines are found to be useful as antioxidant composition in polymers[26] and the treatment of cerebral edema.[27]

EXPERIMENTAL

Material and Methods

All chemicals used were of analytical grade. All the synthesized compounds have been characterized based on chemical properties, elemental and spectral analysis. The melting points were measured in an open glass capillary and are uncorrected.IR spectra in KBr were recorded on instrument Perkin Elmer - Spectrum RX-IFTIR. ^{1}H-NMR spectra were recorded on FT NMR Spectrometer model Advance-II (Bruker) It's ^{1}H frequency is 400 MHz 13C the frequency is 100 MHz ($CDCl_3$ and DMSO-d6) using TMS as an internal standard. All reactions were monitored by TLC using silica gel 60-f-254 plates. All reactions were carried out in a scientific microwave oven (Scientific microwave system model RG31lL1, 700w, 2450MHz). Satisfactory C, H, N analysis were carried out for most of the compounds on Thermo Scientific (FLASH 2000) CHN Elemental Analyzer at RSIC, Punjab University, Chandigarh.

Synthesis of 3,5-(substituted phenyl)-6 phenyl-3,3a,5,-trihydro -2H-pyrazolo[3,4-d] thiazoles (IIa-IIh)

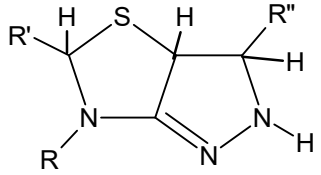
The reaction is completed in the following two steps:

Synthesis of 2-(substituted phenyl)-3-phenylthiazolidin-4-ones (Ia-Ih)

A neat reaction technology for one-pot synthesis of the starting material of 2-(substituted phenyl)-3-phenylthiazolidin)-4-ones by condensation of different aromatic aldehydes (0.01M), aniline(0.01M), and thioglycolic acid(0.01M), Carried out under scientific microwave oven. The irradiation time is 1-1.5 min. The reaction mixtures were cooled at room temperature and poured into ice-cold water. The products thus separated were filtered and crystallized from ethanol to get fine crystals of 2-(substituted phenyl)-3-phenylthiazolidin-4-one. (Ia- Ih) compounds.

Synthesis of 3,5-(substitutedphenyl)-6 phenyl-3,3a,5,-trihydro -2H-pyrazolo[3,4-d] thiazole(IIa-IIh)

This section reported the one-pot solid-phase synthesis of novel 3,5-(substitutedphenyl)-6 phenyl-3,3a,5,-trihydro-2H-pyrazolo[3,4-d] thiazoles (IIa-IIh) by condensation of 2-(substituted phenyl)-3-phenylthiazolidin-4-one(Ia- Ih)(0.01M) with hydrazine hydrate(0.015)and aromatic aldehyde (0.02M) in presence of solid-phase catalyst Alumina under microwave irradiation, then mixture was cooled at room temperature and poured into dilute hydrochloric acid , the product thus obtained were filtered, washed with water and recrystallized from ethanol to get the compounds (IIa-IIh).



(IIa-IIh)
Fig.-1

Analytical Discussion

Synthesis of 3-(2,4-dicholorophenyl)-5,6-diphenyl-3,3a,5,-trihydro-2H-pyrazolo[3,4-d] thiazole(IIb)-

The compound (IIb) is a brown crystalline solid having M. P..254^{0}C,molecular formula $C_{22}H_{17}Cl_2N_3S$, %C -61.97, %N-9.86 , %S -7.52, %H- 4.02 %Cl-16.63.

Spectral Study (IR Study in cm^{-1})

3332,m,NH Strech ,3032,s, C-H(aromatic), 2924,w, C-H stretch(aliphatic), 1952-1814,m, Combination band, 1671,s, C=N, 1595,1496,1456,s, C=C, 1496,m, NH bend,1385,s,C-N, 1112,1075,s,C-Cl aryl, 898,s, 1,2,4 trisubstituted oop, 730,693,s, Monosustituted oop.

(PMR in δ ppm) -3.54,s(NH), 4.02 ,d(-CH(J=1.4)), 4.06,d(-CH (J=1.4), 6.5,s,(-CH),7.40,d,2H, (Ar-H(-CH)J=8.5 Hz , 7.31,d,2H,(Ar-H(-CH)J=8.5 Hz , 7.21-7.32,m,8H, Ar-H .

The CMR spectrum of compound (IIb) was reported in (DMSO-d6) with TMS as an internal standard. The observed chemical shifts can be correlated as follows: C_3=C_5(63.48), C_{3a}(32.73), C_{6a}(170.49), C_7(140.04), C_8=C_{12}(125.48), C_9=C_{11}=C_{17}=C_{15}(128.62), C_{10}(124), C_{13}(136), C_{14}=C_{18}(129.97), C_{16}(126.97), C_{19}(137.64), C_{20}(128.42), C_{21}=C_{23}(128.67), C_{22}=C_{24}(126.36).

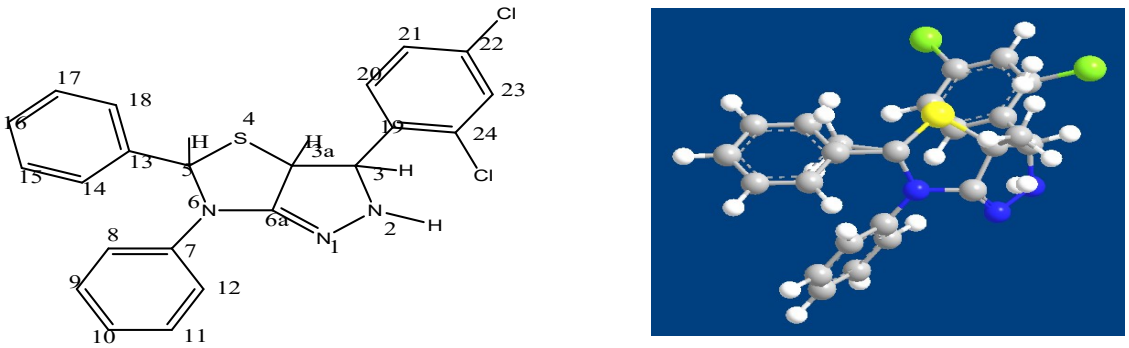
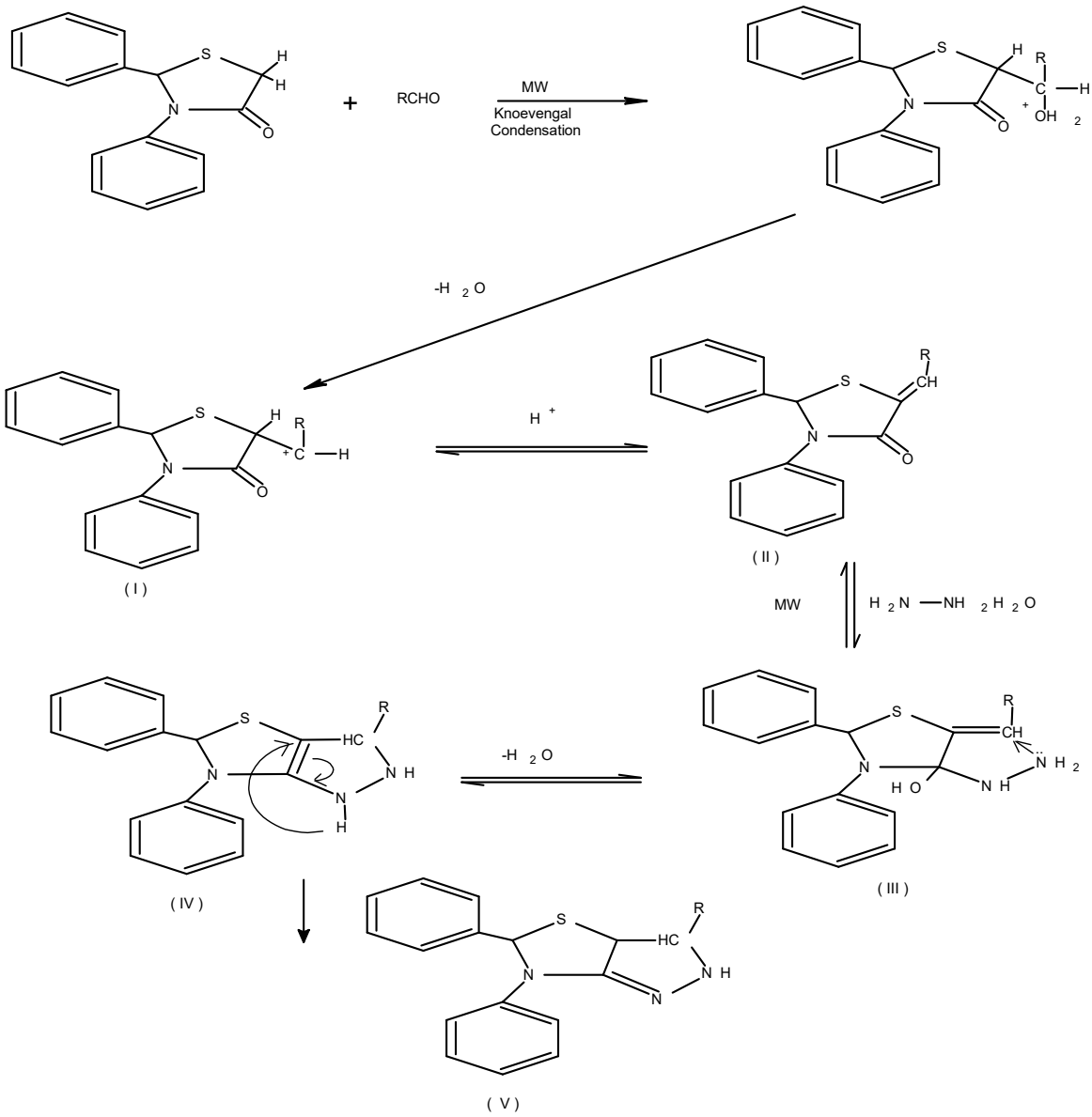


Fig.-2

Probable Mechanism

In the present work, three-component condensation between thiazolidione, aldehyde and hydrazine hydrate over basic alumina in solvent free condition under microwave irradiation lead to the target molecules. In this proposed mechanism, the first step concerned with Knoevenagel condensation of thiazolidione and aldehyde *in situ* by absorption at basic alumina. Being M.W. transparent basic alumina provides surface and also catalyses the reaction β unsaturated ketone through carbonium ion intermediate. In second step nucleophilic attack of nitrogen of the reagent on electron-deficient carbonyl carbon of thiazolidione and the carbonyl oxygen gets hydroxylated. At end nitrogen of the hydrazine hydrate bond with β carbon of intermediate II leads to pyrazoline molecule through cyclodehydration.



Scheme-1

Synthesis of 3-(4-bromophenyl)-5-(2,4-dicholorophenyl)-6-phenyl-3,3a,5,-trihydro-2H-pyrazolo[3,4-d]thiazole (IId)

The compound (IId) is a brown crystalline solid having M. P..267^{0}C, the molecular formula of the compound as $C_{22}H_{16}BrCl_2N_3S$.

Table-1: Synthesis of 3,5-(substituted phenyl)-6 phenyl-3,3a,5,-trihydro -2H-pyrazolo[3,4-d] thiazoles (IIa-IIh).

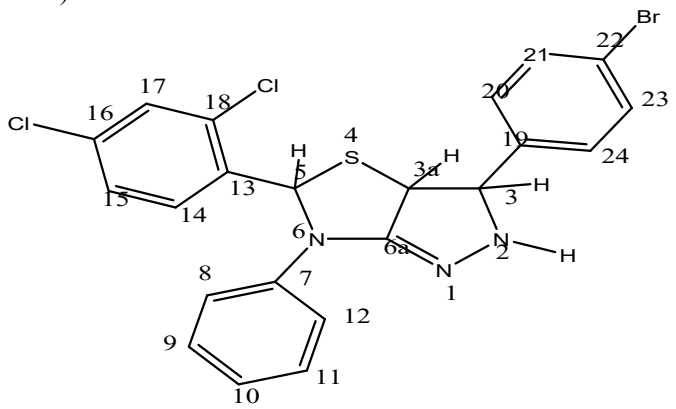
S.No.	R	R'	R"	M.P. (^{0}C)	M.F.	Yeild(%)
IIa	$-C_6H_5$	$-C_6H_4OH$	$-C_6H_4Br$	231	$C_{22}H_{18}BrN_3OS$	78
IIb	$-C_6H_5$	$-C_6H_5$	$-C_6H_3Cl_2$	254	$C_{22}H_{17}Cl_2N_3S$	82
IIc	$-C_6H_5$	C_2H_5	$-C_6H_4Br$	231	$C_{18}H_{18}BrN_3S$	84
IId	$-C_6H_5$	$-C_6H_3Cl_2$	$-C_6H_4Br$	267	$C_{22}H_{16}BrCl_2N_3S$	79
IIe	$-C_6H_5$	$-C_6H_4-OCH_3$	$-C_6H_4OH$	284	$C_{23}H_{21}N_3O_2S$	85
IIf	$-C_6H_5$	$-C_6H_3Cl_2$	$-C_6H_4Cl$	251	$C_{22}H_{16}Cl_3N_3S$	87
IIg	$-C_6H_5$	$C_6H_4-OCH_3$	$-C_6H_4Br$	258	$C_{23}H_{20}BrN_3OS$	83
IIh	$-C_6H_5$	$-C_6H_4OH$	$-C_6H_4Br$	263	$C22H_{18}BrN_3OS$	84

Spectral Study (IR in Cm^{-1})

3362,m,NH; 3041,s, C-H (aromatic); 2977, w, C-H stretch(aliphatic); 1913,m, Combination band;1692,s, C=N;1597,1490(s) C=C; 1410(s) CH_2 bend; 1365(s) C-N , 1100,1071(s) C-Cl(aryl halide),1028,1010(s) C-Cl (aryl halide); 904(s) 1,2,4 trisubstituted oop.; 840(s) Parasubstituted oop.

(PMR in δ ppm) 3.5(broad),-NH , 3.99(d) -CH(J=15.7), 4.0(d), -CH (J=15.7), 6.5(s)-CH , 7.47(d),2H Ar-H(-CH)J=8.46 Hz., 7.36(d), 2H Ar-H (–CH) J=8.46 Hz , 7.1-7.4(m) 8H Ar-H.

The CMR spectrum of compound (IId) was reported in (DMSO-d6) with TMS as an internal standard. There is good agreement in calculated and observed chemical shifts can be correlated as follows: C_3=C_5(62.76), C_{3a}(32.71),C_{6a}(170.39),C7(139.56), C_8=C_{12}(125.48), C_9=C_{11}(129.24), C_{10}(119),C13(139.56), C_{14}(131.37), C_{15}=C_{17}(128.67), C_{16}=C_{18}(139.43), C_{19}(126.49), C_{20}=C_{24}(128.76), C_{21}=C_{23}(131.57), C_{22}(121.38).



(IId)

Fig.-3

RESULTS AND DISCUSSION

From the chemical properties, elemental result and spectral data, the compounds 3, 5-(Substituted Phenyl)-6- Phenyl-3,3a, 5, Trihydro-2H-Pyrazolo [3, 4-D]Thiazoles (IIa-IIh) show the confirmatory results.

CONCLUSION

The microwave technique has a beneficial effect on reaction if a mode reaction needs heating. Many new compounds 3, 5-(Substituted Phenyl)-6- Phenyl-3,3a, 5, Trihydro-2H-Pyrazolo [3, 4-D] Thiazoles (IIa-IIh) were successfully synthesized by microwave irradiation with high yield and short reaction time. Chemistry plays an integral part in our lives. Sustainability, eco-friendly and green chemistry are new principles that are guiding the development of the next generation of products and processes "Green chemistry is considered an essential piece of a comprehensive program to protect human health and the

environment." In its essence green chemistry is a science-based non-regulatory and economically driven approach to achieving the goals of environmental protection and sustainable development**.**

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