



Eco-friendly Synthesis of 1-Aryl-8-methoxythiazolo [2', 3' : 3, 4] [1, 2, 4] triazino [5, 6-b] Indoles under Microwave IR-Radiations

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ABSTRACT

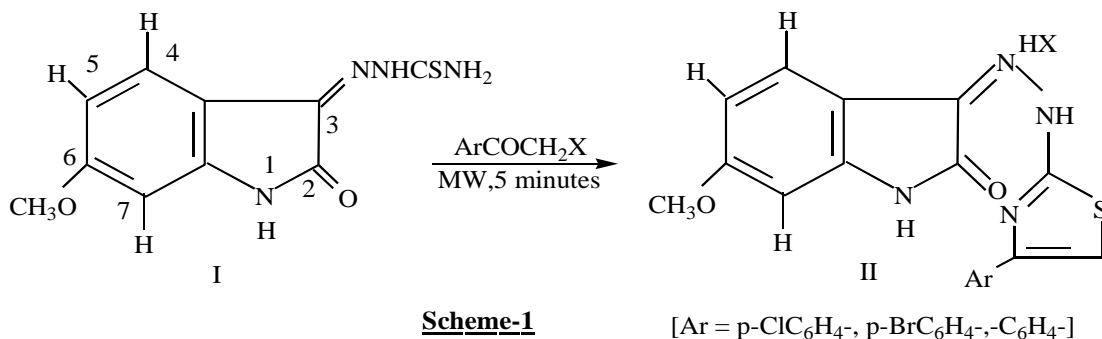
The different 1-Aryl-8-methoxythiazolo [2', 3' : 3, 4] [1, 2, 4] triazino [5, 6-b] indoles are synthesized in high yield in shorter reaction time under microwave irradiations keeping in view their antihistaminic, antithyroid, antitubercular, antifungal & antibacterial activities.

Key words: Indole, Microwave, Isatin, Heterocyclic.

INTRODUCTION

The indoles exhibiting antihistaminic, antithyroid, antitubercular, antifungal, antibacterial activities¹⁻³, anthelminitics, antidepressants, platelet aggregation inhibitors, antineoplastic, vulcanization accelerators, photographic sensitizers⁴⁻¹¹ properties are already been synthesized by different method but they requires longer reaction time and tedious workup.¹²⁻²¹ Microwave assisted reactions are gaining much more importance in synthetic organic chemistry due to dramatic reduction in time from days to hours and hours to minutes or seconds.²²⁻²³

The present work reports the synthesis of 1-Aryl-8-methoxythiazolo [2', 3' : 3, 4] [1, 2, 4] triazino [5, 6-b] indoles in a multi-step preparation in high yield in shorter reaction time (Scheme-1). Our work started by reacting 6-methoxyisatin with thiosemicarbazide in Anhyd. ethanol under microwave irradiation at 560W for 5-minutes to give 6-Methoxyisatin-3-thiosemicarbazone (I). After separation, the 6-Methoxyisatin-3-thiosemicarbazone(I) reacts with p-chlorophenacyl bromide under microwave irradiation at 560W for 5-minutes to give 6-Methoxyisatin-3-(4-p-chlorophenyl-2-thiazoly1) hydrazone hydrobromide (IIa; Ar = p-C₁C₆H₄) (See Scheme-1).



Similarly, 6-Methoxyisatin-3-thiosemicarbazone (I) was also irradiated with p-bromophenacyl bromide, phenacyl bromide, under microwave irradiation at 560W for 5-minutes to give 6-Methoxyisatin-3-(4-p-bromopheny1-2-thiazoly1)

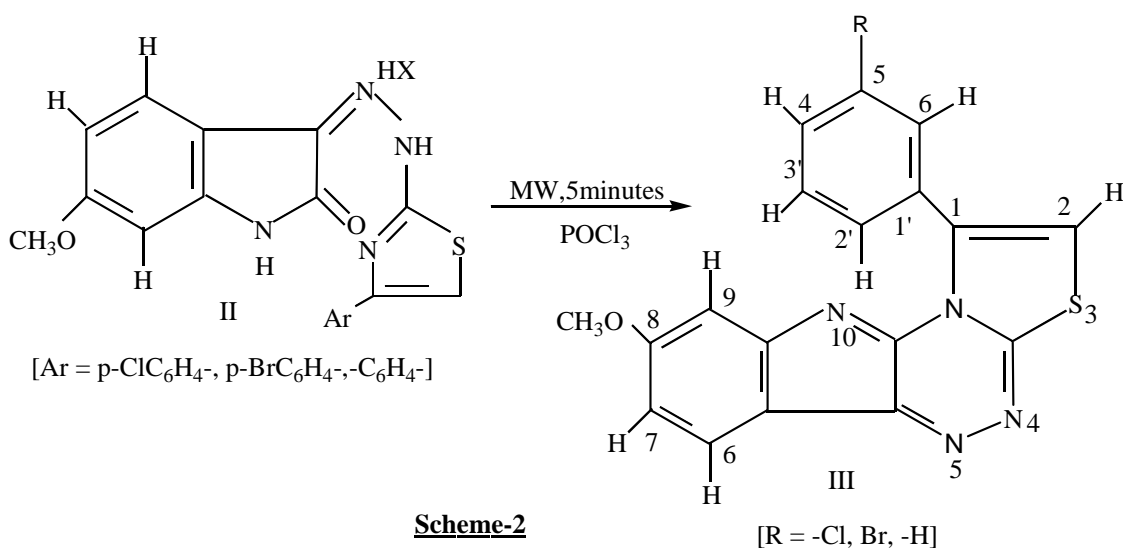
hydrazone hydrobromide (IIb, Ar = p-Br C₆H₄) and 6-Methoxyisatin-3-(pheny1-2-thiazoly1) hydrazone hydrobromide (IIc; Ar = C₆H₅) respectively. The results are shown in Table-1.

Table 1: 6-Methoxyisatin-3-(aryl-2-thiazoly1) hydrazone hydrobromide

S. NO.	Substrate(R)	Time(in minutes)	Yield(%)	m.p.(°C)
1.	-pClC ₆ H ₄ -(IIa)	5	94	> 250°C
2.	-pBrC ₆ H ₄ -(IIb)	5	92	> 250°C
3.	-C ₆ H ₅ (IIc)	5	97	> 250°C

We further explore our work by irradiated 6-Methoxyisatin-3-(4-p-chloropheny1-2-thiazoly1) hydrazone hydrobromide (IIa; Ar = p-C1C₆H₄) in a POCl₃ under microwave irradiation at 560W for 5-

minutes to give 1-(p-Chloropheny1)-8-methoxythiazolo [2', 3' : 3, 4] [1, 2, 4] triazino [5, 6-b] indole (IIIa, R = Cl). (See Scheme-2).



Similarly, 6-Methoxyisatin-3-(4-p-bromophenyl-2-thiazoly1) hydrazone hydrobromide (IIb; Ar = p-BrC₆H₄) and 6-Methoxyisatin-3-(phenyl-2-thiazoly1) hydrazone hydrobromide (IIa; Ar = p-C₁C₆H₄) (IIc; Ar = C₆H₅) were also irradiated in a mixture of POCl₃ under

microwave irradiation at 560W for 5-minutes to give 1-(p-bromophenyl)-8-methoxythiazolo [2', 3' : 3, 4] [1, 2, 4] triazino [5, 6-b] indole (IIIb, R = Br) and 1-(phenyl)-8-methoxythiazolo [2', 3' : 3, 4] [1, 2, 4] triazino [5, 6-b] indole (IIIc, R = H) respectively. The results are shown in Table-2.

Table 2: 1-(p-Chlorophenyl)-8-methoxythiazolo [2', 3' : 3, 4] [1, 2, 4] triazino [5, 6-b] indole

S. NO.	Substrate(R)	Time(in minutes)	Yield(%)	m.p.(°C)
1.	-Cl(IIIa)	5	89	> 250°C
2.	-Br(IIIb)	5	86	> 250°C
3.	-H(IIIc)	5	93	> 250°C

EXPERIMENTAL

All the melting points reported are uncorrected. Infrared spectra (n_{\max} in cm⁻¹) were recorded in nujol mull or KBr on a Perkin-Elmer 842/Beckman IR-20 / Hitachi 215 spectrometers. The proton magnetic resonance spectra were recorded on a VXR-200 MHz or R-32 Perkin-Elmer 90 MHz spectrometer in CDC₁₃ or DMSO-d₆ using tetramethylsilane (TMS) as internal reference standard. The chemical shifts are expressed in (ppm) units downfield from TMS. Mass spectra were scanned on a Jeol JMX-DX-300 spectrometer operating at 70 eV. Carbon, hydrogen and nitrogen analyses were carried out on a Yanaco MT-3 (JAPAN) instrument. Thin layer chromatography (TLC) were performed on silica-gel plates using acetone-benzene (1 : 3 or 1 : 2) as solvent system and iodine chamber as visualizing agent.

Typical procedure for the synthesis of 6-Methoxyisatin-3-thiosemicarbazone(I)

A mixture of 6-methoxyisatin (0.18g, 0.001 mol) in Anhyd. ethanol (2ml) and thiosemicarbazide (0.1g, 0.0011 mol) in a mixture of water (2 ml) and glacial acetic acid (0.5 ml) was irradiated under microwave irradiation at 560W for 5-minutes. A yellow coloured solid formed during irradiation. The solid was filtered, washed well with water and crystallized from ethanol-DMF furnishing yellow crystals. Yield 0.247g (95%), m.p. 265°C. [Found : N, 22.68, S, 12.62. C₁₀H₁₀N₄O₂S requires N, 22.40;

S, 12.80%]; IR: 825, 860 (1, 2, 4-trisubstituted benzene ring), 1115 (C=S), 1125 & 1370 (C-O-C stretching), 1620 (C=N), 1700 (C=O), 3200, 3280, 3400 (NH, NH₂).

Typical procedure for the synthesis of 6-Methoxyisatin-3-(4-p-chlorophenyl-2-thiazoly1) hydrazone hydrobromide (IIa, Ar = p-C₁C₆H₄ -)

6-Methoxyisatin-3-thiosemicarbazone (I, 0.250g, 0.001 mole) and p-chlorophenacyl bromide (0.234 g, 0.001 mol) in DMF (6 ml) was irradiated under microwave irradiation at 560W for 5-minutes, and poured into ice-water. The solid thus separated, was filtered, washed with water and crystallized from aq. DMF to give IIa as yellow crystals, yield 0.437g (94%), m.p. > 250°C [Found : N, 12.20; S, 6.90. C₁₈H₁₄N₄O₂SClBr requires N, 12.03; S, 6.87%]; IR : 810, 870 (1, 2, 4-trisubstituted benzene ring), 1150, 1370 (C-O-C stretching), 1630 (C=N), 1690 (C=O), 3180, 3300 (N-H stretching).

Following members of the series were also prepared in a similar way

IIb (Ar = p-BrC₆H₄-): yield 0.469g (92%), m.p. > 250° [Found : N, 11.16 S, 6.42. C₁₈H₁₄N₄O₂SBr₂ requires N, 10.98; S, 6.27%]; IR: 1535 (C-N stretching), 1610 (C=N), 1685 (C=O), 3170 (N-H stretching).

IIc (Ar = C₆H₅): yield 0.418g (97%), m.p. > 250° [Found : N, 14.54; S, 8.47. C₁₈H₁₅N₄O₂SBr

requires N, 14.49; S, 8.27%]; IR: 1515 (C-N stretching), 1610 (C=N), 1690 (C=O), 3180 (N-H stretching).

Typical procedure for the synthesis of 1-(p-Chlorophenyl)-8-methoxythiazolo [2', 3' : 3, 4] [1, 2, 4] triazino [5, 6-b] indole (IIIa, R = C1)

Compound IIa (0.465g, 0.001mole) in POC₁₃ (4ml) was irradiated under microwave irradiation at 560W for 5-minutes. The reaction mixture was poured into water and neutralised with aq. K₂CO₃ solution. The solid, thus separated, was filtered, washed well with water and crystallised from aq. DMF to furnish IIIa as yellow crystals, yield 0.325g (89%), m.p. > 250° [Found: C, 59.10; H, 3.12; N, 15.38; S, 8.55. C₁₈H₁₁N₄OSC1 requires C, 58.93; H, 3.01; N, 15.27; S, 8.73%]; IR : 1575 (C-N), 1610 (C=N); PMR (DMSO-d): d3.95 (3H, s, C₈-OCH₃); 7.95 (1H, s, C₂-H); 6.4-8.4 (7H, m, ArH).

Following members of the series were also prepared in a similar way

IIIb (R = Br): yield 0.353g (86%), m.p. > 250° [Found : C, 52.76; H, 2.80; N, 13.87; S, 7.84. C₁₈H₁₁N₄OSBr requires C, 52.55; H, 2.67; N, 13.62; S, 7.78%]; IR: 1570 (C-N stretching), 1600, 1610 (C=N).

IIIc (R = H) : yield 0.308g (93%), m.p. > 250° [Found : C, 65.21; H, 3.74; N, 16.66; S, 9.52. C₁₈H₁₂N₄OS requires C, 65.06; H, 3.61; N, 16.86; S, 9.63%]; IR: 1570 (C-N stretching), 1600, 1620 (C=N).

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