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Synthesis of novel bioactive heterocyclic compounds - 4 - thiazolidinone via solvent - free microwave mediated technology

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ABSTRACT

A rapid & solvent free approach involving microwave technique by solid catalyst for synthesis of 4-(arylidene)-phenyl azo benzene 3a-j is presented in this paper. A series of 4-thiazolidinones 4a-f have been prepared by reaction of 4-(arylidene)-phenyl azo benzene 3a-f with mercaptoacetic acid. Azomethines 3a-j have been prepared by condensation of 4-amino azo benzene 1 with substituted aryl aldehydes 2a-j using conventional as well as microwave method. All products have been characterised by IR, ^{1}H NMR and elemental analysis.

Key words: Solvent-free synthesis, 4-thiazolidinones, azomethines, 4-amino azo benzene.

INTRODUCTION

Arylidene derivatives are important intermediates for the synthesis of bioactive compounds e.g. β-lactams, which also reported to show a variety of interesting biological actions including antimouse hepatitis virus (MHV), inhibition of herpes simplex virus type 1 (HSV-1) and adenovirus type 5 (Ad 5), antimosquito larvae and it has been suggested that the presence of azomethine linkage might be responsible for the biological activities displayed by arylidene derivatives[1]. The existence of an azo moiety in different types of compounds has caused arylidene derivatives to show biological activities containing antibacterial and pesticidal activities[2]. Furthermore arylidene derivative has good antimicrobial, fungicidal and pharmaceutical applications and it can be prepared by an acid catalyzed reaction of amines and ketones or aldehydes[3]. Thiazolidinone derivatives are well known for their diverse biological activities such as fungicidal, bactericidal, insecticidal, herbicidal, viruscidal, anti-inflammatory, anti-tubercular, anthelmintic, antithyroidal, cardiovascular, potential to pentobarbital induced sleeping potentials[4].

They are also associated with pharmacological activities such as antitumor, antidiabetic, antiparkinsons, antiviral and analgesic effects[5]. Commercial microwave oven is used as a convenient source of heat in the laboratory. The microwave assisted organic reactions are pollution free, eco-friendly, rapid, safe and with higher chemical yields[6]. These features render the microwave method superior to conventional one.
These observations stimulated us for the synthesis of 4-Thiazolidinone derivatives. Condensation of 4-amino azo benzene 1 with substituted aryl aldehydes 2a-j was carried out using conventional and microwave method to yield schiff bases 3a-j. In conventional method, reaction was carried out in

ethanol for 8-10 hr. but these products were obtained only in 2-3 min under microwave irradiation using alumina as support (Table 1). Reaction of the schiff bases 3a-f with mercaptoacetic acid in ethanol was carried out for 10-12 hr to get 4-Thiazolidinones 4a-f (Table 2) (Scheme 1). Structures of the synthesised compounds 3a-j and 4a-f have been confirmed by IR, ^{1}H NMR and elemental analysis (Table 3).

MATERIAL AND METHODS

The reactions were monitored on TLC plates (solvents of varying polarity). The melting points were determined in open capillaries and are uncorrected. IR spectra were recorded using F.T. Infra-Red Spectrometer Model RZX (Perkin Elmer) in KBr disc. ^{1}H NMR spectra were recorded on (Perkin Elmer) FT-NMR Cryo-magnet Spectrometer

Table 1: Comparative study in terms of yield and reaction period (Conventional and MWI method) & physical data of compounds (3a-j)

Comp.	R	m.p. (°C)	Conventional method Yield (%) (Period/hr)	Microwave method Yield (%) (Period/hr)
3a	2-OH-C_6H_4-	152	76(8.0)	80(3.0)
3b	-C_6H_5	115	82(8.5)	89(1.5)
3c	3-NO_2-C_6H_4-	150	74(9.0)	83(3.0)
3d	4-OCH_3-C_6H_4-	145	80(10.0)	88(2.5)
3e	4-N $(CH_3)_2$-C_6H_4-	178	71(10.0)	79(1.5)
3f	2-NO_2-C_6H_4-	142	75(9.5)	87(2.5)
3g	4-OH-C_6N_4-	185	79(10.0)	86(2.5)
3h	-CH=CH-C_6H_5	135	81(10.0)	90(2.0)
3i	4-F-C_6H_4-	110	78(10.0)	85(2.5)
3j	3, 4-$(OCH_3)_2$-C_6H_3-	148	83(9.5)	92(3.0)

400MHz (Bruker) using DMSO-d_6 as solvent, TMS was used as an internal standard (chemical shifts in δ ppm). The reactions were carried out in a microwave oven (KENSTAR- OM- 20DSP, 2450 MHz).

Synthesis of 4-(2'-hydroxy benzylidene)-phenyl azo benzene 3a.

Conventional method

A mixture of 4-amino azo benzene 1 (1.97g, 0.01mol) and salicylaldehyde 2a (1.22g, 0.01mol) was refluxed in ethanol for 8 hr. After completion of reaction, solvent was removed under reduced pressure and the residue was purified by crystallization from appropriate solvent to give 3a. IR (KBr): 3458(str, OH), 3047(str, Aromatic C-H), 1611(str, C=N), 1560(str, N=N), 754(1,2 disubstituted benzene ring) cm^{-1}, ^{1}H NMR (400MHz, DMSO-d_6): δ 13.04 (s, 1H, OH), 8.80 (s, 1H, N=CH), 6.97-8.02 (m, 13H, Ar-H).

Table 2: Characterization data of compounds (4a-f)

Compd	R	m.p. (°C)	Yield (%)
4a	2-OH-C_6H_4-	146	74
4b	-C_6H_5	100	80
4c	3-NO_2-C_6H_4-	118	81
4d	4-OCH_3-C_6H_4-	120	76
4e	4-N $(CH_3)_2$-C_6H_4-	125	78
4f	2-NO_2-C_6H_4-	112	79

Microwave method

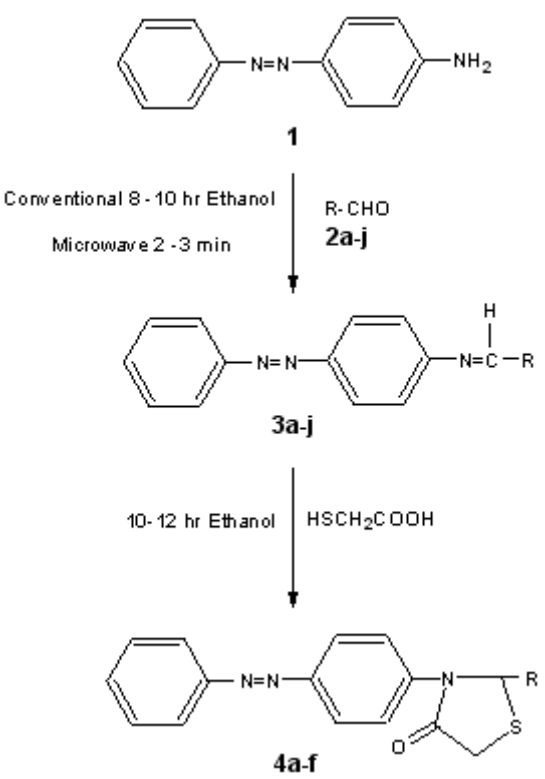
A mixture of 4-amino azo benzene 1 (1.97g, 0.01mol) , salicylaldehyde 2a (1.22g, 0.01mol) and 2g alumina in R.B. flask was irradiated inside microwave oven (KENSTAR- OM- 20DSP, 2450 MHz) for 3 min. Reaction mixture was cooled

at room temp. followed by extraction with ethanol, removal of the solvent and subsequent recrystallisation to give 3a. Compounds 3b-j was also prepared by the similar method using 2b-j (Table 1)

Synthesis of 2-(2'-hydroxy phenyl)-3-(phenyl azo benzene)-thiazolidin-4-one 4a.

A mixture of 4-(2'-hydroxy benzylidene)-phenyl azo benzene 3a (1.50 g, 0.005 mol) and mercaptoacetic acid (0.46 g 0.005 mol) in ethanol was refluxed for 10 hr. On cooling the reaction mixture, solid product thus separated was filtered, washed with solvent ether and recrystallised from suitable solvent to give 4a. IR (KBr): 3375(str, OH), 3050 (str, Aromatic C-H), 2917 (str, CH_2), 1615 (C=O thiazolidinone ring), 1567(str, N=N), 750(1,2 disubstituted benzene ring), 686.4 (str, C-S-C 4-thiazolidinone ring) cm^{-1}, ^1H NMR (400MHz, DMSO-d_6): δ 8.78 (s, 1H, OH), 6.95-7.58 (m, 13H, Ar-H), 3.03(s, 2H, CH_2).

Compounds 4b-f were synthesised from 3b-f using similar method. (Table 2)



Scheme 1

Table 3: Elemental analysis data of 3a-j and 4a-f

Compd	Mol. Formula	Mol. Wt	Elemental analysis Calculated (Found) (%)		
			C	H	N
3a	$C_{19}H_{15}N_3O$	301	75.73(75.71)	5.02(5.00)	13.94(13.91)
3b	$C_{19}H_{15}N_3$	285	79.97(79.95)	5.29(5.27)	14.73(14.70)
3c	$C_{19}H_{14}N_4O_2$	330	69.08(69.05)	4.27(4.25)	16.96(16.94)
3d	$C_{20}H_{17}N_3O$	315	76.17(76.14)	5.43(5.41)	13.32(13.30)
3e	$C_{21}H_{20}N_4$	328	76.80(76.77)	6.14(6.12)	17.06(17.03)
3f	$C_{19}H_{14}N_4O_2$	330	69.08(69.06)	4.27(4.24)	16.96(16.93)
3g	$C_{19}H_{15}N_3O$	302	75.73(75.70)	5.02(5.01)	13.94(13.92)
3h	$C_{21}H_{17}N_3$	311	81.00(80.98)	5.50(5.48)	13.49(13.47)
3i	$C_{21}H_{19}N_3O_2$	345	73.02(73.00)	5.54(5.51)	12.16(12.14)
3j	$C_{19}H_{14}N_3F$	303	75.23(75.21)	4.65(4.63)	13.85(13.82)
4a	$C_{21}H_{17}N_3SO_2$	375	67.18(67.16)	4.56(4.54)	11.19(11.16)
4b	$C_{21}H_{17}N_3OS$	359	70.17(70.15)	4.76(4.73)	11.69(11.67)
4c	$C_{21}H_{16}SO_3N_4$	404	62.36(62.34)	3.98(3.95)	13.85(13.83)
4d	$C_{22}H_{19}N_3O_2S$	389	67.84(67.82)	4.91(4.89)	10.78(10.76)
4e	$C_{23}H_{22}N_4SO$	402	68.63(68.61)	5.50(5.48)	13.91(13.89)
4f	$C_{21}H_{16}SO_3N_4$	404	62.36(62.32)	3.98(3.96)	13.85(13.82)

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