Heteroatom Chemistry
Volume 20, Number 4, 2009

Indium Trichloride–Catalyzed Synthesis of Some Novel 2,2′-(*N*,*N*′-Diarylamino)-4,4′-diaryl-5,5′-arylidenebisthiazoles and Their Insecticidal Activity

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Received 19 February 2009; revised 30 April 2009

ABSTRACT: *A series of novel 2,2′-(N,N′-diarylamino)-4,4′-diaryl-5,5′-arylidene-bisthiazoles* **2** *were rapidly and smoothly prepared in good yields by using non conventional techniques i.e. microwave or ultrasonic irradiation, through indium trichloride catalyzed electrophilic substitution reaction of 2-(N-arylamino)-4-arylthiazoles* **1** *with various arylaldehydes. All the synthesized compounds were characterized on the basis of their elemental analyses and spectral data (IR, PMR and Mass). The synthesized compounds were also evaluated for their insecticidal activity against* Helicoverpa armigera *and gave promising results.* © 2009 Wiley Periodicals, Inc. Heteroatom Chem 20:224–231, 2009; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20537

INTRODUCTION

Thiazoles and their derivatives are useful intermediates in organic synthesis and possess a broad range of biological activities such as anti-inflammatory [1], antiviral [2], antibacterial [3], antitumor [4], analgesic [5], antioxidant [6], anticonvulsant [7], antihypertensive [8], and hypoglycemic [9] activities. Thiazoles have also found application in other fields such as polymers [10], liquid crystals [11], photonucleases [12], fluorescent dyes [13], insectides [14], and antioxidants [15]. Furthermore, the molecules that incorporate a bithiazole moiety in which two thiazole rings are joined directly such as in bleomycin [16] or a bisthiazole unit in which the two thiazole rings are connected through a few intervening bonds also exhibit antibacterial [17], anticancer [18], and antiarthritic [19] activities.

Aminothiazole derivatives are highly electron rich at position 5 of the ring and as a result are readily substituted by electrophilic reactants. The entry of the electrophilic reactants at position 5 or 5′ of the bisthiazole system depends on the nature of the residue present at position 4 [20]. The acid-catalyzed substitution reaction of electron-rich heterocyclic compounds with *p*-dimethylaminobenzaldehyde is known as Ehrlich test [21] for π-electron excessive heterocycles. Protic acids and Lewis acids are both known to promote this type of reaction.

Recently, indium trichloride has been found to act as a mild and water-tolerant Lewis acid catalyst in synthetic organic chemistry, for example, Mukaiyama aldol reaction [22], Mannich-type

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Contract grant sponsor: Centre of Advanced Studies, Department of Chemistry, University of Rajasthan, Jaipur, India.
Contract grant number: JRF (to D.S.).

reaction [23], Diels-Alder reaction [24], aziridination reaction [25], Friedal-Crafts reaction [26], Barbier reaction [27], and Biginelli reaction [28]. It can be conveniently used in both aqueous and nonaqueous mediums. Moreover, indium(III) chloride is stable under air and in water, and constitutes an interesting catalyst for clean and green chemistry due to possibility of recovery and recycling [29]. In addition, it has a high coordination number and possesses a fast coordination-dissociation equilibrium in aqueous solutions. This behavior of indium trichloride prompted us to investigate its catalytic activity for the electrophilic substitution reaction of *N*-arylaminothiazoles.

Although the synthesis of 5,5′-bis-1,3-thiazoles [30], 2,2′-bis-1,3-thiazoles [31], and 4,4′-(1,4-biphenylene)bis-1,3-thiazoles [32] has been reported, there is no report on the synthesis of 2,2′-(*N*,*N*′-diarylamino)-4,4′-diaryl-5,5′-arylidenebisthiazoles **2** by the condensation of *N*-arylaminothiazoles and aldehydes. Interest in their synthesis comes from the fact that the cystothiazoles [33], having a (2,4′)bisthiazole component, demonstrate potent antifungal activity and function as novel inhibitors of mitochondrial oxidation at a specific site on cytochrome bc_1 complex and bis(aminothiazolyl)-methanes, which have been synthesized by reacting dichloropentadiones with thiourea and show anticholinesterase activity [34].

As environmental consciousness in chemical research and industry increases, the challenge for a sustainable environment calls for clean procedures. So, several procedures are now recommended for green chemistry [35] involving new ecofriendly reagents or catalysts, selective medium such as water, ionic liquids, or solvent-free reactions, or nonconventional energy sources such as ultrasound or microwaves. Encouraged by these observations and as a part of our ongoing research program on arylaminothiazoles [36], we herein report environmentally desirable synthesis of 2,2′-(*N*,*N*′-diarylamino)-4,4′-diaryl-5,5′-arylidenebisthiazoles **2** using green chemistry techniques (microwave irradiation and ultrasonicaton) via indium trichloride–catalyzed electrophilic substitution reaction. All the synthesized compounds showed promising results when screened for their insecticidal activity against *Helicoverpa armigera*.

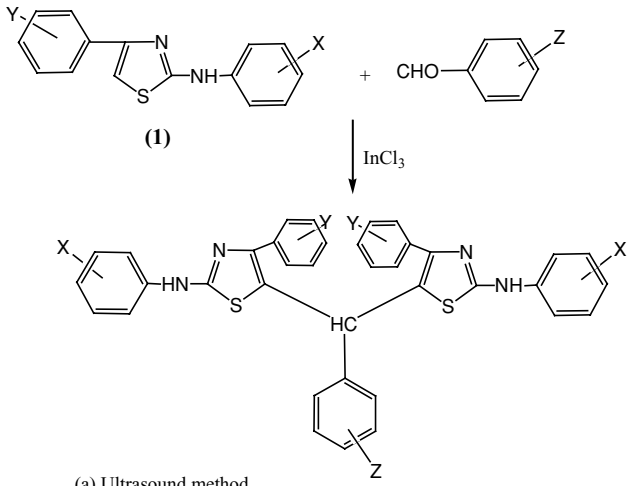
Ultrasound and microwave have been widely recognized as important enabling technologies in organic synthesis due to a range of ensuing benefits such as improved yields, shorter times, and enhanced selectivity [37] in comparison with conventional conditions. These techniques can induce reactions that would otherwise be very laborious and may bring out peculiar chemoselectivities, thus opening up new synthetic methods [38]. Although it has been widely presumed that ultrasound and microwave provide differential assistance to completely different reaction pathways [39], there has been a dearth of reports wherein the competitive efficacy of ultrasound and microwave toward selective formation of competing procedures has been clearly discerned.

A survey of literature revealed that no work has been done on the synthesis of 2,2′-(*N*,*N*′-diarylamino)-4,4′-diaryl-5,5′-arylidenebisthiazoles **2** using indium trichloride (20 mol%) via microwave or ultrasound and any other method.

RESULTS AND DISCUSSION

Synthesis

A series of 2,2′-(*N*-*N*′-diarylamino)-4,4′-diaryl-5,5′-arylidenebisthiazoles **2** has been synthesized and identified. Electrophilic substitution reaction of 2-(*N*-arylamino)-4-arylthiazoles **1** with various arylaldehydes in the molar ratio of 2:1 along with a catalytic amount of anhydrous indium trichloride under microwave or ultrasonic irradiation was performed in good to excellent yields (Scheme 1). In



(a) Ultrasound method
(b) Microwave method
(c) Conventional method

2	X	Y	Z
a	H	H	H
b	H	H	4-Cl
c	H	4-Cl	H
d	H	4-Cl	4-Cl
e	H	H	4-F
f	H	4-Br	4-Cl
g	H	4-Br	4-F
h	H	4-Cl	4-F
i	H	4-Br	4-OCH_3
j	3-Cl; 4-F	4-Br	4-OCH_3

SCHEME 1

TABLE 1 Physical and Analytical Data of 2,2′-(*N*,*N*′-Diarylamino)-4,4′-diaryl-5,5′-arylidenebisthiazoles **2a–j**

						Analyses [Calculated (Found)] (%)			
Compound	*X*	*Y*	*Z*	*Molecular Formula*	*Melting Point (°C)*	*C*	*H*	*N*	*S*
2a	H	H	H	$C_{37}H_{28}N_4S_2$	217	75.00 (74.83)	4.72 (4.59)	9.45 (9.41)	10.81 (10.77)
2b	H	H	4-Cl	$C_{37}H_{27}ClN_4S_2$	220	70.92 (70.79)	4.31 (4.34)	8.94 (8.89)	10.22 (10.15)
2c	H	4-Cl	H	$C_{37}H_{26}Cl_2N_4S_2$	218	67.27 (67.18)	3.93 (3.89)	8.48 (8.42)	9.69 (8.54)
2d	H	4-Cl	4-Cl	$C_{37}H_{25}Cl_3N_4S_2$	210	63.97 (63.91)	3.60 (3.53)	8.06 (8.09)	9.22 (9.13)
2e	H	H	4-F	$C_{37}H_{27}FN_4S_2$	165	72.78 (72.72)	4.42 (4.45)	9.18 (9.14)	10.49 (10.51)
2f	H	4-Br	4-Cl	$C_{37}H_{25}Br_2ClN_4S_2$	195	56.34 (56.26)	3.17 (3.11)	7.10 (7.05)	8.12 (8.05)
2g	H	4-Br	4-F	$C_{37}H_{25}Br_2FN_4S_2$	219	57.96 (57.87)	3.26 (3.21)	7.31 (7.26)	8.35 (8.30)
2h	H	4-Cl	4-F	$C_{37}H_{25}Cl_2FN_4S_2$	194	65.48 (65.44)	3.68 (3.57)	8.25 (8.21)	9.43 (9.36)
2i	H	4-Br	4-OCH_3	$C_{38}H_{28}Br_2N_4OS_2$	212	58.61 (58.65)	3.59 (3.53)	7.19 (7.12)	8.22 (8.14)
2j	3-Cl; 4-F	4-Br	4-OCH_3	$C_{38}H_{24}Br_2Cl_2F_2N_4OS_2$	110	51.70 (51.66)	2.72 (2.65)	6.34 (6.38)	7.25 (7.29)

the classical approach, the reaction proceeds with a low yield of the products (15%–22%) by refluxing the reactants for 16–22 h in dichloromethane. In an attempt to improve the yields of reaction and acknowledging the benefits of "green chemistry," the same reaction was performed under solvent-free conditions (microwave and ultrasound irradiation).

In the ultrasonic approach, sonication of 2-(*N*-arylamino)-4-arylthiazoles **1** with various arylaldehydes using indium trichloride as a catalyst in an ultrasonic cleaning bath gave 72%–84% yield of the corresponding bisthiazole derivatives in 3–5 h. The reaction rates and yields were dramatically enhanced by sonic waves because of cavitational collapse under mild conditions. The same reactants were thoroughly mixed without solvent and irradiated for 10–20 min in a domestic microwave oven to afford the title compounds in 80%–92% yield. Under solvent-free conditions, the reaction is completed with higher yield because the eutectic mixture having a uniform distribution of the reactants brings the reacting species in close proximity to react than in the solvent.

The physical and analytical data of compounds **2** are given in Table 1. The synthetic step is illustrated in Scheme 1. The comparative data of various procedures are tabulated in Table 2. All the synthesized compounds were characterized by their IR, ^{1}H NMR, and fast atomic bombardment (FAB) mass spectral data (Table 3).

In the IR spectra of 2-(*N*-arylamino)-4-arylthiazoles **1**, absorption bands at 3450–3100,

TABLE 2 Yield (%) and Time for the synthesis of 2,2′-(*N*,*N*′-Diarylamino)-4,4′-diaryl-5,5′-arylidenebisthiazoles **2a–j**

	Yield (%)			*Time (min)*		
Compound	*Ultrasound*	*Microwave*	*Conventional*	*Ultrasound*	*Microwave*	*Conventional*
2a	73.0	80.0	15.0	[5]	20	[20]
2b	73.8	84.0	18.0	[4.5]	15	[18]
2c	74.6	85.0	18.0	[4]	12	[18]
2d	76.0	87.5	20.0	[4]	15	[21]
2e	72.0	81.7	15.0	[5]	20	[22]
2f	80.0	91.0	21.0	[3.5]	10	[20]
2g	81.5	88.5	20.0	[3]	12	[16]
2h	80.4	87.0	20.0	[4]	15	[22]
2i	82.2	91.5	21.0	[4]	20	[20]
2j	84.7	92.0	22.0	[3]	10	[16]

Values given in square brackets are in hours.

TABLE 3 Spectral Data of 2,2′-(*N*,*N*′-Diarylamino)-4,4′-diaryl-5,5′-arylidenebisthiazoles **2a–j**

Compound	*IR (KBr) (ν_{max}) (cm^{-1})*	*^{1}H NMR (in $CDCl_3$) (δ ppm)*	*FAB Mass (m/z) (M^+)*
2a	3120 (N—H str.), 3045 (aromatic C—H str.), 2840 (aliphatic C—H str.), 1570 (aromatic C=C str.), 1500 (C=N str.), 1310 (C=S str.)	7.01–7.34 (m, ArH, 25H) 7.38 (s, NH, 2H), 6.02 (s, CH, 1H)	592
2b	3150 (N—H str.), 3050 (aromatic C—H str.), 2850 (aliphatic C—H str.), 1580 (aromatic C=C str.), 1510 (C=N str.), 1350 (C=S str.), 670 (C—Cl str.)	6.89–7.35 (m, ArH, 25H) 7.37 (s, NH, 2H), 6.53 (s, CH, 1H)	626/628
2c	3155 (N—H str.), 3059 (aromatic C—H str.), 2853 (aliphatic C—H str.), 1588 (aromatic C=C str.), 1516 (C=N str.), 1352 (C=S str.), 675 (C—Cl str.)	7.01–7.46 (m, ArH, 23H) 7.59 (s, NH, 2H), 6.64 (s, CH, 1H)	660/662
2d	3160 (N—H str.), 3055 (aromatic C—H str.), 2900 (aliphatic C—H str.), 1593 (aromatic C=C str.), 1510 (C=N str.), 1349 (C=S str.), 688 (C—Cl str.)	7.01–7.47 (m, ArH, 22H) 7.62 (s, NH, 2H), 6.64 (s, CH, 1H)	694/696
2e	3220 (N—H str.), 3055 (aromatic C—H str.), 2995 (aliphatic C—H str.), 1615 (aromatic C=C str.), 1518 (C=N str.), 1356 (C=S str.), 1114 (C—Cl str.)	6.90–7.45 (m, ArH, 24H) 7.62 (s, NH, 2H), 6.50 (s, CH, 1H)	610
2f	3217 (N—H str.), 3065 (aromatic C—H str.), 2993 (aliphatic C—H str.), 1620 (aromatic C=C str.), 1519 (C=N str.), 1358 (C=S str.), 692 (C—Cl str.), 561 (C-Br str.)	6.83–7.49 (m, ArH, 22H) 7.72 (s, NH, 2H), 6.49 (s, CH, 1H)	788/790
2g	3157 (N—H str.), 3062 (aromatic C—H str.), 2900 (aliphatic C—H str.), 1620 (aromatic C=C str.), 1512 (C=N str.), 1356 (C=S str.), 1100 (C—F str.), 575 (C-Br str.)	6.91–7.36 (m, ArH, 22H) 7.49 (s, NH, 2H), 6.60 (s, CH, 1H)	766/768
2h	3158 (N—H str.), 3050 (aromatic C—H str.), 2960 (aliphatic C—H str.), 1610 (aromatic C=C str.), 1515 (C=N str.), 1355 (C=S str.), 1110 (C—F str.), 690 (C—Cl str.)	6.87–7.36 (m, ArH, 22H) 7.42 (s, NH, 2H), 6.48 (s, CH, 1H)	678/680
2i	3158 (N—H str.), 3060 (aromatic C—H str.), 2950 (aliphatic C—H str.), 1600 (aromatic C=C str.), 1520 (C=N str.), 1355 (C=S str.), 560 (C-Br str.)	6.91–7.48 (m, ArH, 22H) 7.86 (s, NH, 2H), 6.59 (s, CH, 1H), 3.82 (s, OCH_3, 3H)	778/780
2j	3255 (N—H str.), 3070 (aromatic C—H str.), 2995 (aliphatic C—H str.), 1625 (aromatic C=C str.), 1526 (C=N str.), 1360 (C=S str.), 1120 (C—F str.), 680 (C—Cl str.), 570 (C-Br str.)	7.02–7.86 (m, ArH, 18H) 8.10 (s, NH, 2H), 6.81 (s, CH, 1H)	882/884/886

1560–1530, and 1352–1330 cm^{-1} are attributed to >NH, >C=N, and >C=S stretching vibrations, respectively. The aromatic double bond (>C=C<) appears between 1600–1594 cm^{-1}. The IR spectra of 2,2′-(*N*,*N*′-diarylamino)-4,4′-diaryl-5,5′-arylidenebisthiazoles **2** exhibits the >NH stretching vibration at 3255–3120 cm^{-1} and phenyl ring skeletal >C=C< vibrations at 1625–1570 cm^{-1}. The prominent peak between (1526–1500) cm^{-1} has been attributed to >C=N stretching vibrations and (1360–1310) cm^{-1} have been assigned to >C=S stretching frequencies. The strong absorption bands at 575–560, 690–670, and 1114–1100 cm^{-1} have been attributed to Ar-Br, Ar-Cl, and Ar-F stretching modes. An additional peak between 2995 and 2840 cm^{-1} attributed to aliphatic C—H stretching vibration that was not present earlier in compounds **1** is also observed.

In the PMR spectra of compounds **1**, methine proton at C-5 position of thiazole moiety shows a resonance signal at δ 5.9–6.2 ppm and the resonance signal of N—H is observed in the region from δ 7.3 to 7.8 ppm as a singlet, which is D_2O exchangeable. Aromatic protons are observed as a multiplet from δ 6.9 to 7.8 ppm. In the ^{1}H NMR spectra of 2,2′-(*N*,*N*-diarylamino)-4,4′-diaryl-5,5′-arylidenebisthiazoles **2**, the disappearance of resonance signal due to methine =C—H proton at C-5 position of thiazole moiety and the appearance of a sharp singlet at δ 6.25–6.64 ppm support the formation of bisthiazoles. The position of aromatic and N—H resonance signals remains unaltered. Aromatic protons appear as a complex multiplet in the region from δ 6.83 to 7.86 ppm and the resonance signal of N—H appears as a singlet from δ 7.36 to 8.10 ppm, which is D_2O exchangeable.

Final confirmation is achieved from FAB mass spectra, which exhibit molecular ion peak (M^+) of compounds **2** corresponding to their molecular masses. Mass spectrum of compound **2i** shows characteristic molecular ion cluster *m*/*z* at 778/780(base peak)/782 due to the presence of two bromine atoms

TABLE 4 Percentage Mortality of *Helicoverpa armigera* on 1, 3, 5, and 7 Days After the Treatment by Food Dipping Method for Compounds **2a–j**

	1 Day		*3 Days*		*5 Days*		*7 Days*	
Compound	*0.05*	*0.025*	*0.05*	*0.025*	*0.05*	*0.025*	*0.05*	*0.025*
2a	35 (36.17)	25 (29.94)	50 (45.00)	40 (39.15)	65 (53.72)	50 (45.00)	85 (67.79)	60 (50.78)
2b	35 (36.25)	30 (33.17)	50 (44.99)	40 (39.19)	75 (60.06)	50 (45.00)	90 (71.86)	65 (53.82)
2c	50 (45.01)	30 (33.11)	60 (50.78)	50 (45.00)	75 (60.06)	60 (50.78)	95 (77.92)	65 (53.72)
2d	55 (47.91)	35 (36.21)	65 (53.75)	50 (45.00)	85 (67.79)	65 (53.75)	100 (85.94)	70 (56.79)
2e	40 (39.17)	30 (33.17)	55 (47.87)	40 (39.22)	70 (56.83)	55 (47.90)	90 (71.86)	65 (53.75)
2f	55 (47.88)	40 (39.16)	70 (56.94)	50 (45.00)	90 (71.86)	65 (53.83)	100 (85.94)	70 (56.98)
2g	60 (50.80)	35 (36.21)	70 (56.83)	50 (45.00)	100 (85.94)	60 (50.78)	100 (85.94)	75 (60.20)
2h	55 (47.90)	40 (39.23)	85 (67.79)	60 (50.80)	100 (85.94)	70 (56.83)	100 (85.94)	75 (60.20)
2i	50 (45.00)	35 (36.25)	65 (53.82)	55 (47.88)	80 (63.52)	60 (50.80)	100 (85.94)	65 (53.82)
2j	60 (50.77)	40 (39.20)	85 (67.79)	55 (47.90)	100 (85.94)	70 (56.83)	100 (85.94)	80 (63.52)
Endosulfan	25 (29.94)		40 (39.22)		60 (50.80)		75 (60.20)	
Control	0 (4.05)		0 (4.05)		0 (4.05)		0 (4.05)	
Standard Error of Mean SEm±	1.79		1.97		1.48		1.76	
Critical difference 5%	5.06		5.58		4.19		4.98	
Coefficient of variance %	9.43		8.41		5.19		5.42	

Figures in parenthesis are angular transformation values.

in the peak ratio of 1.2:2.3:1. When two bromine atoms are present in the compound, the ideal condition for the peak ratio is 1:2:1 due to M^+, M + 2, and M + 4 ions [40]. Slight variation that is observed from the ideal values can be attributed to the contribution by isotopic sulfur, carbon, and hydrogen. Other peaks at 705 (22.85%), 602 (14.28%), 571 (20.0%), 525 (65.71%), 449 (34.28%), 422 (34.28%), 407 (17.14%), 390 (2.85%), 328 (8.57%), 299 (8.57%), 258 (77.14%), and 195 (14.28%) were also observed.

Insecticidal Activity

Helicoverpa armigera (Lepidoptera; Noctuidae), the old-world worm, is a highly polyphagous insect. This moth is a major pest threat because its larva can feed on a wide range of economically important crops including cotton, corn, tomato, legumes, and tobacco. Polyphagy, high mobility, high fecundity, and facultative diapauses are its key physiological, behavioral, and ecological characteristics that facilitate its survival even under unstable habitats.

In the present study, all the synthesized compounds **2a–j** were screened for their insecticidal activity, which was measured on third instar larvae of *H armigera* at the Department of Entomology, Agricultural Research Station, Durgapura, Jaipur, by food dipping method [41]. Different instar larvae were collected from the local chickpea (*Cicer arietinum* L.) fields in January and a larva along with chickpea leaves was placed in a plastic container with a perforated lid (10-g capacity) to avoid cannibalism. The stock culture was maintained.

A test solution was prepared by dissolving the compound in 1–2 mL of acetone, then adding water to make up the volume up to 1 L. Two doses of 0.05% and 0.025% were selected for inoculation. For control, only acetone and water mixture was used. For comparison, a standard 0.05% solution of endosulfan was also prepared in a similar way. The third instar larvae were used from the stock culture. Five insects were kept together in a container and four such replicates were prepared for both the concentrations of each compound. Chickpea shoots (2–3 g) were soaked in solutions for 10 s and dried for 3–4

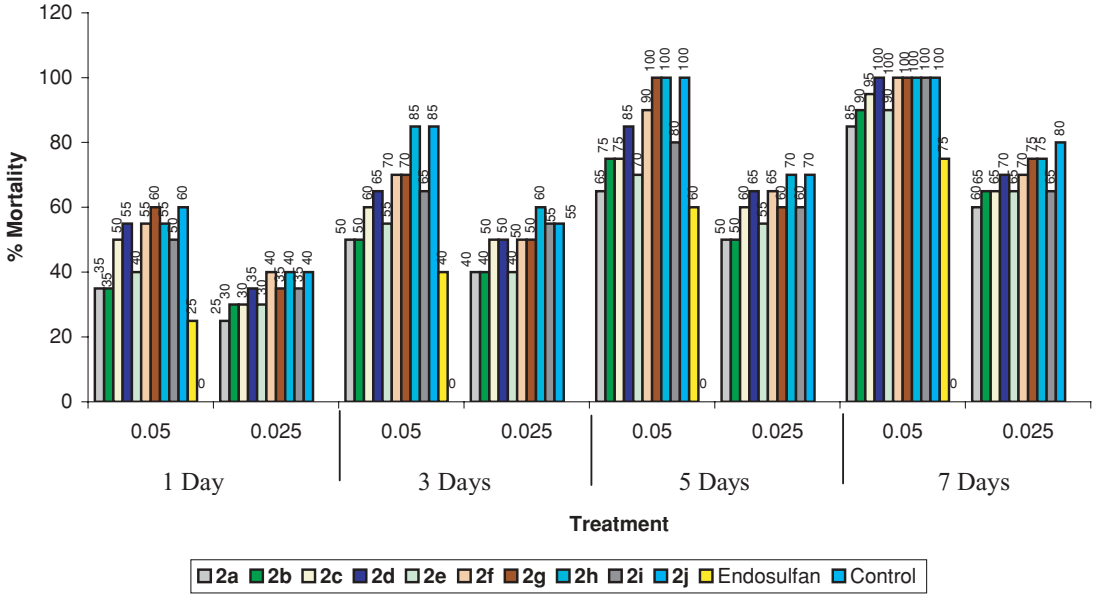


FIGURE 1 Percentage mortality of *Helicoverpa armigera* on 1, 3, 5, and 7 days after the treatment.

min at room temperature. These shoots were then introduced in the plastic container containing larvae. The percentage mortality of the larvae was recorded after 1, 3, 5, and 7 days. The moribund insects were also considered dead.

The percentage figures were then converted to the angular transformation values, which were then subjected to statistical analysis of completely randomized design technique [42]. The results obtained are presented in Table 4 (Fig. 1).

Initially after 24 h of the treatment, compound **2j** showed higher activity (60% mortality at 0.05 ppm and 40% mortality at 0.025 ppm), but after 3 days, both compounds **2j** and **2h** showed higher bioactivity than the others. At this time, compound **2j** (X = 3-Cl, 4-F, Y = 4-Br, Z = 4-OCH_3) was found to be the most potent at both the concentrations. Compound **2h** (X = H, Y = 4-Cl, Z = 4-F) was at par with compound **2j** and was also found to be a better insecticide. After 5–7 days, all the synthesized compounds showed significantly higher bioactivity, even better than endosulfan at same dosage level. No mortality was found in the untreated control. Final observation regarding the mortality was performed after 7 days of the treatment. The results are discussed with respect to the variation associated with the aryl moiety.

By comparing the insecticidal activities of compounds **2a–j**, it was found that their activities against *H. armigera* increased in the following order: **2j** > **2h** > **2g** > **2f** > **2d** > **2i** > **2c** > **2e** > **2b** > **2a**. So, it can be concluded that with the increase of electron-withdrawing power, insecticidal activity of 2,2′-(*N*,*N*′-diarylamino)-4,4′-diaryl-5,5′-arylidenebisthiazoles against the old-world worm increases.

CONCLUSION

In summary, we have developed a simple, novel, and efficient synthetic protocol for the synthesis of 2,2′-(*N*,*N*′-diarylamino)-4,4′-diaryl-5,5′-arylidenebisthiazoles using a catalytic amount of anhydrous indium trichloride under microwave or ultrasonic irradiation by electrophilic substitution reaction of 2-(*N*-arylamino)-4-arylthiazoles **1** with various arylaldehydes. The short reaction time coupled with the simplicity of the reaction procedure makes this method one of the most efficient methods for the synthesis of this class of compounds. On the basis of insecticidal evaluation, compounds **2h** and **2j** seem to be very attractive as insecticidal agents against *H. armigera*.

EXPERIMENTAL

All melting points were determined in open glass capillary tubes and are uncorrected. IR spectra (υ_{max} in cm^{-1}) were recorded on an FT-IR model Shimadzu-8400S grating infrared spectrophotometer using KBr pellets. PMR spectra were recorded on a JEOL-AL 300 spectrophotometer at 300 MHz using TMS as an internal standard (chemical shift in δ ppm) and $CDCl_3$ as a solvent. IR and PMR spectra were recorded at the Department of Chemistry, University of Rajasthan, Jaipur. FAB mass

spectra were recorded on a JEOL SX 102/DA-6000 mass spectrometer/data system using argon/xenon (6 kV, 10 mA) as the FAB gas. An Elentar Vario EL III automatic CHNS analyzer was used for elemental analyses. FAB mass spectra and CHNS analyses were recorded at the Central Drug Research Institute, Lucknow, India. Microwave irradiation was carried out in an LG MS-194A household microwave oven with a maximum 800 W power and 2450 MHz frequency. Sonication was performed in a Toshcon model SW 4 cleaner (with a frequency of 37 kHz and operating at a maximum power of 150 W). The purity of the compounds was checked by TLC using silica gel (60–120 mesh) as the adsorbent, under UV light or iodine-accomplished visualization. All common reagents and solvents were used as obtained from commercial suppliers without further purification. 2-(*N*-Arylamino)-4-arylthiozoles **1** were prepared by the following literature method [43].

Method a

A mixture of 2-(*N*-Arylamino)-4-arylthiazole (1 mmol), arylaldehyde (0.5 mmol), and anhydrous indium trichloride (20 mol%, 0.44 g) in CH_2Cl_2 (20 mL) was taken in a Pyrex conical flask (250 mL). The reaction flask was then placed in the maximum energy area in an ultrasonic cleaning bath (observation of the surface of the reaction solution during vertical adjustment of flask depth shows the optimum position by the point at which maximum surface disturbance occurs) and then it was sonicated for the time period as indicated in Table 2. The bath temperature (30°C–35°C) was controlled by the addition or removal of water. The progress of the reaction was monitored by TLC using C_6H_6:EtOAC (95:5) as the solvent system. Sonication was continued until reactants disappeared as indicated by TLC. After the completion of the reaction, the mixture was cooled to room temperature, diluted with water, and extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and evaporated to dryness under reduced pressure. Further purification was accomplished by column chromatography using silica gel (60–120 mesh) as the stationary phase and solvent of increasing polarity as the mobile phase. Pure bisthiazole was obtained in pet ether:benzene (20:80) as yellow crystalline needles.

Method b

2-(*N*-Arylamino)-4-arylthiazole (1 mmol), arylaldehyde (0.5 mmol), and anhydrous indium trichloride (20 mol%, 0.44 g) as a catalyst were mixed into a conical flask (100 mL) and exposed to microwave irradiation for 10–20 min (intermittently with 1-min cooling interval) at maximum power (800 W). The progress of the reaction was monitored by TLC using C_6H_6:EtOAC (95:5) as the eluant and the reaction was run to completion. When irradiation was stopped, the final temperature was measured by introducing a glass thermometer into the reaction mixture (65°C–70°C). After cooling it to room temperature, the reaction mixture was quenched with water and extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and evaporated to dryness under reduced pressure. Further purification was accomplished by column chromatography using silica gel (60–120 mesh) as the stationary phase and solvent of increasing polarity as the mobile phase. Pure bisthiazole was obtained in pet ether:benzene (20:80) as yellow crystalline needles.

Method c

2-(*N*-Arylamino)-4-arylthiazole (1 mmol) and arylaldehyde (0.5 mmol) in dichloromethane were refluxed in the presence of anhydrous indium trichloride (20 mol%, 0.44 g) as a catalyst for 16–22 h. After the reaction was complete (checked by TLC), the resulting mixture was poured into ice-cold water and extracted with CH_2Cl_2 (3×10 mL). The organic layers were combined, dried over anhydrous Na_2SO_4, filtered, and evaporated to dryness under reduced pressure. Further purification was accomplished by column chromatography using silica gel (60–120 mesh) as the stationary phase and solvent of increasing polarity as the mobile phase. Pure bisthiazole was obtained in pet ether:benzene (20:80) as yellow crystalline needles.

ACKNOWLEDGMENTS

The authors thank Dr. K. P. Madhusudanan, Deputy Director and Head, Sophisticated Analytical Instrument Facility, Central Drug Research Institute, Lucknow, India, for elemental analyses and spectral data. The authors also thank Dr. Swaroop Singh, Durgapura Agricultural Research Station, Jaipur, India, for providing necessary facilities during insecticidal evaluation.

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