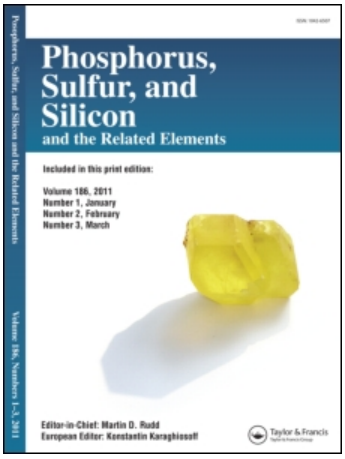

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Rapid Synthesis and Biological Activities of Some New Derivatives of Benzothiazolylhexahydro-s-triazine

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RAPID SYNTHESIS AND BIOLOGICAL ACTIVITIES OF SOME NEW DERIVATIVES OF BENZOTHIAZOLYLHEXAHYDRO-s-TRIAZINE

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1,3,5-Tri(6-substituted benzothiazolyl)-2,4,6-substitutedhexahydro-1,3,5-s-triazine derivatives were synthesized by condensation of substituted benzothiazoles with aldehydes by conventional as well as microwave irradiation (solvent free and solid support) methods. All compounds were tested for antibacterial and antifungal activities, and results have been compared with standard drugs. Acaricidal and antifeedant activities were also tested.

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Keywords Acaricidal activity; antifeedant activity; antimicrobial activity; benzothiazole; solid support MW synthesis; 1,3,5-s-triazine

INTRODUCTION

Nitrogen- and sulfur-containing heterocycles play an important role, not only for life science, but also in many other industrial fields related to special and fine chemistry. Among them, benzothiazoles comprise a class of therapeutic compounds that exert a wide range of biological activities such as antibacterial,[1–5] antifungal,[6–9] antihelmintic,[10,11] antiviral,[12,13] etc. 2-(4-Aminophenyl)benzothiazole derivatives have been extensively studied for their anticancer action.[14,15]

s-Triazine derivatives have revealed new biological activities with interesting potential in therapeutic applications besides their traditional employment as herbicidal[16–18] and antiviral[19–23] agents. They have also been reported to possess anti-HIV,[24] anticancer,[25–30] antithyroid,[31] and diuretic[32] activities. Triaminotriazine aniline amides possess potent p38 enzyme activity.[33] The synthesis of hexahydro 1,3,5-tricarbalkoxy-s-triazine and octahydro-1,3,5,7-tetracarbalkoxy tetrazocines has also been reported.[34]

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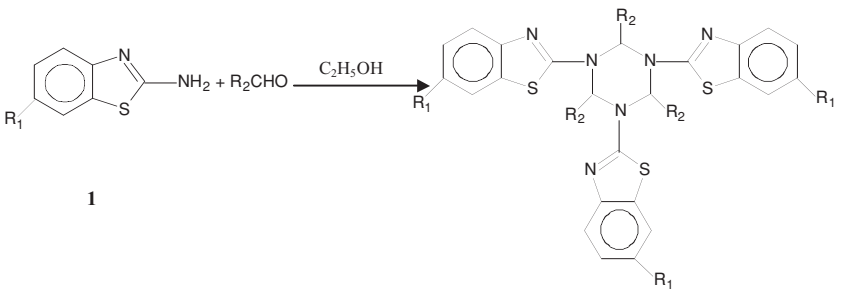
The application of microwave irradiation using solid support, used for carrying out chemical transformations that are pollution-free, ecofriendly, and are associated with high reaction yields, render the microwave method superior to conventional methods. Hence with a view to further assess the pharmacological profile of benzothiazoles, s-triazine derivatives, and benefits associated with microwave synthesis, it was thought worthwhile to synthesize some new derivatives by incorporating the 2-aminobenzothiazole and s-triazine moieties in a single molecular framework. This article deals with the synthesis of 1,3,5-tri-(6-substituted benzothiazolyl)-2,4,6-substitutedhexahydro-1,3,5-s-triazines followed by antimicrobial susceptibility test (AST) against *Lactobacillus sp.*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Micrococcus leutius*, *Kocuria rosea*, *Aspergillus niger*, and *Aspergillus candidus* using standard methods and in comparison with standard drugs. All the synthesized derivatives were also screened for their acaricidal and antifeedant activities.

RESULTS AND DISCUSSION

2-Amino-6-substitutedbenzothiazoles were synthesized by the earlier reported methods.[35,36] 1,3,5-Tri(6-substituted benzothiazolyl)-2,4,6-substitutedhexahydro-1,3,5-s-triazines were synthesized by the condensation reaction of substituted benzothizoles (1.0 mol) and aldehydes (1.0 mol) in ethanol with continuous stirring and refluxing for 13 h.

In view of long reaction time, moderate yields (Table I), tedious workup after the reaction, and requirement of large quantity of solvent associated with conventional methods, a relatively more versatile yet simplified procedure was conceived in which substituted benzothizoles and aldehydes could be made to react without using any solvent (without, as well as with, solid support). Microwave synthesis has received attention as a new strategy for organic synthesis due to the fact that many reactions seem to proceed with much alacrity under such conditions as opposed to the corresponding thermal-assisted reactions.[37] The strategy worked well and afforded the desired product in improved yields in significantly lower reaction time (Tables I and II). The synthesized compounds are characterized by their analytical and IR, ^{1}H NMR, and mass spectral data.



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Scheme 1

EXPERIMENTAL

Reagent grade chemicals were used without further purification. The substrates and solvents were used as received. All the melting points are taken in open capillaries and

Table I Preparation of 1,3,5-tri(6-substituted benzothiazolyl)-2,4,6-substitutedhexahydro-1,3,5-s-triazines

				Conventional heating		Microwave (neat reaction)	
Compound	R_1	R_2	Mp °C	Time (h)	Yield (%)	Time (min)	Yield (%)
2a	OCH_3	H	100	13	50	3.5	60
2b	OCH_3	CH_3	110	13	52	3.0	60
2c	OCH_3	$CH_3CH{=}CH-$	135	13	50	3.5	60
2d	OC_2H_5	H	125	13	58	3.0	60
2e	OC_2H_5	CH_3	130	13	50	3.0	65
2f	OC_2H_5	$CH_3CH{=}CH-$	132	13	58	3.0	66
2g	CH_3	H	128	13	50	3.0	63
2h	CH_3	CH_3	95	13	55	3.0	65
2i	CH_3	$CH_3CH{=}CH-$	129	13	50	3.0	63
2j	NO_2	H	112	13	51	3.5	65
2k	NO_2	CH_3	140	13	55	3.0	60
2l	NO_2	$CH_3CH{=}CH-$	127	13	52	3.0	65
2m	CI	H	120	13	48	3.5	62
2n	Cl	CH_3	98	13	52	3.5	65
2o	Cl	$CH_3CH{=}CH-$	135	13	50	3.5	62
2p	Br	H	102	13	56	3.0	65
2q	Br	CH_3	117	13	53	3.5	55
2r	Br	$CH_3CH{=}CH-$	170	13	55	3.5	65

Table II Preparation of 1,3,5-tri(6-substituted benzothiazolyl)-2,4,6-substitutedhexahydro-1,3,5-s-triazines

	Solid supported microwave irradaition							
	Silica		Alumina basic		Alumina neutral		Alumina acidic	
Compound	Time (min)	Yield (%)	Time (min)	Yield (%)	Time (min)	Yield (%)	Time (min)	Yield (%)
2a	4.0	50	3.5	55	2.0	65	1.5	75
2b	4.0	50	3.5	65	2.0	75	1.5	80
2c	2.5	50	2.5	55	1.5	65	1.0	80
2d	4.0	58	3.5	60	2.0	68	1.5	75
2e	4.0	50	3.5	60	2.0	65	1.5	78
2f	2.5	58	2.0	60	1.5	68	1.0	80
2g	4.0	55	3.5	60	2.0	66	1.5	75
2h	4.0	52	3.5	65	2.0	78	1.0	84
2i	2.5	55	2.0	66	1.5	82	1.0	92
2j	4.5	55	3.5	60	2.0	68	1.5	78
2k	3.5	50	3.0	58	2.5	65	2.0	75
2l	2.5	55	2.0	58	1.5	68	1.0	80
2m	4.0	55	3.5	60	2.0	65	1.5	76
2n	4.0	57	3.5	59	2.0	68	1.5	72
2o	2.5	55	2.0	58	1.0	65	0.5	85
2p	2.5	58	2.0	68	1.5	80	1.0	87
2q	4.0	58	3.5	60	2.0	67	1.5	78
2r	2.5	58	2.0	61	1.5	65	1.0	92

are uncorrected. The purity of synthesized compounds was checked by thin layer chromatographic studies. IR spectra were measured on FT IR Perkin Elmer (Spectrum RX1) spectrophotometer (υ in cm^{-1}) using KBr disc. ^1H NMR were recorded in $CDCl_3$ and DMSO with tetramethylsilane (TMS) as the internal standard at 300 MHz on a Bruker DRTX-300 spectrophotometer. The chemical shifts are reported as parts per million (ppm). Fast atom bombardment mass spectra (FABMS) were recorded at room temrature on a Jeol SX-102/DA-6000 mass spectrophotometer/data system using Argon/Xenon (6 kV, 10 mA) as the FAB gas. The accelerating potential was 10 kV. Microwave synthesis was carried out in a Q-pro-M Modified Microwave system. The elemental analysis of compounds was performed on a Carlo Erba-1108 elemental analyzer.

General Procedure for the Synthesis of 1,3,5-Tri-(6-substituted benzothiazolyl)-2,4,6-substitutedhexahydro-1,3,5-s-triazines

Conventional method. 2-Amino-6-substituted benzothiazoles (0.1 mol) and aldehydes (0.1 mol) were taken in a round bottom flask dissolved in absolute ethanol (10 mL) with constant stirring for 30 min. The reaction was stirred and heated for a further 13 h. The desired triazines were separated out with evaporation of ethanol under vacuum. The impurities were dissolved in diethyl ether and the desired product was obtained by washing with petroleum ether (40–60°C).

Microwave method. 2-Amino-6-substituted benzothiazoles (0.01 mol) and aldehydes (0.01 mol) were taken in a round bottom flask and subjected to microwave irradiation. On completion of the reaction as monitored by TLC (at an interval of 30 sec), the reaction mixture was cooled and the sticky mass obtained was triturated with a few drops of petroleum ether (40–60°C). It was dried and recrystallized from ethanol.

Solid supported microwave synthesis. To a mixture of 2-amino-6-substituted benzothiazoles (0.01 mol) and aldehydes (0.01 mol), solid support alumina (acidic/basic/neutral) and silica gel were mixed thoroughly in a mortar, then the reaction mixture was transferred to a round bottom flask and irradiated in a microwave oven at 30 sec intervals of specified times. Upon completion of the reaction as monitored by TLC, the reaction mixture was cooled and the sticky mass obtained was titurated with a few drops of petroleum ether (40–60°C). It was dried and recrystallized from ethanol.

1,3,5-Tri(6-methoxybenzothiazolyl)-2,4,6-hexahydro-1,3,5-s-triazine (2a). ^1H NMR: 3.91 (s, 9H), 7.32–7.91 (m, 9H), 1.76 (s, 6H); Mass: 576 (M^+); IR (cm^{-1}): ν_{max} 1057, 1140, 1170, 1350, 1460, 1465, 1545, 1586, 2960; Anal. Calcd. For $C_{27}H_{24}N_6O_3S_3$: C, 56.23; H, 4.19; N, 14.57; O, 8.32; S, 16.68; Found: C, 56.20; H, 4.15; N, 14.54; O, 8.30; S, 16.63.

1,3,5-Tri(6-methoxybenzothiazolyl)-2,4,6-trimethylhexahydro-1,3,5-s-triazine (2b). ^1H NMR: 3.92 (s, 9H), 7.33–7.90 (m, 9H), 3.84 (q, $J = 6.9$ Hz, 3H), 1.25–1.27 (d, $J = 6.3$ Hz, 9H); Mass: 618 (M^+); IR (cm^{-1}): ν_{max} 1000, 1050, 1150, 1180, 1210, 1540, 1585; Anal. Calcd. For $C_{30}H_{30}N_6O_3S_3$: C, 58.23; H, 4.89; N, 13.58; O, 7.76; S, 15.54; Found: C, 58.21; H, 4.85; N, 13.51; O, 7.72; S, 15.52.

1,3,5-Tri(6-methoxybenzothiazolyl)-2,4,6-tri(1-propenyl)-hexahydro-1,3,5-s-triazine (2c). ^1H NMR: 3.91 (s, 9H), 7.33–7.91 (m, 9H), 3.95 (d, $J = 5.1$ Hz, 3H), 2.95 (d, $J = 5.9$ Hz, 9H), 6.20 (dd, $J = 6.3$ Hz, $J = 6.2$ Hz, 3H), 6.92 (dq, $J = 3.1$ Hz, $J = 2.9$ Hz, 3H); Mass: 696 (M^+); IR (cm^{-1}): ν_{max} 1058, 1140, 1170, 1460, 1550, 1590, 1625, 2960, 3059; Anal. Calcd. For $C_{36}H_{36}N_6O_3S_3$: C, 62.05; H, 5.21; N, 12.06; O, 6.89; S, 13.80; Found: C, 62.00; H, 5.15; N, 12.02; O, 6.81; S, 13.79.

1,3,5-Tri(6-ethoxybenzothiazolyl)-2,4,6-hexahydro-1,3,5-s-triazine (2d). ^{1}H NMR: 2.32 (t, $J = 6.6$ Hz, 9H), 4.21 (q, $J = 6.0$ Hz, 6H), 7.32–7.91 (m, 9H), 2.17 (s, 6H); Mass: 618 (M^+); IR (cm^{-1}): ν_{max} 1054, 1224, 1350, 1355, 1460, 1468, 1540, 1595, 2973; Anal. Calcd. For $C_{30}H_{30}N_6O_3S_3$: C, 58.23; H, 4.89; N, 13.58; O, 7.76; S, 15.54; Found: C, 58.20; H, 4.87; N, 13.88; O, 7.73; S, 15.56.

1,3,5-Tri(6-ethoxybenzothiazolyl)-2,4,6-trimethylhexahydro-1,3,5-s-triazine (2e). ^{1}H NMR: 2.62 (t, $J = 6.1$ Hz, 9H), 3.41 (q, $J = 7.1$ Hz, 6H), 7.44–7.89 (m, 9H), 3.91 (q, $J = 6.7$ Hz, 3H), 1.54–1.57 (d, $J = 6.1$ Hz, 9H); Mass: 660 (M^+); IR (cm^{-1}): ν_{max} 920, 1040, 1150, 1200, 1460, 1530, 1595; Anal. Calcd. For $C_{33}H_{36}N_6O_3S_3$: C, 59.98; H, 5.49; N, 12.72; O, 7.26; S, 14.55; Found: C, 59.95; H, 5.47; N, 12.68; O, 7.22; S, 14.52.

1,3,5-Tri(6-ethoxybenzothiazolyl)-2,4,6-tri(1-propenyl)-hexahydro-1,3,5-s-triazine (2f). ^{1}H NMR: 2.62 (t, $J = 6.2$ Hz, 9H), 7.45–7.88 (m, 9H), 3.40 (q, $J = 7.1$ Hz, 6H), 3.90 (q, $J = 6.6$ Hz, 3H), 2.90 (d, $J = 5.8$ Hz, 9H), 6.20 (dd, $J = 6.3$ Hz, $J = 6.2$ Hz, 3H), 6.91 (dq, $J = 3.1$ Hz, $J = 3.0$ Hz, 3H); Mass: 738 (M^+); IR (cm^{-1}): ν_{max} 1050, 1150, 1158, 1186, 1455, 1530, 1620, 2900, 3075; Anal. Calcd. For $C_{39}H_{42}N_6O_3S_3$: C, 63.39; H, 5.73; N, 11.37; O, 6.50; S, 13.02; Found: C, 63.36; H, 5.70; N, 11.32; O, 6.48; S, 13.00.

1,3,5-Tri(6-methylbenzothiazolyl)-2,4,6-hexahydro-1,3,5-s-triazine (2g). ^{1}H NMR: 2.25 (s, 9H), 7.72–8.29 (m, 9H), 2.17–2.18 (s, 6H); Mass: 528 (M^+); IR (cm^{-1}): ν_{max} 1150, 1360, 1460, 1468, 1540, 1585, 2878, 2900; Anal. Calcd. For $C_{27}H_{24}N_6S_3$: C, 61.34; H, 4.58; N, 15.90; S, 18.19; Found: C, 61.31; H, 4.55; N, 15.89; S, 18.16.

1,3,5-Tri(6-methylbenzothiazolyl)-2,4,6-trimethylhexahydro-1,3,5-s-triazine (2h). ^{1}H NMR: 2.24 (s, 9H), 7.71–8.22 (m, 9H), 3.98 (q, $J = 6.8$ Hz, 3H), 1.96 (d, $J = 6.1$ Hz, 9H); Mass: 570 (M^+); IR (cm^{-1}): ν_{max} 980, 1150, 1210, 1540, 1586, 2860, 2900; Anal. Calcd. For $C_{30}H_{30}N_6S_3$: C, 63.13; H, 5.30; N, 14.72; S, 16.85; Found: C, 63.12; H, 5.28; N, 14.71; S, 16.81.

1,3,5-Tri(6-methylbenzothiazolyl)-2,4,6-tri(1-propenyl)-hexahydro-1,3,5-s-triazine (2i). ^{1}H NMR: 2.21 (s, 9H), 7.74–8.21 (m, 9H), 3.85 (d, $J = 5.2$ Hz, 3H), 2.95 (d, $J = 5.9$ Hz, 9H), 6.00 (dd, $J = 6.4$ Hz, $J = 6.3$ Hz, 3H), 6.71 (dq, $J = 3.2$ Hz, $J = 3.0$ Hz, 3H); Mass: 648 (M^+); IR (cm^{-1}): ν_{max} 1150, 1460, 1540, 1586, 1650, 2860, 2900, 3090; Anal. Calcd. For $C_{36}H_{36}N_6S_3$: C, 66.64; H, 5.59; N, 12.95; S, 14.82; Found: C, 66.62; H, 5.57; N, 12.94; S, 14.80.

1,3,5-Tri(6-nitrobenzothiazolyl)-2,4,6-hexahydro-1,3,5-s-triazine (2j). ^{1}H NMR: 2.59–2.64 (s, 6H), 7.51–7.99 (m, 9H); Mass: 621 (M^+); IR (cm^{-1}):ν_{max} 1320, 1330, 1385, 1465, 1505, 1539, 1580; Anal. Calcd. For $C_{24}H_{15}N_9O_6S_3$: C, 46.37; H, 2.43; N, 20.28; O, 15.44; S, 15.47; Found: C, 46.35; H, 2.40; N, 20.22; O, 15.43; S, 15.45.

1,3,5-Tri(6-nitrobenzothiazolyl)-2,4,6-trimethylhexahydro-1,3,5-s-triazine (2k). ^{1}H NMR: 2.17 (d, $J = 6.3$ Hz, 9H), 7.55–7.91 (m, 9H), 3.64–3.66 (q, $J = 6.8$ Hz, 3H); Mass: 663 (M^+); IR (cm^{-1}): ν_{max} 970, 1215, 1330, 1385, 1465, 1505, 1539, 1580; Anal. Calcd. For $C_{27}H_{21}N_9O_6S_3$: C, 48.86; H, 3.19; N, 18.99; O, 14.46; S, 14.49; Found: C, 48.84; H, 3.17; N, 18.95; O, 14.44; S, 14.47.

1,3,5-Tri(6-nitrobenzothiazolyl)-2,4,6-tri(1-propenyl)-hexahydro-1,3,5-s-triazine (2l). ^{1}H NMR: 2.42 (d, $J = 6.0$ Hz, 9H), 7.51–7.95 (m, 9H), 3.98 (d, $J = 5.0$ Hz, 3H), 6.01 (dd, $J = 6.4$ Hz, $J = 6.3$ Hz, 3H), 6.22 (dq, $J = 3.4$ Hz, $J = 3.2$ Hz, 3H); Mass: 741 (M^+); IR (cm^{-1}): ν_{max} 1330, 1385, 1465, 1505, 1539, 1580, 1626, 3025; Anal. Calcd. For $C_{33}H_{27}N_9O_6S_3$: C, 53.43; H,3.67; N,16.99;O,12.94;S,12.97;Found: C, 53.41; H,3.65; N,16.94;O,12.93;S,12.96.

1,3,5-Tri(6-chlorobenzothiazolyl)-2,4,6-hexahydro-1,3,5-s-triazine (2m). ^{1}H NMR: 2.52–2.62 (s, 6H), 7.37–7.93 (m, 9H); Mass: 589 (M^+); IR (cm^{-1}): ν_{max} 864, 1310, 1450, 1468, 1535, 1580; Anal. Calcd. For $C_{24}H_{15}N_6S_3Cl_3$: C, 48.86; H, 2.56; N, 14.25; S, 16.30; Cl, 18.03; Found: C, 48.83; H, 2.52; N, 14.22; S, 16.29; Cl, 18.01.

1,3,5-Tri(6-chlorobenzothiazolyl)-2,4,6-trimethylhexahydro-1,3,5-s-triazine (2n). ^{1}H NMR: 3.54–3.59 (q, $J = 7.0$ Hz, 3H), 7.34–7.99 (m, 9H), 1.95 (d, $J = 5.6$ Hz, 9H); Mass: 635 (M^+); IR (cm^{-1}): ν_{max} 817, 1100, 1310, 1320, 1466, 1479, 1528, 1587; Anal. Calcd. For $C_{27}H_{24}N_6S_3Cl_3$: C, 51.07; H, 3.81; N, 13.23; S, 15.14; Cl, 16.75; Found: C, 51.05; H, 3.80; N, 13.21; S, 15.12; Cl, 16.72.

1,3,5-Tri(6-chlorobenzothiazolyl)-2,4,6-tri(1-propenyl)-hexahydro-1,3,5-s-triazine (2o). ^{1}H NMR: 2.23 (d, $J = 6.2$ Hz, 9H), 7.31–7.96 (m, 9H), 6.02 (dd, $J = 6.5$ Hz, $J = 6.4$ Hz, 3H), 6.30 (dq, $J = 3.5$ Hz, $J = 3.4$ Hz, 3H), 4.12 (d, $J = 5.0$ Hz, 3H); Mass: 710 (M^+); IR (cm^{-1}): ν_{max} 864, 1310, 1450, 1535, 1580, 1625, 3010; Anal. Calcd. For $C_{33}H_{27}N_6O_3S_3$: C, 55.81; H, 3.83; N, 11.83; S, 13.54; Cl, 14.98; Found: C, 55.80; H, 3.80; N, 11.81; S, 13.52; Cl, 14.96.

1,3,5-Tri(6-bromobenzothiazolyl)-2,4,6-hexahydro-1,3,5-s-triazine (2p). ^{1}H NMR: 2.55–2.65 (s, 6H), 7.21–7.89 (m, 9H); Mass: 723 (M^+); IR (cm^{-1}): ν_{max} 856, 1320, 1340, 1460, 1465, 1531, 1588; Anal. Calcd. For $C_{24}H_{15}N_6S_3Br_3$: C, 39.85; H, 2.09; N, 11.62; S, 13.30; Br, 33.14; Found: C, 39.81; H, 2.08; N, 11.60; S, 13.29; Br, 33.13.

1,3,5-Tri(6-bromobenzothiazolyl)-2,4,6-trimethylhexahydro-1,3,5-s-triazine (2q). ^{1}H NMR: 3.55–3.60 (q, $J = 7.0$ Hz, 3H), 7.23–7.85 (m, 9H), 1.85 (d, $J = 6.0$ Hz, 9H); Mass: 768 (M^+); IR (cm^{-1}): ν_{max} 854, 1110, 1320, 1350, 1460, 1531, 1589; Anal. Calcd. For $C_{27}H_{24}N_6S_3Br_3$: C, 42.20; H, 3.15; N, 10.94; S, 12.52; Br, 31.20; Found: C, 42.18; H, 3.12; N, 10.90; S, 12.51; Br, 31.16.

1,3,5-Tri(6-bromobenzothiazolyl)-2,4,6-tri(1-propenyl)-hexahydro-1,3,5-s-triazine (2r). ^{1}H NMR: 4.18 (d, $J = 4.9$ Hz, 3H), 7.23–7.88 (m, 9H), 2.21 (d, $J = 6.1$ Hz, 9H), 6.00 (dd, $J = 6.4$ Hz, $J = 6.1$ Hz, 3H), 6.44 (dq, $J = 3.6$ Hz, $J = 3.4$ Hz, 3H); Mass: 843 (M^+); IR (cm^{-1}): ν_{max} 854, 1320, 1460, 1531, 1582, 1620, 3025; Anal. Calcd. For $C_{33}H_{27}N_6S_3Br_3$: C, 46.99; H, 3.23; N, 9.96; S, 11.40; Br, 28.42; Found: C, 46.96; H, 3.21; N, 9.95; S, 11.37; Br, 28.40.

Antimicrobial, Antiacarial, and Antifeedant Activities

All the synthesized compounds were tested for their antibacterial activity against *Lactobacillus sp.*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Micrococcus leutius* and *Kocuria rosea* and antifungal activity against *Aspergillus candidus* and *Aspergillus niger* using the paper disc method. The acaricidal activity of these compounds was carried out by the leaf dip method.[38,39] The antifeedant activity of these compounds was also carried out by the leaf dip method.[38,39] The results are summarized in Tables III–V (available online in the Supplemental Materials).

CONCLUSION

Antibacterial Activity

The substituted benzothiazoles show very low activity against all the bacteria under study. But 1,3,5-tri(6-substituted benzothiazolyl)-2,4,6-substitutedhexahydro-1,3,5-s-triazines derivatives show enhanced activity comparable to standard drugs. Compounds

2j, **2m**, and **2q** exhibit considerable antibacterial activity against *Lactobacillus sp.*. Compounds **2l**, **2o**, and **2r** show good activity against *Pseudomonas aeruginosa.* Compounds **2f**, **2i**, and **2l** exhibit significant activity against *Staphylococcus aureus.* Compounds **2f**, **2i**, and **2r** show good results against *Kocuria rosea.*

Antifungal Activity

1,3,5-Tri(6-substituted benzothiazolyl)-2,4,6-substitutedhexahydro-1,3,5-s-triazines exhibit higher antifungal activities as compared to corresponding benzothiazoles, but only moderate activity as compared to standard drugs.

Acaricidal Activity

It is evident from LD_{50} values, which are given in Table III (available online in the Supplemental Materials), compound **2e** has lowest LD_{50} value, and so possesses more contact toxicity against insects. The decreasing order of contact toxicity of compounds is as follows: **2e** > **2i** = **2k** = **2m** = **2p** = **2q** = **2r** > **2f** = **2n** > **2b** > **2a** = **2g** = **2j** > **2d** > **2c** = **2o** > **2l** > **2h**.

Antifeedant Activity

It is evident from LD_{50} values, which are given in Table IV (available online in the Supplemental Materials), compound **2k** has the lowest LD_{50} value, and so possesses more contact toxicity against insects. The decreasing order of contact toxicity of compounds is as follows: **2k** > **2i** > **2e** > **2r** > **2n** > **2h** > **2p** > **2f** = **2g** > **2c** > **2o** > **2j** > **2d** = **2m** > **2l** > **2b** > **2a** = **2q**.

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