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Synthesis and Chemical Reactivity of Novel Functionally Substituted-5,6-Diphenyl-1,2,4-Triazines

J M Morsy, F Ismail, R M Abdel-Rahman* and H A Amine

Chemistry Department, Faculty of Education, Ain-Shams University, Roxy, Cairo, Egypt

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An improved synthesis of some new fully substituted-5,6-diphenyl-1,2,4-triazines starting from 4H-2-cyanomethyl/aryl-5,6-diphenyl-1,3,4-oxadiazines (3a-d) has been reported. The structures were determined through elemental analysis and spectral data. The mass spectra of the synthesized compounds were also studied. Some of these compounds exhibited significant antimicrobial activity.

Key words: Synthesis, Fully substituted-1,2,4-triazines, Elemental analysis, Triazines.

Introduction

In continuation of the earlier works of authors on 5,6-diphenyl-1,2,4-triazine derivatives (Abdel-Rahman and Islam 1993; Abdel-Rehman *et al* 1993 a,b; 1994), a facile synthesis of functionally substituted 5,6-diphenyl-1,2,4-triazines starting from 1,3,4-oxadiazine derivatives has been described here in a modified approach. Their reactivity towards some nucleophilic nitrogen reagents under different reaction conditions was tested and has been described.

Experimental

Melting points are uncorrected. IR spectra were recorded in KBr on a FT-IR 1650 spectrophotometer (λ_{max} in cm^{-1}), 90 MHz ^{1}H-NMR spectra in DMSO-d6 on an JNM-PMX 60 spectrophotometer using TMS as internal standard (chemical shift in δ ppm) whereas UV spectra (λ_{max} in nm) in absolute ethanol on Perkin Elmer lambda 3B and mass spectra on a gas chromatographic GC-MS_{qp} 1000 ex Shimadzu instrument at 70eV. The purity of the compounds was checked by ascending TLC ($CHCl_3$-MeOH) (Scheme I).

*Synthesis of fully substituted 1,2,4-triazine derivatives (**4a-d**): I a. Reaction of I with ethyl cyanoacetate: Formation of **2a**.* A mixture of benzoin hydrazine (**1**) (0.01 mol) and ethyl cyanoacetate (0.01 mol) in dry benzene (20 ml) was refluxed for 2 h and on concentration, a solid was obtained. It was recrystallized to give **2a** (Table 1); IR: 3500 (OH), 3050 (NH), 2220 (C=N), 1700 (C=O), 1610 (C=N), 1480 (def. CH_2) and 900 cm^{-1} (phenyl groups).

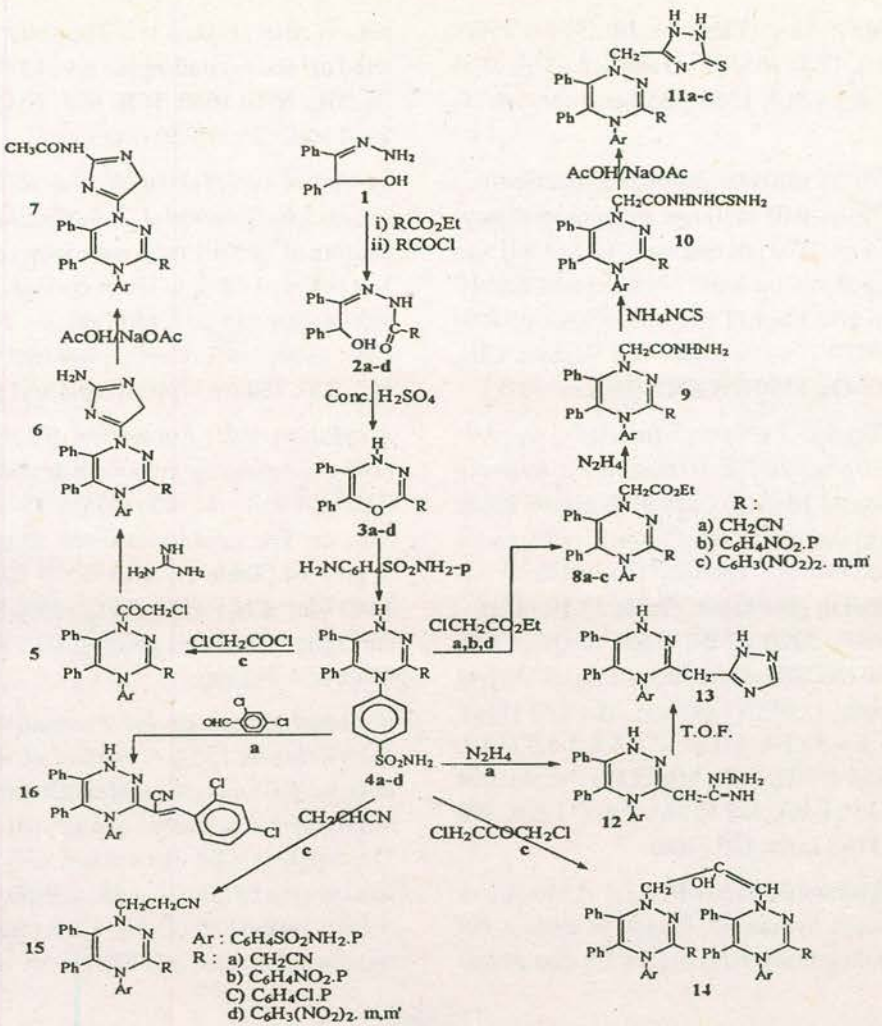
*I b. Reaction of aroyl chlorides with I: Formation of **2b-d**.* A mixture of benzoin hydrazine (**1**) (0.01 mol) and the appropriate aroyl chlorides: *p*-nitrobenzoyl chloride, *p*-chlorobenzoyl chloride and 3,5-dinitorbenzoyl chloride (0.01 mol) in DMF (20 ml) was refluxed for 15 min, cooled and poured onto crushed ice. The solid obtained was filtered off and crystallized to give **2b-d** (Table 1); IR (**2b**) 3500-3100 (b.NH, OH), 1720-1700 (C=O), 1580 (C=N), 1530, 1340 cm^{-1} (asy. & sy. NO_2). UV (**2b**): 312.40 (ε 0.726) and 250.0 (ε 0.912) nm.

*II.Synthesis of 4H-2-cyanomethyl/aryl-5,6-diphenyl-1,3,4-oxadiazines (**3a-d**).* Compounds **2a-d** (1g) were stirred with conc H_2SO_4 (2ml) for 2 h and poured onto crushed ice with stirring. The solids thus obtained were filtered off and crystallized to give **3a-d** (Table 1); IR (3a): υ_{max}, 3100 (NH), 2205 (C≡N) 1610, 1590 (2C=N), 1480 (def. CH_2), 1060 (cyclic C-O-C) and 880, 790 cm^{-1} (phenyl groups). UV (**3a**): 205.5 (ε 1.555)nm.

*III.Synthesis of IH-3-cyanomethyl/aryl-5,6-diphenyl-4-(p-sulphamido-benzene)-1,2,4-triazines (**4a-d**).* A mixture of **3a-d** (0.01 mol) and sulfanilamide (0.01 mol) in dry pyridine (20 ml) was refluxed for 10-12 h, cooled and poured onto crushed ice. The solids obtained were filtered off and crystallized to give **4a-d** (Table 1); IR (**4a**): υ 3206-2950 (b. NH, aromatic and aliphatic CH), 2200 (C≡N), 1440, 1470 (def. CH_2), 1250 (SO_2) and 850, 780 cm^{-1} (phenyl groups); UV (**4a**) λmax:244.4 (ε 1.643) and 203.6 (ε 2.380) nm; ^{1}H-NMR (**4a**): δ 3.8-4.2 (2H, CH_2CN), δ 7.0-8.2 (14H, aromatic protons), δ 11.0-12.1 (3H, NH, NH_2 protons). Mass spectra (**4a**), M/e (intensity%): 429 (1.17), 412 (0.86), 385 (16.37), 358 (1.98),293 (6.95); 178 (23.0), and 115 (12.62), 105 (100); 273 (2.85). 233 (28.16). IR (**4b**): υ_{max} 3200-3020 (b. NH_2, NH), 1600 (C=N), 1520, 1340 (asy. & sy. NO_2), 1230 (SO_2) and 800, 780 cm^{-1} (phenyl and aryl groups); UV (**4b**): 256.2 (ε 1.426)nm.

*Acylation of **4c**: Formation of N-chloroacetyl deriva-*

*Author for correspondence



Scheme 1

tive 5. A mixture of **4c** (0.01 mol) and chloroacetyl chloride (0.01 mol) in DMF (20 ml) was refluxed for 1 h, cooled and poured onto crushed ice. The solid thus obtained was crystallized to give 5 (Table 1); IR: υ 1680 (C=O), 1610 (C=N), 1470 (def.CH_2), 1260 (SO_2), and 820, 800, 780 (phenyl and aryl groups).

Synthesis of 2-Amino -5-dihydro-4 (3,4-diaryl-5,6-diphenyl-1,2,4-triazin-l-yl) imidazoline (6). A mixture of **5** (0.01 mol) and guanidine hydrochloride (0.01 mol, in 5 ml H_2O), in DMF (50 ml) was refluxed for 10 h, cooled and poured onto crushed ice. The resultant solid was crystallized to give **6** (Table 1); IR:υ 3424 (NH_2), 3057 (aromatic CH), 2918 (aliphatic CH), 1630 (deformation NH_2), 1599 (C=N), 1288 (SO_2), 782 (phenyl group) and 694 cm^{-1} (C-Cl).

Acylation of 6: Formation of N-acetylamino derivative 7. A suspension of **6** (0.01 mol) in glacial acetic acid (20 ml), with fused sodium acetate (5 g) was refluxed for 4 h, cooled and poured onto ice. The solid thus produced was filtered and crystallized to give **7** (Table 1); IR:υ 3100 (NH_2, NH), 1680 (C=O), 1600, 1590 (C=N), 1440 (deformation CH2); 1250 (SO_2) and 850, 820, 770 cm^{-1} (aryl and phenyl groups).

Alkylation of 4a, 4b and 4d: Formation of N'-ethyl acetate derivatives 8a-c. An equimolar amount of **4a, 4b, 4d** and ethyl chloroacetate in DMF (20 ml) was refluxed for 2 h, cooled and poured onto ice. The solid thus resulted was filtered and crystallized to give **8a-c** (Table 1); IR (8b): 3020, 2990 (aromatic and aliphatic CH), 1760 (C=O), 1600, 1580 (C=N), 1520, 1330 (asy. & sy. NO_2), 1050 (C-O-C) and 800, 780 cm^{-1} (phenyl and aryl groups).

Preparation of acetic acid hydrazide derivatives 9a-c. A mixture of **8a-c** (0.01 mol) and hydrazine hydrate (0.012 mol), in abs. ethanol (25 ml) was refluxed for 3 h, cooled and poured onto crushed ice. The solid obtained was filtered off

and crystallized to give **9a-c** (Table 1); IR (**9b**):υ 3500-3000(broad, NH_2, NH), 1700-1650 (C=O and def. NH_2), 1590 (C=N), 1480, 1440 (def. CH_2), 1520, 1350 cm^{-1} (asy. & sy. NO_2).

*Preparation of N¹-acyl thiosemicarbazide derivatives **10a-c**.* A mixture of **9a-c** (0.01 mol) and ammonium thiocyanate (0.01 mol) in ethanol (20 ml) and conc. HCl (3 ml) was refluxed for 2 h, cooled and the solid obtained was filtered off and crystallized to give **10a-c** (Table 1). IR (**10a**): υ 3500-3050 (b. NH_2, NH), 3020-2980 (aromatic and aliphatic CH), 2180 (C≡N), 1680 (C=O), 1350 (NCSN) 1250 cm^{-1} (SO_2).

*Synthesis of 1,2-dihydro-3-thioxo-5-(methyl-1-yl-3,4-disubstituted-5,6-diphenyl-1,2,4-triazine)-s-triazole (**11a-c**).* A suspension of **10a-c** (0.01 mol) in glacial acetic acid (50 ml) and fused sodium acetate (5 g) was refluxed for 4 h, cooled and poured onto ice. The solid thus obtained was filtered and crystallized to give **11a-c,** (Table 1). IR (**11a**): υ 3378–3058 (NH-NH), 2220 (C≡N), 1600 (C=N), 1470, 1440 (def. CH_2), 1350 (NCSN), 1250 (SO_2), 1170 (C-S) and 850, 820 780 cm^{-1} (phenyl and aryl groups). ^{1}H-NMR (**11a**): δ 3.5 (2H, CH_2CN), δ 4.5 (2H, N-CH_2-C), δ 6.5-8.5 (14H, aromatic protons) and 9.5 (1H, NH). M/e (**11b**) (Int.%): 624 (0.26), 511 (0.94), 114 (1.46), 389 (0.28), 310 (11.26), 298 (3.45), 178 (20.77), 119 (3.03), 105 (100).

Synthesis of iminohydrazine derivative 12. A mixture of **4a** (0.01 mol), hydrazine hydrate (0.01 mol) in ethanol (20 ml) and piperidine (2 drops) was refluxed for 2 h, cooled and poured onto crushed ice. The solid thus produced was filtered off and crystallized to give **12** (Table 1); IR: 3300-3050 (b. NH_2, NH), 1630, 1610 (def. NH_2, C=NH), 1590 (C=N), 1480 (def. CH_2), 1260 (SO_2) cm^{-1}.

*Synthesis of 1H-5-[methyl-3-yl-4-(p-sulphamido benzene)-5,6-diphenyl-1,2,4-triazine]-s-triazole (**13**).* A mixture of **12** (0.01 mol) and triethyl orthoformate (0.02 mol) was refluxed for 2 h. Upon cooling, the solid obtained was recrystallized to give **13** (Table 1). IR: υ 3300-3100 (b.NH, NH), 1600, 1590 (C=N), 1440 (def. CH_2), 1250 (SO_2) and 850, 800, 780 cm^{-1} (phenyl and aryl groups).

*Alkylation of **4c**: Formation of 1,3-diheteroaryl acetone (**14**).* An equimolar amount of **4c** and 1,3-dichloroacetone in DMF (20 ml) was refluxed for 15 min, cooled and poured onto ice. The solid isolated was filtered off and crystallized to give **14** (Table 1); IR: υ 3500 (OH), 1670 (C=O), 1470, 1440 (def. CH_2) 1250 (SO_2), 850, 820, 800, 780 and 750 cm^{-1} (phenyl and aryl groups); UV: λ_{max} 370.2 (ε 0.003) and 234.0 (ε 1.842)nm.

*Cyanoethylation of **4c**: Formation of fully substituted 1,2,4-triazine (**15**).* A mixture of **4c** (0.01 mol) and acrylonitrile (0.01 mol) in pyridine (30 ml) and water (10 ml) was refluxed for 4 h, cooled and poured onto crushed ice-HC1. The resulting solid was washed with cold water and crystallized to give **15** (Table 1); IR: υ 2950, 2880 (CH_2, CH_2), 2200 (C≡N), 1600-1570 (C=N), 1250 (SO_2), 850, 820, 780 (aryl and phenyl groups) and 690 cm^{-1} (C-C1).

Table 1

Physical and analytical data of the prepared compounds 2-16

No.	m.p. °C	yield (%)*	M.F. (M.Wt.)	Analysis, Found/Calculated (%) C	H	N	X-ray Cl	S
2a	188	85[a]	$C_{17}H_{15}N_3O_2$ 293	69.05 (69.62)	4.90 (5.12)	13.80 (14.33)	-	-
2b	189	87[b]	$C_{21}H_{17}N_3O_4$ 375	67.25 (67.73)	4.30 (4.53)	10.81 (11.2)	-	-
2c	194	75[b]	$C_{21}H_{17}N_2O_2Cl$ 364	68.79 (69.23)	4.50 (4.67)	7.09 (7.69)	8.95 (9.61)	-
2d	194	74[b]	$C_{21}H_{16}N_4O_6$ 420	59.81 (60.00)	3.55 (3.80)	13.01 (13.33)	-	-
3a	120	86[b]	$C_{17}H_{13}N_3O$ 275	74.00 (74.18)	4.52 (4.72)	15.01 (15.27)	-	-
3b	212	70[b]	$C_{21}H_{15}N_3O_2$ 341	73.55 (73.90)	4.40 (4.39)	12.00 (12.31)	-	-
3c	185	76[b]	$C_{21}H_{15}N_2OCl$ 346	72.40 (72.83)	4.12 (4.33)	7.79 (8.09)	9.25 (10.11)	-
3d	255	80[b]	$C_{21}H_{14}N_4O_5$ 402	62.15 (62.68)	3.14 (3.48)	13.50 (13.93)	-	-
4a	270	68[a]	$C_{23}H_{19}N_5SO_2$ 429	64.02 (64.33)	4.50 (4.42)	15.98 (16.31)	-	6.75 (7.45)

(Cont'd.....)

(Table 1 cont'd.....)

4b	187	77[c]	$C_{27}H_{21}N_5SO_4$ 511	63.00 (63.40)	4.00 (4.10)	13.50 (13.69)	-	5.85 (6.26)
4c	196	60[c]	$C_{27}H_{21}N_4SO_2Cl$ 500	64.31 (64.80)	4.10 (4.20)	10.85 (11.20)	6.71 (7.00)	5.74 (6.40)
4d	290	65[b]	$C_{27}H_{20}N_6SO_6$ 556	58.01 (58.27)	3.35 (3.59)	14.79 (15.10)	-	5.40 (5.75)
5	255	80[d]	$C_{29}H_{22}N_4SO_3Cl$ 541	63.93 (64.32)	4.00 (4.06)	10.01 (10.35)	5.84 (6.46)	5.60 (5.91)
6	230	75[d]	$C_{30}H_{24}N_7SO_2Cl$ 581	61.63 (61.96)	4.00 (4.13)	16.33 (16.86)	5.79 (6.02)	5.31 (5.50)
7	226	78[e]	$C_{32}H_{26}N_7SO_3Cl$ 623	61.31 (61.63)	3.89 (4.17)	15.25 (15.73)	5.33 (5.61)	5.00 (5.13)
8a	145	60[f]	$C_{27}H_{25}N_5SO_4$ 515	62.55 (62.91)	4.59 (4.85)	13.18 (13.59)	-	5.95 (6.21)
8b	194	75[g]	$C_{31}H_{27}N_5SO_6$ 597	62.01 (62.31)	4.32 (4.52)	11.25 (11.72)	-	5.53 (5.36)
8c	245	69[g]	$C_{31}H_{26}N_6SO_8$ 642	62.88 (63.05)	4.01 (4.40)	14.00 (14.23)	-	4.80 (4.98)
9a	285	80[h]	$C_{25}H_{23}N_7SO_3$ 501	59.39 (59.88)	4.28 (4.59)	19.09 (19.56)	-	6.00 (6.38)
9b	242	64[g]	$C_{29}H_{25}N_7SO_5$ 583	59.30 (59.69)	4.00 (4.28)	16.50 (16.80)	-	5.02 (5.48)
9c	285	67[g]	$C_{29}H_{24}N_8SO_7$ 628	55.01 (55.41)	3.55 (3.82)	17.35 (17.83)	-	4.20 (5.09)
10a	285	80[d]	$C_{26}H_{24}N_8S_2O_3$ 560	55.39 (55.71)	4.01 (4.28)	19.81 (20.00)	-	10.70 (11.42)
10b	233	84[g]	$C_{30}H_{26}N_8S_2O_5$ 642	55.87 (56.07)	3.90 (4.04)	17.00 (17.44)	-	8.98 (9.96)
10c	262	75[g]	$C_{30}H_{25}N_9S_2O_7$ 687	52.01 (52.40)	3.33 (3.63)	18.21 (18.34)	-	8.85 (9.31)
11a	280	60[a]	$C_{26}H_{22}N_8S_2O_2$ 542	57.14 (57.56)	3.59 (4.05)	20.15 (20.66)	-	10.85 (11.80)
11b	227	72[a]	$C_{30}H_{24}N_8S_2O_4$ 624	57.41 (57.69)	3.58 (3.84)	17.55 (17.94)	-	10.20 (10.25)
11c	267	67[g]	$C_{30}H_{23}N_9S_2O_6$ 669	53.55 (53.81)	3.50 (3.43)	18.38 (18.83)	-	9.01 (9.56)
12	240	70[i]	$C_{23}H_{23}N_7SO_2$ 461	59.48 (59.86)	4.69 (4.98)	21.00 (21.25)	-	5.99 (6.94)
13	290	65[i]	$C_{24}H_{21}N_7SO_2$ 471	60.91 (61.14)	4.15 (4.45)	20.55 (20.80)	-	6.01 (6.79)
14	205	78[b]	$C_{57}H_{44}N_8S_2O_5Cl_2$ 1055	64.53 (64.83)	3.88 (4.17)	10.33 (10.61)	6,51 (6.72)	5.40 (6.06)
15	220	65[a]	$C_{30}H_{24}N_5SO_2CI$ 553	64.59 (65.09)	4.01 (4.33)	12.50 (12.65)	5.95 (6.32)	5.70 (5.78)
16	115	80[b]	$C_{30}H_{21}N_5SO_2CI$ 550	65.09 (65.45)	3.57 (3.81)	12.75 (12.72)	5.89 (6.36)	5.30 (5.81)

*Solvents: a, MeOH; b, isopropyl alcohol; c, dil isopropyl alcohol; d, dil MeOH; e, benzene; f, EtOH; g, dil DMF; h, dil pyridine; i, DMF-MeOH (1:1).

*Condensation of **15** with 2,4-dichlorobenzaldehyde: Formation of **16**.* A mixture of **4a** (0.01 mol) and 2,4-dichlorobenzaldehyde (0.01 mol) in glacial acetic acid (50 ml) with fused sodium acetate (5 g) was refluxed for 4 h, cooled and poured onto crushed ice. The solid separated was filtered off, washed with cold water and crystallized to give **16** (Table 1); IR: υ 3200-3100 (NH), 2150 (C≡N), 1620 (C=C), 1600, 1580 (C=N), 1280 (SO_2), 900, 880, 800, 780 (aryl and phenyl groups) and 700-690 cm^{-1} (C-Cl); UV: λ_{max} 211.2 (ε 2.918)nm.

Results and Discussion

The synthesis of fully substituted-1,2,4-triazines (**4a-d**) was achieved through treatment of benzoin hydrazine (**1**) with ethyl cyanoacetate in dry benzene to give **2a.** It was followed by dehydration via stirring with conc H_2SO_4 (Rao and Rao

Table 2

Minimal inhibitory concentration (MIC in ug ml^{-1}) of the biologically active compounds*

Compd. No.	Bacteria				Fungi	
	S aureus	*B subtilis*	*E.coli*	*P vulgaris*	*A niger*	*P lnotatum*
4b	100	100	100	100	250	250
4d	25	25	25	25	25	25
6	250	250	250	250	250	250
7	500	500	500	500	500	500
10	25	25	25	25	100	100
11b	250	250	250	250	250	500
11c	25	25	25	100	25	25
13	500	500	500	500	500	500
14	250	500	250	500	500	500
16	500	500	500	500	500	500

*Biologically inactive compound (MIC>500 ug ml^{-1}).

1985) produceing **3a,** which on cyclocondensation with sulphanilamide in dry pyridine (Singh *et al* 1994) gave **4a** [Scheme I].

The structure of **4a** was elucidated on the basis of elemental analysis and spectral data (Table 1). Thus, UV absorption spectrum of **4a** revealed λ_{max} at 244.4 and 203.6 nm while that of **3a** recorded λ_{max} at 205nm. IR spectrum of **4a** showed broad band υ 3206-2950 cm^{-1} in addition to characteristic bands for C≡N, SO_2 and NH_2 groups. 1H-NMR spectrum of **4a** expressed signals due to presence of NH, NH_2, aliphatic and aromatic protons. Also, the mass spectrum of 4a displayed the molecular ion peak at m/e 429 (1.17%). Loss of NH_3, HCN, N_2 and SO_2 moieties yielded peak at m/e 105 (100% base peak), and loss of benzene sulphamido, H_2C-CN, N_2 and HCN yielded a prominent peak at m/e 178 (23.06%) with a typical 5,6-diphenyl-1,2,4-triazine fission (Palmer *et al* 1994). Acylation of compound **1** using aroyl chloride in the presence of DMF afforded **2b-d** which were further treated with conc. H_2SO_4 to get **3b-d** that easily underwent nucleophilic reaction with sulphanilamide in dry pyridine to furnish **4b-d** [Scheme I].

Similarly, structures of **4b-d** were preferred on the following grounds: (i) Microanalytical data, (ii) their UV spectra showed λ_{max} 256.2 nm in comparison with that of **2b** which recorded λ_{max} at 250 and 312 nm and (iii) their infrared spectra showed broad bands due to NH, NH_2, NO_2 and SO_2 functional groups.

In view of the chemical reactivity of functionally 5,6-diphenyl-1,2,4-triazines **4a-d**, acylation of **4c** using chloroacetyl chloride in DMF (Abdel Rahman *et al* 1989) was carried out affording N-chloroacetyl derivative **5** which underwent cyclocondensation reaction with guanidine hydrochloride in the presence of DMF to give 2-amino-4-(3,4-diaryl-5,6-diphenyl-1,2,4-triazine-1-yl)-imidazoline (**6**). Presence of amino group in compound **6** was established from treatment with AcOH to give N-acetylamino derivative **7** [Scheme I].

Since the prepared compounds **5-7** were new, their structures were verified by elemental analysis and spectral data. IR spectrum of **5** exhibited absorption bands due to C=O, aliphatic and aromatic functional groups, while that of **6** showed stretching bands attributable to NH_2, NH, C=N and SO_2 groups. In addition, IR spectrum of **7** revealed the presence of absorption bands due to C=O with absence of NH_2 and NH bands. Mercapto-1,2,4-triazoles are associated with diverse biological activities (Abdel Rehman 1987). These observations prompted us to prepare mercapto-s-triazole incorporating the substituted 1,2,4-triazine moiety. Thus, alkylation of **4a-c** with ethyl chloroacetate in the presence of DMF produced **8a-c**. Hyrazinolysis of **8** by refluxing with hydrazine hydrate in absolute ethanol yielded **9a-c,** which on addition reaction with ammonium thiocyanate gave N^1-acylthiosemicarbazide **10a-c.** Refluxing of compound **10** with glacial acetic acid/ fused sodium acetate (Abdel Rehman 1990) furnished 1,2 dihydro-3-thioxo-5 (methyl-l-yl-3,4-diaryl-5,6-diphenyl-1,2,4-triazine)-s-triazole (**11a-c**) respectively [Scheme I].

Structures of compounds **8-11** were deduced from elemental analysis and spectral data. IR spectrum of **8b** showed the presence of C=O, alkyl and aryl functional groups while that of **9b** revealed broad peaks between υ3500-3000 cm^{-1} attributable to NH_2-NH, and 1700-1650 cm^{-1} due to C=O groups. As a representative case, the IR spectrum of **10** a exhibited absorption bands due to NH-NH, NH-CS-NH and C=O groups. Also, structure of compound **11** was confirmed from elemental analysis as well as, IR, ^{1}H-NMR and mass spectral data.

IR spectrum of 11a showed the stretching band at υ 3378-3058 cm^{-1} due to NH-NH while ^{1}H-NMR of it showed the signals attributable to CH_2, CH_2CN, NH and aromatic protons. On the other hand, mass spectrum of **11b** showed molecular ion peak at m/e 624 (0.26%) and the presence of a peak at m/e 511 and 114 in moderate intensity. Peak appeared at m/e 511, under elimination of SO_2, NH_2, C_6H_5 and diphenylacetylene produced azinobenzene radical at m/e 105 (100%) as base peak was found to be in conformity with the assigned structure (Sayed and Kjosen 1981).

The iminohydrazine **12** was obtained from addition of hydrazine hydrate to **4a** in the presence of ethanol-piperidine (Abdel Rehman *et al* 1991). The compound **12** on cyclocondensation with triethyl orthoformate produced 1H-5-(methyl-3-yl-1-H-4-aryl-5,6-diphenyl-1,2,4-triazine)-s-triazole **13** (Scheme I). IR spectrum of 12 indicated the

presence of NH_2, NH and $C{=}NH_2$ groups while that of **13** revealed the absence of both NH and NH_2 functional groups.

Our next study was the reactivity of compound **4** towards trifunctional agents. Thus, 1,3-diheteroarylacetone **14** was isolated from treatment of **4c** with 1,3-dichloroacetone in the presence of DMF. Under experimental conditions, it was found that compound **14c** did not allow to cyclize in basic or acidic media which is due to the enol $\rightleftharpoons$ keto form. Structure of **14** was supported by elemental analysis and spectral data. IR spectrum of **14** showed the presence of enolic OH group with absence of C-O group, while its UV spectrum revealed the absorption bands at λ_{max} 370 (0.003) and 234 (1.482)nm. The higher absorption band in UV is relatively due to the extension of conjugated system of enolic form.

Alkylation of compound **4c** using acrylontrile in the presence of pyridine-water afforded 1-cyanoethyl-3-(p-chlorophenyl)-4-(*p*-sulphonamidophenyl)-5,6-diphenyl-1,2,4-triazine; **15**. IR spectrum of 15 showed characteristic absorption bands in the regions of CN, CH_2 and aromatic groups.

Finally, condensation of compound **4a** with 2,4-dichlorobenzaldehyde in acetic acid/fused sodium acetate furnished ethylenic derivative **16**. Structure of **16** was deduced booth from the elemental analysis and spectral data. Its IR spectrum showed the presence of NH, CN and exo C=C groups, while its UV spectrum revealed the absorption at λ_{max} 211.2 nm. Lowering absorption bands of **16** is due to the interaction between chlorine atom of aryl group and N_2 of 1,2,4-triazine, which caused the inhibition of conjugation.

Antimicrobial activity. The products **6-16** and their parent **4b** and **4d** were tested *in vitro* for their antimicrobial activity against *Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Proteus vulgaris* as bacteria and *Aspergillus niger* and *Penicillium notatum* as fungi by using diffusion method (Abdel Rehman *et al* 1990) with DMF as solvent. Only compounds **4d, 10** and **11d** were active against the tested organisms, due to the presence of thiosemicarbazido and mercapto 1,2,4-triazole (Table 2).

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