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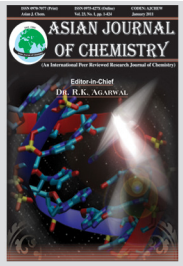

Synthesis of Some Substituted Phenylthiazolyl 1,3,5-Triazine Derivatives

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A series of some substituted phenylthiazolyl 1,3,5-triazine derivatives **4b-12b** were obtained by two steps substitution reaction of cyanuric chloride with various nucleophilic amines like diisopropylamine, morpholine, diphenyl amine in presence of aqueous media and subsequently with, synthesized substituted phenylthiazolyl-2-amines. Molecular structures of the synthesized compounds were confirmed by FTIR, ^{1}H NMR, ^{13}C NMR and elemental analyses.

Key Words: Synthesis, Phenylthiazolyl, 1,3,5-Triazine derivatives.

INTRODUCTION

1,3,5-Triazine derivatives have been found widespread application in the pharmaceutical, textile, plastic and rubber industries[1] and used as a pesticide or herbicide components in agriculture[2], medicines[3], polymers[4], optical bleaches[5], dye-stuff[6], explosive[7] and surface active agents[8]. The continuous demand to develop synthetic methods for the selective preparation of compounds under mild conditions by using stable, nonvolatile, non-toxic and less expensive reagents, has prompted the researchers to investigate the use of 1,3,5-triazine derivatives, such as cyanuric chloride in organic synthetic applications[9]. In continuation of previous work on 1,3,5-triazines[10], we herein report two step synthesis of 1,3,5-triazines derivatives by substitution of first two chlorines in cyanuric chloride with various amines and subsequently conversion of these diamino 1,3,5-triazine, with three higher bulky groups like 4-substituted phenylthiazole-2-amines to furnish a series of substituted phenylthiazolyl 1,3,5-triazines.

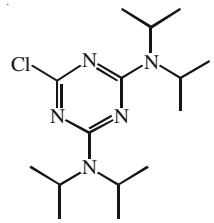
EXPERIMENTAL

The synthesized compounds were characterized by their melting point, % yield, UV, FTIR, ^{1}H NMR and ^{13}C NMR spectroscopy and elemental analysis. Melting point ranges of products were determined by the melting point apparatus (electrothermic model, MP-1) and were uncorrected. UV (ethanol) were recorded on Hitachi U-2001 spectroscope and FTIR (KBr pellet) were taken on Perkin-Elmer-spectrum RX-I spectroscope. Proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded on Bruker Avance II 400 NMR spectroscope and (^{13}C NMR) were recorded on Bruker Avance II 100 NMR spectroscope. Chemical shifts are expressed as δ values (ppm), downfield from tetramethylsilane (TMS) used as internal standard. Elemental analyses were performed on Vario EL III CHNOS elemental analyzer.

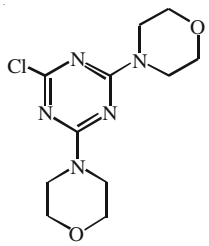
Diamino 1,3,5-triazine (1a-3a): These derivatives were prepared according to published procedure[11]. Cyanuric chloride was dissolved in 100 mL of 1,4-dioxane, fine slurry was prepared by adding solution into 150 mL well stirred ice-water. Diphenyl amine and equivalent of $KHCO_3$ was added and the mixture was stirred for 1 h. The product was filtered and washed with cold water. Filtered immediately in suction filter and recrystallize to afford pure product.

6-Chloro-N^2,N^2,N^4,N^4-tetraisopropyl-1,3,5-triazine-2,4-diamine (1a): m.p. (ºC) 86-88; Yield 84.11 %; UV (ethanol) 227.5 nm; FTIR (KBr, cm^{-1}): 2969, 1582, 1324, 1019; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (d, J = 6.9, 24H, 8 × CH_3-CH), 2.04 (m, 4H, 4 × -CH-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) 20.53 (CH_3-), 47.35 (-CH-), 163.56 (ar C-Cl), 168.96 (ar C-N). Anal. calcd. (%) for $C_{15}H_{28}N_5Cl$: C, 57.40; H, 8.99; Cl, 11.30; N, 22.31. Found (%): C, 57.45; H, 8.98; Cl, 11.35; N, 22.25.

2-Chloro-4,6-dimorpholino-1,3,5-triazine (2a): m.p. (ºC) 132-135, Yield 73.32 %; UV (ethanol) 249.4 nm; FTIR (KBr, cm^{-1}): 2966, 1574-1451, 1362, 1116; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.70 (t, J = 4.9, 8H, 4 × CH_2-N), 3.78 (t, 8H, 4 × CH_2-O); ^{13}C NMR (100 MHz, $CDCl_3$) 43.86 (CH_2-N), 66.56 (CH_2-O), 164.48 (ar C-N), 169.69 (ar C-Cl). Anal. calcd.



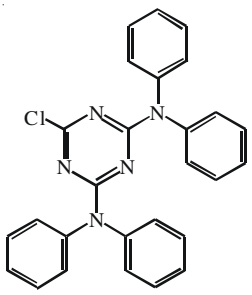
1a



2a

(%) for $C_{11}H_{16}N_5O_2Cl$: C, 46.24; H, 5.64; Cl, 12.41; N, 24.51. Found (%): C, 46.28; H, 5.58; Cl, 12.45; N, 24.56.

6-Chloro-N^2,N^2,N^4,N^4-tetraphenyl-1,3,5-triazine-2,4-diamine (3a): m.p. (ºC) 96-98; Yield 84.16 %; UV (ethanol) 318.5 nm; FTIR (KBr, cm^{-1}): 3055, 1548-1446, 1342, 1079; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27(d, *J* = 1.4, 8H, 8 × CH-), 7.32 (t, *J* = 1.2, 4H, 4 × =CH-), 7.40 (t, *J* = 1.4, 8H, 8 × =CH-); ^{13}C NMR (100 MHz, $CDCl_3$) 127.23, 129.36 (ar C), 143.16 (ar C-N,) 165.85 (ar C-Cl), 173.56 (ar C-N, s-triazine). Anal. calcd. (%) for $C_{27}H_{20}N_5Cl$: C, 72.07; H, 4.48; Cl, 7.88; N, 15.57. Found (%): C, 72.12; H, 4.53; Cl, 7.81; N, 15.62.



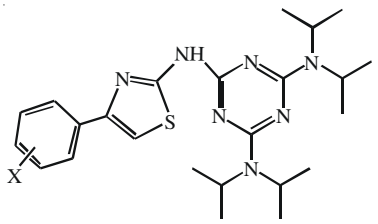
3a

Substituted phenylthiazolyl-1,3,5-triazine (4b-12b): Phenyl-, 4-chlorophenyl- and 4-nitrophenyl thiazole-2-amine derivatives were synthesized according to known procedures[12,13], with the help of corresponding acetophenone, thiourea, thionyl chloride and bromine. A mixture of diamino-1,3,5-triazine and synthesized phenyl-, 4-chlorophenyl- and 4-nitrophenyl thiazole-2-amine in 1,4-dioxane was refluxed for 5 h during which equimolar K_2CO_3 solution was added in fractions (0.2 g) over 2 h. The content was then poured into crushed ice, product isolated. Extracted with ethyl acetate, petroleum ether was added to afford these products.

N^2,N^2,N^4,N^4-Tetraisopropyl-N^6-(4-phenylthiazol-2-yl)-1,3,5-triazine-2,4,6-triamine (4b): m.p. (ºC) 274-276; Yield 47.83 %; UV (ethanol) 312.4 nm; FTIR (KBr, cm^{-1}): 3436, 2970, 2923, 2860, 1578-1302; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (d, *J* = 8.3, 24 H, 8 × -CH-CH_3), 1.85 (m, 4H, 4 × -CH-CH_3), 4.41 (s, NH), 6.71 (thiazole -CH), 7.75 (t, aromatic -CH), 7.77 (t, aromatic -CH), 7.82 (d, aromatic-CH); ^{13}C NMR (100 MHz, $CDCl_3$) 47.65 (-CH-), 100.43, 148.04 (C-thiazole),126.37,131.96,136.62, 137.58 (ar CH), 163.52, 168.64 (ar C-N, s-triazine). Anal. calcd. (%) for $C_{24}H_{35}N_7S$: C, 63.54; H, 7.78; N, 21.61; S, 7.07. Found (%): C, 63.58; H, 7.82; N, 21.65; S, 7.12

N^2-(4-(4-Chlorophenyl)thiazol-2-yl)-N^4,N^4,N^6,N^6-tetraisopropyl-1,3,5-triazine-2,4,6-triamine (5b): m.p. (ºC) 247-248; Yield 40.15 %; UV (ethanol) 303.5 nm; FTIR (KBr, cm^{-1}) 3263, 2965, 2869, 2784, 1572-1497, 1092; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (d, *J* = 8.3,24 H, 8 × -CH-CH_3), 1.85 (m, 4H, 4 × -CH-CH_3), 4.42 (s, NH), 7.14 (thiazole -CH), 7.63 (t, aromatic -CH), 7.71 (d, aromatic-CH); ^{13}C NMR (100 MHz, $CDCl_3$) 47.56 (-CH-), 100.42, 148.56 (C-thiazole), 128.92, 132.44, 137.54, 138.08 (ar CH), 163.56, 168.96 (ar C-N, s-triazine). Anal. calcd. (%) for $C_{24}H_{34}ClN_7S$: C, 59.06; H, 7.02; Cl, 7.26; N, 20.09; S, 6.57. Found (%): C, 59.12; H, 7.08; Cl, 7.30; N, 20.12; S, 6.58.

N^2,N^2,N^4,N^4-Tetraisopropyl-N^6-(4-(4-nitrophenyl)-thiazol-2-yl)-1,3,5-triazine-2,4,6-triamine (6b): m.p. (ºC) 214-216; Yield 42.19 %; UV (ethanol) 318.2 nm; FTIR (KBr, cm^{-1}): 3399, 2970-2860, 1566, 1343, 839; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (d, *J* = 8.3, 24 H, 8 × -CH-CH_3), 1.85 (m, 4H, 4 × -CH-CH_3), 4.42 (s, NH), 7.26 (thiazole -CH), 8.31 (t, aromatic -CH), 8.35 (d, aromatic-CH); ^{13}C NMR (100 MHz, $CDCl_3$) 47.55 (-CH-), 100.41, 148.58 (C-thiazole), 125.42, 133.76, 142.56, 152.53 (ar CH), 163.56, 168.97 (ar C-N, s-triazine). Anal. calcd. (%) for $C_{24}H_{34}N_8O_2S$: C, 57.81; H, 6.87; N, 22.47; S, 6.43. Found (%): C, 57.72; H, 6.77; N, 22.57; S, 6.41.



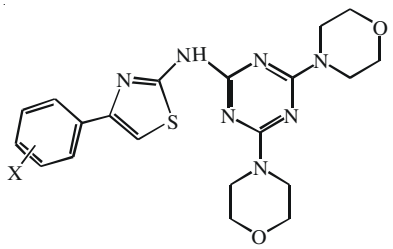
4b X= -H
5b X= -C
6b X= -NO_2

4,6-Dimorpholino-N-(4-phenylthiazol-2-yl)-1,3,5-triazin-2-amine (7b): m.p. (ºC) 196-198; Yield 88.83 %; UV (ethanol) 294.5 nm; FTIR (KBr, cm^{-1}): 3061, 1741, 1488-1340, 1120; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.03 (t, *J* = 8.3,8 H, morpholine CH), 2.15 (t, 8H, morpholine CH), 5.84 (thiazole -CH), 6.91 (d, aromatic C-H), 7.07(t, aromatic -CH), 7.10 (t, aromatic-CH); ^{13}C NMR (100 MHz, $CDCl_3$) 43.95 (CH_2-N morholine), 66.57 (CH_2-O, morpholine), 108.47, 157.36 (C-thiazole), 126.48, 135.88, 144.54, 153.54 (ar C), 164.52, 167.56 (ar C- N, s-triazine). Anal. calcd. (%) for $C_{20}H_{23}N_7O_2S$: C, 56.45; H, 5.45; N, 23.04; S, 7.54. Found (%): C, 56.42; H, 5.44; N, 23.10; S, 7.52.

N-(4-(4-Chlorophenyl) thiazol-2-yl)-4,6-dimorpholino-1,3,5-triazin-2-amine (8b): m.p. (ºC) 114-118; Yield 81.84 %; UV (ethanol) 298.0 nm; FTIR (KBr, cm^{-1}): 3403, 2852, 1578-1342, 1116; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.13 (t, *J* = 8.3, 8H, morpholine CH), 2.15 (t, 8H, 4 × -CH-CH_3), 5.86 (thiazole -CH), 7.01 (d, aromatic C-H), 7.35 (d, aromatic -CH); ^{13}C NMR (100 MHz, $CDCl_3$) 45.26 (CH_2-N), 66.59 (CH_2-O), 108.92, 157.39 (C-thiazole), 126.86, 136.87, 145.56, 153.62 (ar C), 165.11, 167.8 (ar C- N, s-triazine). Anal. calcd. (%) for $C_{15}H_{28}N_5Cl$: C, 57.40; H, 8.99; Cl, 11.30; N, 22.31. Found (%): C, 57.45; H, 8.98; Cl, 11.35; N, 22.25.

4,6-Dimorpholino-N-(4-(4-nitrophenyl)phiazol-2-yl)-1,3,5-triazin-2-amine (9b): m.p. (ºC) 145-148; Yield 81.82 %; UV (ethanol) 298.5 nm; FTIR (KBr, cm^{-1}): 3399, 2860,1578, 1518-1345, 839; ^{1}H NMR (400 MHZ, $CDCl_3$) δ

2.15 (t, *J* = 8.3,8 H, Morpholine CH), 2.17 (t, 8H, 4× -CH-CH_3), 5.95 (thiazole -CH), 6.95 (d, aromatic C-H), 7.20 (d, aromatic -CH); ^{13}C NMR (100 MHz, $CDCl_3$) 46.67 (CH_2-N), 66.89 (CH_2-O), 109.22, 158.23 (C-thiazole), 127.12, 137.24, 145.62, 162.14 (ar C), 165.57, 168.21 (ar C- N, s-triazine). Anal. calcd. (%) for $C_{15}H_{28}N_5Cl$: C, 57.40; H, 8.99; Cl, 11.30; N, 22.31. Found (%): C, 57.45; H, 8.98; Cl, 11.35; N, 22.25.

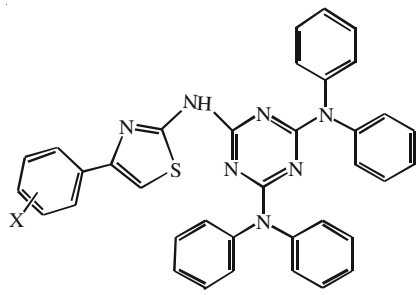


7b X= -H
8b X= -Cl
9b X= - NO_2

N^2,N^2,N^4,N^4-Tetraphenyl-N^6-(4-phenylthiazol-2-yl)-1,3,5-triazine-2,4,6-triamine (10b): m.p. (ºC) 48-49; Yield 54.43 %; UV (ethanol) 318.5 nm; FTIR (KBr, cm^{-1}): 3361, 3039, 1566-1430; ^{1}H NMR (400 MHz, $CDCl_3$) 7.48 (d, 2H aromatic C-H), 7.32 (t, 2H aromatic C-H), 7.22 (t, 1H aromatic C-H), 7.01 (t, 8H, aromatic C-H), 6.68 (t, 8H, aromatic C-H), 6.42 (s, thiazole), 6.4(s, 8H, aromatic C-H), 4.04 (N-H amino thiazole); ^{13}C NMR (100 MHz, $CDCl_3$) 102.48, 150.42, 162.24 (C-thiazole), 120.24, 121.12, 132.52, 145.45 (C-phenyl-N), 132.41, 134.24, 135.62, 136.72 (C-phenyl thiazole), 167.84, 169.23 (ar C- N, s-triazine). Anal. calcd. (%) for $C_{15}H_{28}N_5Cl$: C, 57.40; H, 8.99; Cl, 11.30; N, 22.31. Found (%): C, 57.45; H, 8.98; Cl, 11.35; N, 22.25.

N^2-(4-(4-Chlorophenyl)thiazol-2-yl)-N^4,N^4,N^6,N^6-tetraphenyl-1,3,5-triazine-2,4,6-triamine (11b): m.p. (ºC) 52-56; Yield 54.59 %; UV (ethanol) 323.5 nm; FTIR (KBr, cm^{-1}): 3340, 3042, 1566-1430, 1078; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, 2H aromatic C-H), 7.44 (t, 2H aromatic C-H), 7.02 (t, 8H, aromatic C-H), 6.67 (t, 8H, aromatic C-H), 6.46 (s, thiazole), 6.49 (s, 8H, aromatic C-H), 4.06 (N-H amino thiazole); ^{13}C NMR (100 MHz, $CDCl_3$) 103.34, 151.12, 162.87 (C-thiazole), 120.26, 121.22, 132.58, 145.56 (C-phenyl-N), 132.58, 134.65, 137.12, 138.72 (C-phenyl thiazole), 167.98, 169.29 (ar C- N, s-triazine). Anal. calcd. (%) for $C_{15}H_{28}N_5Cl$: C, 57.40; H, 8.99; Cl, 11.30; N, 22.31. Found: C, 57.45; H, 8.98; Cl, 11.35; N, 22.25.

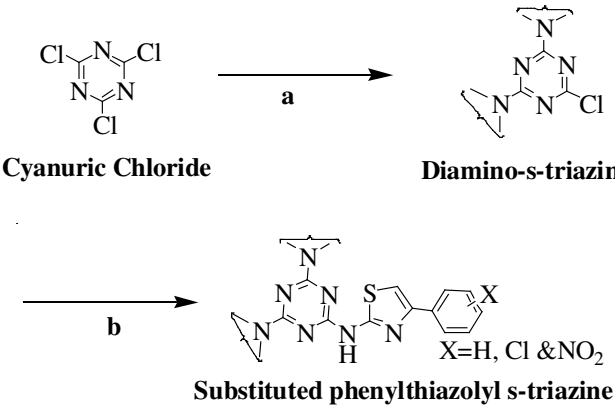
N^2-(4-(4-Nitrophenyl)thiazol-2-yl)-N^4,N^4,N^6,N^6-tetraphenyl-1,3,5-triazine-2,4,6-triamine (12b): m.p. (ºC) 40-42; Yield 57.19 %; UV (ethanol) 325.5 nm; FTIR (KBr, cm^{-1}): 3362, 3042, 1566, 1490, 1342, 826; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, 2H aromatic C-H), 7.64 (t, 2H aromatic C-H), 7.11 (t, 8H, aromatic C-H), 6.78 (t, 8H, aromatic C-H), 6.51 (s, thiazole), 6.48(s, 8H, aromatic C-H), 4.10 (N-H amino thiazole); ^{13}C NMR (100 MHz, $CDCl_3$) 103.52, 151.76, 163.16 (C-thiazole), 120.94, 121.84, 132.97, 145.94 (C-phenyl-N), 132.97, 136.14, 138.56, 139.54 (C-phenyl thiazole), 168.44, 169.42 (ar C- N, s-triazine). Anal. calcd. (%) for $C_{15}H_{28}N_5Cl$: C, 57.40; H, 8.99; Cl, 11.30; N, 22.31. Found (%): C, 57.45; H, 8.98; Cl, 11.35; N, 22.25.



10b X= -H
11b X= -Cl
12b X= -NO_2

RESULTS AND DISCUSSION

The compounds were prepared in two step reactions, first step consists of nucleophilic substitution of two chlorines in cyanuric chloride in presence of aqueous dioxane with various amines like diisopropylamine, morpholine and diphenyl amine to furnish diamino 1,3,5-triazine and second step involves further substitution of these synthesized diamino-1,3,5-triazines in presence of 1,4-dioxane with previously synthesized substituted thiazole-2-amine to obtain a series of substituted phenylthiazolyl 1,3,5-triazine (**Scheme-I**).



Cyanuric Chloride **Diamino-s-triazine**

Substituted phenylthiazolyl s-triazine

Reagents and conditions: (a) 1,4-dioxane/water, amine (diisopropyl amine, morpholine, diphenyl amine), $KHCO_3$, 0.5-1.0 h; (b) 1,4-dioxane, 4-sustituted phenyl thiazole-2-amine, K_2CO_3 reflux, 5-6 h

Scheme-I: Synthesis of substituted phenylthiazolyl 1,3,5-triazine derivatives

UV of the compound was found to be at about 300 nm due to n-π* transition. FTIR spectra of the products displayed characteristic absorption in the region 1550-1200 cm^{-1} due to -C=C-, -C=N stretching. ^{1}H NMR spectra of class of compounds showed a singlet at δ 4.4- 4.6 due to -NH group of phenyl thiazolyl-2-amine groups and aromatic C-NH lies at *ca.* 4.3-3.3 ppm, disappearance of primary amine peak associated with substituted phenyl thiazole-2-amine further confirmed the formation of this class of derivatives and ^{13}C NMR state that carbon signal appear at about 168-178 ppm, respectively.

Water has high dielectric constant with permanent dipole moment which allows the ease of nucleophilic substitution of various amines and isolation of pure product is also facilitated due to decreased solubility of organic material upon post reaction and cooling.

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