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Short communication

The synthesis and photophysical studies of pyridinyl-1,2,4-triazine derivatives and use as a fluorescent sensor for ferric salts

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ABSTRACT

A simple method is described for the efficient synthesis of bisaryl-3-pyridinyl-1,2,4-triazine derivatives via condensation of cinnamils with pyridine carboxtrisamidrazone in methanol under both conventional heating and microwave irradiation in high yield (85–66%). Photophysical analysis revealed that the derivatives displayed good fluorescent properties and bisaryl-3-pyrazine-1,2,4-triazine derivatives selectively bound Fe(III) ions.

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1. Introduction

The structural diversity and biological importance of nitrogen containing heterocycles have made them attractive synthetic targets over many years and they are found in various natural products. Substituted 1,2,4-triazines represent an important class of nitrogen containing heterocycles. 1,2,4-Triazines and their derivatives occupy a pivotal position in modern medicinal chemistry because of their high potential for biological activity [1]. Thus, the 1,2,4-triazine ring is a prominent structural motif found in numerous natural and synthetic biologically active compounds. For example well-known antiviral drug azaribine is structurally based on the 1,2,4-triazine scaffold [1,2]. In addition, certain azanucleosides, for example, 6-azacytosine and 6-azauracil, bearing the 1,2,4-triazine heterocycle, have displayed an impressive array of biological activities such as antimicrobial [3], antiviral [4], anti-inflammatory [5] and antimalarial.[6] activities. Furthermore, 6-azaisocytosine (3-amino-1,2,4-triazin-5(2H)-one), an isosteric isomer of 6-azacytosine and 6-azauracil, is a great biological interest due to its resistance to deaminase [7].

The 1,2,4-triazine core is a versatile synthetic platform to access a wide range of condensed heterocyclic ring systems *via* intramolecular Diels–Alder reactions with a vast array of dienophiles. In addition, the triazine ring system is a key component of commercial dyes, herbicides, insecticides and more recently, pharmaceutical compositions [8]. As our efforts are directed at an iterative analog library approach to support nascent medicinal chemistry programs, this latter application for the triazine scaffold attracted our attention.

Fluorescent property is the ultimate tool for the identification of chromosomes and ultra fast DNA sequencing by showing different colours with each DNA base pairs *via* fluorescence resonance energy transfer [9,10]. Many nitrogen containing heterocyclic compounds have displayed photoluminescence and electroluminescence properties. Compounds with fused 1,2,4-triazine aromatic rings are used as raw material for organic light-emitting devices, light emitting cells and optoelectronic devices [11–13].

The wide-ranging biological activity associated with 1,2,4-triazine derivatives, both naturally occurring and synthetic, ensures that the synthesis of this important ring system remains a topic of current interest. Various methods for the preparation of these compounds have been reported. However these methods suffer from tedious synthetic routes, longer reaction time, drastic reaction conditions, as well as narrow substrate scope [14–17]. To the best of our knowledge, there have been very few reports for the synthesis of 1,2,4-triazine derivatives in literature [18–21]. As part of our ongoing research on the development of novel synthetic routes for the synthesis of biologically active heterocyclic compounds and use

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of green chemical techniques in organic synthesis [22–24], herein, we report a simple and facile one pot procedure for the synthesis of 1,2,4-triazine derivatives under reflux condition.

2. Experimental

2.1. General

All the substituted aldehydes, biacetyl, and all the substituted cyanopyridines were purchased from Aldrich Chemicals. Piperidine and other reagents were purchased from S. D. Fine. Chem. India Limited. Methanol was distilled with Mg/I_2 under nitrogen and stored over 3A° molecular sieves. IR measurements were done as KBr pellets for solids using Perkin Elmer Spectrum RXI FT-IR. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ using TMS as internal standard with JEOL 500 MHz and Bruker 300 MHz high resolution NMR spectrometer respectively. Multiplicities were abbreviated as follows: singlet (s), doublet (d), triplet (t), multiplet (m), and broad (br). Mass spectra were recorded using Electron Spray Ionization method with Thermo Finnigan mass spectrometer. Melting points were determined in capillary tubes and are uncorrected. Analytical TLC was performed on precoated plastic sheets of silica gel G/UV-254 of 0.2 mm thickness (Macherey-Nagel, Germany). Elemental analysis data were recorded using Thermo Finnigan FLASH EA 1112 CHN. The electronic spectral measurements were carried out in Perkin–Elmer Lambda 35 double beam spectrometer at room temperature. The steady state emission spectra were recorded on Hitachi 650–40 spectrofluorometer at room temperature. Time-resolved fluorescence measurements were determined using picosecond laser excited Horibajobinyvon time correlated single photon counting spectrofluorometer. The excitation source was a tunable Ti-sapphire laser (Tsunami, Spectrometer, USA) with a pulse width of <2 ps and repetition rate of 82 MHz, Ar–*H*. The sample was excited at its corresponding wavelength and the emission was monitored between 400 to 600 nm using a MCP-PMT detector. Decay traces were deconvulated using a non-linear least-squares analysis using IBH software.

2.2. General procedure for the synthesis of bisaryl-3-pyridinyl-1,2,4-triazine derivatives (**3a**–**l**)

Method: A

A mixture of cinnamil (1.0 mmol) and pyridine carboxtrisamidrazone (1.0 mmol) in methanol (30 mL) was refluxed for the appropriate time as described in Table 1. After completion of the reaction, as indicated by TLC, the precipitated solid was filtered, washed with water and dried. The obtained crude solid was purified further by recrystalization with ethanol.

Method: B

A mixture of cinnamil (1.0 mmol) and pyridine carboxtrisamidrazone (1.0 mmol) in methanol (2 mL) was irradiated in a microwave oven (BPL BMG 800 TS model) at 80 W for the appropriate time displayed in Table 1. After completion of the reaction, as indicated by TLC, the precipitated solid was filtered, washed with water and then dried. The obtained crude product was recrystallized with ethanol.

2.2.1. **3a**. 5,6-bis[(E)-2-phenylvinyl]-3-pyridin-2-yl-1,2,4-triazine (Table 1 entry 1)

Yellow solid; mp 72–74 °C; R_f 0.80 (40% AcOEt/Petroleum ether); IR (KBr): 1072, 1365, 1484, 1623 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.38–7.43 (m, 8H, –Ar–*H*), 7.45 (d, 1H, J = 8.4 Hz, –Ar–*H*), 7.50 (s, 1H, –Ar–*H*), 7.67–7.70 (m, 3H, –Ar–*H*), 7.91–7.94 (m, 1H, –Ar–*H*), 8.13 (d, 1H, –Ar–*H*), 8.39 (d, 1H, J = 15.3 Hz, –Ar–*H*), 8.69 (d, 1H, J = 7.6 Hz, –Ar–*H*), 8.89 (d, 1H, J = 3.8 Hz, –Ar–*H*); ^{13}C NMR (75 MHz, DMSO-d_6): 118.5, 119.4, 127.8, 128.3, 129.0, 129.1, 129.7, 130.5, 135.3, 135.9, 139.2, 143.2, 144.6, 145.6, 145.9, 148.8, 151.4, 152.6, 159.1; MS (EI): m/z 363.27 [$M^+ + H^+$]; $C_{24}H_{18}N_4$. Anal. Calcd for $C_{24}H_{18}N_4$. C 79.54 H 5.01 N 15.46. Found: C 79.49 H 5.03 N 15.49.

2.2.2. **3b**. 5,6-bis[(E)-2-(4-methylphenyl)vinyl]-3-pyridin-2-yl-1,2,4-triazine (Table 1, entry 2)

Yellow solid; mp 168–170 °C; R_f 0.83 (40% AcOEt/Petroleum ether); IR (KBr): 1065, 1180, 1363, 1400, 1481, 1623 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 2.40 (s, 3H, Ar–C*H*$_3$), 2.41 (s, 3H, Ar–C*H*$_3$), 7.22–7.26 (m, 4H, –Ar–*H*), 7.30–7.39 (m, 2H, –Ar–*H*), 7.54–7.60 (m, 2H, –Ar–*H*), 8.10 (d, 1H, J = 15.3 Hz, –Ar–*H*), 8.30 (d, 1H, J = 15.3 Hz, –Ar–*H*), 8.43 (d, 1H, J = 6.1 Hz, –Ar–*H*), 8.82 (d, 1H, J = 4.6 Hz, –Ar–*H*); ^{13}C NMR (75 MHz, DMSO-d_6): 21.4, 21.5, 117.9, 118.8, 124.0, 125.1, 127.7, 128.2, 129.6, 129.7, 132.9, 133.4, 137.0, 138.3, 139.7, 140.7, 142.6, 150.3, 151.4, 152.2, 153.4, 160.3; MS (EI): m/z 391.20 [$M^+ + H^+$]; Anal. Calcd for $C_{26}H_{22}N_4$. C 79.97 H 5.68 N 14.35. Found: C 79.87 H 5.66 N 14.29.

2.2.3. **3c**. 5,6-bis[(E)-2-(4-methoxyphenyl)vinyl]-3-pyridin-2-yl-1,2,4-triazine (Table 1, entry 3)

Yellow solid; mp 62–64 °C; R_f 0.64 (40% AcOEt/Petroleum ether); IR (KBr): 822, 1026, 1171, 1278, 1301, 1508, 1602 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 3.84 (s, 6H, Ar–OC*H*$_3$), 6.92 (d, 5H, J = 9.2 Hz, –Ar–*H*), 7.22–7.30 (m, 2H, –Ar–*H*), 7.59 (d, 2H, J = 16.1 Hz, –Ar–*H*), 7.63 (d, 2H, J = 16.1 Hz), 8.09 (d, 1H, J = 16.1 Hz, –Ar–*H*), 8.30 (d, 1H, J = 16.1 Hz, –Ar–*H*), 8.71 (d, 1H, J = 2.3 Hz, –Ar–*H*), 8.81 (d, 1H, J = 2.3 Hz, –Ar–*H*), 8.84 (d, 1H, J = 1.6 Hz, –Ar–*H*); ^{13}C NMR (75 MHz, DMSO-d_6): 55.3, 55.4, 117.2, 117.6, 123.8, 125.0, 127.2, 128.4, 129.0, 129.2, 129.5, 129.9, 130.8, 136.4, 137.0, 137.7, 142.0, 147.4, 150.2, 151.3, 152.1, 155.5, 160.7; MS (EI): m/z 423.27 [$M^+ + H^+$]; Anal. Calcd for $C_{26}H_{22}N_4O_2$. C 73.92 H 5.25 N 13.26. Found: C 73.84 H 5.23 N 13.23.

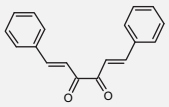
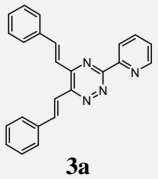
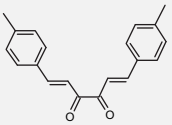
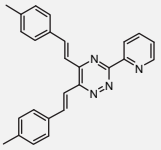
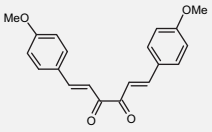
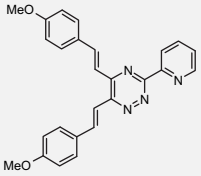
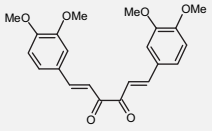
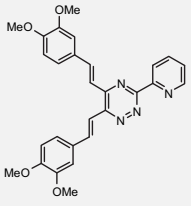
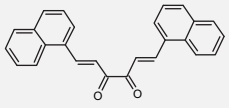
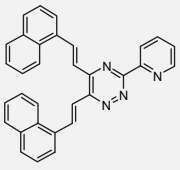
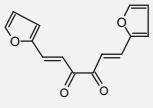
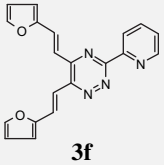
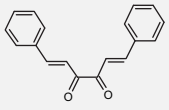
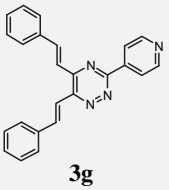
2.2.4. **3d**. 5,6-bis[(E)-2-(3,4-dimethoxyphenyl)vinyl]-3-pyridin-2-yl-1,2,4-triazine (Table 1, entry 4)

Yellow solid; mp 180–182 °C; R_f 0.35 (40% AcOEt/Petroleum ether); IR (KBr): 963, 1019, 1140, 1260, 1511, 1624 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 3.90 (s, 6H, Ar–OC*H*$_3$), 3.92 (s, 3H, Ar–OC*H*$_3$), 3.93 (s, 3H, Ar–OC*H*$_3$), 6.88 (d, 2H, J = 8.4 Hz, –Ar–*H*), 7.15–7.23 (m, 4H, –Ar–*H*), 7.25–7.31 (m, 2H, –Ar–*H*), 7.41–7.43 (m, 1H, –Ar–*H*), 7.87–7.90 (m, 1H, –Ar–*H*), 8.02 (d, 1H, J = 16.2 Hz, –Ar–*H*), 8.29 (d, 1H, J = 15.3 Hz, –Ar–*H*), 8.65 (d, 1H, = 7.6 Hz, –Ar–*H*), 8.87 (d, 1H, J = 4.6 Hz, –Ar–*H*); ^{13}C NMR (75 MHz, DMSO-d_6): 55.9, 56.0, 110.2, 110.7, 111.3, 117.1, 117.8, 121.5, 122.2, 123.9, 125.0, 128.7, 129.3, 137.0, 138.0, 142.3, 149.2, 150.2, 150.5, 151.1, 151.3, 152.1, 153.4, 160.0; MS (EI): m/z 483.20 [$M^+ + H^+$]; Anal. Calcd for $C_{28}H_{26}N_4O_4$. C 69.70 H 5.43 N 11.61. Found: C 69.81 H 5.45 N 11.57.

2.2.5. **3e**. 5,6-bis[(E)-1-napthylvinyl]-3-pyridin-2-yl-1,2,4-triazine (Table 1, entry 5)

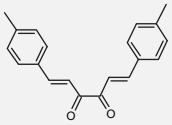
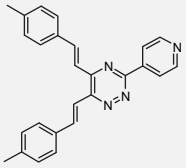
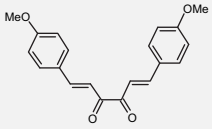
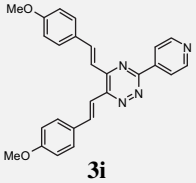
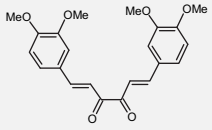
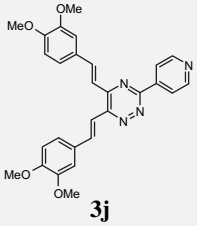
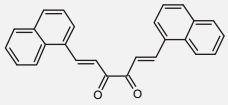
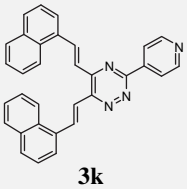
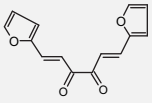
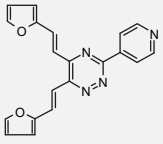
Yellow solid; mp 68–70 °C; R_f 0.82 (40% AcOEt/Petroleum ether); IR (KBr): 1024, 1251, 1395, 1465, 1621 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 6.88–6.93 (m, 6H, –Ar–*H*), 7.22–7. 32 (m, 4H, –Ar–*H*), 7.41–7.43 (m, 1H, –Ar–*H*), 7.56–7.64 (m, 5H, –Ar–*H*), 7.76 (d, 1H, J = 16.1 Hz), 7.86–7.88 (m, 1H, –Ar–*H*), 8.05 (d, 1H, J = 15.3 Hz, –Ar–*H*), 8.33 (d, 1H, J = 15.3 Hz, –Ar–*H*), 8.64 (d, 1H, J = 15.3 Hz, –Ar–*H*), 8.86 (d, 1H, J = 3.6 Hz, –Ar–*H*); ^{13}C NMR (75 MHz, DMSO-d_6): 121.0, 121.8, 122.1, 123.4, 123.7, 124.5, 125.3, 125.6, 126.3, 126.4, 126.9, 127.1, 128.7, 128.9, 130.0, 130.8, 132.9, 133.8, 136.0, 139.7, 150.7; MS (EI): m/z 463.27 [$M^+ + H^+$]; $C_{32}H_{22}N_4$.

Table 1
Synthesis of bisaryl-3-pyridinyl-1,2,4-triazine derivatives.

Entry	Cinnamil	2	Triazine[a]	Conventional heating		Microwave irradiation	
				Time (h)	Yield (%)[b]	Time (min)	Yield (%)[b]
1	 **1a**	**2a**	 **3a**	2.5	81	12.0	84
2	 **1b**	**2a**	 **3b**	1.5	85	14.0	86
3	 **1c**	**2a**	 **3c**	2.0	84	12.0	86
4	 **1d**	**2a**	 **3d**	2.5	80	11.0	86
5	 **1e**	**2a**	 **3e**	4.0	76	14.0	78
6	 **1f**	**2a**	 **3f**	2.5	79	12.0	81
7	 **1a**	**2b**	 **3g**	3.0	76	12.0	79

(*continued on next page*)

Table 1 (*continued*)

Entry	Cinnamil	2	Triazine[a]	Conventional heating		Microwave irradiation	
				Time (h)	Yield (%)[b]	Time (min)	Yield (%)[b]
8	 **1b**	**2b**	 **3h**	3.5	74	12.0	78
9	 **1c**	**2b**	 **3i**	4.0	71	14.0	74
10	 **1d**	**2b**	 **3j**	4.5	69	14.0	75
11	 **1e**	**2b**	 **3k**	4.5	66	14.0	76
12	 **1f**	**2b**	 **3l**	4.0	71	14.0	76

[a] All products were confirmed by IR, NMR, mass and elemental analysis.
[b] Isolated yield.

Anal. Calcd for $C_{32}H_{22}N_4$. C 83.09 H 4.79 N 12.11. Found: C 83.04 H 4.78 N 12.07.

2.2.6. ***3f****. 5,6-bis[(E)-2-furyl vinyl]-3-pyridin-2-yl-1,2,4-triazine (Table 1, entry 6)*

Yellow solid; mp 148–151 °C; R_f 50 (40% AcOEt/Petroleum ether); IR (KBr): 1375, 1470, 1511, 1615 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 6.51–6.53 (m, 2H, –Ar–*H*), 6.63 (d, 1H, J = 3.1 Hz, –Ar–*H*), 7.33–7.46 (m, 3H, –Ar–*H*), 7.54–7.57 (m, 2H, –Ar–*H*), 7.90–7.93 (m, 1H, –Ar–*H*), 7.95(d, 1H, J = 16.1 Hz, –Ar–*H*), 8.20 (d, 2H, J = 15.3 Hz, –Ar–*H*), 8.65 (d, 1H, J = 8.4 Hz, –Ar–*H*), 8.88 (d, 1H, J = 3.9 Hz, –Ar–*H*); ^{13}C NMR (75 MHz, DMSO-d_6): 112.5, 112.8, 113.6, 115.4, 116.4, 117.1, 124.0, 124.6, 125.1, 125.2, 128.6, 137.1, 144.1, 145.0, 150.4, 150.9, 151.7, 152.4, 152.6, 154.4, 160.2; MS (EI): m/z 343.33 [$M^+ + H^+$]; Anal. Calcd for $C_{20}H_{14}N_4O_2$. C 70.17 H 4.12 N 16.37. Found: C 70.30 H 4.11 N 16.32.

2.2.7. ***3g****. 5,6-bis[(E)-2-phenylvinyl]-3-pyridin-4-yl-1,2,4-triazine (Table 1, entry 7)*

Yellow solid; mp 192–194 °C; R_f 0.80 (40% AcOEt/Petroleum ether); IR (KBr): 1070, 1363, 1401, 1482, 1622 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.38–7.46 (m, 8H, –Ar–*H*), 7.47–7.49 (m, 4H, –Ar–*H*), 8. 13 (d, 1H, J = 16.1 Hz, –Ar–*H*), 8.31 (d, 1H, J = 15.3 Hz, –Ar–*H*), 8.43 (d, 2H, J = 15.3 Hz, –Ar–*H*), 8.82 (d, 2H, J = 6.2 Hz, –Ar–*H*); ^{13}C NMR (75 MHz, DMSO-d_6): 118.2, 119.4, 121.6, 127.8, 128.3, 129.0, 129.1, 129.7, 130.5, 135.3, 135.9, 138.7, 142.5, 142.7, 150.6, 152.2, 159.1; MS (EI): m/z 363.27 [$M^+ + H^+$]; Anal. Calcd for $C_{24}H_{18}N_4$. C 79.54 H 5.01 N 15.46. Found: C 79.60 H 5.00 N 15.42.

2.2.8. ***3h****. 5,6-bis[(E)-2-(4-methylphenyl)vinyl]-3-pyridin-4-yl-1,2,4-triazine (Table 1, entry 8)*

Yellow solid; mp 182–184 °C; R_f 0.83 (40% AcOEt/Petroleum ether); IR (KBr): 1065, 1180, 1363, 1400, 1481, 1623 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 2.40 (s, 3H, Ar–CH_3), 2.41 (s, 3H, Ar–CH_3), 7.22–7.26 (m, 4H, –Ar–H), 7.30–7.39 (m, 2H, –Ar–H), 7.54–7.60 (m, 4H, –Ar–H), 8.10 (d, 1H, J = 15.3 Hz, –Ar–H), 8.30 (d, 1H, J = 15.3 Hz, –Ar–H), 8.43 (d, 2H, J = 6.1 Hz, –Ar–H), 8.82 (d, 2H, J = 4.6 Hz, –Ar–H); ^{13}C NMR (75 MHz, DMSO-d_6): 23.3, 23.4, 119.2, 120.2, 123.5, 129.7, 130.2, 131.6, 131.8, 134.6, 135.2, 140.5, 141.9, 142.9, 144.3, 144.8, 152.5, 152.7, 154.2, 160.9; MS (EI): m/z 391.20 [$M^+ + H^+$]; Anal. Calcd for $C_{26}H_{22}N_4$. C 79.97 H 5.68 N 14.35. Found: C 79.87 H 5.66 N 14.29.

2.2.9. ***3i****. 5,6-bis[(E)-2-(4-methoxyphenyl)vinyl]-3-pyridin-4-yl-1,2,4-triazine (Table 1, entry 9)*

Yellow solid; mp 178–180 °C; R_f 0.64 (40% AcOEt/Petroleum ether); IR (KBr): 1253, 1294, 1479, 1512, 1601 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 3.84 (s, 3H, Ar–OCH_3), 3.86 (s, 3H, Ar–OCH_3), 6.93–6.96 (m, 4H, –Ar–H), 7.18–7.26 (m, 2H, –Ar–H), 7.57–7.65 (m, 4H, –Ar–H), 8.07 (d, 1H, J = 16.1 Hz, –Ar–H), 8.26 (d, 1H, J = 15.3 Hz, –Ar–H), 8.40 (d, 2H, J = 6.2 Hz, –Ar–H), 8.79 (d, 2H, J = 5.4 Hz, –Ar–H); ^{13}C NMR (75 MHz, DMSO-d_6): 55.5, 55.6, 117.3, 11.9, 123.7, 125.4, 127.2, 128.5, 129.1, 129.4, 129.6, 130.0, 130.9, 136.5, 137.1, 137.9, 142.2, 147.5, 150.2, 151.4, 152.3, 155.6, 160.8; MS (EI): m/z 422.48 [$M^+ + H^+$]; $C_{26}H_{22}N_4O_2$. Anal. Calcd for $C_{26}H_{22}N_4O_2$. C 73.92 H 5.25 N 13.26. Found: C 73.80 H 5.29 N 13.30.

2.2.10. ***3j****. 5,6-bis[(E)-2-(3,4-dimethoxyphenyl)vinyl]-3-pyridin-4-yl-1,2,4-triazine (Table 1, entry 10)*

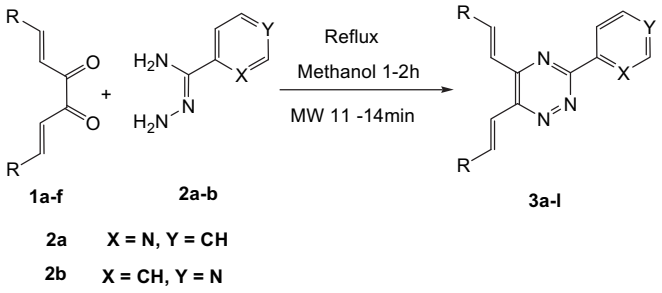
Yellow solid; mp 208–210 °C; R_f 0.35 (40% AcOEt/Petroleum ether); IR (KBr): 1023, 1135, 1260, 1419, 1478, 1260, 1419, 1478, 1514, 1598, 1623 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 3.93 (s, 3H, Ar–OCH_3), 3.95 (s, 3H, Ar–OCH_3), 3.96 (s, 12H, Ar–OCH_3), 6.91–6.95 (m, 2H, –Ar–H), 7.16–7.24 (m, 2H, –Ar–H), 7.25–7.28 (m, 3H, –Ar–H), 7.30–7.34 (m, 1H, –Ar–H), 8.08 (d, 1H, J = 15.3 Hz, –Ar–H), 8.29 (d, 1H, J = 15.3 Hz, –Ar–H), 8.44 (d, 2H, J = 6.2 Hz, –Ar–H), 8.82 (d, 2H, J = 5.4 Hz, –Ar–H); ^{13}C NMR (75 MHz, DMSO-d_6): 56.0, 56.1, 56.2, 110.2, 110.7,111.4, 116.6, 117.4, 121.7, 122.4, 128.5, 129.2, 138.5, 142.3, 142.9, 149.3, 149.4, 150.6, 150.7, 150.9, 151.4, 152.3, 158.9; MS (EI): m/z 483.27 [$M^+ + H^+$]; $C_{28}H_{26}N_4O_4$. Anal. Calcd for $C_{28}H_{26}N_4O_4$. C 69.70 H 5.43 N 11.61. Found: C 69.61 H 5.41 N 11.58.

2.2.11. ***3k****. 5,6-bis[(E)-1-napthylvinyl]-3-pyridin-4-yl-1,2,4-triazine (Table 1, entry 11)*

Yellow solid; mp 180–182 °C; R_f 0.82 (40% AcOEt/Petroleum ether); IR (KBr): 959, 1071, 1359, 1401, 1482, 1616 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.34–7. 42 (m, 8H, –Ar–H), 7.55–7.67 (m, 10H, –Ar–H), 7.96 (d, 1H, J = 15.3 Hz, –Ar–H), 8.28–8.34 (m, 2H, –Ar–H), 9.02–9.04 (m, 1H, –Ar–H); ^{13}C NMR (75 MHz, DMSO-d_6): 112.4, 112.8, 113.8, 115.4, 115.8, 116.9, 121.6, 124.7, 128.1, 142.9, 144.1, 145.1, 150.3, 151.7, 152.1, 152.4, 158.6; MS (EI): m/z 464.40 [$M^+ + H^+$]; $C_{32}H_{22}N_4$. Anal. Calcd for $C_{32}H_{22}N_4$. C 83.09 H 4.79 N 12.11. Found: C 83.04 H 4.80 N 12.15.

2.2.12. ***3l****. 5,6-bis[(E)-2-furyl vinyl]-3-pyridin-4-yl-1,2,4-triazine (Table 1, entry 12)*

Yellow solid; mp 174–176 °C; R_f 0.5 (40% AcOEt/Petroleum ether); IR (KBr): 1019, 1258, 1311, 1356, 1399, 1456, 1621, cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 6.49–6.60 (m, 3H, –Ar–H), 6.73 (s, 1H, –Ar–H), 7.22–7.31 (m, 2H, –Ar–H), 7.51 (s, 1H, –Ar–H), 7.56 (s, 1H, –Ar–H), 7.91(d, 1H, J = 15.3 Hz, –Ar–H), 8.06 (d, 1H, J = 4.6 Hz, –Ar–H), 8.38 (d, 2H, J = 4.6 Hz), 8.77 (d, 2H, J = 3.8 Hz –Ar–H); ^{13}C NMR (75 MHz, DMSO-d_6): 112.7, 113.1, 114.0, 115.7, 116.2, 117.2, 121.8, 125.0, 128.4, 143.1, 144.4, 145.4, 150.4, 150.7, 152.0, 152.5, 152.7, 159.0; MS (EI): m/z 343.20 [$M^+ + H^+$]; $C_{20}H_{14}N_4O_2$. Anal. Calcd for $C_{20}H_{14}N_4O_2$. C 70.17 H 4.12 N 16.37. Found: C 70.10 H 4.11 N 16.40.



Scheme 1. Synthesis of bisaryl-3-pyridinyl-1,2,4-triazine derivatives.

*2.3. General procedure for the synthesis of bisaryl-3-pyrazine-1,2,4-triazine derivatives (****5a****–****e****)*

Method: A

A mixture of cinnamil (1 mmol) and pyrazine-2-carboxtrisamidrazone (1 mmol) in methanol (30 ml) was refluxed for the appropriate time as displayed in Table 3. After completion of the reaction, as indicated by TLC, the solid precipitated was filtered, washed with water, dried and recrystallized with ethanol.

Method: B

A mixture of cinnamil (1 mmol) and pyrazine-2-carboxtrisamidrazone (1 mmol) in water (2 ml) was irradiated in microwave oven (BPL BMG 800 TS model) irradiated at 80 W for the appropriate time listed in Table 3. The progress of the reaction was monitored by TLC. After completion of the reaction, the precipitated solid was filtered, washed with water and then dried. The obtained crude product was purified by recrystalization with ethanol.

2.3.1. ***5a****. 5,6-bis[(E)-2-phenylvinyl]-3-pyrazin-2-yl-1,2,4-triazine (Table 3, entry 1)*

Yellow solid; mp 78–80 °C; R_f 0.61 (40% AcOEt/Petroleum ether); IR (KBr): 970, 1070, 1362, 1395, 1488, 1624 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.41–7.48 (m, 7H, –Ar–H), 7.51 (s, 1H, –Ar–H), 7.68–7.72 (m, 4H, –Ar–H), 8.18 (d, 1H, J = 16.1 Hz, –Ar–H), 8.38 (d, 1H, J = 16.1 Hz, –Ar–H), 8.75 (d, 1H, J = 2.3 Hz, –Ar–H), 8.85 (s, 1H,

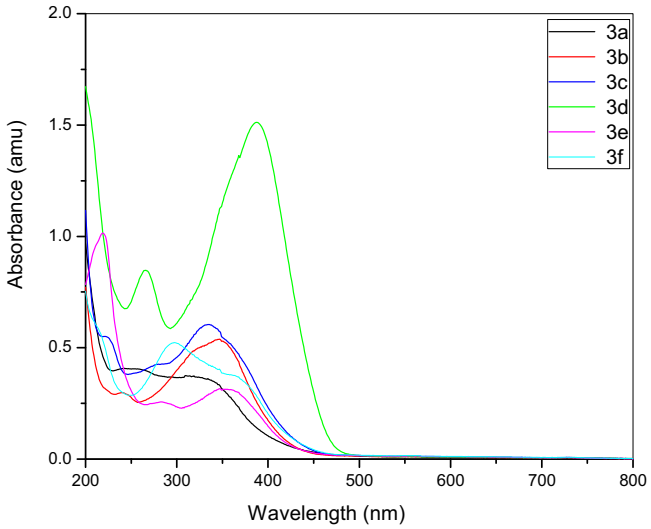


Fig. 1. Absorption spectrum of compounds **3a**–**f**.

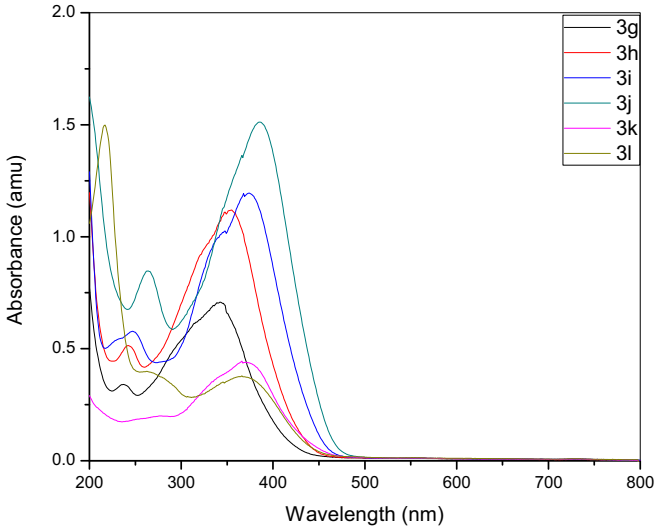


Fig. 2. Absorption spectrum of compounds **3g**–**l**.

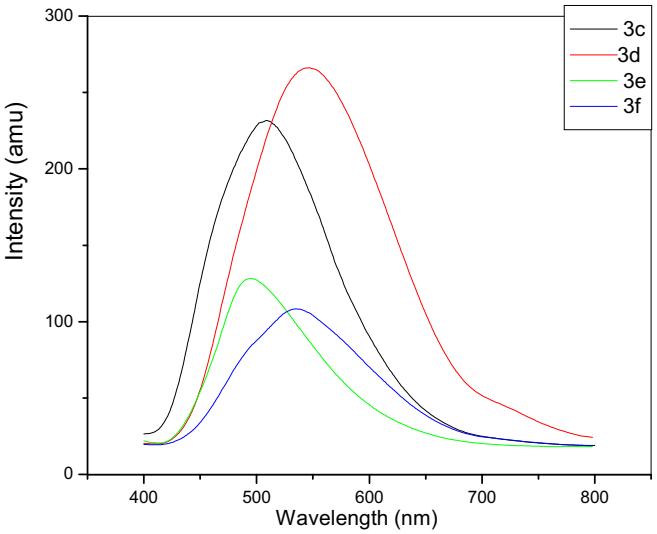


Fig. 3. Emission spectrum of compounds **3c**–**f**.

–Ar–*H*), 9.88 (d, 1H, *J* = 1.6 Hz); ^{13}C NMR (75 MHz, DMSO-d_6): 118.8, 119.8, 124.0, 125.2, 127.8, 128.2, 128.8, 128.9, 129.0, 129.5, 130.2, 135.5, 136.1, 137.1, 138.5, 142.7, 150.3, 151.3, 152.1, 153.2, 160.4; MS (EI): *m*/*z* 364.13 [$M^+ + H^+$]; $C_{23}H_{17}N_5$. Anal. Calcd for $C_{23}H_{17}N_5$. C 76.01 H 4.71 N 19.27. Found: C 75.95 H 4.70 N 19.23.

2.3.2. ***5b****. 5,6-bis[(E)-2-(4-methoxyphenyl)vinyl]-3- pyrazin-2-yl-1,2,4-triazine (Table 3, entry 2)*

Yellow solid; mp 78–80 °C; R_f 0.29 (40% AcOEt/Petroleum ether); IR (KBr): 815, 1025, 1174, 1254, 1375, 1474, 1602 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.86 (s, 6H, Ar–O*CH*$_3$), 6.95 (d, 4H, *J* = 9.2 Hz –Ar–*H*), 7.25–7.34 (m, 2H, –Ar–*H*), 7.61–7.67 (m, 4H, –Ar–*H*), 8.11 (d, 1H, *J* = 16.1 Hz), 8.33 (d, 1H, *J* = 15.3 Hz, –Ar–*H*), 8.73 (d, 1H, *J* = 1.3 Hz, –Ar–*H*), 8.83 (s, 1H, –Ar–*H*), 9.86 (d, 1H, *J* = 1.3 Hz, –Ar–*H*); ^{13}C NMR (75 MHz, DMSO-d_6): 55.4, 55.5, 114.4, 114.5, 116.1, 116.8, 128.2, 128.8, 129.4, 130.1, 138.5, 142.6, 144.6, 145.7, 149.0, 151.5, 152.6, 158.7, 160.9, 161.6; MS (EI): *m*/*z* 424.70 [$M^+ + H^+$]; Anal. Calcd for $C_{25}H_{21}N_5O_2$. C 70.91 H 5.00 N 16.54. Found: C 70.84 H 5.01 N 16.57.

2.3.3. ***5c****. 5,6-bis[(E)-2-(3,4-dimethoxyphenyl)vinyl]-3- pyrazin-2-yl-1,2,4-triazine (Table 3, entry 3)*

Yellow solid; mp 194–196 °C; R_f 0.11 (40% AcOEt/Petroleum ether); IR (KBr): 803, 1022, 1262, 1471, 1514, 1621 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.93 (s, 6H, Ar–O*CH*$_3$), 3.92 (s, 6H, Ar–O*CH*$_3$), 6.91–6.93 (m, 2H, –Ar–*H*), 7.17–7.19 (m, 2H, –Ar–*H*), 7.23–7.26 (m, 2H, –Ar–*H*), 7.29–7.32 (m, 2H, –Ar–*H*), 8.08 (d, 1H, *J* = 16.2 Hz, –Ar–*H*), 8.30 (d, 1H, *J* = 15.3 Hz, –Ar–*H*), 8.73 (d, 1H, *J* = 2.3 Hz, –Ar–*H*), 8.83 (d, 1H, *J* = 2.3 Hz, –Ar–*H*), 9.86 (d, 1H, *J* = 1.6 Hz, –Ar–*H*); ^{13}C NMR (75 MHz, DMSO-d_6): 55.4, 55.5, 114.4, 114.5, 116.1, 116.8, 128.2, 128.8, 129.4, 130.0, 130.9, 138.4, 142.5, 144.5, 145.4, 145.6, 149.0, 151.4, 152.5, 158.7, 160.9, 161.5; MS (EI): *m*/*z* 484.20 [$M^+ + H^+$]; Anal. Calcd for $C_{27}H_{25}N_5O_4$. C 67.07 H 5.21 N 14.48. Found: C 67.20 H 5.19 N 14.43.

2.3.4. ***5d****. 5,6-bis[(E)-1-napthylvinyl]-3- pyrazin-2-yl-1,2,4-triazine (Table 3, entry 4)*

Yellow solid; mp 168–170 °C; R_f 0.70 (40% AcOEt/Petroleum ether); IR (KBr): 1077, 1293, 1511, 1615 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52–7.60 (m, 8H, –Ar–*H*), 7.88–7. 92 (m, 6H, –Ar–*H*), 8.32 (d, 2H, *J* = 8.5 Hz, –Ar–*H*), 8.77 (s, 1H, –Ar–*H*), 8.87 (s, 1H, –Ar–*H*), 9.04 (d, 1H, *J* = 15.3 Hz, –Ar–*H*), 9.21 (d, 1H, *J* = 15.3 Hz, –Ar–*H*), 9.93 (s, 1H, –Ar–*H*); ^{13}C NMR (75 MHz, DMSO-d_6): 112.1, 112.7, 113.4, 115.4, 116.7, 121.4, 124.5, 128.0, 130.2, 140.7, 142.6, 145.1,

Table 2
Photo physical properties of bisaryl-3-pyridinyl-1,2,4-triazine derivatives.

Entry	λ_{max} (nm)	λ_{emi} (nm)	Life time of pyrido-1,2,4-triazines derivatives	
			τ (ns)	χ^2
3a	251.75, 311.35,	nt	nt	nt
3b	328.54	nt	nt	nt
3c	333.83	507.92	2.96 (92.16), 1.12 (7.84)[a]	1.09
3d	386.85	545.02	3.98 (85.67), 0.68 (14.33)[a]	1.15
3e	356.46	535.37	0.71 (62.69), 1.42 (20.18), 2.84 (17.14)[b]	1.22
3f	351.93	491.49	0.9 (28.4), 4.24 (71.6)[a]	1.25
3g	343.05	nt	nt	nt
3h	355.56	nt	nt	nt
3i	373.86	542.55	4.13 (13.93), 1.10 (86.07)[a]	1.19
3j	387.82	572.55	3.88 (90.34), 0.57 (9.66)[a]	1.05
3k	374.58	500.60	4.91 (52.04), 1.33 (47.96)[a]	1.08
3l	374.28	553.93	3.63 (66.37), 1.32 (33.63)[a]	1.12

nt-not studied.
[a] Fluorescence lifetime associated with the bi exponentials.
[b] Fluorescence lifetimes associated with the tri exponentials.

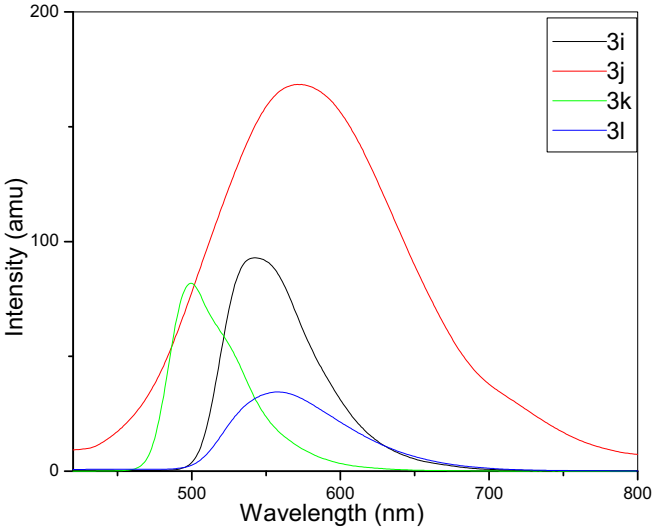


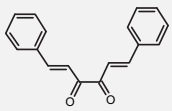
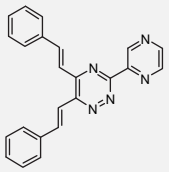
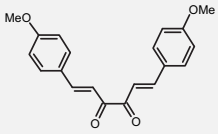
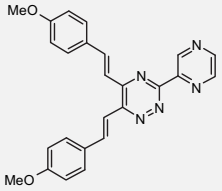
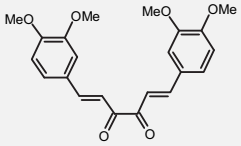
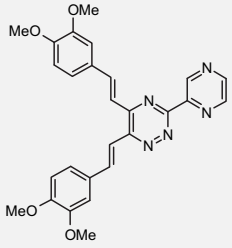
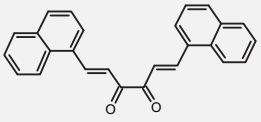
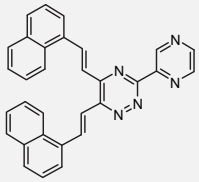
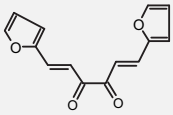
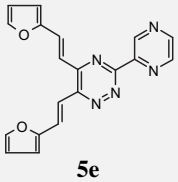
Fig. 4. Emission spectrum of compounds **3i**–**l**.

150.1, 151.4, 153.2, 155.6, 158.6; MS (EI): *m/z* 464.20 [$M^+ + H^+$]; Anal. Calcd for $C_{31}H_{21}N_5$. C 80.32 H 4.57 N 15.11. Found: C 80.40 H 4.58 N 15.16.

2.3.5. ***5e****. 5,6-bis[(E)-2-furyl vinyl]-3- pyrazin-2-yl-1,2,4-triazine (Table 3, entry 5)*

Yellow solid; mp 168–170 °C; R_f 0.53 (40% AcOEt/Petroleum ether); IR (KBr): 1079, 1204, 1295, 1379, 1408, 1576, 1616 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 6.50–6.52 (m, 2H, –Ar–*H*), 6.63 (d, 1H, *J* = 3.1 Hz, –Ar–*H*), 6.73 (d, 1H, *J* = 3.1 Hz, –Ar–*H*), 7.25–7.37 (m, 2H, –Ar–*H*), 7.53 (d, 2H, *J* = 16.2 Hz, –Ar–*H*), 7.96 (d, 1H, *J* = 16.1 Hz, –Ar–*H*), 8.15 (d, 1H, *J* = 15.3 Hz, –Ar–*H*), 8.72 (d, 1H, *J* = 16.1 Hz, –Ar–*H*), 8.81 (s, 1H, –Ar–*H*), 9.83 (d, 1H, *J* = 1.6 Hz, –Ar–*H*); ^{13}C NMR (75 MHz, DMSO-d_6): 112.4, 112.8, 113.9, 115.7, 115.9, 116.7, 125.1, 128.8, 144.2, 144.5, 145.1, 145.3, 145.7, 148.9, 150.9, 152.1, 152.4; MS (EI): *m/z* 344.20 [$M^+ + H^+$]; $C_{19}H_{13}N_5O_2$. Anal. Calcd for $C_{19}H_{13}N_5O_2$. C 66.47 H 3.82 N 20.40. Found: C 66.37 H 3.83 N 20.34.

Table 3
Synthesis of bisaryl-3-pyrazine-1,2,4-triazine derivatives.

Entry	Cinnamil	Triazine[a]	Conventional Heating		Microwave Irradiation	
			Time (h)	Yield (%)[b]	Time (min)	Yield (%)[b]
1	 **1a**	 **5a**	3.0	75	12.0	79
2	 **1b**	 **5b**	3.5	78	13.0	81
3	 **1c**	 **5c**	4.0	81	14.0	85
4	 **1d**	 **5d**	4.5	68	14.0	74
5	 **1e**	 **5e**	4.0	76	15.0	81

[a] All products were confirmed by IR, NMR, mass and elemental analysis.
[b] Isolated yield.

3. Results and discussion

On continuation of earlier work [22], in an initial endeavor, we carried out the reaction of tolylcinnamil (**1b**) and pyridine-2-carboxtrisamidrazone [20,21] (**2**) in various solvents at reflux temperature. Excellent results were obtained with methanol as a solvent at reflux temperature in the shorter reaction time. After completion of the reaction, the reaction mixture was poured into ice cold water and extracted with ethyl acetate and then dried with sodium sulphate. The crude product was purified by using column chromatography. The purified bisaryl-3-pyridin-2-yl-1,2,4-triazine derivative gave good yield of 85% (Scheme 1).

The substrate scope of the reaction under the optimized conditions was investigated, and the reaction was amendable to a wide variety of substituents on cinnamils. We extended our investigation on microwave irradiated synthesis of substituted triazines and the results, are summarized in Table 1. Microwave reactions were rapid and resulted in high yields of substituted 1,2,4-triazine derivatives.

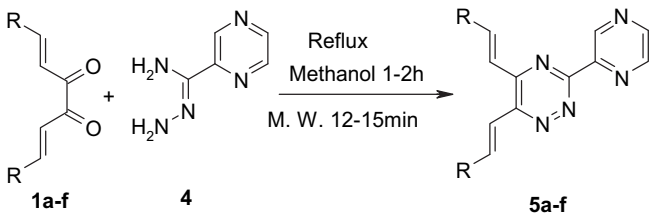
The structures of products **3a**–**l** were confirmed by spectral studies and elemental analysis as exemplified for compound **3b** as follows: The IR spectrum showed a peak at 1623 cm^{-1} which indicated the presence of C═N group. In the ^1H NMR spectrum, aromatic protons resonated in the region of δ: 7.22–8.82 ppm. The trans olefinic protons were demonstrated at δ: 8.10 (J = 15.2 Hz) and methyl protons appeared at chemical shift values of δ: 2.40 and 2.41 ppm. The ^{13}C NMR studies showed aromatic carbons in the region of δ: 119.2–160.9 ppm and the methyl carbons were seen at δ: 23.3 and 23.4 ppm. The mass spectrum displayed molecular ion peak at m/z 391.20.

3.1. Photo physical properties of bisaryl-3-pyridinyl-1,2,4-triazine derivatives

The photo physical properties of bisaryl-3-pyridinyl-1,2,4-triazine derivatives were studied in acetonitrile (1×10^{-4} M). The λ_{max} values of bisaryl-3-pyridinyl-1,2,4-triazine derivatives were observed in the range of 280–400 nm are due to $\pi-\pi^*$ and $n-\pi^*$ electronic transition in quinoxaline. The absorbance values increase with the increase in electron donating ability of the substituents present in the triazine moiety. The bathochromic shift was observed due to increase in electron donating ability of the substituents present in the triazine molecule. (Figs. 1 and 2).

The fluorescence spectral data of triazine derivatives (**3c**–**f** and **3i**–**l**) in acetonitrile is shown in Table 2, Figs. 3 and 4. Their fluorescence emission maximum shifted to longer wavelength region λ_{emi}, which mainly depends on the electronic character of the substituents present in the triazene derivatives. Substituents with higher electron donating character lead to longer λ_{emi} values. Moreover extended conjugation with fused rings are also responsible for the higher λ_{emi} value.

Time correlated single photon counting experiments exhibited that triazine derivatives have longer life times. Except **3e** all other



Scheme 2. Synthesis of bisaryl-3-pyrazine-1,2,4-triazine derivatives.

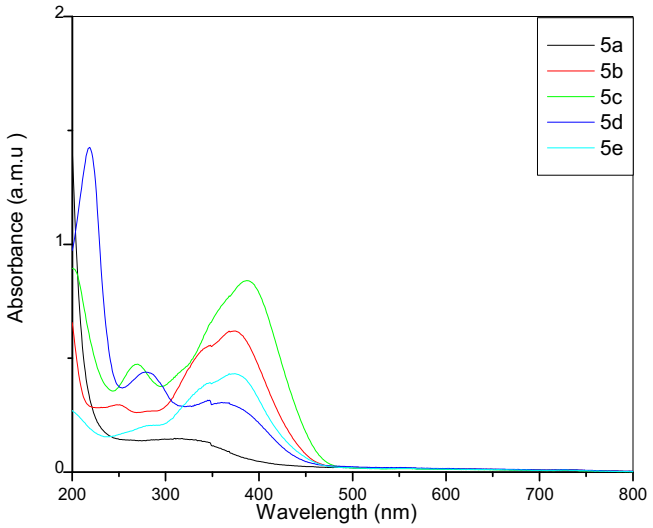


Fig. 5. Absorption spectrum of compounds **5a**–**e**.

triazine derivatives exhibit a bi-exponential decay and **3e** exhibit a tri-exponential decay. The value of chi-square is in the order of one, comparatively a good fit with experimental results shown in Table 2.

Based on the above results, we extended our protocol to the synthesis of bisaryl-3-pyrazine-1,2,4-triazine derivatives under optimized condition. 1,6-Diphenylhexa-l,5-diene-3,4dione and pyrazine-2-carboxtrisamidrazone in methanol under reflux condition gave bisphenyl-3-pyrazine-1,2,4-triazine derivative in good yield. (Table 3, Scheme 2) To explore the utility of bisphenyl-3-pyrazine-1,2,4-triazine derivative, reaction under the optimized conditions were investigated and the reaction was amendable to a variety of substituted cinnamils bearing ethers, aromatic ring and hydrocarbons.

The structure of compounds (**5a**–**e**) were evaluated based on detailed spectroscopic studies as exemplified for compound **5d** as follows: IR spectrum of compound (**5d**) showed an absorption band in the region of 1615 cm^{-1} for C═N functional group. Aromatic protons appeared in the region of δ: 7.52–9.93 in the ^1H NMR. In ^{13}C

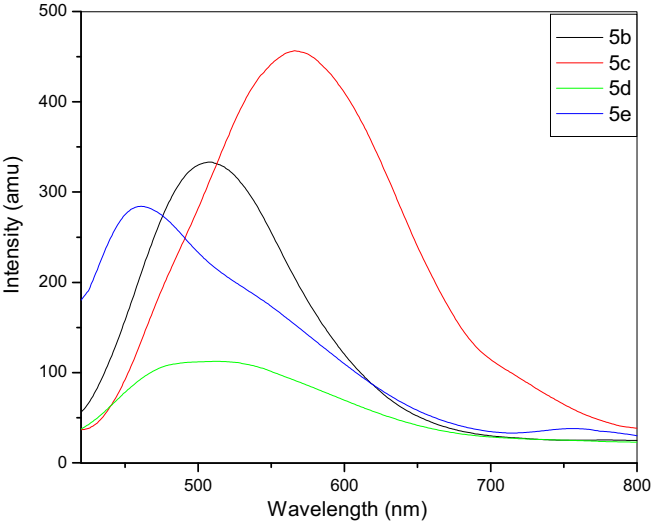


Fig. 6. Emission spectrum of compounds **5b**–**e**.

Table 4
Photo physical properties of bisaryl-3-pyrazine-1,2,4-triazine derivatives.

Entry	λ_{max} (nm)	λ_{emi} (nm)	Life time of pyrazine-1,2,4-triazines	
			τ (ns)	χ^2
5a	344.58	nt	nt	nt
5b	373.44	506.60	3.96 (91.44), 2.1 (8.56)[a]	1.06
5c	390.41	568.89	4.2 (78.44), 2.2 (21.66)[a]	1.12
5d	369.77	467.93	2.83 (55.46), 1.41 (44.54)[a]	1.16
5e	375.22	510.14	3.33 (68.79), 0.74 (31.21)[a]	1.19

nt-not studied.
[a] fluorescence lifetime associated with the bi-exponential.

NMR spectra all the aromatic carbons resonated in the region of δ: 112.1–158.6. The mass spectra displayed the $[M^+ + H^+]$ peak at m/z 464.20.

3.2. Photo physical properties of bisaryl-3-pyrazine-1, 2,4-triazine derivatives

The optical properties of bisaryl-3-pyrazinyl-1,2,4-triazine derivatives were studied in acetonitrile (1×10^{-4} M). The λ_{max} values of bisaryl-3-pyrazine-1,2,4-triazine derivatives observed in the range of 280–400 nm are due to $\pi-\pi^*$ and $n-\pi^*$ electronic transition in quinoxaline. The absorbance values increase with the increase in electron donating ability of the substituents present in the triazine moiety. The bathochromic shift was observed due to increase in electron donating ability of the substituents present in the triazine molecule (Fig. 5).

Bisaryl-3-pyrazinyl-1,2,4-triazine derivatives (**5b**–**e**) showed longer photoluminescence maxima than that of bisaryl-3-pyridinyl-1,2,4-triazine derivatives. The red shift maxima observed in the region of 450–600 nm which strongly depends on the electron donating character of the substituents present in the pyrazinyl-1,2,4-triazine moiety. Stronger electron donating groups present in the pyrazinyl-1,2,4-triazine moiety lead to longer emission values (Fig. 6 and Table 4).

All bisaryl-3-pyrazinyl-1,2,4-triazine derivatives of entry (**5b**–**e**) showed a bi exponential decay. The value of chi-square is in the order of one comparatively a good fit with experimental results.

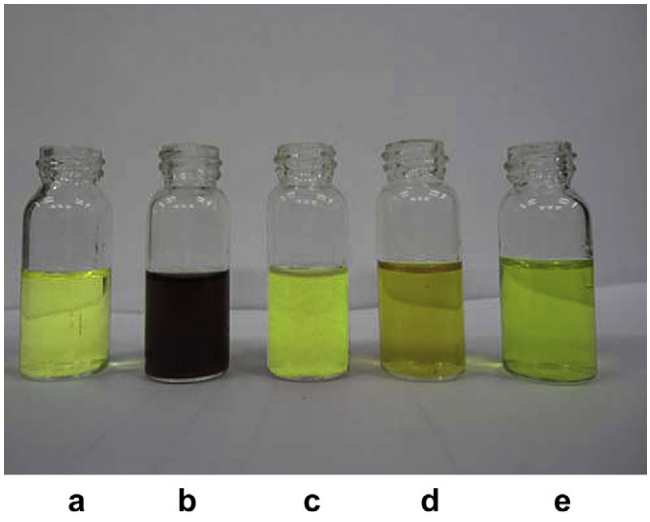


Fig. 7. (a) Compound **5b** of conc. (b) **5b**(50 μM) + Fe(III)(50 μM); (c) **5b**(50 μM) + Fe(II) (100 μM); (d) **5b**(50 μM) + Cu(II) (100 μM); (e) **5b**(50 μM) + Co(II) (100 μM) in acetonitrile.

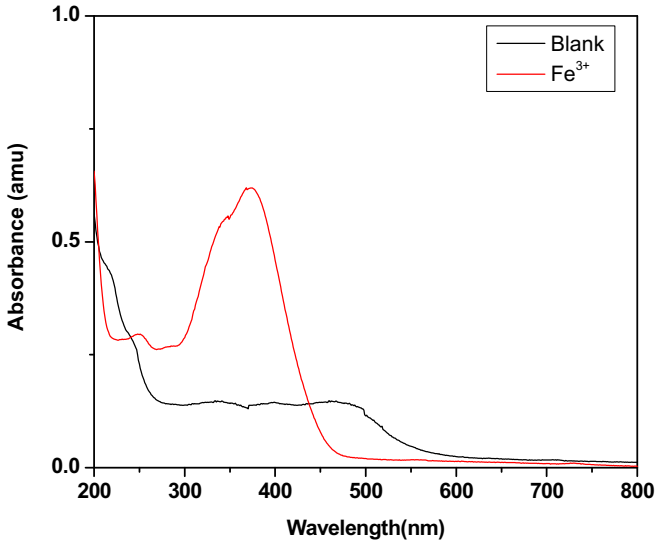


Fig. 8. The effect addition of Fe(III) in the absorption spectrum of compound **5b** in acetonitrile.

The fluorescence lifetimes of bisaryl-3-pyrazinyl-1,2,4-triazine derivatives show higher values on comparison to pyridinyl-1,2,4-triazine derivatives as shown in Table 4.

Fluorescence modulation upon metal binding is expected when a fluorophore interacts directly with a nonbonded electron pair belonging to a metal chelating group. Fluorescence intensity of the molecules (**5b**) has been found to change in the presence of Fe(II) (Ferrous salt of Chloride, Fluoride, Oxalate, Iodide and sulphate), Fe(III) (Ferric salt of Chloride, Fluoride, Oxalate, Iodide and sulphate), Co(II) (cobalt salt of Chloride, Fluoride and Iodide) and Cu(II) (cupric salt of Chloride, Fluoride and Nitate) ions. In the case of Fe(III), the original green fluorescence has been found to change to reddish brown upon the addition of 50 μM of metal ion to 50 μM of compound **5b** (Fig. 7) and the corresponding UV and fluorescence spectral changes are shown Figs. 8 and 9.

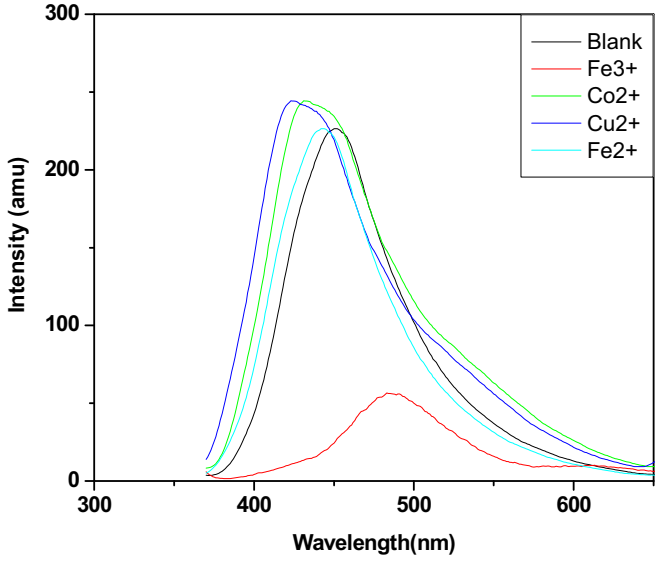


Fig. 9. The effect addition of Fe(III), Fe(II), Cu(II) and Co(II) in the fluorescence spectrum of compound **5b** in acetonitrile.

4. Conclusion

In conclusion, we have demonstrated a simple and convenient method for the synthesis of novel bisaryl-3-pyridinyl-1,2,4-triazine derivative and bisaryl-3-pyrazine-1,2,4-triazine derivatives. This protocol offers several advantages such as inexpensive starting material, very simple route of synthesis, no undesired side products and high yield of products without employing any purification techniques like column chromatography or recrystallisation, which makes it an useful and attractive process for the synthesis of substituted 1,2,4-triazine derivatives. Bisaryl-3-pyrazine-1,2,4-triazine derivatives showed good sensor property with Fe(III)ions even in micro level concentrations also. Further studies to delineate the scope and limitations of the present methodology are underway.

Acknowledgments

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Appendix. Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.dyepig.2010.07.013.

References

[1] Boger DL. Diels–Alder reactions of heterocyclic azadienes: scope and applications. Chemical Reviews 1986;86:781–93.
[2] Khramov Dimitri M, Bielawski CW. Triazene formation via reaction of imidazol-2-ylidenes with azides. Chemical Communications; 2005:4958–60.
[3] Benson SC, Li JH, Snyder JK. Indole as a dienophile in inverse electron demand Diels–Alder reactions. Intramolecular reactions with 1,2,4-triazines to access the Canthine skeleton. Journal of Organic Chemistry 1992;57:5285–7.
[4] Grembecka J, Mucha A, Cierpicki T, Kafarski P. The most potent organophosphorus inhibitors of leucine aminopeptidase. Structure-based design, chemistry and activity. Journal of Medicinal Chemistry 2003;46:2641–5.
[5] Mitchel WL, Hill ML, Newtons RH, Ravenscroft P, Scopes DK. Synthesis of C-nucleoside isosteres of 9-(2-hydroxyethoxymethyl)guanine (acyclovir). Journal of Heterocyclic Chemistry 1984;21:697–9.
[6] Salahuddin NA, El-Barbary AA, Abdo NI. Delivery systems for some biologically active 1,2,4-triazine derivatives: synthesis and release. Polymers for Advanced Technologies 2009;20:122–9.
[7] Sztanke K, Pasternak K, Rajtar B, Sztanke M, Majek M, Polz-Dacewicz M. Identification of antibacterial and antiviral activities of novel fused 1,2,4-triazine esters. Bioorganic Medicinal Chemistry 2007;15:5480–6.
[8] Hurst DT. Progress in heterocyclic chemistry, vol. 7. Oxford, United Kingtom: Elsevier Science Limited; 1995. p. 244–267.
[9] Ho H, Najari A, Leclerc M. Optical detection of DNA and proteins with cationic polythiophenes. Accounts of Chemical Research 2008;41:168–78.
[10] Metzker ML, Lu J, Gibbs RA. Electrophoretically uniform fluorescent dyes for automated DNA sequencing. Science 1996;271:1420–2.
[11] Khramov Dimitri M, Bielawski CW. Donor–acceptor triazenes: synthesis, characterization, and study of their electronic and thermal properties. Journal of Organic Chemistry 2007;72:9407–17.
[12] Zhang J, Tan W, Meng X, Tian H. Soft mimic gear-shift with a multi-stimulus modified diarylethene. Journal of Materials Chemistry 2009;19:5726–9.
[13] Jiang Y, Wang Y, Hua J, Tang J, Li B, Qian S, et al. Multibranched triarylamine end-capped triazines with aggregation-induced emission and large two-photon absorption cross-sections. Chemical Communications 2010;46:4689–91.
[14] Kozhevnikov VN, Kozhevnikov DN, Shabunina OV, Rusinov VL, Chupakhin ON. An efficient route to 5-(hetero)aryl-2,4′- and 2,2′-bipyridines through readily available 3-pyridyl-1,2,4-triazines. Tetrahedron Letters 2005;46:1791–3.
[15] Hajbi Y, Suzenet F, Khouili M, Lazar S, Guillaumet G. Polysubstituted 2,3-dihydrofuro[2,3-b]pyridines and 3,4-dihydro-2H-pyrano[2,3-b]pyridines via microwave-activated inverse electron demand Diels–Alder reactions. Tetrahedron 2007;63:8286–97.
[16] Ławecka J, Olender E, Piszcz P, Rykowski A. Sequential homo-coupling Diels–Alder/retro Diels–Alder reaction of 5,5′-bi-1,2,4-triazine-containing thiamacrocycles as a new route to thiacrown ethers incorporating a 2,2′-bipyridine subunit. Tetrahedron Letters 2008;49:723–6.
[17] Adam F, Burton AJ, Cardwell KS, Cox RA, Henson RA, Mills K, et al. Novel syntheses of the amino-1,2,4-triazine GW356194: identification of a synthesis amenable to scale up. Tetrahedron Letters 2003;44:5657–9.
[18] Diring S, Retailleau P, Ziessel R. Intramolecular inverse electron demand Diels–Alder reactions of imidazoles with 1,2,4-triazines: a new route to 1,2,3,4-tetrahydro-1,5-naphthyridines and related heterocycles. Journal Organic Chemistry 2007;69:7171–82.
[19] Zhao Z, Leister WH, Strauss KA, Wisnoski DD, Lindsley CW. Broadening the scope of 1,2,4-triazine synthesis by the application of microwave technology. Tetrahedron Letters 2003;44:1123–7.
[20] Pabst GR, Sauer J. The new and simple 'LEGO' system: its application to the synthesis of superbranched oligopyridines. Tetrahedron Letters 1998;39:8817.
[21] Pabst OC, Sauer J. The new and simple 'LEGO' system for the synthesis of thienyl substituted 2,6-oligopyridines. Tetrahedron Letters 1998;39:8821–4.
[22] Thirumurugan P, Muralidharan D, Perumal PT. The synthesis and photophysical studies of quinoxaline and pyridopyrazine derivatives. Dyes and Pigments 2009;81:245–53.
[23] Thirumurugan P, Nandakumar A, Muralidharan D, Perumal PT. Simple and convenient approach to the Kr€ohnke pyridine type synthesis of functionalized indol-3-yl pyridine derivatives using 3-cyanoacetyl indole. Journal of Combinatorial Chemistry 2010;12:161–7.
[24] Thirumurugan P, Perumal PT. A simple one-pot synthesis of functionalised 6-(indol-3-yl)-2,2'-bipyridine derivatives via multi-component reaction under neat condition. Tetrahedron Letters 2009;50:4145–50.