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Novel 5,6-bis-(4-substitutedphenyl)-2*H*(3)-pyridazinones: Synthesis and reactions

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Abstract A series of 5,6-bis(4-substitutedphenyl)-2*H*(3)-pyridazinones **2a–f** have been synthesized from the condensation of the corresponding benzil monohydrazones **1** either with ethyl cyanoacetate or diethyl malonate in ethanol. The synthesized pyridazinones were converted to the corresponding 3-chloro derivatives **3a–f** by the action of phosphoryl chloride. Reaction of the latter halogenated pyridazines with various aromatic amines led to the formation of new 3-aminoaryl pyridazines (**4**) in moderate yield. The structures of all new compounds **2b,c,e,f**, **3b–e**, **4** were fully identified by the analysis of their ¹H and ¹³C NMR and mass spectra. Some of these synthetic heterocyclic compounds were screened for their antimicrobial activities but they were almost negative.

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1. Introduction

In recent years, a great deal of work have been directed to the organic synthesis of pyridazines. These nitrogen heterocyclic compounds are of biological importance and therefore, design and strategy for their synthesis is important. Pyridazines, and in particular 3-pyridazinone derivatives, are known for a wide range of biological activities. They possess antibacterial

(Ibrahim et al., 1993; Seada et al., 1989; Kamal El-Dean and Radwan, 1998), antifungal (Kamal El-Dean and Radwan, 1998; Ralph et al., 1988) and insecticidal (Numata et al., 1988) activities. Further, a number of these nitrogen heterocycles showed a promising pharmacological activities such as 6-phenyl 2*H*(3)-pyridazinones as antihypertensive (Demirayak et al., 2004; Wermuth et al., 1989; Curran and Adma Ross, 1944; McEvoy and Allen, 1974), cardiotonic (Cignarella et al., 1986; Howson et al., 1988; Okushimo et al., 1987), antinociceptive (Piaz et al., 2003; Frank and Heinisch, 1992) agents as well as coagulants (Cignarella et al., 1986; Sotelo et al., 2002; Coelho et al., 2004; Sircar et al., 1985).

Also, many of *N*-alkylated 3-pyridazinones have been found to be inhibitors of Interleukin-1 β production (Matsuda et al., 2001a,b). In view of the above mentioned biological and pharmacological importance of the title compounds, and due to our increased activity involved in the synthesis of a variety of nitrogen-containing heterocycles during the past few years (El-Baih et al., 2000; El-Baih, 2003; El-Baih et al., 2006a,b;

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El-Shehry et al., 2008), we report herein the synthesis of a series of novel 5,6-bis(4-substitutedphenyl)-3-(2*H*)-pyridazinones (**2a–f**), the corresponding chloro derivatives (**3a–e**), and coupling products of the latter compounds with some aromatic amines (**4**). All synthesized compounds have been structurally elucidated on the basis of spectroscopic means.

2. Experimental

Starting materials were obtained from commercial suppliers and used without further purification. Melting points are determined on an electrothermal's IA9000 series digital capillary melting point apparatus and are uncorrected. IR spectra were run (KBr discs) on Perkin Elmer FT spectrophotometer 1000. ^1H and ^{13}C NMR spectra were recorded on a JEOL ECP 400 NMR spectrometer operating at 400 MHz in $\text{DMSO}-d_6$ unless otherwise stated with TMS as internal standard. DEPT and HETCOR experiments were recorded on 500 MHz instrument (Bruker, J.F.B. 288) at King Saud University (Pharmacy Research Centre). Chemical shifts are given in δ ppm and coupling constants (J) are given in Hz. Electron impact (EI) MS spectra were carried on Shimadzu GCMSQP5050A spectrometer, DB-1 glass column 30 m, 0.25 mm, ionization energy 70 eV, at Chemistry Department, College of Science, King Saud University. The reactions were monitored by TLC.

2.1. Benzil monohydrazones (**1a–c**)

A mixture of benzil derivative (0.075 mol) and hydrazine hydrate 99% (0.075) was heated in 50 ml ethanol (96%) on oil bath, and the reaction was monitored by TLC. After reaction completion which takes 9 h, 29 h and 11 h, respectively, the mixture was kept to cool overnight at 0–5 °C. The precipitate was filtered, washed by ethanol and recrystallised from ethanol.

2.1.1. 2-Hydrazono-1,2-diphenylethanone (**1a**)

White powder, m.p. 154–156 °C, lit. (Druey and Schemidt, 1957) 151 °C, yield 79%; IR (cm^{-1}): 1626 ($\text{C}=\text{O}$), 1441.2 ($\text{C}=\text{N}$); MS: m/z 212 [M^+]; ^1H NMR(CDCl_3): δ 6.30 (2H, s, NH_2), 7.35 (2H, d, $J = 8.08$ Hz, H-2',6'), 7.46 (3H, t, $J = 7.32$ Hz, H-3',4',5'), 7.53 (3H, t, $J = 7.36$ Hz, H-3'',4'',5''), 7.96 (2H, dd, $J = 6.60$ Hz, $J = 4.40$ Hz, H-2'',6''); ^{13}C NMR(CDCl_3): δ 145.5 ($\text{C}=\text{N}$), 191.9 ($\text{C}=\text{O}$), 127.80 (C-3',5'), 129.00 (C-3'',5''), 129.30 (C-2',4',6'), 130.20 (C-2'',6''), 131.60 (C-4''), 129.80 (C-1'), 138.20 (C-1'').

2.1.2. 1,2-Bis(4-bromophenyl)-2-hydrazonoethanone (**1b**)

White needles, m.p. 185–186 °C, yield 63%; IR (cm^{-1}): 1622.6 ($\text{C}=\text{O}$), 1348.7 ($\text{C}=\text{N}$); MS: m/z 384 [$\text{M} + 4$] ($\text{C}_{14}\text{H}_{10}\text{N}_2\text{O}^{81,81}\text{Br}_2$) (25.71%), 382 [$\text{M} + 2$] ($\text{C}_{14}\text{H}_{10}\text{N}_2\text{O}^{79,79}\text{Br}_2$) (52.16%), 380 [M^+] ($\text{C}_{14}\text{H}_{10}\text{N}_2\text{OBr}_2$) (29.03%); ^1H NMR ($\text{DMSO}-d_6$): δ 8.23 (2H, s, NH_2), 6.69 (2H, d, $J = 8.08$ Hz, H-3',5'), 7.06 (2H, d, $J = 8.80$ Hz, H-2',6'), 7.14 (2H, d, $J = 8.80$ Hz, H-3'',5''), 7.31 (2H, dd, $J = 8.80$, 2.20 Hz, H-2'',6''); ^{13}C NMR ($\text{DMSO}-d_6$): δ 146.1 ($\text{C}=\text{N}$), 190.19 ($\text{C}=\text{O}$), 123.37 (C-4'), 126.25 (C-4''), 127.72 (C-1'), 130.32 (C-2',6'), 130.63 (C-3',5'), 131.07 (C-2'',6''), 132.07 (C-1''), 132.00 (C-3'',5'').

2.1.3. 1,2-Bis(4-methoxyphenyl)-2-hydrazonoethanone (**1c**)

Yellowish needles, m.p. 132–134 °C, yield 65%; IR (cm^{-1}): 1628 ($\text{C}=\text{O}$), 1412.3 ($\text{C}=\text{N}$); MS: m/z 284 [M^+] ($\text{C}_{16}\text{H}_{16}\text{N}_2\text{O}_3$) (42.88%), 149 [$\text{M}^+ - \text{C}_8\text{H}_7\text{O}_2$] (100%), 135

[$\text{M}^+ - \text{C}_8\text{H}_9\text{N}_2\text{O}$] (51.36%); ^1H NMR(CDCl_3): δ 6.18 (2H, s, NH), 3.83, 3.85 (each 3H, s, $2\times\text{OCH}_3$), 6.92 (2H, dd, $J = 8.80$, 1.48 Hz, H-3',5'), 7.02 (2H, dd, $J = 8.80$, 2.20 Hz, H-3'',5''), 7.29 (2H, dd, $J = 6.60$, 2.20 Hz, H-2',6'), 8.00 (2H, dd, $J = 8.80$, 6.60 Hz, H-2'',6''); ^{13}C NMR(CDCl_3): δ 145.9 ($\text{C}=\text{N}$), 190.57 ($\text{C}=\text{O}$), 55.40 (OCH_3), 55.00 (OCH_3), 113.20 (C-3',5'), 114.70 (C-3'',5''), 122.00 (C-1'), 130.40 (C-2',6'), 130.60 (C-1''), 132.70 (C-2'',6''), 160.10 (C-4''), 162.60 (C-4').

2.2. General procedure for the preparation of pyridazinones (**2a–f**)

A solution of sodium metal (0.1 mol) in absolute alcohol (150 ml) was prepared. This solution was gradually added to a solution of equimolar amounts of 0.1 mole of the appropriate hydrazone **1a–c** and 0.1 mole of ethyl cyanoacetate or diethyl malonate in absolute ethanol (150 ml). Then, the mixture was refluxed for some hours as judged by TLC. The time was 6, 16, 16 h for **2a–c** and 11, 17, 18 h for **2d–f**, respectively. The reaction mixture was then evaporated under reduced pressure until dryness, then, ice was added to the residue acidified by HCl solution (2 N). The formed precipitate was filtered, washed with distilled water and recrystallized from ethanol for **2a–c** and from benzene **2d–f**, to give the required pyridazinone **2** with moderate yield. NMR data of **2a–f** were reported in Table 1.

2.2.1. 3-Oxo-5,6-diphenyl-2,3-dihydropyridazine-4-carbonitrile (**2a**)

White powder, m.p. 272–274 °C, lit. (Schemidt and Druey, 1954) 272–273 °C, yield 50%; IR (cm^{-1}): 1660.6 ($\text{C}=\text{O}$), 2229.4 (CN); MS: m/z 273 [M^+] ($\text{C}_{17}\text{H}_{11}\text{N}_3\text{O}$) (100%), 274 [$\text{M}^+ + 1$] ($\text{C}_{17}\text{H}_{12}\text{N}_3\text{O}$) (15.56%); NMR (δ_{H} , δ_{C}): Table 1.

2.2.2. 5,6-Bis(4-bromophenyl)-3-oxo-2,3-dihydropyridazine-4-carbonitrile (**2b**)

White powder, m.p. 275–276 °C, yield 49%; IR (cm^{-1}): 1700.6 ($\text{C}=\text{O}$), 2228.4 (CN); MS: m/z 429 [M^+] ($\text{C}_{17}\text{H}_9\text{N}_3\text{OBr}_2$) (40.55%), 431 [$\text{M}^+ + 2$] ($\text{C}_{17}\text{H}_{11}\text{N}_3\text{OBr}_2$) (71.89%), 433 [$\text{M}^+ + 4$] ($\text{C}_{17}\text{H}_{12}\text{N}_3\text{OBr}_2$) (38.77%); NMR (δ_{H} , δ_{C}): Table 1.

2.2.3. 5,6-Bis(4-methoxyphenyl)-3-oxo-2,3-dihydropyridazine-4-carbonitrile (**2c**)

Yellowish needles, m.p. 235–236 °C, yield 59%; IR (cm^{-1}): 1661 ($\text{C}=\text{O}$), 2227.13 (CN); MS: m/z 333 [M^+] ($\text{C}_{19}\text{H}_{15}\text{N}_3\text{O}_3$) (100%), 318 [$\text{M}^+ - \text{CH}_3$] (9.29%), 302 [$\text{M}^+ - \text{OCH}_3$] (5.37%); NMR (δ_{H} , δ_{C}): Table 1.

2.2.4. Ethyl 3-oxo-5,6-diphenyl-2,3-dihydropyridazine-4-carboxylate (**2d**)

White powder, m.p. 224–226 °C, lit. (Druey and Schemidt, 1957) 219–220 °C, yield 51%; IR (cm^{-1}): 1647.11 ($\text{C}=\text{O}$), 1737.14 (COO); MS: m/z 320 [M^+] ($\text{C}_{19}\text{H}_{16}\text{N}_2\text{O}_3$) (62.70%), 291 [$\text{M}^+ - \text{C}_2\text{H}_5$] (2.77%), 275 [$\text{M}^+ - \text{C}_2\text{H}_5\text{O}$] (43.85%); NMR (δ_{H} , δ_{C}): Table 1.

2.2.5. Ethyl 5,6-bis(4-bromophenyl)-3-oxo-2,3-dihydropyridazine-4-carboxylate (**2e**)

White powder, m.p. 248–250 °C, yield 61%; IR (cm^{-1}): 1645 ($\text{C}=\text{O}$), 1743 (COO); MS: m/z 476 [M^+] ($\text{C}_{19}\text{H}_{14}\text{N}_2\text{O}_3^{79,79}\text{Br}_2$) (42.83%), 478 [$\text{M}^+ + 2$] ($\text{C}_{19}\text{H}_{16}\text{N}_2\text{O}_3^{79,81}\text{Br}_2$) (100%), 480 [$\text{M}^+ + 4$] ($\text{C}_{19}\text{H}_{14}\text{N}_2\text{O}_3^{81,81}\text{Br}_2$) (44.80%); NMR (δ_{H} , δ_{C}): Table 1.

Table 1 NMR Spectral data (CDCl₃, DMSO-*d*₆) of chloro-pyridazines **2a–f**.

Compound No.	Chemical shifts (δ_H) in ppm	Chemical shifts (δ_C) in ppm
2a*	14.11 (1H, s, NH), 7.10 (2H, d, J = 8.08 Hz, H-3',5'), 7.30 (5H, m, H-3'',4',5',2',6'), 7.44 (3H, m, H-2'',4'',6'')	158.0 (C=O), 114.42 (CN), 113.98 (C-4), 128.44 (2C), 128.96 (2C), 129.11 (C-4'), 129.32 (2C), 129.62 (2C), 130.44 (C-4''), 133.86 (C-1'), 135.29 (C-1''), 146.45 (C-5), 152.38 (C-6)
2b*	33.03 (1H, s, NH), 7.05 (2H, d, J = 8.08 Hz, H-3',5'), 7.21 (2H, d, J = 8.80 Hz, H-2',6'), 7.43 (2H, d, J = 8.80 Hz, H-3'',5''), 7.61 (2H, d, J = 8.04 Hz, H-2'',6'')	162.74 (C=O), 116.13 (CN), 121.79 (C-4'), 123.53 (C-4''), 131.38 (C-2',6'), 131.65 (C-2'',3',5',6''), 132.10 (2C), 134.03 (C-4), 136.07 (C-1''), 143.85 (C-1'), 145.50 (C-5), 154.00 (C-6)
2c*	13.96 (2H, s, NH), 3.71, 3.85 (each 3H, s, 2X-OCH ₃), 6.81 (2H, d, J = 8.80 Hz, H-3',5'), 6.96 (2H, d, J = 8.80 Hz, H-2',6'), 7.02 (2H, d, J = 8.80 Hz, H-3'',5''), 7.22 (2H, d, J = 8.80 Hz, H-2'',6'')	160.92 (C=O), 114.79 (CN), 55.67, 55.83 (2X-OCH ₃), 113.43 (C-4), 113.90 (C-3',5'), 114.46 (C-3'',5''), 125.93 (C-1'), 127.76 (C-1''), 131.02 (2C), 131.22 (2C), 146.37 (C-5), 152.17 (C-6), 158.13 (C-4'), 159.89 (C-4'')
2d	12.62 (1H, s, NH), 0.97 (3H, t, J = 7.32 Hz, CH ₃), 4.13 (2H, q, J = 7.32 Hz, CH ₂), 7.12 (3H, d, J = 6.60 Hz, H-3',4',5'), 7.20 (3H, t, J = 8.08 Hz, H-3'',4'',5''), 7.33 (4H, m, H-2',2'',6',6'')	163.8 (COO), 158.88 (C=O), 13.77 (CH ₃), 62.11 (CH ₂), 128.09 (C-2',6'), 128.44 (C-3',4',5'), 128.80 (C-3'',4'',5''), 129.31 (C-2'',6''), 133.82 (C-4), 133.91 (C-1''), 134.90 (C-1'), 143.28 (C-5), 147.70 (C-6)
2e	12.57 (1H, s, NH), 1.04 (3H, t, J = 6.60 Hz, CH ₃), 4.14 (2H, q, J = 7.36 Hz, CH ₂), 6.98 (4H, t, J = 8.80 Hz, H-2',3',5',6'), 7.36 (2H, d, J = 8.08 Hz, H-3'',5''), 7.44 (2H, d, J = 8.80 Hz, H-2'',6'')	163.36 (COO), 158.55 (C=O), 13.83 (CH ₃), 62.39 (CH ₂), 123.66 (C-4'), 124.12 (C-4''), 130.35 (C-2',6'), 130.81 (C-2'',6''), 132.55 (C-3',5'), 131.98 (C-3'',5''), 137.33 (C-4), 133.47 (C-1''), 134.19 (C-1'), 141.74 (C-5), 146.20 (C-6)
2f	12.67 (1H, s, NH), 1.02 (3H, t, J = 7.32 Hz, CH ₃), 3.73, 3.76 (each 3H, s, 2X-OCH ₃), 4.15 (2H, q, J = 7.32 Hz, CH ₂), 6.72 (2H, d, J = 8.80 Hz, H-3',5'), 6.79 (2H, d, J = 8.76 Hz, H-3'',5''), 7.03 (4H, d, J = 8.80 Hz, H-2',2'',6',6'')	164.17 (COO), 160.24 (C=O), 13.91 (CH ₃), 55.29, 55.34 (2X-OCH ₃), 62.02 (CH ₂), 113.53 (C-3',5'), 113.89 (C-3'',5''), 126.15 (C-4), 127.55 (C-1'), 128.40, 130.34 (2C), 130.69 (2C), 133.65 (C-1''), 142.99 (C-5), 147.57 (C-6), 159.04 (C-4'), 159.89 (C-4'')

2.2.6. Ethyl 5,6-bis(4-methoxyphenyl)-3-oxo-2,3-dihydropyridazine-4-carboxylate (**2f**)

White powder, m.p. 204–206 °C, yield 54%; IR (cm⁻¹): 1642 (C=O), 1740 (COO); MS: m/z 380 [$M^+ - C_{21}H_{20}N_2O_5$] (100%), 351 [$M^+ - C_2H_5$] (2.20%), 335 [$M^+ - C_2H_5O$] (17.02%); NMR (δ_H , δ_C): [Table 1](#).

2.3. General procedure for the preparation of 3-chloro-pyridazinones (**3a–e**)

A mixture of the pyridazinone **2a,c–f** (0.002 mol) and phosphoryl chloride (6 ml) was heated to 100 °C on oil bath for some hours. After cooling, excess reagent was removed under reduced pressure and the mixture was poured into a mixture of ice and 10% ammonia. The precipitate was filtered, washed with water and recrystallised from ethanol. NMR data of **3a–e** were reported in [Table 2](#).

2.3.1. 3-Chloro-5,6-diphenyl-pyridazine-4-carbonitrile (**3a**)

Beige powder, reaction time 8 h, m.p. 136–138 °C, lit. ([Brit. Patent, 1959](#)) 114 °C, yield 42%; IR (cm⁻¹): 2238.25 (CN); MS: m/z 291 [M^+] (C₁₇H₁₀N₃Cl) (61.17%); ¹H NMR and ¹³C NMR: [Table 2](#).

2.3.2. 3-Chloro-5,6-bis(4-methoxyphenyl)-pyridazine-4-carbonitrile (**3b**)

White powder, reaction time 9 h, m.p. 162–164 °C, yield 57%; IR (cm⁻¹): 2240.15 (CN); MS: m/z 351 [M^+] (C₁₉H₁₄N₃O₂³⁵Cl) (100%); ¹H NMR and ¹³C NMR: [Table 2](#).

2.3.3. 3-Chloro-5,6-diphenyl-pyridazine-4-carboxylic acid ethyl ester (**3c**)

Yellowish needles, reaction time 12 h, m.p. 132–134 °C, lit. ([Brit. Patent, 1959](#)) 134 °C, yield 63%; IR (cm⁻¹): 1734.1

(C=O); MS: m/z 338 [M^+] (C₁₉H₁₅N₂O₂³⁵Cl) (42.28%); ¹H NMR and ¹³C NMR: [Table 2](#).

2.3.4. 5,6-Bis(4-bromophenyl)-3-chloro-pyridazine-4-carboxylic acid ethyl ester (**3d**)

Light brown powder, reaction time 15 h, m.p. 132–134 °C, yield 65%; IR (cm⁻¹): 1731.20 (C=O); MS: m/z 494 [M^+] (C₁₉H₁₃N₂O₂^{79,79}Br₂³⁵Cl) (22.21%); ¹H NMR and ¹³C NMR: [Table 2](#).

2.3.5. 3-Chloro-5,6-bis(4-methoxyphenyl)-pyridazine-4-carboxylic acid ethyl ester (**3e**)

Brown needles, reaction time 8 h, m.p. 122–124 °C, yield 55%; IR (cm⁻¹): 1732.20 (C=O); MS: m/z 398 [M^+] (C₂₁H₁₉N₂O₄³⁵Cl) (100%); ¹H NMR and ¹³C NMR: [Table 2](#).

2.4. Typical procedure for preparation of 3-arylaminopyridazines (**4**)

Compounds **4a–r** were synthesized following the usual way for nucleophilic substitution of chlorine by an organic amine. A mixture of 3-chloropyridazine **3** (0.002 mol) and substituted aniline (0.04 mol) was refluxed in EtOH (30–40 ml) on an oil bath for some hours following the reaction by TLC. After reaction completion, the mixture evaporated to dryness and the precipitate washed with cold water and recrystallised from ethanol. Physical properties as well as IR and mass spectral data are depicted in [Table 3](#).

2.4.1. 5,6-Diphenyl-3-(*p*-tolylamino)-pyridazine-4-carbonitrile (**4a**)

Yellow needles; MS: m/z 362 [M^+] (C₂₄H₁₈N₄) (76.67%); ¹H NMR(CDCl₃): δ 2.38 (3H, s, CH₃), 7.62 (2H, d, J = 8.80 Hz,

Table 2 NMR spectral data (CDCl₃) of chloro-pyridazines **3a–e**.

Compound No.	Chemical shifts (δ_H) in ppm	Chemical shifts (δ_C) in ppm
3a	7.28 (2H, t, J = 5.60 Hz, H-4',4''), 7.33 (2H, t, J = 5.60 Hz, H-3',5'), 7.39 (2H, t, J = 5.60 Hz, H-3'',5''), 7.43 (2H, t, J = 6.00 Hz, H-2',6'), 7.48 (2H, t, J = 6.00 Hz, H-2'',6'')	159.72 (C-3), 114.85 (CN), 112.55 (C-4), 128.38 (C-2',6'), 129.12 (C-2'',6''), 129.24 (C-3',5'), 129.79 (C-4'), 129.90 (C-3'',5''), 130.59 (C-4''), 132.21 (C-1''), 134.68 (C-1'), 143.73 (C-5), 154.02 (C-6)
3b	3.80, 3.85 (each 3H, s, 2X-OCH ₃), 6.81 (2H, d, J = 6.80 Hz, H-3',5'), 6.94 (2H, d, J = 6.80 Hz, H-3'',5''), 7.22 (2H, d, J = 7.20 Hz, H-2',6'), 7.29 (2H, d, J = 6.80 Hz, H-2'',6'')	159.42 (C-3), 114.46 (CN), 55.32, 55.41 (2X-OCH ₃), 113.02 (C-4), 113.96 (C-3',5'), 114.70 (C-3'',5''), 124.32 (C-1''), 126.88 (C-1'), 130.98 (C-2',6'), 131.44 (C-2'',6''), 143.33 (C-5), 153.42 (C-6), 160.88 (C-4'), 161.36 (C-4'')
3c	1.06 (3H, t, J = 5.60 Hz, CH ₃), 4.19 (3H, q, J = 5.60 Hz, CH ₂), 7.16 (2H, d, J = 5.60 Hz, H-3',5'), 7.27 (2H, d, J = 6.00 Hz, H-2',6'), 7.39 (6H, m, H-2'',3'',4'',5'',6'')	163.38 (C=O), 150.7 (C-3), 13.59 (CH ₃), 62.60 (CH ₂), 128.12 (C-2',6'), 128.58 (C-2'',6''), 129.06 (C-3',5'), 129.17 (C-4'), 129.29 (C-4''), 129.27 (C-3'',5''), 133.24 (C-4), 133.34 (C-1''), 135.32 (C-1'), 137.88 (C-5), 159.83 (C-6)
3d	1.13 (3H, t, J = 5.60 Hz, CH ₃), 4.23 (2H, q, J = 5.60 Hz, CH ₂), 7.04 (2H, d, J = 6.40 Hz, H-2',6'), 7.24 (2H, d, J = 6.40 Hz, H-2'',6''), 7.44 (2H, d, J = 6.40 Hz, H-3',5'), 7.50 (2H, d, J = 6.80 Hz, 3'',5'')	163.08 (C=O), 151.1 (C-3), 13.69 (CH ₃), 62.90 (CH ₂), 124.23 (C-4''), 124.31 (C-4'), 130.60 (C-2',6'), 131.44 (C-2'',6''), 131.64 (C-3',5'), 131.89 (C-4), 132.16 (C-3'',5''), 133.20 (C-1''), 133.90 (C-1'), 136.49 (C-5), 158.47 (C-6)
3e	1.13 (3H, t, J = 6.00 Hz, CH ₃), 3.80, 3.82 (each 3H, s, 2X-OCH ₃), 4.22 (3H, q, J = 6.00 Hz, CH ₂), 6.81 (2H, d, J = 6.80 Hz, H-3',5'), 6.86 (2H, d, J = 7.20 Hz, H-3'',5''), 7.09 (2H, d, J = 6.80 Hz, H-2',6'), 7.30 (2H, d, J = 7.20 Hz, 2'',6'')	163.75 (C=O), 150.15 (C-3), 13.76 (CH ₃), 55.24 (OCH ₃), 55.29 (OCH ₃), 62.54 (CH ₂), 113.71 (C-3',5'), 114.21 (C-3'',5''), 125.62 (C-4), 127.18 (C-1'), 130.49 (C-2',6'), 131.43 (C-2'',6''), 133.13 (C-1''), 137.37 (C-5), 159.59 (C-6), 160.32 (C-4'), 163.73 (C-4'')

Table 3 Physical properties, IR and Ms spectra of 3-arylamino-pyridazines **4a–r**.

Compound No.	m.p. (°C)	Reaction time (h)	Yield (%)	Molecular weight	IR (cm ⁻¹)
4a	210–212	27	39	C ₂₄ H ₁₈ N ₄	2222 (CN), 3345 (NH)
4b	222–223	26	50	C ₂₆ H ₂₂ N ₄ O ₂	2227 (CN), 3331 (NH)
4c	158–160	26	32	C ₂₅ H ₂₀ N ₄	2229 (CN), 3289 (NH)
4d	194–195	28	49	C ₂₇ H ₂₄ N ₄ O ₂	2229 (CN), 3330 (NH)
4e	218–220	26	51	C ₂₃ H ₁₅ N ₄ Cl	2222 (CN), 3234 (NH)
4f	241–242	26	48	C ₂₅ H ₁₉ N ₄ O ₂ Cl	2229 (CN), 3329 (NH)
4g	288–290	27	50	C ₂₃ H ₁₄ N ₄ Cl ₂	2231 (CN), 3295 (NH)
4h	274–275	28	35	C ₂₅ H ₁₈ N ₄ O ₂ Cl ₂	2230 (CN), 3240 (NH)
4i	98–100	27	56	C ₂₆ H ₂₃ N ₃ O ₂	1734 (C=O), 3367 (NH)
4j	191–192	31	51	C ₂₆ H ₂₁ N ₃ O ₂ Br ₂	1703 (C=O), 3363 (NH)
4k	99–100	26	39	C ₂₇ H ₂₅ N ₃ O ₂	1692 (C=O), 3342 (NH)
4l	179–180	18	75	C ₂₇ H ₂₃ N ₃ O ₂ Br	1710 (C=O), 3364 (NH)
4m	160–162	28	40	C ₂₉ H ₂₉ N ₃ O ₄	1708 (C=O), 3367 (NH)
4n	154–156	26	47	C ₂₅ H ₂₀ N ₃ O ₂ Cl	1716 (C=O), 3401 (NH)
4o	217–218	17	52	C ₂₅ H ₁₈ N ₃ O ₂ Br ₂ Cl	1690 (C=O), 3313 (NH)
4p	171–172	28	67	C ₂₇ H ₂₄ N ₃ O ₄ Cl	1707 (C=O), 3369 (NH)
4q	180–182	26	53	C ₂₅ H ₁₉ N ₃ O ₂ Cl ₂	1716 (C=O), 3354 (NH)
4r	181–182	26	77	C ₂₅ H ₁₇ N ₃ Br ₂ Cl ₂	1703 (C=O), 3361 (NH)

H-2'',6''), 7.42 (3H, m, NH, H-2',6'), 7.25 (10H, m, others aromatic protons); ¹³C NMR(CDCl₃): δ 21.10 (CH₃), 100.22 (C-4), 122.78 (C-2'',6''), 128.43 (2C), 128.70 (C-4'), 129.09 (2C), 129.57 (2C), 129.83 (2C), 129.87 (2C), 130.02 (C-4''), 155.01 (C-3), 153.10 (C-6), 143.53 (C-1'''), 137.18, 136.72 (C-1',1''), 134.51, 133.36 (C-5,4''').

2.4.2. 5,6-Bis(4-methoxyphenyl)-3-(p-tolylamino)-pyridazine-4-carbonitrile (**4b**)

Yellow needles; MS: m/z 422 [M⁺] (C₂₆H₂₂N₄O₂) (63.90%); ¹H NMR(CDCl₃): δ 2.37 (3H, s, CH₃), 3.79 (6H, s, 2OCH₃), 6.78 (2H, d, J = 8.76 Hz, H-3',5'), 6.92 (2H, d, J = 8.76 Hz, H-3'',5''), 7.25 (7H, m, others aromatic protons), 7.61 (2H, d, J = 8.80 Hz, H-2'',6''); ¹³C NMR(CDCl₃): δ 21.04 (CH₃), 55.32, 55.44 (2X-OCH₃), 113.73 (C-3',5'), 114.54 (2C), 114.01 (C-4), 121.84 (C-6'''), 129.86 (3C), 130.97 (C-2',6'), 131.01

(2C), 134.94 (C-1',1''), 145.50 (C-5), 152.73 (C-1'''), 153.49 (C-6), 160.42 (C-4',4''), 161.15 (C-3).

2.4.3. 3-(Ethylphenylamino)-5,6-diphenylpyridazine-4-carbonitrile (**4c**)

Orange needles; MS: m/z 376 [M⁺] (C₂₅H₂₀N₄) (37.08%); ¹H NMR(CDCl₃): δ 1.26 (3H, t, J = 7.30 Hz, CH₂CH₃), 2.70 (2H, q, J = 7.30 Hz, CH₂CH₃), 7.03 (1H, d, J = 7.32 Hz, H-3'), 7.27 (7H, m, others aromatic protons), 7.32 (2H, t, J = 7.32 Hz, H-4',4''), 7.42 (3H, m, NH, H-2',6'), 7.56 (1H, s, NH), 7.60 (1H, d, J = 8.08 Hz, H-2''); ¹³C NMR(CDCl₃): δ 15.64 (CH₃), 28.97 (CH₂), 100.37 (C-4), 118.89 (C-6'''), 120.96 (C-2'''), 124.64 (C-4'''), 128.21 (C-2',6'), 128.81 (C-5'''), 129.02 (2C), 129.36 (2C), 129.64 (2C), 130.24 (C-4''), 133.45 (C-3'''), 135.37 (C-1'''), 137.58 (C-1',1''), 143.64 (C-3), 145.70 (C-4'), 153.10 (C-6), 153.67 (C-5).

2.4.4. 3-(Ethylphenylamino)-5,6-bis(4-methoxyphenyl)-pyridazine-4-carbonitrile (**4d**)

Light brown powder; MS: m/z 436 [M^+] ($C_{27}H_{24}N_4O_2$) (60.20%); 1H NMR($CDCl_3$): δ 1.26 (3H, t, $J = 7.36$ Hz, CH_2CH_3), 2.69 (2H, q, $J = 8.08$ Hz, CH_2CH_3), 3.79 (6H, s, $2OCH_3$), 6.78 (2H, d, $J = 8.80$ Hz, H-3',5'), 6.91 (2H, d, $J = 8.80$ Hz, H-3'',5''), 7.01 (1H, d, $J = 7.36$ Hz, H-4'''), 7.26 (4H, m, H-2'',6'',2''',6'''), 7.31 (2H, t, $J = 8.08$ Hz, H-2',6'), 7.57 (1H, s, NH), 7.61 (1H, d, $J = 8.08$ Hz, H-6'''); ^{13}C NMR($CDCl_3$): δ 15.64 (CH_3), 28.98 (CH_2), 55.31, 55.43 ($2X-OCH_3$), 100.11 (C-4), 113.72 (C-3',5'), 114.35 (CN), 114.52 (C-3'',5''), 120.64 (C-2'''), 118.59 (C-6'''), 124.27, 125.65 (C-1', C-4'''), 128.02 (C-1''), 129.19 (C-5'''), 130.95 (2C), 131.00 (2C), 137.90 (C-5), 145.64 (C-1''',3'''), 153.00, 153.55 (C-3, C-6), 160.02, 161.04 (4',4'').

2.4.5. 3-(4-Chlorophenylamino)-5,6-diphenylpyridazine-4-carbonitrile (**4e**)

Yellowish needles; MS: m/z 382 [M^+] ($C_{23}H_{15}N_4^{35}Cl$) (63.05%); 1H NMR ($DMSO-d_6$): δ 7.28 (5H, m, H-2'',3'',4'',5'',6''), 7.33-7.44 (7H, other aromatic protons), 7.74 (2H, d, $J = 8.80$ Hz, H-3''',5'''), 9.57 (1H, s, NH); ^{13}C NMR ($DMSO-d_6$): δ 101.04 (C-4), 123.88 (C-2'',6'''), 127.68 (C-4'''), 128.45 (2C), 128.83 (C-4'), 128.99 (2C), 129.11 (2C), 129.82 (2C), 129.90 (2C), 130.08 (C-4''), 134.38 (C-1'), 136.59 (C-1''), 138.91 (C-5), 143.71 (C-1'''), 153.74 (C-6), 154.69 (C-3).

2.4.6. 3-(4-Chlorophenylamino)-5,6-bis(4-methoxyphenyl)-pyridazine-4-carbonitrile (**4f**)

Yellowish needles; MS: m/z 442 [M^+] ($C_{25}H_{19}N_4O_2^{35}Cl$) (82.34%); 1H NMR($CDCl_3$): δ 3.84 (6H, s, $2OCH_3$), 6.79 (2H, dd, $J = 5.12$ Hz, H-3',5'), 6.92 (2H, dd, $J = 8.80$ Hz, H-3'',5''), 7.25 (4H, m, H-2''',6''',3''',5'''), 7.35 (3H, dd, $J = 8.80$ Hz, H-2',6', NH), 7.71 (2H, dd, $J = 8.08$ Hz, H-2'',6''); ^{13}C NMR($CDCl_3$): δ 55.34, 55.46 (OCH_3), 112.50 (C-4), 113.79 (2C), 114.60 (2C), 115.00 (C-4'''), 117.50 (C-1'), 122.56 (C-2'',6'''), 125.34 (C-1''), 127.43 (C-5), 129.31 (2C), 130.00 (C-1'''), 130.97 (2C), 131.07 (C-3''',5'''), 153.35 (C-6), 153.37 (C-3), 160.25 (C-4'), 161.22 (C-4'').

2.4.7. 3-(3,4-Dichlorophenylamino)-5,6-diphenylpyridazine-4-carbonitrile (**4g**)

Yellowish powder; MS: m/z 416 [M^+] ($C_{23}H_{14}N_4^{35}Cl_2$) (45.23%); 1H NMR ($DMSO-d_6$): δ 7.28 (5H, m, H-2''',4',4'',5'',6'''), 7.33 (2H, d, $J = 7.32$ Hz, H-3',5'), 7.42 (3H, d, $J = 5.12$ Hz, H-3'',5'',6''), 7.62 (1H, d, $J = 8.80$ Hz, H-2'), 7.73 (1H, dd, $J = 8.80$ Hz, H-6''), 8.08 (1H, d, $J = 2.20$ Hz, H-2''), 9.72 (1H, s, NH); ^{13}C NMR ($DMSO-d_6$): δ 101.69 (C-4), 121.97 (C-6'''), 123.11 (C-2'''), 125.17 (C-4'''), 128.48 (C-2',6'), 128.94 (C-4'), 129.13 (C-2'',6''), 129.81 (C-3',5'), 129.94 (C-3'',5''), 130.14 (C-4''), 130.94 (C-5'''), 131.30 (C-3'''), 134.28 (C-1'), 136.47 (C-1''), 140.26 (C-5), 143.89 (C-1'''), 154.23 (C-6), 154.43 (C-3).

2.4.8. 3-(3,4-Dichlorophenylamino)-5,6-bis(4-methoxyphenyl)pyridazine-4-carbonitrile (**4h**)

Greenish needles; MS: m/z 476 [M^+] ($C_{25}H_{18}N_4O_2^{35}Cl_2$) (100%); 1H NMR ($DMSO-d_6$): δ 3.35 (6H, s, $2X-OCH_3$), 6.85 (2H, d, $J = 8.04$ Hz, H-3',5'), 7.01 (2H, d, $J = 8.08$ Hz, H-3'',5''), 7.20 (2H, d, $J = 8.80$ Hz, H-2',6'), 7.27 (2H, d, $J = 8.80$ Hz, H-2'',6''), 7.61 (1H, d, $J = 8.80$ Hz, H-6'''), 7.84

(1H, d, $J = 8.80$ Hz, H-5'''), 8.07 (1H, s, $J = 8.80$ Hz, H-2'''), 9.63 (1H, s, NH).

2.4.9. 5,6-Diphenyl-3-(p-tolylamino)-pyridazine-4-carboxylic acid ethyl ester (**4i**)

Greenish needles; MS: m/z 409 [M^+] ($C_{26}H_{23}N_3O_2$) (53.81%); 1H NMR($CDCl_3$): δ 0.70 (3H, t, $J = 6.60$ Hz, CH_2CH_3), 2.34 (3H, s, CH_3), 4.17 (2H, q, $J = 8.04$ Hz, CH_2CH_3), 7.37 (14H, m, NH, other hydrogen), 7.54 (1H, d, $J = 8.04$ Hz, H-2''). ^{13}C NMR($CDCl_3$): δ 13.14 ($-CH_2CH_3$), 21.01 (CH_3), 62.74 ($-CH_2CH_3$), 163.52 (CO).

2.4.10. 5,6-Bis(4-bromophenyl)-3-(p-tolylamino)-4-carboxylic acid ethyl ester (**4j**)

Greenish needles; MS: m/z 565 ($C_{26}H_{21}N_3O_2Br_2$); 1H NMR($CDCl_3$): δ 0.80 (3H, t, $J = 7.24$ Hz, CH_2CH_3), 2.34 (3H, s, CH_3), 4.01 (2H, q, $J = 7.36$ Hz, CH_2CH_3), 6.94 (2H, d, $J = 8.04$ Hz, H-2'',6'''), 7.11 (2H, d, $J = 8.08$ Hz, H-3''',5'''), 7.17 (2H, d, $J = 8.80$ Hz, H-2',6'), 7.35 (2H, d, $J = 8.80$ Hz, H-2'',6''), 7.46 (2H, d, $J = 8.04$ Hz, H-3',5'), 7.64 (2H, d, $J = 8.80$ Hz, H-3'',5''), 8.34 (1H, s, NH). ^{13}C NMR($CDCl_3$): δ 13.42 ($-CH_2CH_3$), 20.96 (CH_3), 62.41 ($-CH_2CH_3$), 114.57 (C-4'), 121.05 (C-2''',6'''), 129.58 (C-2',6'), 130.64 (C-2'',6''), 131.23 (C-3''',5'''), 131.34 (C-3',5'), 131.74 (C-3'',5''), 122.68 (C-4''), 122.90 (C-4'''), 133.28 (C-4'''), 135.34 (C-1'), 135.47 (C-1''), 136.30 (C-5), 137.47 (C-1'''), 152.45 (C-6), 152.86 (C-3), 166.1 (CO).

2.4.11. 3-(Ethylphenylamino)-5,6-diphenylpyridazine-4-carboxylic acid ethyl ester (**4k**)

Greenish needles; MS: m/z 423 [M^+] ($C_{27}H_{25}N_3O_2$) (50.40%); 1H NMR($CDCl_3$): δ 0.71 (3H, t, $J = 6.60$ Hz, $C-CH_2CH_3$), 1.26 (3H, t, $J = 8.08$ Hz, $O-CH_2CH_3$), 2.68 (2H, q, $J = 8.08$ Hz, $C-CH_2CH_3$), 3.95 (2H, q, $J = 7.32$ Hz, $O-CH_2CH_3$), 6.93 (1H, d, $J = 7.32$ Hz, H-6'''), 7.07 (2H, d, $J = 7.32$ Hz, H-3',5'), 7.30 (10H, m, other hydrogen), 7.62 (1H, s, H-2''), 7.66 (1H, d, $J = 9.56$ Hz, H-5'''). ^{13}C NMR($CDCl_3$): δ 13.16 ($O-CH_2CH_3$), 15.79 ($C-CH_2CH_3$), 29.07 ($C-CH_2CH_3$), 62.18 ($O-CH_2CH_3$), 113.50 (C-4), 117.99 (C-6'''), 119.99 (C-2'''), 122.84 (C-4'''), 127.83 (2C), 127.94 (C-5'''), 128.31 (2C), 128.40 (C-4'), 128.96 (C-4''), 129.09 (2C), 129.83 (2C), 136.54 (C-1'), 136.60 (C-1''), 138.80 (C-3'''), 139.22 (C-5), 145.33 (C-6), 153.00 (C-1'''), 154.19 (C-3), 167.36 (CO).

2.4.12. 5,6-Bis(4-bromophenyl)-3-(ethylphenylamino)-pyridazine-4-carboxylic acid ethyl ester (**4l**)

Yellowish needles; MS: m/z 409 [M^+] ($C_{27}H_{23}N_3O_2^{79,79}Br_2$) (100%); 1H NMR($CDCl_3$): δ 0.81 (3H, t, $J = 6.60$ Hz, $C-CH_2CH_3$), 1.25 (3H, t, $J = 8.08$ Hz, $O-CH_2CH_3$), 2.67 (2H, q, $J = 7.36$ Hz, $C-CH_2CH_3$), 3.96 (2H, q, $J = 6.60$ Hz, $O-CH_2CH_3$), 6.97 (2H, d, $J = 4.40$ Hz, H-2',6'), 7.12 (2H, d, $J = 8.80$ Hz, H-2'',6''), 7.31 (7H, m, H-4''',6'''), 7.37 (2H, d, $J = 6.60$ Hz, H-3',5'), 7.46 (2H, d, $J = 6.60$ Hz, H-3'',5''), 7.54 (1H, s, H-2'''), 7.60 (1H, d, $J = 8.08$ Hz, H-5'''), 8.61 (1H, s, NH). ^{13}C NMR($CDCl_3$): δ 13.25 ($O-CH_2CH_3$), 15.70 ($C-CH_2CH_3$), 29.01 ($C-CH_2CH_3$), 62.49 ($O-CH_2CH_3$), 115.60 (C-4), 118.63 (C-6'''), 120.65 (C-2'''), 122.90 (C-4'), 123.08 (C-4''), 123.60 (C-4'''), 129.04 (C-5'''), 130.62 (2C), 131.32 (C-2'',3',5',6''), 131.78 (2C), 134.97 (C-1'), 135.54 (C-1''), 138.05 (C-5), 138.54 (C-3'''), 145.44 (C-6), 152.52 (C-1'''), 152.19 (C-1'''), 166.48 (CO).

2.4.13. 3-(Ethylphenylamino)-5,6-bis(4-methoxyphenyl)-pyridazine-4-carboxylic acid ethyl ester (4m)

Yellowish powder; MS: m/z 483 [M^+ - $C_{29}H_{29}N_3O_4$] (54.52%); 1H NMR($CDCl_3$): δ 0.80 (3H, t, J = 7.32 Hz, C- CH_2CH_3), 1.24 (3H, t, J = 7.36 Hz, O- CH_2CH_3), 2.65 (2H, q, J = 7.32 Hz, C- CH_2CH_3), 3.81, 3.78 (each 3H, s, 2X-OCH₃), 3.92 (2H, q, J = 6.60 Hz, O- CH_2CH_3), 6.75 (2H, d, J = 9.56 Hz, H-3',5'), 6.82 (2H, d, J = 8.80 Hz, H-3'',5''), 6.94 (1H, d, J = 6.60 Hz, H-6'''), 6.98 (2H, d, J = 8.80 Hz, H-2',6'), 7.20 (2H, d, J = 8.80 Hz, H-2'',6''), 7.28 (1H, s, J = 8.08 Hz, H-4'''), 7.53 (1H, s, H-2'''), 7.58 (1H, d, J = 7.36 Hz, H-5'''), 8.40 (1H, s, NH). ^{13}C NMR($CDCl_3$): δ 13.42 and 62.19 (O- CH_2CH_3), 15.70 and 29.00 (C- CH_2CH_3), 55.27, 55.41 (2X-OCH₃), 113.43 (2C), 113.70 (C-4), 113.90 (2C), 118.37 (C-6'''), 118.46 (C-2'''), 120.49 (C-4'''), 123.25 (C-5'''), 128.25 (C-1'), 128.75 (C-1''), 130.45 (2C), 130.59 (C-5), 131.11 (2C), 138.81 (C-3'''), 145.36 (C-6), 152.12 (C-1'''), 153.88 (C-3), 159.59 and 159.94 (C-4', C-4''), 166.87 (CO).

2.4.14. 3-(4-Chlorophenylamino)-5,6-diphenylpyridazine-4-carboxylic acid ethyl ester (4n)

Yellowish powder; MS: m/z 429 [M^+] ($C_{25}H_{20}N_3O_2^{35}Cl$) (62.32%); 1H NMR($CDCl_3$): δ 0.67 (3H, t, J = 7.32 Hz, $-CH_2CH_3$), 3.91 (2H, q, J = 7.32 Hz, $-CH_2CH_3$), 7.02 (2H, d, J = 6.60 Hz, H-2''',6'''), 7.29 (10H, m, other hydrogen), 7.72 (2H, d, J = 6.60 Hz, H-2'',6''), 8.52 (1H, s, NH); ^{13}C NMR($CDCl_3$): δ 13.11, 62.34 (O- CH_2CH_3), 116.10 (C-4), 122.04 (C-2''',6'''), 127.88 (2C), 128.34 (2C), 128.10 (C-4'), 128.40 (C-4'''), 128.34 (2C), 128.53 (C-4''), 128.90 (2C), 129.01 (2C), 129.79 (2C), 136.12 (C-1'''), 136.23 (C-1''), 137.60 (C-5), 139.55 (C-1'''), 152.32 (C-6), 154.49 (C-3), 166.93 (CO).

2.4.15. 5,6-Bis(4-bromophenyl)-3-(4-chlorophenylamino)-pyridazine-4-carboxylic acid ethyl ester (4o)

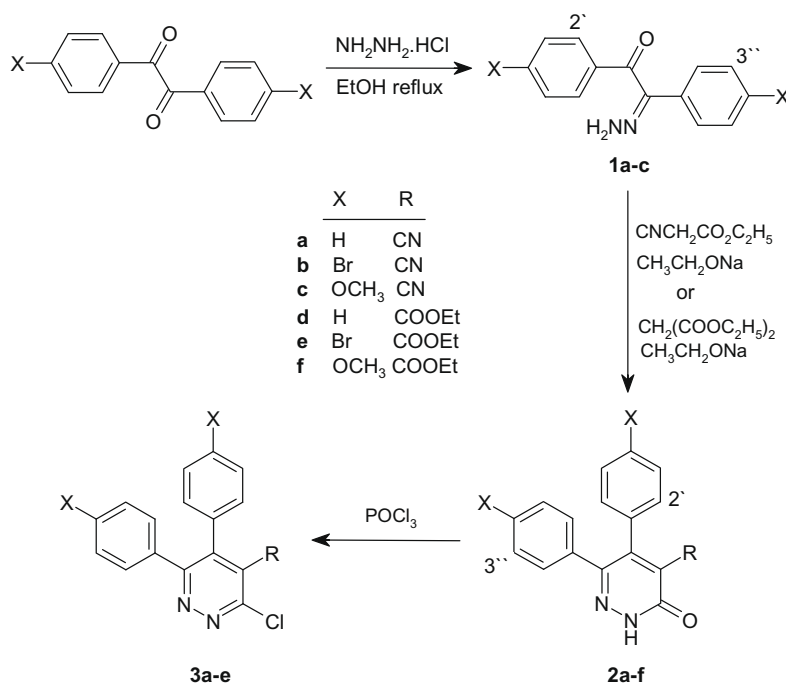
Greenish powder; MS: m/z 585 [M^+] ($C_{25}H_{18}N_3O_2^{79,79}Br_2^{35}Cl$) (100%).

2.4.16. 3-(4-Chlorophenylamino)-5,6-bis(4-methoxyphenyl)pyridazine-4-carboxylic acid ethyl ester (4p)

Yellowish powder; MS: m/z 489 [M^+] ($C_{27}H_{24}N_3O_4^{35}Cl$) (68.53%); 1H NMR($CDCl_3$): δ 0.78 (3H, t, J = 7.36 Hz, O- CH_2CH_3), 3.79, 3.75 (each 3H, s, 2X-OCH₃), 3.98 (2H, q, J = 8.08 Hz, O- CH_2CH_3), 6.73 (2H, d, J = 8.80 Hz, H-2''',6'''), 6.81 (2H, d, J = 8.80 Hz, H-3',5'), 6.97 (2H, d, J = 8.04 Hz, H-3'',5''), 7.19 (2H, d, J = 8.04 Hz, H-3''',5'''), 7.28 (2H, d, J = 8.80 Hz, H-2',6'), 7.73 (2H, d, J = 8.76 Hz, H-2'',6''), 8.23 (1H, s, NH); ^{13}C NMR($CDCl_3$): δ 13.40, 62.28 (O- CH_2CH_3), 55.24, 55.41 (2X-OCH₃), 113.40 and 113.92 (C-3',5',3'',5''), 116.44 (C-4'''), 121.67 (C-2''',6'''), 127.76 (C-1'), 128.50 (C-1''), 128.90 (C-2',6'), 130.42 (2C), 131.10 (2C), 137.98 (C-5), 138.67 (C-1'''), 152.02 (C-6), 154.49 (C-3), 159.54, 159.92 (C-4', C-4''), 167.37 (CO).

2.4.17. 3-(3,4-Dichlorophenylamino)-5,6-diphenylpyridazine-4-carboxylic acid ethyl ester (4q)

Yellow needles; MS: m/z 463 [M^+] ($C_{25}H_{19}N_3O_2^{35,35}Cl$) (66.66%); 1H NMR($CDCl_3$): δ 0.68 (3H, t, J = 6.60 Hz, O- CH_2CH_3), 3.90 (2H, q, J = 6.63 Hz, O- CH_2CH_3), 7.02 (2H, d, J = 7.40 Hz, H-3',5'), 7.29 (m, other hydrogen), 7.35 (1H, d, J = 8.80 Hz, H-2'''), 7.60 (1H, dd, J = 8.80 Hz, H-6'''), 8.02 (1H, d, J = 2.20 Hz, H-5'''), 8.63 (1H, s, NH); ^{13}C NMR($CDCl_3$): δ 13.08, 62.48 (CH_2CH_3), 116.24 (C-4), 120.02 (C-6'''), 122.11 (C-2'''), 126.27 (C-4'''), 127.93 (2C), 128.37 (2C), 128.61 (C-5'''), 128.99 (2C), 129.78 (2C), 130.43



Scheme 1

(C-4',4''), 132.69 (C-3'''), 135.97, 136.02 (C-1',C-1''), 138.57 (C-5), 139.82 (C-1'''), 152.16 (C-6), 154.95 (C-3), 166.85 (CO).

2.4.18. 3-(3,4-Dichlorophenylamino)-5,6-bis(4-bromophenyl)pyridazine-4-carboxylic acid ethyl ester (4r)

Yellow needles; MS: m/z 487 ($C_{25}H_{17}N_3Br_2Cl_2$); 1H NMR- ($CDCl_3$): δ 0.78 (3H, t, $J = 7.36$ Hz, CH_2CH_3), 3.98 (2H, q, $J = 7.32$ Hz, CH_2CH_3), 6.93 (2H, d, $J = 8.04$ Hz, H-2',6'), 7.09 (2H, d, $J = 8.80$ Hz, H-2'',6''), 7.37 (3H, t, $J = 8.08$ Hz, H-3',5',2'''), 7.46 (2H, d, $J = 8.80$ Hz, H-3'',5''), 7.60 (1H, dd, $J = 8.76$ Hz, H-6'''), 8.02 (1H, d, $J = 2.20$ Hz, H-5'''), 8.67 (1H, s, NH); ^{13}C NMR($CDCl_3$): δ 13.19, 62.75 (O- CH_2CH_3), 115.18 (C-4), 120.06 (C-6'''), 122.17 (C-2'''), 123.11 (C-4'), 123.18 (C-4''), 126.48 (C-4'''), 130.47 (C-5'''), 130.56 (C-2',6'), 131.32 (C-2'',6''), 131.36 (2C), 131.82 (2C), 132.75 (C-3'''), 134.87 (C-1'), 134.94 (C-1''), 138.21, 138.41 (C-1''',C-5), 152.37 (C-6), 153.52 (C-3), 166.61 (CO).

3. Results and discussion

The route for the synthesis of pyridazinones **2a–f**, and 3-chloro-pyridazine **3a–e** starting from **1a–c**, is illustrated in Scheme 1. Initially, we planned to prepare 5,6-(4-substituted-phenyl)-3-(2*H*)-pyridazinones (**2a–f**) by using Microwave technique but unfortunately this method led to poor yields of the required pyridazinones. Further more, attempts for obtaining **3a–e** following the latter technique gave mixture of compounds. However, compounds **2a–f** and **3a–f** were obtained in good-moderate yields (see experimental) when the conventional method was used. Therefore, the cyclization of **1a–c** in the presence of sodium hydroxide, through the reaction with ethyl cyanoacetate or diethyl malonate following the latter method afforded the corresponding pyridazinones **2a–f**, which in turn transformed smoothly to **3a–e**. Structures of all synthesised compounds in Scheme 1 were confirmed on the basis of 1H , ^{13}C NMR and MS. IR spectra of monohydrazones **1a–c** showed the expected signals of carbonyl and amine groups. 1H , ^{13}C NMR data were consistent with their structures. The structure of **2a–f** were confirmed on the basis of their spectroscopic analyses. Their IR spectra showed bands in the range 1660–1700 cm^{-1} (C=O in pyridazine ring) in addition to the absorption bands at around 2228 cm^{-1} (C=N) in **2a–c** and at about 1725 cm^{-1} (carbonyl esters) in **2d–f**. Additionally, these spectra showed the stretching bands of CH and C=C bonds in the aromatic substituents. Full analysis of NMR data of **2a–f** reported in Table 2, confirmed their structures. The assignments of all carbons in **2a–f** are basically made by comparison to ^{13}C NMR spectra of structurally related compounds (Csampai et al., 2005) as well as theory

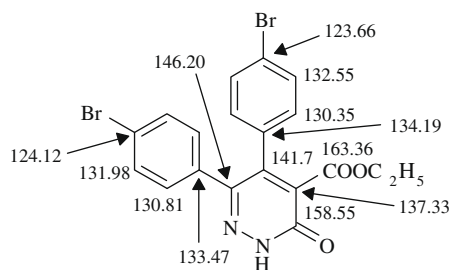
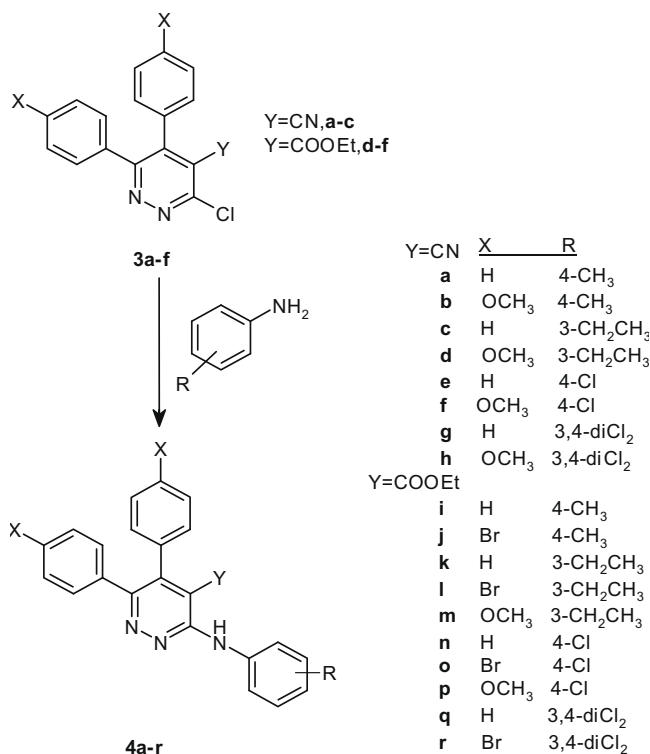


Figure 1 ^{13}C NMR assignments of **2e**.



Scheme 2

ground (Hesse et al., 1997; Lambert and Mazzola, 2004), and the aid of the off resonance, DEPT and HETCOR NMR experiments (Fig. 1).

Reaction of **2a–f** with phosphoryl chloride furnished the corresponding chloro-pyridazine **3a–e** (Scheme 1) after working up in the usual way. The structures of these compounds were assigned on the basis of their various spectral data. IR spectra revealed the disappearance of the carbonyl band in the similar spectra of pyridazinones **2a–f**, while the NMR data of **3a–e** firmly assigned their structures. These data were collected in Table 2. Furthermore, the mass spectra showed the expected molecular ions for these compounds (see experimental). We have included the ^{13}C NMR spectral data of the known compounds **2a,d** (Scheidt and Druey, 1954; Druey and Scheidt, 1957; Brit. Patent, 1959; Shalaby, 1990) and **3a** (Deep et al., 1991) in the experimental for the first time as it seemed for us from literature survey.

Heating of **3a–e** with various substituted anilines led to the formation of a series of corresponding 3-arylaminopyridazines **4a–r** in moderate yields. This reaction is outlined in Scheme 2. Characterization of **4a–r** was based mainly on the spectroscopic means and in particular their NMR data which are depicted in Table 3. The assignments of the resonances in the NMR spectra was based on chemical shifts theory (Hesse et al., 1997; Lambert and Mazzola, 2004), signal intensity arguments and multiplicities, and in part by comparison to ^{13}C NMR spectra of structurally related compounds (Matsuda et al., 2001).

4. Conclusion

In the present work, it is reported the synthesis of novel 5,6-bis(4-substitutedphenyl)-2*H*(3)-pyridazinones **2b,c,e,f**. Reaction

of these pyridazones with phosphoryl chloride led to the formation of the new **3b-e**. Furthermore, a series of the previously unknown **4a-r** have been synthesized in appreciable yields from the reaction of **3a-e** with various arylamines.

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