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Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713618290>

A New Approach for the Synthesis of Some Fused Pyrazolo-, Triazolo-, Tetrazolo-, Diazepino-, Oxazepino-, and Thiazepinopyridazine Derivatives

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Online publication date: 27 October 2010

To cite this Article Shalaby, Alyaa A.(2003) 'A New Approach for the Synthesis of Some Fused Pyrazolo-, Triazolo-, Tetrazolo-, Diazepino-, Oxazepino-, and Thiazepinopyridazine Derivatives', *Phosphorus, Sulfur, and Silicon and the Related Elements*, 178: 2, 199 – 210

To link to this Article: DOI: 10.1080/10426500307951

URL: <http://dx.doi.org/10.1080/10426500307951>

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A NEW APPROACH FOR THE SYNTHESIS OF SOME FUSED PYRAZOLO-, TRIAZOLO-, TETRAZOLO-, DIAZEPINO-, OXAZEPINO-, AND THIAZEPINOPYRIDAZINE DERIVATIVES

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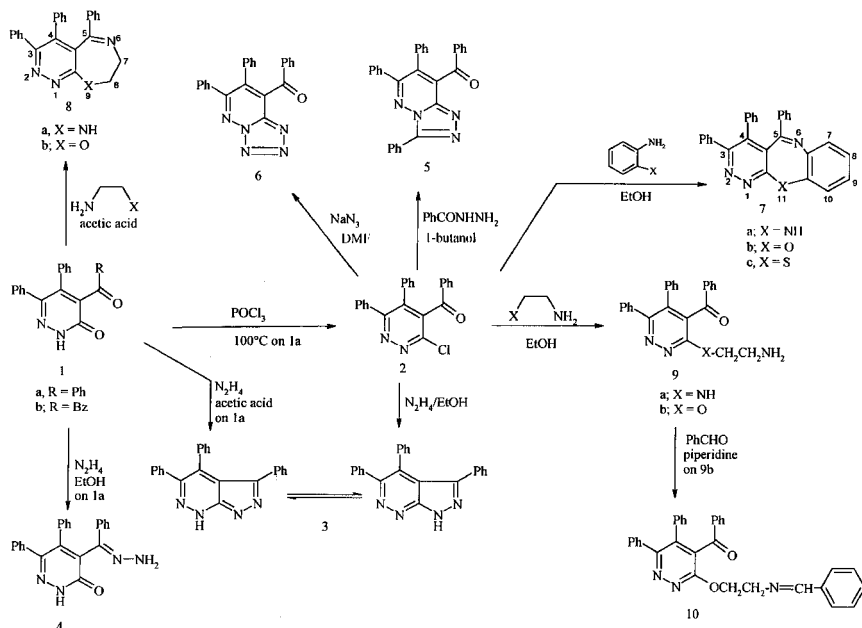
(Received October 30, 2001; accepted April 2, 2002)

*Hydrazinolysis of 4-benzoyl-5,6-diphenyl-pyridazin-3(2H)-one **1a** in acetic acid or 3-chloropyridazine derivative **2** in ethanol afforded the pyrazolo[3,4-c]pyridazine derivative **3**. While boiling **1a** with hydrazine hydrate in ethanol gave the corresponding hydrazono derivative **4**. Reaction of compound **2** with benzhydrazide in refluxing 1-butanol yielded triazolo[4,3-b]pyridazine **5**. On treatment of **2** with sodium azide tetrazolopyridazine **6** resulted. The reaction of **1a** (in acetic acid) or **2** (in ethanol) with o-phenylenediamine and o-aminophenol yielded diazepino- and oxazepinopyridazine derivatives **7a** and **7b**, respectively, while **2** with o-aminothiophenol in ethanol gave thiazepinopyridazine derivative **7c**. Moreover, treatment of **1a** (in acetic acid) or **2** (in ethanol) with ethylenediamine and 2-aminoethanol produced **8a**, **8b** and **9a**, **9b** respectively. Chlorination of the carbinol derivatives **11a** and **11b** with phosphorus oxychloride gave the dichloro derivatives **12a** and **12b**, which reacted with hydrazine to form pyrazolopyridazines **13a** and **13b** respectively. However, thionation of **11b** gave the thionated product **14**. Compound **14** was confirmed by methylation and hydrazinolysis forming **15** and **16** respectively.*

Keywords: Chlorination; fused pyridazines; methylation of pyridazinone derivatives; N-nucleophiles; thionation

In an effort to synthesize new fused pyridazines, I selected 4-benzoyl-5,6-diphenylpyridazin-3(2H)-one¹ **1a** and its chlorinated product 4-benzoyl-3-chloro-5,6-diphenylpyridazine² **2**, 5,6-diphenyl-4-(1,1-diphenyl-1-hydroxymethyl)-2,3-dihydropyridazin-3-one¹ **11a** and 5,6-diphenyl-4-(1,1-dibenzyl-1-hydroxymethyl)-2,3-dihydropyridazin-3-one¹ **11b** as the starting materials. Thus, refluxing **1a** in glacial acetic acid

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SCHEME 1

or **2** in ethanol with hydrazine hydrate afforded the pyrazolo[3,4-*c*]pyridazine derivative **3** (Scheme 1). The structure of the product **3** was deduced from its spectral data. While boiling **1a** with hydrazine hydrate in ethanol for 3 h gave the corresponding hydrazono derivative **4** (Scheme 1). The structure of compound **4** was verified from its spectral data.

The action of benzhydrazide on compound **2** in 1-butanol³ produced triazolo[4,3-b]pyridazine **5** (Scheme 1). The structure of the product **5** was deduced from its analytical and spectral data. The IR spectrum revealed a carbonyl group of an unsaturated ketone at 1669 cm⁻¹. The mass spectrum showed the molecular ion peak [$M^+ = 452$, 3%] and the base peak at [$m/e = 103$], corresponding to the benzonitrile molecule.

Reaction of compound **2** with sodium azide in dimethylformamide⁴ afforded tetrazolo[4,5-b]pyridazine **6** (Scheme 1). This structure was confirmed by its IR spectrum, which showed carbonyl absorption of a conjugated ketone at 1677 cm⁻¹. The ¹H-NMR spectrum showed only a multiplet for 15 protons of the three phenyl groups. The mass spectrum revealed the molecular ion with low intensity [M⁺ = 377, 1%], and the base peak at [m/e = 321], corresponding to [M⁺-2N₂], which was indicative for the expected structure.

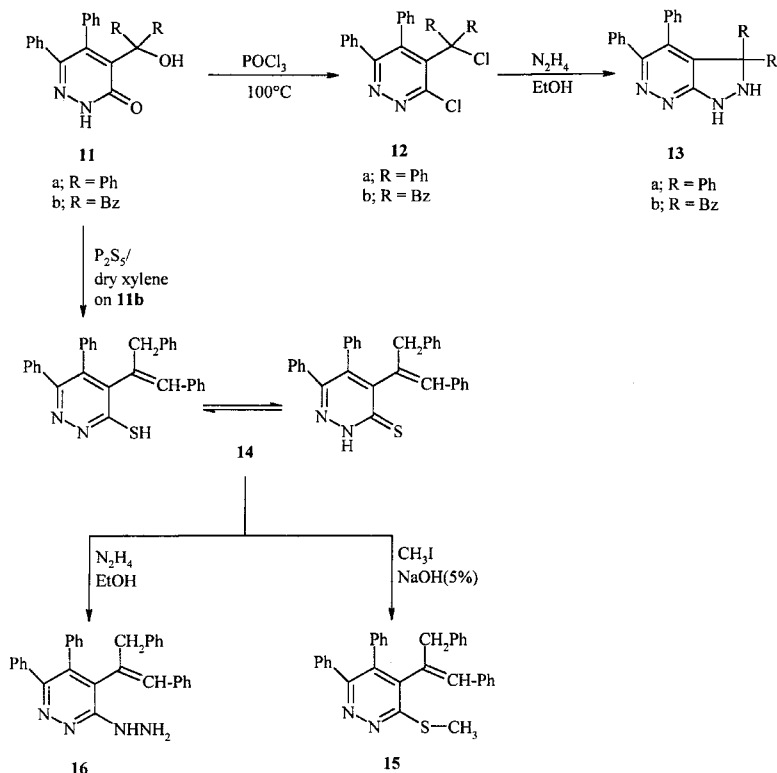
Refluxing compound **2** in ethanol with *o*-phenylenediamine, *o*-aminophenol, and *o*-aminothiophenol gave diazepino-, oxazepino-, and thiazepinopyridazine derivatives **7a–c**, respectively. However, compounds **7a** and **7b** also were obtained by treatment of **1a** in acetic acid with *o*-phenylenediamine and *o*-aminophenol respectively. The structure of the products **7a–c** were verified by their analytical and spectral data (cf. Experimental and Scheme 1).

The reaction of compound **1a** with ethylenediamine and 2-aminoethanol in acetic acid yielded pyridazino-diazepine **8a** and pyridazino-oxazepine **8b**, respectively (Scheme 1). The structures of the products **8a** and **8b** were established by their IR, $^1\text{H-NMR}$, and mass spectra.

However, the reaction of **2** with ethylenediamine and 2-aminoethanol either in ethanol or 1-butanol for a long time afforded the unexpected pyridazine derivatives **9a** and **9b**, respectively (Scheme 1). The structures of these products were verified by their spectral data. Their IR spectra showed carbonyl absorptions of conjugated ketones at 1667 cm^{-1} and two bands at $3428, 3378\text{ cm}^{-1}$ for symmetric and asymmetric stretching vibration of a NH_2 group. The structure of compound **9b** also was confirmed by condensing it with benzaldehyde in the presence of piperidine forming the Schiff's base **10** (Scheme 1). The IR spectrum of **10** lacked the bands characteristic for NH_2 group, which means that compound **9b** is an ether derivative. The mass spectrum of **9b** confirmed the proposed structure.

Moreover, chlorination of the carbinol derivatives¹ **11a** and **11b**, with phosphorus oxychloride yielded the dichloropyridazine derivatives **12a** and **12b** respectively (Scheme 2). The structures for compounds **12a** and **12b** were established from their IR spectra, which lacked the bands characteristic for OH groups. Their $^1\text{H-NMR}$ showed the aromatic protons, besides the methylene protons in case of **12b** and lacked any protons characteristic for OH groups. The mass spectrum for compound **12b** showed a complicated structure due to the presence of the two chlorine atoms and their isotopes.

The dichloro derivatives **12a** and **12b** reacted with hydrazine in ethanol to give pyrazolopyridazines **13a** and **13b**, respectively (Scheme 2). The structures of **13a** and **13b** were verified by their spectral data. Their IR spectra showed bands characteristic for NH groups at $(3214, 3176)$ and $(3271, 3176)\text{ cm}^{-1}$, respectively, their $^1\text{H-NMR}$ spectra revealed two protons for two NH groups at δ 9.15 and 8.35 besides the aromatic and the methylene protons for compound **13b**. The mass spectrum for compound **13a** showed the molecular ion peak with low intensity, but its base peak appeared at m/e 412 corresponding to $[\text{M}^+ - \text{N}]$, while the mass spectrum for compound **13b** lacked the



SCHEME 2

molecular ion peak, but exhibited a peak at m/e 436 (19%), corresponding to $[M^+ - (NH_3, \cdot H)]$ and the base peak at m/e 356.

Thionation of compound **11b** with phosphorus pentasulfide in dry xylene afforded compound **14** (Scheme 2) through elimination of H_2S gas; its structure was deduced from its analytical and spectral data together with its chemical reactions.

Methylation of **14** with methyl iodide afforded a quantitative yield of thiomethyl derivative **15** (Scheme 2). Hydrazinolysis of **14** with hydrazine in ethanol gave **16** (Scheme 2). The structures of compounds **15** and **16** were established from their analytical and spectral data.

EXPERIMENTAL

All melting points were taken on Giffin and George melting point apparatus and are uncorrected. IR absorption spectra were determined with a Moltson-1000 series FTIR spectrometer. 1H -NMR spectra were

determined on Bruker DRX500 or Bruker AC-200. The mass spectra were determined using AMD 604 spectrometer; SHIMADZU single focusing mass spectrometer at a beam energy 70 eV or Finnigan SSQ 7000. Elemental analysis were carried out at the Microanalytical Unit, Faculty of Science, Ain Shams University by using Perkin-Elmer 2400 CHN Elemental Analyzer.

Reaction of 4-Benzoyl-3-chloro-5,6-diphenylpyridazine² 2 or 4-Benzoyl-5,6-diphenylpyridazin-3(2H)-one¹ 1a with Hydrazine Hydrate. Synthesis of 7H-3,4,5-Triphenylpyrazolo[3,4-c]pyridazine 3

A solution of **2** (0.371 g, 0.001 mmol) in ethanol (15 mL) or **1a** (0.352 g, 0.001 mmol) in acetic acid (15 mL) was treated with hydrazine hydrate (0.002 mmol), and the reaction mixture was heated under reflux for 3 h, cooled, and poured on crushed ice. The solid products obtained were filtered off, washed with water, and dried. Recrystallization from benzene yielded identical products **3** as orange crystals. Compound **3** had m.p. 270–271°C (89% yield); IR: cm^{-1} 3146 (NH), 3061 (C–H_{ar}), 1653 (C=N), 1572, 1510, 1445 (pyridazine ring stretching vibrations); ¹H-NMR (CDCl₃): δ 8.9 (s, 1H, NH), 7.45–6.95 (m, 15H, 3 × C₆H₅); MS: m/e [%] 348 [M⁺, 46], 347 [(M⁺–1), 73], 332 [2], 319 [6], 291 [3], 271 [9], 256 [3], 216 [4], 189 [16], 163 [2], 155 [12], 128 [9], 115 [3], 79 [9], 78 [100%], 51 [6].

Reaction of 4-Benzoyl-5,6-diphenylpyridazin-3(2H)-one 1a with Hydrazine Hydrate. Synthesis of 5,6-Diphenyl-4-hydrazonobenzylpyridazin-3(2H)-one 4

Compound **1a** (0.352 g, 0.001 mmol) and excess hydrazine hydrate (0.003 mmol) were refluxed in ethanol (20 mL) for 3 h. The reaction mixture was poured into ice cold water. The solid obtained was filtered off, washed with water, and recrystallized from ethanol to give **4** as yellow crystals. Compound **4** had m.p. 250–252°C (90% yield); IR: cm^{-1} 3358, 3219 (symmetric and unsymmetric stretching for NH₂ group), 3061 (C–H_{ar}), 1680 (CO), 1638 (C=N); ¹H-NMR (CDCl₃): δ 12.4 (broad, 1H, NH for pyridazine moiety), 7.5–6.8 (m, 15H, 3 × C₆H₅), 3.6 (broad =N–NH₂ group).

Reaction of 4-Benzoyl-3-chloro-5,6-diphenylpyridazine 2 with Benzhydrazide. Synthesis of 8-Benzoyl-3,6,7-triphenyl-1,2,4-triazolo[4,3-b]pyridazine 5

A solution of **2** (0.371 g, 0.001 mmol) and benzhydrazide (0.136 g, 0.001 mmol) in l-butanol³ (15 mL) was refluxed for 48 h. On cooling,

a yellow solid was precipitated and filtered. The solid obtained was recrystallized from CHCl_3 to give **5** as yellow crystals (78% yield) m.p. 290–292°C; IR: cm^{-1} 3059 (C-H_{ar}), 1669 (CO), 1598 (C=N), 1463, 1400 (pyridazine ring stretching vibrations); $^1\text{H-NMR}$ (CDCl_3): δ 7.4–6.8 (m, 20H, $4 \times \text{C}_6\text{H}_5$); MS: m/e [%] 452 [M^+ , 4], 451 [15], 450 [41], 436 [13], 348 [12], 347 [$(\text{M}^+ - \text{PhCO})$, 27], 332 [12], 305 [8], 229 [5], 217 [7], 214 [7], 203 [7], 190 [9], 189 [18], 180 [16], 179 [15], 178 [11], 165 [9], 153 [7], 128 [7], 115 [10], 105 [20], 104 [76], 103 [100], 91 [24], 78 [12], 77 [16], 76 [28], 67 [12], 66 [7], 65 [8], 50 [17].

Reaction of 4-Benzoyl-3-chloro-5,6-diphenylpyridazine **2** with Sodium Azide. Synthesis of 8-Benzoyl-6,7-diphenyltetrazolo[4,5-b]pyridazine **6**

A solution of compound **2** (0.25 g) in dimethylformamide (10 mL) and sodium azide⁴ (0.5 g, in few drops of H_2O) was refluxed for 2 h. The reaction mixture was poured into ice cold water. The solid obtained was filtered off, washed with water, and recrystallized from benzene to give **6** (82% yield) as pale yellow crystals, had m.p. 227°C decomp.; IR: cm^{-1} 3059 (C-H_{ar}), 1677 (CO), 1596 (C=N), 1453, 1345 (pyridazine ring), 1229 (C-O); $^1\text{H-NMR}$ (CDCl_3): δ 7.4–6.9 (m, 15H, $3 \times \text{C}_6\text{H}_5$); MS: m/e [%] 377 [M^+ , 1], 353 [2], 337 [13], 322 [25], 321 [$(\text{M}^+ - 2\text{N}_2)$, 100], 320 [45], 306 [25], 292 [13], 265 [10], 217 [11], 216 [53], 189 [9], 163 [4], 105 [43], 77 [34], 51 [24].

Reaction of 4-Benzoyl-3-chloro-5,6-diphenylpyridazine **2** or 4-benzoyl-5,6-diphenylpyridazin-3(2H)-one **1a** with *o*-Phenylenediamine. Formation of 11H-3,4,5-Triphenylbenzo[b]pyridazino[4,3-f][1,4]diazepine **7a**

A solution of compound **2** (0.371 g, 0.001 mmol) in ethanol (20 mL) or **1a** (0.352 g, 0.001 mmol) in acetic acid (15 mL) was treated with *o*-phenylenediamine (0.108 g, 0.001 mmol). The reaction mixture was refluxed for 3 h, filtered while hot, and left to cool. The solid product formed was filtered off and recrystallized from ethanol to give **7a** as pale yellow crystals. Compound **7a** had m.p. 230–232°C (ethanol) (82% yield); IR: cm^{-1} 3270, 3180 (NH), 3054 (C-H_{ar}), 1639 (C=N); $^1\text{H-NMR}$ (CDCl_3): δ 8.25 (s, 1H, NH for pyridazine moiety), 7.4–6.9 (m, 15H, $3 \times \text{C}_6\text{H}_5$); MS: m/e [%] 424 [M^+ , 3], 352 [17], 323 [35], 275 [12], 247 [6], 218 [5], 189 [10], 165 [7], 129 [5], 105 [50], 89 [19], 78 [15], 77 [100], 63 [12], 51 [30].

Analysis Calcd. for $\text{C}_{29}\text{H}_{20}\text{N}_4$: C, 82.05; H, 4.75; N, 13.20. Found: C, 81.76; H, 4.66; N, 13.04.

Reaction of 4-Benzoyl-5,6-diphenylpyridazin-3(2H)-one **1a with *o*-Aminophenol. Synthesis of 3,4,5-Triphenylbenzo[*b*]pyridazino[4,3-*f*][1,4]oxazepine **7b****

Compound **1a** (0.352 g, 0.001 mmol) was heated with *o*-aminophenol (0.109 g, 0.001 mmol) in glacial acetic acid (15 mL) for 4 h. The reaction mixture was poured into ice cold water. The residue was filtered off, dried, and recrystallized from benzene to give **7b** as pink crystals. Compound **7b** had m.p. 271–273°C (63% yield); IR: cm^{-1} 3060 (C–H_{ar.}), 1638 (C=N), 1576, 1464 (pyridazine ring stretching vibrations); ¹H-NMR (CDCl₃): δ 7.5–6.8 (m, 19H, aromatic); MS: *m/e* [%] 427 [M^+ + 2], 1], 415 [31], 414 [97], 413 [57], 337 [28], 336 [25], 335 [56], 323 [7], 307 [12], 287 [22], 286 [100], 279 [12], 278 [14], 277 [14], 276 [12], 265 [12], 259 [18], 257 [14], 232 [13], 231 [11], 230 [9], 229 [20], 202 [10], 189 [10], 165 [19], 152 [10], 85 [24], 83 [35], 77 [2], 51 [50].

Reaction of 4-Benzoyl-3-chloro-5,6-diphenylpyridazine **2 with *o*-Aminothiophenol. Formation of 3,4,5-Triphenylbenzo[*b*]pyridazino[4,3-*f*][1,4]thiazepine **7c****

Compound **2** (0.371 g, 0.001 mmol) was heated with *o*-aminothiophenol (0.015 mmol) in presence of ethanol (20 mL) for 3 h. The reaction solution was concentrated to give **7c** as yellow needles. Compound **7c** had m.p. 193–195°C (ethanol) (85% yield); IR: cm^{-1} 3060 (C–H_{ar.}), 1623 (C=N); ¹H-NMR (DMSO-*d*₆): δ 7.7–7.1 (m, 19H, aromatic); MS: *m/e* [%] 443 [M^+ + 2], 79], 442 [6], 441 [M^+ , 1], 386 [7], 367 [26], 366 [100], 341 [11], 340 [37], 339 [39], 307 [12], 263 [24], 236 [30], 231 [16], 222 [8], 206 [13], 204 [18], 178 [10], 106 [10], 104 [11], 91 [7], 69 [13], 57 [15], 55 [10], 51 [17].

Analysis Calcd. for C₂₉H₁₉N₃S: C, 78.89; H, 4.34; N, 9.52, S, 7.26. Found: C.79.01; H, 4.22; N, 9.60; S, 7.30.

Reaction of 4-Benzoyl-5,6-diphenylpyridazin-3(2H)-one **1a with Ethylenediamine. Synthesis of 7,8-Trihydro-3,4,5-triphenylpyridazino[4,3-*f*][1,4]diazepine **8a****

A solution of compound **1a** (0.352 g, 0.001 mmol) in acetic acid (20 mL) was treated with ethylenediamine (0.015 mmol). The reaction mixture was refluxed for 3 h, filtered while hot, and left to cool. The solid product formed was filtered off and recrystallized from ethanol to give **8a** as white crystals. Compound **8a** had m.p. 270–272°C (78% yield); IR: cm^{-1} 3378 (NH), 3065 (C–H_{ar.}), 2985, 2872 (C–H_{al.}), 1625 (C=N), 1515, 1490, 1446 (pyridazine ring stretching vibrations); ¹H-NMR (CDCl₃): δ 12.05 (s, 1H, NH of diazepine ring), 7.30–6.47 (m, 15H, 3 × C₆H₅), 2.10–2.05 (t, 2H, =N–CH₂); 1.7–1.6 (t, 2H, –HN–CH₂); MS: *m/e* [%] 376 [M^+ , 0],

371 [3], 337 [6], 281 [16], 280 [63], 265 [14], 251 [10], 175 [10], 161 [51], 160 [47], 159 [100], 158 [13], 146 [18], 145 [47], 144 [42], 132 [20], 130 [11], 117 [23], 91 [17], 77 [15], 52 [11].

Reaction of 4-Benzoyl-5,6-diphenylpyridazin-3(2H)-one **1a with 2-Aminoethanol. Synthesis of 7,8-Dihydro-3,4,5-triphenylpyridazino[4,3-f][1,4]oxazepine **8b****

Compound **1a** (0.352 g, 0.001 mmol) in acetic acid (15 mL) was treated with 2-aminoethanol (0.015 mmol). The reaction mixture was refluxed for 3 h, filtered while hot, concentrated, and left to cool to give **8b** as white crystals. Compound **8b** had m.p. 262–264°C (acetic acid, 73% yield); IR: cm^{-1} 3064 (C–H_{ar}), 2986, 2873 (C–H_{al}), 1625 (C=N), 1516, 1490, 1446 (pyridazine ring stretching vibrations) 1265 (C–O); ¹H-NMR (DMSO-*d*₆): δ 7.5–6.8 (m, 15H, 3 × C₆H₅), 4.45 (t, 2H, –OCH₂–), 3.62 (t, 2H, –CH₂N–); MS: *m/e* [%] 377 [*M*⁺, less than 1], 353 [15], 336 [22], 338 [25], 337 [(*M*⁺–N, C₂H₂), 100], 336 [22], 275 [11], 259 [8], 247 [13], 219 [4], 204 [3], 189 [6], 165 [4], 105 [5], 77 [8], 51 [3].

Reaction of 4-Benzoyl-3-chloro-5,6-diphenylpyridazine **2 with Ethylenediamine. Synthesis of 4-Benzoyl-5,6-diphenyl-3-(2-aminoethylamino)pyridazine **9a****

Compound **2** (0.371 g, 0.001 mmol) was treated with ethylene diamine (0.015 mmol) in ethanol (20 mL). The reaction mixture was refluxed for 3 h, filtered while hot, and left to cool. The solid product formed was filtered off and recrystallized from benzene to give **9a** as yellow crystals. Compound **9a** had m.p. 169–171°C (benzene) (76% yield); IR: cm^{-1} 3428, 3378 (NH, NH₂), 3060 (C–H_{ar}), 2930, 2870 (C–H_{al}), 1667 (CO), 1600 (C=N), 1561, 1500, 1472 (pyridazine ring stretching vibrations); ¹H-NMR (DMSO-*d*₆): δ 7.5–6.8 (m, 15H, 3 × C₆H₅), 6.2 (broad, 1H, NH–Ar), 3.5 (broad, 2H, –NH₂), 3.2 (t, 2H, –NH–CH₂–), 2.8 (t, 2H, –CH₂NH₂); MS: *m/e* [%] 394 [*M*⁺, 11], 365 [8], 364 [9], 353 [18], 352 [71], 336 [34], 322 [26], 260 [11], 259 [13], 246 [22], 232 [11], 231 [15], 230 [9], 217 [12], 216 [16], 204 [14], 203 [14], 202 [23], 191 [12], 190 [14], 189 [27], 178 [21], 176 [14], 165 [13], 152 [12], 129 [11], 128 [17], 127 [20], 125 [43], 105 [44], 91 [48], 85 [26], 78 [24], 77 [35], 51 [100].

Reaction of 4-Benzoyl-3-chloro-5,6-diphenylpyridazine **2 with 2-Aminoethanol. Synthesis of 4-Benzoyl-5,6-diphenyl-3-(2-aminoethoxy)pyridazine **9b****

Compound **2** (0.371 g, 0.001 mmol) was refluxed with 2-aminoethanol (0.015 mmol) in ethanol (20 mL) for 3 h. The reaction solution was then concentrated to give **9b**. Compound **9b** had m.p. 183–185°C (benzene,

yellow needles) (72% yield); IR: cm^{-1} 3432, 3372 (NH_2), 3061 (C-H_{ar}), 2930, 2840 (C-H_{al}), 1667 (CO), 1584, 1490 (pyridazine ring stretching vibrations); $^1\text{H-NMR}$ (DMSO-d_6): δ 7.45–6.75 (m, 15H, $3 \times \text{C}_6\text{H}_5$), 6.05 (t, 2H, NH_2), 4.57 (t, 2H, $-\text{OCH}_2$), 3.50 (t, 2H, $-\text{CH}_2\text{NH}_2$); MS: m/e [%] 395 [M^+ , 3], 377 [$(\text{M}^+ - \text{H}_2\text{O})$, 3], 352 [6], 351 [13], 323 [9], 322 [35], 246 [11], 214 [4], 202 [8], 189 [17], 165 [4], 152 [5], 128 [4], 105 [69], 91 [16], 78 [25], 77 [100], 51 [20].

Condensation of Compound 9b with Benzaldehyde. Formation of 4-Benzoyl-5,6-diphenyl-3-(2-benzalaminoethoxy)pyridazine 10

Compound **9b** (0.2 g) in ethanol 15 mL was refluxed with benzaldehyde (0.06 mL) in the presence of piperidine for 3 h. The reaction mixture was concentrated to give **10**. Compound **10** had m.p. 146–148°C; IR: cm^{-1} 3060 (C-H_{ar}), 2930, 2840 (C-H_{al}), 1629 (C=N); $^1\text{H-NMR}$ (DMSO-d_6): δ 7.6–6.8 (m, 20H, $4 \times \text{C}_6\text{H}_5$), 6.3 (s, 1H, $-\text{N=CH}$), 4.52 (t, 2H, $-\text{OCH}_2-$), 3.53 (t, 2H, $-\text{CH}_2-\text{N=}$).

Chlorination of 5,6-Diphenyl-4-(1,1-diphenyl-1-hydroxymethyl)-2,3-dihydropyridazin-3-one¹ 11a. Synthesis of 3-Chloro-5,6-diphenyl-4-(1,1-diphenyl-1-chloromethyl)pyridazine 12a

Compound **11a** (4.30 g, 0.01 mmol) and phosphorus oxychloride (10 mL) were heated on an oil-bath at 100°C for 1 h. After cooling, the reaction mixture was poured into crushed ice and made alkaline with aqueous sodium hydroxide solution. The solid product obtained was filtered off, washed with water, dried, and recrystallized from petroleum ether 80–100°C to give **12a** as colorless crystals. Compound **12a** had m.p. 120–122°C (59% yield); IR: cm^{-1} 3060 (C-H_{ar}), 1653 (C=N); $^1\text{H-NMR}$ (DMSO-d_6): δ 7.7–6.9 (m, 20H, $4 \times \text{C}_6\text{H}_5$).

Analysis Calcd: for $\text{C}_{29}\text{H}_{20}\text{Cl}_2\text{N}_2$: Cl, 15.70. Found: 15.32.

Chlorination of 5,6-Diphenyl-4-(1,1-dibenzyl-1-hydroxymethyl)-2,3-dihydropyridazin-3-one¹ 11b. Synthesis of 3-Chloro-5,6-diphenyl-4-(1,1-dibenzyl-1-chloromethyl)pyridazine 12b

A solution of **11b** (4.59 g, 0.01 mmol) in phosphorus oxychloride (10 mL) was heated on an oil-bath at 100°C for 1 h. After cooling, the reaction mixture was poured on crushed ice and made alkaline with aqueous sodium hydroxide solution. The solid product was filtered off, washed with water, dried, and recrystallized from n-hexane to give **12b** as

colorless crystals (66% yield), had m.p. 106–108°C; IR: cm^{-1} 3050 (C-H_{ar}), 2900–2840 (C-H_{al}), 1600 (C=N); $^1\text{H-NMR}$ (DMSO-d_6): δ 3.85 (s, 4H, $2 \times -\text{CH}_2\text{Ph}$), 7.3–6.8 (m, 20H, $4 \times \text{C}_6\text{H}_5$); MS: m/e [%] 495 [M^+ , 0], 480 [$(\text{M}^+ - \text{NH})$, 19], 164 [100], the spectrum was very complicated.

Analysis Calcd: for $\text{C}_{31}\text{H}_{24}\text{Cl}_2\text{N}_2$: C, 75.15; H, 4.88; N, 5.65; Found: C, 75.10; H, 4.90; N, 5.70.

Hydrazinolysis of 3-Chloro-5,6-diphenyl-4-(1,1-diphenyl-1-chloromethyl)pyridazine 12a. Synthesis of 6,7-Dihydro-3,4,5,5-tetraphenylpyrazolo[3,4-c]pyridazine 13a

Compound **12a** (0.466 g, 0.001 mmol) was refluxed with excess hydrazine hydrate (0.003 mmol) in ethanol (20 mL) for 3 h. The reaction solution was concentrated to give **13a**. Compound **13a** had m.p. 233–235°C (ethanol, 63% yield) as yellow crystals; IR: cm^{-1} 3214, 3176 (2NH), 3057 (C-H_{ar}), 1652 (C=N), 1599, 1561, 1491, 1446 (pyridazine ring stretching vibrations); $^1\text{H-NMR}$ (CDCl_3): δ 9.20, 8.30 (s, for 2NH groups), δ 7.6–7 (m, 20H, $4 \times \text{C}_6\text{H}_5$); MS: m/e [%] 428 [$(\text{M}^+ + 2)$, 5], 426 [M^+ , less than 1], 414 [6], 413 [31], 412 [$(\text{M}^+ - \text{N})$, 100], 370 [7], 355 [13], 317 [4], 294 [18], 265 [12], 239 [1], 215 [2], 189 [2], 176 [1], 165 [1], 139 [1], 95 [1], 77 [1], 51 [1].

Hydrazinolysis of 3-Chloro-5,6-diphenyl-4-(1,1-dibenzyl-1-chloromethyl)pyridazine 12b. Synthesis of 6,7-Dihydro-5,5-dibenzyl-3,4-diphenylpyrazolo-[3,4-c]pyridazine 13b

Compound **12b** (0.496 g, 0.001 mmol) was refluxed with excess hydrazine hydrate (0.003 mmol) in ethanol (20 mL) for 3 h. The reaction solution was concentrated to give **13b**. Compound **13b** had m.p. 205–206°C, pale yellow crystals from petroleum ether 60–80°C (54% yield); IR: cm^{-1} 3271, 3176 (2NH), 3057 (C-H_{ar}), 2927, 2843 (C-H_{al}), 1642 (C=N), 1529, 1492 (pyridazine ring stretching); $^1\text{H-NMR}$ (CDCl_3): δ 9.15, 8.35 (s, for 2NH groups), δ 7.5–6.9 (m, 20H, $4 \times \text{C}_6\text{H}_5$), δ 2.6 and 2.0 (s, 4H, 2×2.0 (s, 4H, $2 \times \text{CH}_2\text{Ph}$); MS: 436 [$(\text{M}^+ - \text{NH}_3)$, H], 19], 375 [14], 361 [28], 356 [100], 324 [25], 313 [25], 295 [44], 280 [43], 267 [41], 231 [19], 213 [31], 199 [17], 186 [28], 152 [26], 106 [52], 50 [19].

Thionation of 5,6-Diphenyl-4-(1,1-diphenyl-1-hydroxymethyl)-2,3-dihydropyridazin-3-one 11b. Synthesis of 4-(1-Benylidenephenethyl)-5,6-diphenyl-2,3-dihydropyridazin-3-thione 14

To a solution of **11b** (4.59 g, 0.01 mmol) in dry xylene (60 mL), phosphorus pentasulfide (4.4 g, 0.02 mmol) was added and the reaction mixture

was heated under reflux for 3 h. The mixture was filtered while hot. The solid product obtained was recrystallized from ethanol to give **14** as orange crystals, m.p. 243–245°C (82% yield); IR: cm^{-1} 3050 (C-H_{ar}), 2940–2900, 2840 (C-H_{al}), 1640 (C=N); $^1\text{H-NMR}$ (DMSO-d_6): δ 4.13 (s, 2H, $-\text{CH}_2\text{Ph}$), 6.7 (s, 1H, $=\text{CH}-\text{Ph}$), 6.8–7.5 (m, 20H, $4 \times \text{C}_6\text{H}_5$), 15 (s, 1H, SH); MS: m/e [%] 456 [M^+ , 0], 418 [1], 386 [2], 367 [1], 357 [3], 356 [10], 355 [37], 354 [100], 353 [83], 339 [5], 325 [8], 324 [20], 323 [18], 322 [44], 321 [21], 320 [10], 305 [3], 295 [4], 275 [5], 244 [6], 231 [5], 215 [5], 202 [6], 189 [10], 165 [5], 140 [3], 115 [5], 91 [4], 78 [3], 77 [2], 51 [3].

Analysis Calcd. for $\text{C}_{31}\text{H}_{24}\text{N}_2\text{S}$: C, 81.55; H, 5.30; N, 6.13; S, 7.02. Found: C, 81.20; H, 5.50; N, 5.90; S, 7.30.

Methylation of 4-(1-Benzylidenephenethyl)-5,6-diphenyl-2,3-dihydropyridazin-3-thione **14**. Synthesis of 4-(1-Benzylidenephenethyl)-5,6-diphenyl-3-methylthiopyridazine **15**

Compound **14** (0.457 g, 0.001 mmol) and methyl iodide (0.015 mmol) were refluxed in 30 mL of sodium hydroxide solution (5%) for 3 h. After cooling, the solid product obtained was filtered off, washed with water, and dried. Recrystallization from ethanol gave **15** as yellow crystals. Compound **15** had m.p. 145–146°C (43% yield); IR: cm^{-1} 3050 (C-H_{ar}), 2940, 2840 (C-H_{al}), 1610 (C=N).

Analysis Calcd. for $\text{C}_{32}\text{H}_{26}\text{N}_2\text{S}$: C, 81.67; H, 5.57; N, 5.95. Found: C, 81.36; H, 5.80; N, 5.73.

Reaction of 4-(1-Benzylidenephenethyl)-5,6-diphenyl-2,3-dihydropyridazin-3-thione **14** with Hydrazine Hydrate. Synthesis of 4-(1-Benzylidenephenethyl)-5,6-diphenyl-3-hydrazinopyridazine **16**

Compound **14** (0.457 g, 0.001 mmol) was treated with excess hydrazine hydrate (0.002 mmol) in ethanol (20 mL). The reaction mixture was refluxed for 3 h, then concentrated to give **16** as yellow crystals. Compound **16** had m.p. 124–126°C (methanol) (69% yield); IR: cm^{-1} 3380, 3200 (NH , NH_2), 3050 (C-H_{ar}), 2940–2900, 2840 (C-H_{al}), 1645 (C=N); $^1\text{H-NMR}$ (DMSO-d_6): δ 3.9 (s, 2H, $-\text{CH}_2\text{Ph}$), 4.83 (d, 2H, $-\text{NH}_2$), 6.7 (s, 1H, $=\text{CH}-\text{Ph}$), 6.9–7.45 (m, 20H, $4 \times \text{C}_6\text{H}_5$), 9.65 (broad, 1H, $-\text{NH}-$); MS: m/e [%] 454 [M^+ , less than 1], 391 [3], 356 [19], 355 [78], 354 [100], 325 [12], 324 [32], 323 [39], 264 [15], 263 [66], 245 [8], 233 [4], 218 [5], 209 [7], 195 [18], 178 [7], 165 [5], 140 [5], 130 [14], 115 [12], 104 [6], 103 [9], 91 [36], 77 [6], 65 [7], 51 [4].

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