PYRIDAZINE AND ITS RELATED COMPOUNDS, PART 27.1
SYNTHESIS AND INSECTICIDAL ACTIVITY OF SOME PYRIDAZINE DERIVATIVES

Ali Deeb[a,⁎], Elsayed Mourad[b] and Diaa Elenany[b]

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An effective method has been developed for the preparation under mild conditions of novel pyridazine derivatives from the easily accessible starting materials benzilmonohydrazone, p,p'-dichlorobenzilmonohydrazone, diethyl malonate and ethyl phenylacetate. All the synthesized compounds were fully characterized and some of them displayed good insecticide activities against Mucsa domestica and Macrosiphum pisi in preliminary insecticide activity tests.

Introduction

Many pyridazine are well known to possess a wide range of bioactivities and are often employed as plant virucides,⁵ antitumor agents,⁶ fungicides,⁷ insecticides,⁸ herbicides⁹ and anti-inflammatory agents.⁹ They have immense potential in agricultural science as plant growth regulators and crop protection agents. Several derivatives of these compounds incorporating 1,3,4-thiadiazole, 1,3,4-oxadiazole and oxazolidin-2-one rings have been shown to display moderate to good insecticide activities.⁸ The present investigation, which is a continuation of our previous work⁹ on pyridazine derivatives and related compounds, deals with the synthesis of different substituted pyridazines and studies their insecticidal activities.

Materials and Methods

Preparation of ethyl 3-chloro-5,6-diarylp yridazine-4-carboxylates (3a,b)

A mixture of pyridazinone derivatives 1a,b (10 mmol) and phosphoryl chloride (10 mL) was refluxed for 4 hours. The cooled reaction mixture was poured onto ice-H₂O (50 mL), the precipitate was filtered off, dried and recrystallized from ethanol to give 3a,b.

**Ethyl 3-chloro-5,6-diphenylpyridazine-4-carboxylate (3a):** Yield as 95%; Mp. 118-120 °C; IR (KBr) cm⁻¹: 3050, 2983, 1735, 761. ¹H NMR, δ ppm (DMSO-d₆): 7.43-7.30 (m, 10H, 2Ph-H), 4.31 (q, 2H, CH₂), 1.20 (t, 3H, CH₃). Anal. Calcd for C₁₉H₁₅ClN₂O₂: C, 67.36; H, 4.46; N, 8.27. Found: C, 67.20; H, 4.30; N, 8.10.

**Ethyl 3-chloro-5,6-bis(4-chlorophenyl)pyridazine-4-carboxylate (3b):** Yield 96%; Mp. 80-82 °C; IR (KBr) cm⁻¹: 3050, 2983, 1735, 761. ¹H NMR, δ ppm (DMSO-d₆): 7.79-7.41 (m, 8H, 2Ar-H), 4.30 (q, 2H, CH₂), 1.29 (t, 3H, CH₃). Anal. Calcd for C₁₉H₁₃Cl₃N₂O₂: C, 55.97; H, 3.21; N, 6.87. Found: C, 55.90; H, 3.00; N, 6.70.

Preparation of ethyl 6,7-diaryltetrazolo[1,5-b]pyridazine-8-carboxylates (4a,b)

Sodium azide (0.65g, 10.0 mmol) was added to a solution of ethyl 3-chloro-5,6-diarylp yridazine-4-carboxylates 3a,b (4.0 mmol) in ethanol (20 mL). The stirred reaction mixture was heated under reflux for 6 hours. The solvent was evaporated under reduced pressure, then the solid residue was diluted with H₂O (100 mL) and the precipitated product was isolated by suction, dried and recrystallized from ethanol to give title compounds 4a,b.
Synthesis and insecticidal activity of some pyrazidine derivatives

**Ethyl 6,7-diphenyltetrazolo[1,5-b]pyrazidine-8-carboxylate (4a)**: Yield 76%, Mp. 147-148 °C (as reported).11)

**Ethyl 6,7-bis(4-chlorophenyl)tetrazolo[1,5-b]pyrazidine-8-carboxylate (4b)**: Yield 72%, Mp. 145-147 °C; IR (KBr) cm⁻¹: 3205, 2981, 1731, 730. 'H NMR, δ ppm (DMSO-d₆): 7.78-7.42 (m, 8H, 2 Ar-H), 4.30 (q, 2H, CH₂), 1.29 (t, 3H, CH₃). MS (m/z): 288 (M⁺, 56.8%), 287 (M⁺, - CO₂Et, 100%), 231 (M⁺ - HNNCCO₂Et, 7.0%).

**Preparation of 4,5-diaryl-3-oxo-1,2-dihydropyridazine-4-carboxylic acids (9a,b)**

A slurry of carboxylic acid derivatives 8a,b (3.0 mmol), water (15 mL), and conc. HCl (30 mL) was cooled to 5 °C. To this slurry was added a solution of sodium nitrite (1.1 g) in water (5 mL) dropwise, after the addition, the cooling bath was removed, the mixture was allowed to warm slowly to room temperature, transferred to a steam bath until dissolution occurred. Continued heating was a companied by gas evolution followed by precipitation. After cooling, the solid was filtered, washed several times with water, dried and recrystallized from ethanol to give title compounds 9a,b.

**5,6-Diphenyl-3-oxo-4-carboxydrazine (8a)**: Yield 73%; mp 123-125 °C, (as reported)11).

**6,7-Diphenyltetrazolo[1,5-b]pyrazidine-8-carboxylate (4a)**: Yield 98.9%, Mp 110-112 °C; IR (KBr) cm⁻¹: 3422, 3189, 1651. 'H NMR, δ ppm (DMSO-d₆): 7.88-7.22 (m, 10H, 2Ph-H), 4.0 (s, 1H, pyrazolo NH), 7.42-7.79 (m, 10H, 2-Ph-H). MS (m/z): 375 (M⁺, 1.1%). Anal. Calcd. for C₁₉H₁₃N₅O₂: C, 54.42; H, 3.22; N, 14.93. Found: C, 54.30; H, 3.10; N, 14.80.

**Preparation of 2-carbethoxy-4,5-diphenyl-3-oxo-1H-pyrazolo[3,4-c]pyrazidine (6)**

A mixture of 3-hydroxy derivative 5a (1.2 g, 4.0 mmol) and ethyl chloroformate (5 mL) was heated under reflux for 3 hr, upon cooling the solid product formed was filtered off, dried and recrystallized from ethanol to give title compound 6, yield 98.9%, Mp. 110-112 °C; IR (KBr) cm⁻¹: 3057, 2980, 1760. 'H NMR, δ ppm (DMSO-d₆): 1.29 (t, 3H, CH₃), 4.0 (s, 1H, NH), 4.13 (q, 2H, CH₂), 7.41-7.79 (m, 10H, 2Ph-H). MS (m/z): 360 (M⁺, 59%), 287 (M⁺ - CO₂Et, 100%), 231 (M⁺ - HINNCOCO₂Et, 9.1%). Anal. Calcd. for C₁₉H₁₃N₅O₂: C, 66.56; H, 4.47; N, 15.55. Found: C, 66.50; H, 4.30; N, 15.30.

**Preparation of N-ethylthio-4,5-diphenyl-3-oxo-1,2-dihydropyrazolo[3,4-c]pyrazidine-2-carboxamidine (7)**

To a solution of 3-hydroxy derivative 5a (1.8 g, 6.0 mmol) in dry acetone (50 mL), ethyl isothiocyanate (0.87 g, 10.0 mmol) and potassium hydroxide (0.6 g, 10.0 mmol) were added. The reaction mixture was refluxed for 5 hours. The cooled reaction mixture was poured onto water (50 mL) and upon neutralization with hydrochloric acid, a precipitate which obtained was filtered, washed several times with water, dried and recrystallized from ethanol, to afford compound 7, yield 91%; Mp. 230-232 °C. IR (KBr) cm⁻¹: 3169, 3085, 2818, 1656, 1164. 'H NMR, δ ppm (DMSO-d₆): 0.86 (t, 3H, CH₃), 1.57 (q, 2H, CH₂), 2.0 (s, 1H, NH), 4.0 (s, 1H, pyrazolo NH), 7.42-7.79 (m, 10H, 2-Ph-H). MS (m/z): 375 (M⁺, 1.1%). Anal. Calcd. for C₁₀H₁₃N₅O₂: C, 54.42; H, 3.22; N, 14.93. Found: C, 54.30; H, 3.10; N, 14.80.

**Preparation of 5,6-diaryl-3-oxo-2,3-dihydropyridazine-4-carboxylic acids (9a,b)**

A slurry of carboxylic acid derivatives 8a,b (3.0 mmol), water (15 mL), and conc. HCl (30 mL) was cooled to 5 °C. To this slurry was added a solution of sodium nitrite (1.1 g) in water (5 mL) dropwise, after the addition, the cooling bath was removed, the mixture was allowed to warm slowly to room temperature, transferred to a large beaker, and heated on a steam bath until dissolution occurred. Continued heating was a companied by gas evolution followed by precipitation. After cooling, the solid was filtered, washed several times with water, dried and recrystallized from ethanol to give title compound 9a,b.
Hydrolysis of 4-carboethoxy-5,6-diarylpipridazin-3(2H)-ones (1a,b)

6-Carboethoxy derivatives 1a,b (1.1 mmol) were separately dissolved in ethanol (15 mL). Following addition of sodium hydroxide (0.5 g), the reaction mixture was placed on a steam bath, when the solvent had evaporated, the residues were dissolved in warm water (10 mL) and filtered. The filtrates were acidified with hydrochloric acid, and the resulting precipitates were separated by filtration, dried and recrystallized from ethanol, to give 78 and 79% yield respectively that were identical with compounds 9a,b.

Preparation of 3-chloro-5,6-diaryl-4-phenylpyridazines (10a,b)

A mixture of pyridazinone derivatives 2a,b (9.0 mmol) and phosphoril chloride (6 mL) was refluxed for 5 hrs. The cooled reaction mixture was poured into ice-H2O (50 mL), the precipitate was filtered, dried and recrystallized from ethanol to give the title compounds 10a,b.

3-Chloro-4,5,6-triphenylpyridazine (10a): Yield 94%; Mp. 170-172 °C as reported.

Preparation of 6,7-diaryl-8-phenyltetrazolo[1,5-b]pyridazine (11b)

Sodium azide (0.06 g, 0.9 mmol) was added to a solution of compounds 10a,b (1.0 mmol) in ethanol (20 mL). The reaction mixture was heated under reflux for 10 hours. The solvent was evaporated under reduced pressure, then the solid residue was diluted with water (100 mL) and the precipitate obtained was filtered, washed several times with water, dried and recrystallized from ethanol.

Preparation of 6,7,8-Triphenyltetrazolo[1,5-b]pyridazines (11a,b)

To a solution of compound 11a (1.7 g, 4.8 mmol) in 1,2-dichlorobenzene (10 mL), triphenylphosphine (1.57 g, 5.9 mmol) was added, the reaction mixture was refluxed for 6 hours, the solvent was evaporated and the residue was washed with petroleum ether 40/60 °C, the precipitate was filtered, dried and recrystallized from ethanol. Yield 88 %; Mp. 212-214 °C. IR (KBr) cm-1: 3055, 1597, 1537. 1H NMR, δ ppm (DMSO-d6): 6.81-7.93 (m, 30H, 6Ph-H). Anal. Calcd for C26H27N3O: C, 82.31; H, 5.18; N, 7.19. Found: C, 82.20; H, 5.10; N, 7.10.

Preparation of 5,6-diaryl-3-β-hydroxyethylamino-4-phenylpyridazine (13a,b)

A mixture of compound 10a,b (0.9 mmol) and ethanolamine (5 mL) was refluxed for 2 hours. The cooled reaction mixture was poured onto water (100 mL). A precipitate which obtained was filtered, washed several times with water, dried and recrystallized from benzene to give the title compounds 13a,b.

4,5,6-Triphenylpyridazine-3-β-hydroxynapipyridazine (13a): Yield 84%; Mp. 185-187 °C as reported.

6-Bis[4-chlorophenyl]-3-β-hydroxyethylamino-4-phenylpyridazine (13b): Yield 91.7 %; Mp. 85-87°C. IR (KBr) cm−1: 3259, 3081, 2909, 767. 1H NMR, δ ppm (DMSO-d6): 3.48-3.65 (m, 5H, CH2CH2OH), 4.0 (s, 1H, NH), 7.41-7.98 (m, 13H, aromatic-H). MS (m/z): 435 (M⁺ + 1, 2.7%), 416 (M⁺ - H2O, 14%), 404 (M⁺ - CH2OH, 19%), 390 (M⁺ - CH2CH2OH, 100%). Anal. Calcd. for C27H19Cl2N3O: C, 73.66; H, 4.39; N, 9.63. Found: C, 66.00; H, 4.30; N, 9.50.

Preparation of 5,6-diaryl-3-morpholino-4-phenylpyridazines (13c,d)

A mixture of 3-chloro derivatives 10a,b (1.0 mmol) and morpholine (4 mL) was refluxed for 3 hours. The cooled mixture was poured onto water (100 mL). A precipitate which obtained was filtered, washed several times with water, dried and recrystallized from ethanol.

4,5,6-Triphenyl-morpholinopyridazine (13c): Yield 91 %; Mp. 190-191 °C. IR (KBr) cm−1: 3390, 3060, 2912, 1115. 1H NMR, δ ppm (DMSO-d6): 3.57 (m, 4H, CH2NCH2), 3.69 (m, 4H, CH2OCH2), 7.41-7.98 (m, 13H, aromatic-H). MS (m/z): 416 (M⁺ + 1, 61%), 404 (M⁺ - CH2OH, 100%), 390 (M⁺ - CH2CH2OH, 100%). Anal. Calcd. for C26H22N3O: C, 79.16; H, 4.79; N, 10.65. Found: C, 79.00; H, 6.00; N, 10.40.

4,5,6-Bis[4-chlorophenyl]-3-morpholinopyridazine (13d): Yield 87 %; Mp. 219-221 °C. IR (KBr) cm−1: 3409, 3058, 2912, 1115. 1H NMR, δ ppm (DMSO-d6): 3.56 (m, 4H, CH2NCH2), 3.65 (m, 4H, CH2OCH2), 7.41-7.98 (m, 13H, aromatic-H). MS (m/z): 462 (M⁺ + 1, 66.9%), 460 (M⁺ - H2, 61%), 376 (M⁺-morpholino, 8.27%). Anal. Calcd. for C27H24N3O: C, 76.39; H, 4.79; N, 9.07. Found: C, 76.20; H, 4.40; N, 9.00.

Preparation of 5,6-ary1-4-phenyl-3-piperidinopyridazine (13e,f)

To a solution of 3-chloro derivative 10a,b (1.0 mmol) in ethanol (25 mL), piperidine (1 mL, 12.0 mmol) was added, the reaction mixture was refluxed for 15 hours. The cooled reaction mixture was poured onto water (100 mL). A precipitate which obtained was filtered, washed several times with water, dried and recrystallized from benzene to give 13e,f.
4,5,6-Triphenyl-3-piperidinopyridazine (13c): yield 68.1 %; Mp. 235-237 °C; as reported.10c

5,6-Bis(4-chlorophenyl)-3-piperidino-4-phenylpyridazine (13f): yield 85%; Mp. 208-210 °C. IR (KBr) cm\(^{-1}\): 3052, 2844, 760. \(^{1}\)H NMR, δ ppm (DMSO-\(d_6\)): 1.53-1.59 (m, 6H, CH\(_2\)CH\(_2\)CH\(_3\) ), 3.71 (t, 4H, CH\(_2\)NCH\(_2\) ), 7.41-7.79 (m, 13H, aromatic-H). Anal. Calcd for C\(_{25}\)H\(_{23}\)N\(_5\)S: C, 70.56; H, 5.44; N, 16.46. Found: C, 70.40; H, 5.30; N, 16.40.

Preparation of 5,6-diarylo-3-hydrazino-4-phenylpyrazidines (13g,h)

To a solution of 3-chloro derivatives 10a,b (10.0 mmol) in 1-butanol (20 mL), hydrazine hydrate (6 mL, 80%) was added. The reaction mixture was refluxed for 8 hours, after cooling the solid product formed was filtered, dried and recrystallized from ethanol.

3-Hydrazino-4,5,6-triphenylpyridazine (13g): Yield 88 %; Mp. 229-231 °C. IR (KBr) cm\(^{-1}\): 3470, 3355, 3200, 1620, 1560. \(^{1}\)H NMR, δ ppm (DMSO-\(d_6\)): 7.50-7.70 (m, 15H, Ph-H). MS (m/z): 391 (M\(^+\), 0.6%), 363 (M\(^+\) - C\(_2\)H\(_5\), 100%). Anal. Calcd for C\(_{25}\)H\(_{23}\)N\(_5\): C, 76.40; H, 5.10; N, 17.60. Found: C, 76.10; H, 4.80; N, 18.20.

5,6-Bis(4-chlorophenyl)-3-hydrazino-4-phenylpyridazine (13h): Yield 65%; Mp. 220-222 °C; IR (KBr) cm\(^{-1}\): 3247, 3262, 3063, 1491, 730. \(^{1}\)H NMR, δ ppm (DMSO-\(d_6\)): 2.0 (s, 2H, NH\(_2\) ), 4.0 (s, 1H, NH), 7.41-7.79 (m, 13H, aromatic-H). Anal. Calcd for C\(_{25}\)H\(_{23}\)N\(_5\): C, 76.40; H, 3.96; N, 13.76. Found: C, 76.40; H, 3.80; N, 13.60.

Preparation of N-(4,5,6-triphenylpyridazin-3-yl)-N’-[alkylthio(carbamoyl)]hydrazine (14a,b)

A solution of 3-hydrazino derivative 13g (1.7 g, 5.0 mmol) and equimolar amount of alkyl isothiocyanate (5.0 mmol) in acetone (30 mL), potassium hydroxide (0.6 mL, 2N) was added. The reaction mixture was heated under reflux for 6 hrs; the solvent was evaporated under reduced pressure. The residue was dissolved in water (100 mL) and neutralized with hydrochloric acid. The solid product obtained was filtered, dried and recrystallized from ethanol to give the title compounds 15a,b

3-Methylamino-6,7,8-triphenyl-1,2,4-triazolo[4,3-b]pyridazine (15a): Yield 56.5%; Mp. 215-217 °C. IR (KBr) cm\(^{-1}\): 3375, 3049, 2979. \(^{1}\)H NMR, δ ppm (DMSO-\(d_6\)): 2.91 (s, 3H, CH\(_3\) ), 4.0 (s, 1H, NH), 7.41-7.79 (m, 15H, 3Ph-H). MS (m/z): 377 (M\(^+\), 3%), 362 (M\(^+\) - CH\(_3\) , 1.4%). Anal. Calcd for C\(_{25}\)H\(_{23}\)N\(_5\): C, 76.70; H, 5.07; N, 18.56. Found: C, 76.10; H, 4.80; N, 18.20.

3-Ethylamino-6,7,8-triphenyl-1,2,4-triazolo[4,3-b]pyridazine (15b): Yield 51 %; Mp. 220-221 °C. IR (KBr) cm\(^{-1}\): 3365, 3020, 2969. \(^{1}\)H NMR, δ ppm (DMSO-\(d_6\)): 1.14 (t, 3H, CH\(_3\) ), 3.47 (q, 2H, CH\(_2\) ), 7.41-7.79 (m, 15H, 3Ph-H). MS (m/z): 391 (M\(^+\), 0.6%), 363 (M\(^+\) - C\(_2\)H\(_5\) , 100%). Anal. Calcd for C\(_{26}\)H\(_{25}\)N\(_5\): C, 76.70; H, 5.41; N, 17.89. Found: C, 76.40; H, 5.10; N, 17.60.

Method B: To a solution of compound 14a,b (5.0 mmol) in acetone (30 mL), potassium hydroxide (0.6 mL, 2N) was added. The reaction mixture was refluxed for 6 hours, the same work-up as in method A, gave 70% yield of 15a and 66% yield of 15b. It was identical with that prepared by method A.

Insecticidal activity

Out of the synthesized compounds, only compounds 3a, 5a, 10b, 12, 13a and 15b were examined for their insecticidal activity against two insects viz. *Mucsa domestica* and Aphid. *Macrophium pisi* by dipping method\(^{(2)}\) at 500 ppm concentration.

Results and Discussion

The parents 4-carboethoxy-5,6-diarylpyrazidin-3(H)-ones 1a,b and 5,6-diaryl-4-phenyl-pyrazidin-3(2H)-ones 2a,b required in the present work were prepared more conveniently and in higher yields starting from benzil (p,p’-dichlorobenzilmonohydrazone with diethyl malonate and with ethyl phenylacetate in presence of sodium ethoxide as described earlier\(^{(18)}\) (Scheme 1).

Ethyl 3-chloro-5,6-diarylpyrazidin-4-carboxylates 3a,b were conveniently prepared in good yields by treatment of 4-carboethoxy-5,6-diarylpyrazidin-3(2H)-ones 1a,b with phosphoryl chloride at refluxing temperature. The structures of compounds 3a,b were established on the basis of their spectroscopic data. The IR spectra showed an absorption bands at 1735 and at 1734 cm\(^{-1}\) referred to ester carbonyl groups and no absorption bands referred to amide carbonyl groups.
On reacting compounds 3a,b with one equivalent of sodium azide in boiling ethanol gave the corresponding tetrazolopyridazine derivatives 4a,b.\(^\text{11}\) Wherein 3-azido derivatives were formed at the first step in these reactions and intramolecular cyclization to the tetrazole derivatives 4a,b occurred immediately. The predominant existence of tetrazole derivatives were supported by the IR spectral data, which exhibited no absorption bands around 2200 cm\(^{-1}\). The mass spectrum of ethyl 6,7-bis(4-chlorophenyl)tetrazolo-[1,5-b]pyridazine-8-carboxylate 4b could be accounted as follows: the molecular ion at m/z 414 underwent the following fragmentation. It could be lose COOEt to give the ion at m/z 343, which in turn gives rise to the ion at m/z 330 by lose of (N, COOEt), this ion lose 2N to give the ion at m/z 303.

Scheme 2.

The starting 3a,b required for the synthesis of pyrazolopyridazines 5a,b is important synthesis for annelations of pyrazole such compounds 3a,b on reaction with hydrazine hydrate in boiling 1-butanol gave 3-hydroxy-4,5-diaryl-1H-pyrazolo[3,4-c]pyridazine 5a,b in a good yields. Mechanistically the formation of 5a,b involve the nucleophilic substitution of hydrazine at carbon-3, which undergoes immediate intramolecular nucleophilic cyclathion of the hydrazine primary amino group to the carboxethoxy group with elimination of ethanol molecule (Scheme 3).

Scheme 3.

With a view of studying some of the reaction of 5a, it was allowed to react with excess of ethyl chloroformate at reflux temperature, a crystals deposited during the refluxing time, as a single product. The isolated product was proven to be 2-carbethoxy-4,5-diphenyl-3-oxo-1H-pyrazolo[3,4-c]pyridazine 6. As the progress of the reaction was monitored by TLC, the possibility of a side reaction through the oxygen substituted could not obtain. The assignment of structure 6 was based on an analytical and spectral data.

Also, the reaction of compound 5a with ethyl isothiocyanate in presence of potassium hydroxide in boiling acetone furnished 2-substituted product 7 as the only product.

Heating a mixture of 4-carbethoxy-5,6-diarylpyridazin-3(2H)-ones 1a,b with hydrazine hydrate in 1-butanol gave the corresponding 4,6-diaryl-2,3-dihydro-3-oxopyridazine-4-carbocydrazone 8a,b (Scheme 4). The reaction of this carbohydrazide with one equivalent of sodium nitrite in hydrochloric acid at 5°C, afforded the acid azide intermediate, the latter when heated gave the carboxylic acid derivatives 9a,b rather than the corresponding 4-amino derivatives, via Curtius rearrangement on the basis of spectral data and elemental analysis. The formation of 4-carboxy derivatives involves a nucleophilic substitution of water to the 4-carbonylazide group with elimination of hydrazoic acid. Also, the structures were assigned by comparison with authentic samples prepared from the basic hydrolysis followed by neutralization of 4-carboxethoxy derivatives 1a,b.

Scheme 4.

Compounds 2a,b were also separately reacted (Scheme 5) with phosphoryl chloride at refluxing temperature gave the corresponding 3-chloro derivatives 10a,b. Since the reactivity of the chlorine atoms were expected, the compounds were subjected to nucleophilic substitution reactions to obtained the next derivatives of the ring systems.

On reacting compounds 10a,b with sodium azide afforded tetrazolo derivatives 11a,b in a single step in 73% and 79% respectively.

The pyridazine derivatives 12 was easily obtained in 88% yield by the reaction of 6,7,8-triphenyltetrazolo[1,5-a]pyridazine 11a with triphenylphosphine in refluxing 1,2-dichlorobenzene (b.p. 179°C).

Compounds 10a,b were also separately reacted with ethanolamine, morpholine, piperidine and/or hydrazine to afforded 3-substituted pyridazines 13a-f.

Reacting equimolecular quantities of the 3-hydrazino derivatives 13e and alkyl isothiocyanate in boiling acetone yielded the corresponding N-(4,5,6-triphenylpyridazin-3-yl)-N′-alkylthio(carbomyl)hydrazines 14a,b in 95% and 92% yield respectively. On the other hand, reaction of compound 13a with alkyl isothiocyanate in boiling 2N acetic potassium hydroxide afforded, unexpectedly a single product. The isolated product was proved to be
identical in every respect with 3-alkylamino-6,7,8-triphenyl-1,2,4-triazolo[3,4-b]pyridazines \(15a,b\). Mechanistically, the formation of tricyclic derivatives \(15a,b\) from \(13\) involves the initial formation of \(14a,b\) which undergo immediate intramolecular nucleophilic attack of ring-2 nitrogen on thione group with elimination of hydrogen sulfide molecule. This mechanism was proved by converting \(14a,b\) to \(15a,b\) upon boiling in acetone potassium hydroxide indicates that \(14a,b\) are thermostable at the boiling point of acetone.

The compounds \(5b\) and \(13a\) showed good activities (Table 1). The other tested compounds showed lower activity as compared to the standard insecticides Diazinox and Carbosulfan. From the insecticidal data, it is clear that the combination of chloro atom at position 4 of the phenyl ring with hydroxyprazolopyridazine works better, the maximum (+++) against \(Mucsa domestica\) was observed with compound \(5b\). Ethanolamino derivative in compound \(13a\) has the maximum (+++) against \(Macrosiphum pisi\).

\[
\varphi = 100 \times \frac{N_1}{N_2} \quad (1)
\]

where
- \(\varphi\) - mortality in %
- \(N_1\) - no. of dead insects
- \(N_2\) - no. of insects released

Mortality is indicated by symbols (-) \(\approx 0-20\%\), (+) \(\approx 21-40\%\), (+++) \(\approx 41-60\%\), (++++) \(\approx 61-80\%\), (++++) \(\approx > 80\%\).

### Table 1. Insecticidal activity (mortality %) of compounds \(3a, 5a, 6, 10b, 12, 13a\) and \(15b\)

<table>
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<th>Compounds</th>
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<th>(Macrosiphum pisi)</th>
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<tbody>
<tr>
<td>(3a)</td>
<td>++</td>
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<tr>
<td>(5a)</td>
<td>++</td>
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<tr>
<td>(5b)</td>
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<td>(6)</td>
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<td>(10b)</td>
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<td>(12)</td>
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<td>(13a)</td>
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<td>(16b)</td>
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Table 1. Insecticidal activity (mortality %) of compounds \(3a, 5a, 6, 10b, 12, 13a\) and \(15b\)

**References**


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