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SYNTHESIS OF PYRIDAZINE DERIVATIVES—V[1]

FORMATION OF s-TRIAZOLO-(4,3-b)-PYRIDAZINES AND BIS-s-TRIAZOLO-(4,3-b,3',4'-f)-PYRIDAZINES

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Abstract—3-Substituted s-triazolo-(4,3-b)-pyridazines (III) and some derivatives have been prepared from II or IV by oxidative or thermal cyclization. The reaction has been extended to the preparation of 3,6-di-substituted bis-s-triazolo-(4,3-b,3',4'-f)-pyridazines (VIII)—a new heterocyclic system—also formed from a bis-arylidene derivative of 3,6-dihydrazinopyridazine (X) in one reaction step.

IN ADDITION to the formation of some bicyclic heterocyclic systems based on pyridazine and described recently,[2] the preparation of different bis-s-triazolo-(4,3-b,3',4'-f)-pyridazines with a ring system hitherto unknown are now reported.

The route was either via (1) the appropriate s-triazolo-(4,3-b)-pyridazines with formations of a new triazole ring or (2) an appropriate pyridazine and formation of both triazole rings in one reaction step. The formation of s-triazolo-(4,3-b)-pyridazines[3] have been described only in a few cases. The products of various β-keto esters with 4-amino-1,2,4-triazole formulated as derivatives of s-triazolo-(4,3-b)-pyridazine, have not had their structures unambiguously ascertained.[7–9] Some controversy arose regarding these structures as the reaction[10] of acetoacetic ester with 4-amino-1,2,4-triazole yields 6-methyl-8-hydroxy-s-triazolo-(4,3-b)-pyridazine as first postulated[8] and not 8-methyl-5,6-dihydro-6-oxo-s-triazolo-(4,3-b)-pyridazine as suggested later.[11] Another method for the preparation of the desired ring system was treatment of a hydrazinopyridazine with formic acid, ethyl formate, triethyl orthoformate or acetic anhydride[5,12] and this method was used successfully for the preparation of the parent compound.[13]

In an attempt to extend this cyclization for the formation of a second fused triazole ring it was found that under conditions similar to those applied for the preparation of the s-triazolo-(4,3-b)-pyridazines, only the 6-formylhydrazino derivative

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[2] A. Pollak and M. Tišler, *Tetrahedron* **21**, 1323 (1965).
[3] The s-triazolo-(4,3-b)-pyridazine system is referred to in the literature as a 2,3,7-triazaindolizine[4] or a 2,3-triazolo-7,0'-pyridazine.[5,6]
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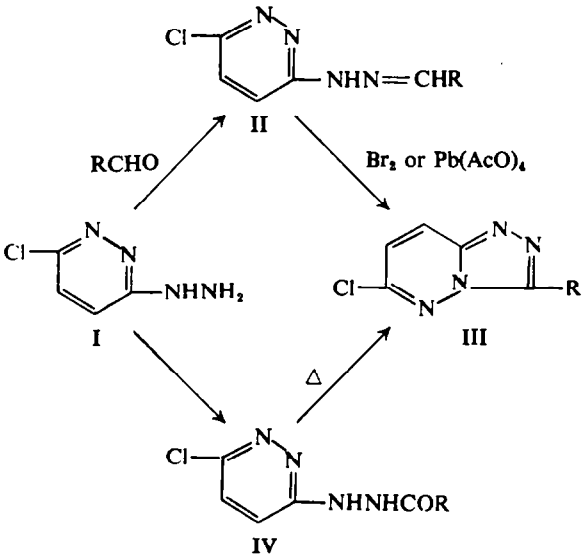
was obtained.[10] Thus ring closure to a bis-s-triazolo-(4,3-b,3',4'-f)-pyridazine proved unsuccessful.

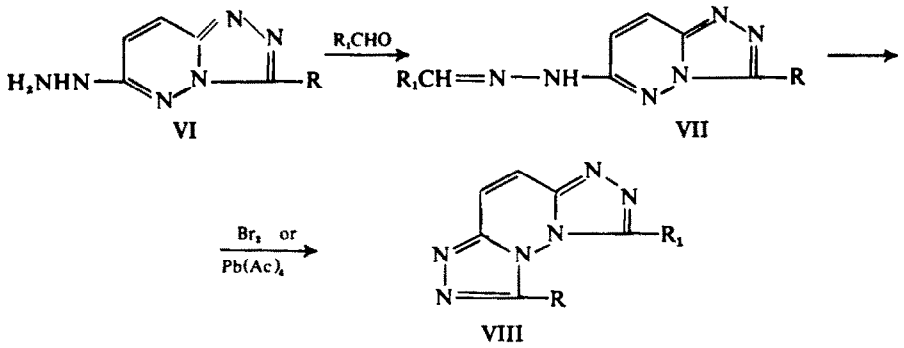
For the preparation of different s-triazolo-(4,3-b)-pyridazines two different methods have been used. The first utilized the condensation of 3-hydrazino-6-chloropyridazine (I) with different aldehydes giving rise to the corresponding alkylidene or arylidene derivatives (II) which could be cyclized by means of bromine in acetic acid or with lead tetraacetate to III. The second method involved the use of acylated hydrazinopyridazine (IV, R = C_6H_5—) which on heating and dehydration was transformed into the same ring system.



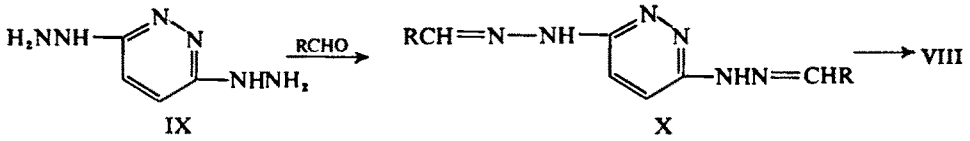
Since III as a starting material has interesting possibilities for further synthetic work, the chlorine was replaced with different nucleophiles and mercapto, substituted mercapto, amino, substituted amino and hydrazino derivatives (V, R_1 = SH, SCH_3, SCH_2OH, SC_6H_5, NH_2, NRR, $NHNH_2$, R = C_6H_5 or CH_3) were prepared.

The 3-phenyl-6-mercapto-s-triazolo-(4,3-b)-pyridazine can exist in the mercapto or the alternative thioamide form, but the proposed structure (V, R = C_6H_5, R_1 = SH) is supported by the presence of a typical SH absorption band at 2545 cm^{-1} in the IR spectrum.

The route described for the preparation of III was extended to the preparation of VIII. Thus a 3-substituted 6-hydrazino-s-triazolo-(4,3-b)-pyridazine (VI) was condensed with an aliphatic or aromatic aldehyde and the corresponding alkylidene or arylidene derivative (VII) converted into the tricyclic compound (VIII) following the dehydrogenative cyclization used for the preparation of III.



Alternatively, this ring system can be obtained by direct cyclization. 3,6-Dihydrazinopyridazine (IX) was converted into the bis-arylidene derivative (X) which was then dehydrocyclized to VIII.



Both dehydrogenative cyclizations using bromine in acetic acid or lead tetraacetate afford the same cyclic compounds in reasonably good yields. It is quite probable that a similar reaction mechanism—a substitution-elimination process—is operating in each case. It is known that bromination of arylidene hydrazones includes substitution of the methine hydrogen,[14] but benzylidene-2-pyridylhydrazones behave differently and form first an addition product which can be isolated and in the presence of bases the elimination of hydrogen bromide is followed by cyclization.[15] Lead tetraacetate has been used for purposes of preparing azaheterocyclic compounds,[16–20] but if arylhydrazones or carbethoxyhydrazones of aliphatic or aromatic ketones were treated with $Pb(AcO)_4$, the corresponding azo compounds, e.g. azoacetates[16,21,22] were obtained and for this reaction a free radical mechanism sequence was proposed. The azoacetates could be further cyclized in the presence of a Lewis acid,[16] but in the above cyclizations the formation of such intermediates were not observed.

A correlation of the UV spectral data of II with those of III indicates that the cyclization results in a shift of the short and long wavelength bands to longer wavelengths. This displacement of the $n \rightarrow \pi^*$ band is consistent with the introduction of two more nitrogens in the new heteroaromatic ring system[23–25] and a similar

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displacement is observed when comparing the spectra of related pyrido-(2,1-c)-s-triazoles[25] with those of III. This shift is a result of the replacement of an α-CH=group in the pyridine ring by nitrogen. The UV spectrum of VIII differs from that of III in that it exhibits only one absorption band in the 245–296 mμ region. This is consistent with the contribution of both s-triazole ring systems[26,27] the properties of which dominate over those of the central pyridazine ring.

Finally, the NMR spectra of III (R = CH_3), V (R = C_6H_5, R_1 = CH_3S) and VIII (R = R_1 = CH_3) were recorded and are consistent with the proposed structures.

EXPERIMENTAL

UV spectra were measured with a Beckman Model DU spectrophotometer. IR spectra were obtained with a Perkin–Elmer spectrophotometer Model 21 equipped with a NaCl prism. NMR spectra were determined using a Varian A-60 at approximately 40° and concentration of 0·5 M. M.ps were determined on a Kofler heating microscope.

6-Hydrazino-s-triazolo-(4,3-b)*-pyridazine* was synthesized from 6-chloro-s-triazolo-(4,3-b)-pyridazine[5] (λ_{max}^{EtOH} 290 mμ, ε 2,160) according to the procedure of Takahayashi,[18] m.p. 222–223°, λ_{max}^{EtOH} 290 mμ (ε 8,100). *3-Methyl-6-chloro-s-triazolo-*(4,3-b)*-pyridazine* was prepared according to Takahayashi,[5] m.p. 104–105°, λ_{max}^{EtOH} 270 and 314 mμ (ε 3,680 and 2,140). NMR (pyridine, TMS as internal standard): singlet τ_{CH_3} = 8·15 and quartet centered at τ_{H_7,H_8} = 1·82, J = 10 c/s in ratio 3:2. *3-Hydrazino-6-chloropyridazine* was prepared from 3,6-dichloropyridazine.[28]

Formation of hydrazones of 3-hydrazino-6-chloropyridazine (II)

The hydrazones were prepared from the appropriate aliphatic or aromatic aldehydes and 3-hydrazino-6-chloropyridazine by adopting the general procedure.[29,30] The hydrazones were purified from a mixture of toluene and N,N-dimethylformamide (2:1).

(i) *6-Chloropyridazinyl-3-hydrazone of acetaldehyde* (II, R = CH_3), m.p. 205–206°. (Found: C, 42·57; H, 4·31; N, 32·90 $C_6H_7ClN_4$ requires: C, 42·42; H, 4·13; N, 32·84%), λ_{max}^{EtOH} 270 mμ (ε 22,050).

(ii) *6-Chloropyridazinyl-3-hydrazone of benzaldehyde* (II, R = C_6H_5), m.p. 263–264°. (Found: C, 56·67; H, 4·10; N, 23·97; $C_{11}H_9ClN_4$ requires: C, 56·78; H, 3·90; N, 24·08%), λ_{max}^{EtOH} 225 and 316 mμ (ε 11,150 and 32,800).

(iii) *6-Chloropyridazinyl-3-hydrazone of p-chlorobenzaldehyde* (II, R = *p*-Cl—C_6H_4—), m.p. 295–296°. (Found: C, 49·60; H, 3·29; N, 20·88. $C_{11}H_8Cl_2N_4$ requires: C, 49·46; H, 3·01; N, 20·97%), λ_{max}^{EtOH} 240 and 323 mμ (ε 12,750 and 35,700).

(iv) *6-Chloropyridazinyl-3-hydrazone of p-methoxybenzaldehyde* (II, R = *p*-CH_3O—C_6H_4—), m.p. 225–226°. (Found: C, 55·19; H, 4·35; N, 21·54. $C_{12}H_{11}ClN_4O$ requires: C, 54·86; H, 4·23; N, 21·33%), λ_{max}^{EtOH} 250 and 323 mμ (ε 8,750 and 35,400).

Benzoyl derivative of 3-hydrazino-6-chloropyridazine (IV)

To a stirred solution of I (1·45 g) in pyridine (15 ml) benzoyl chloride (1·4 g) was added dropwise. After the exothermic reaction had subsided, the mixture was left at room temp for 3 hr and thereafter poured onto 60 g ice. The crude product was washed with water, air dried and crystallized from AcOEt yielding 1·65 g (65%) of colourless crystals, m.p. 83–84°. (Found: C, 52·91; H, 4·06; N, 22·23. $C_{11}H_9ClN_4O$ requires: C, 53·13; H, 3·64; N, 22·53%), λ_{max}^{EtOH} 274 mμ (ε 17,700).

3-Phenyl-6-chloro-s-triazolo-(4,3-b)*-pyridazine* (III, R = C_6H_5)

a. Compound II (R = C_6H_5; 1·16 g) was suspended in glacial AcOH (50 ml) and anhydrous AcONa (1·23 g) was added. To this stirred mixture a solution of Br_2 (0·8 g) in glacial AcOH (10 ml)

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was added dropwise. The hydrazone dissolved and the solution after 30 min was poured into water (200 ml). The separated crystals were collected, washed with water, dried and crystallized from AcOEt, m.p. 200–201°. (Found: C, 56·86; H, 3·52; N, 24·49. $C_{11}H_7ClN_4$ requires: C, 57·28; H, 3·06; N, 24·29%), λ_{max}^{EtOH} 252 and 339 mμ (ε 22,350 and 1,960).

b. Compound II (R = C_6H_5; 0·8 g) was heated on an oil bath at 160° and from the resulting melt after few min crystals began to separate. Heating was continued for 10 min and the crude product (0·65 g) then crystallized from AcOEt as colourless needles, m.p. 201–202°. Mixed m.p. with the compound obtained under (a) showed no depression.

Similarly, as described under (a) the following compounds were prepared:

(i) 3-(p-*Chlorophenyl*)-6-*chloro-s-triazolo*-(4,3-b)-*pyridazine* (III, R = *p*-Cl—C_6H_4), m.p. 193–194°. (Found: C, 49·84; H, 2·08; N, 21·16. $C_{11}H_6Cl_2N_4$ requires: C, 49·84; H, 2·28; N, 21·13%), λ_{max}^{EtOH} 260 and 328 mμ (ε 22,900 and 1,865).

(ii) 3-(p-*Methoxyphenyl*)-6-*chloro-s-triazolo*-(4,3-b)-*pyridazine* (III, R = *p*-CH_3O—C_6H_4), m.p. 211–212°. (Found: C, 55·28; H, 3·65; N, 21·78. $C_{12}H_9ClN_4O$ requires: C, 55·29; H, 3·48, N, 21·50%), λ_{max}^{EtOH} 267 and 350 mμ (ε 19,350 and 1,500).

3-*Phenyl-6-mercapto-s-triazolo*-(4,3-b)-*pyridazine* (V, R = C_6H_5, R_1 = SH)

In a freshly prepared ethanolic solution of KHS (1·4 g KOH were dissolved in 25 ml EtOH and H_2S introduced until pH 7) 3-phenyl-6-chloro-s-triazolo-(4,3-b)-pyridazine (2·3 g) was suspended and the mixture refluxed for 3 hr. After cooling 100 ml water were added and the mixture acidified with conc. HCl to pH 1. The resulting precipitate was filtered off and thoroughly washed with water. After drying *in vacuo* the product was dissolved in a 5% $NaHCO_3$aq, filtered and the filtrate acidified to pH 1 with HCl. The resulting precipitate was washed with water, dried in *vacuo* and recrystallized from AcOEt as yellow crystals, m.p. 151–152°, yield 2·0 g (88%). (Found: C, 58·23; H, 3·82; N, 24·27; S, 13·65. $C_{11}H_8N_4S$ requires: C, 57·90; H, 3·53; N, 24·55; S, 14·02%), λ_{max}^{EtOH} 238 mμ (ε 16,700). The IR spectrum showed a band at 2545 cm^{-1} (SH).

3-*Phenyl-6-methylmercapto-s-triazolo*-(4,3-b)-*pyridazine* (V, R = C_6H_5, R_1 = SCH_3)

Compound V (R = C_6H_5, R_1 = SH) was dissolved in KOHaq (0·3 g in 10 ml water) and a solution of 0·75 g MeI in 5 ml EtOH added. The mixture was shaken vigorously and after few min crystals separated but shaking was continued for 30 min. The product was washed with water, dried (1·0 g, 83%) and crystallized from AcOEt as colourless needles, m.p. 141–142°. (Found: C, 59·64; H, 4·45; N, 22·93; S, 13·50. $C_{12}H_{10}N_4S$ requires: C, 59·50; H, 4·16; N, 23·13; S, 13·21%), λ_{max}^{EtOH} 228 and 268 mμ (ε 15,100 and 19,500). NMR (acetone, TMS as internal standard): quartet centered at τ_{H_7,H_8} = 1·85 and 2·75, multiplet centered at τ_ϕ = 2·40, J = 10 c/s in ratio 2:5.

3-*Phenyl-6-phenylmercapto-s-triazolo*-(4,3-b)-*pyridazine* (V, R = C_6H_5, R_1 = SC_6H_5)

Sodium (0·12 g) was allowed to react in abs. EtOH (20 ml) and thereafter thiophenol (0·55 g) and 3-phenyl-6-chloropyridazine (1·1 g) were added. The reaction mixture was heated under reflux for 2 hr and after cooling was diluted with 100 ml water. The colourless precipitate was filtered off and washed with water. The dried product (1·2 g, 80%) was crystallized from EtOH–AcOEt (1:1), affording colourless crystals, m.p. 212–213°. (Found: C, 67·15; H, 3·95; N, 18·45; S, 10·78. $C_{17}H_{12}N_4S$ requires: C, 67·09; H, 3·98; N, 18·41; S, 10·52%), λ_{max}^{EtOH} 272 mμ (ε 20,490).

3-*Phenyl-6-hydroxymethylmercapto-s-triazolo*-(4,3-b)-*pyridazine* (V, R = C_6H_5, R_1 = SCH_2OH)

To 1·1 g of V (R = C_6H_5, R_1 = SH) 35% HCHOaq (2 ml) were added. After the initial exothermic reaction the mixture was left at room temp for 3 hr. The crude product was crystallized from AcOEt, m.p. 160–161°, yield 1·0 g (80%). (Found: C, 56·06; H, 4·09; N, 21·89; S, 12·31. $C_{12}H_{10}N_4OS$ requires: C, 55·81; H, 3·90; N, 21·70; S, 12·40%), λ_{max}^{EtOH} 275 mμ (ε 22,500).

3-*Phenyl-6-amino-s-triazolo*-(4,3-b)-*pyridazine* (V, R = C_6H_5, R_1 = NH_2)

A mixture of III (R = C_6H_5, 2·3 g) and 35 ml liquid ammonia were placed in an autoclave and heated 2 hr at 75°. On cooling the autoclave was vented and to the residue 50 ml water was added. The reaction product was washed with water and dried to yield 2·0 g crude material which crystallized from AcOEt–EtOH (5:1) as colourless crystals, m.p. 226–227°. (Found: C, 62·81; H, 4·71; N, 33·16. $C_{11}H_9N_5$ requires: C, 62·55; H, 4·30; N, 33·16%), λ_{max}^{EtOH} 266 mμ (ε 21·750).

3-Phenyl-6-piperidino-s-triazolo-(4,3-b)-pyridazine (V, R = C_6H_5, R_1 = $N(CH_2)_5$)

A solution of III (R = C_6H_5; 1·15 g) in EtOH (10 ml) and piperidine (1·5 g) was refluxed for 3 hr. The solvent was evaporated *in vacuo* and 30 ml water was added to the residue. The resulting precipitate was dried and recrystallized from AcOEt yielding 1·2 g (84%) colourless crystals, m.p. 166–167°. (Found: C, 68·42; H, 6·13; N, 25·29. $C_{16}H_{17}N_5$ requires: C, 68·79; H, 6·13; N, 25·07%), λ_{max}^{EtOH} 272 mμ (ε 20,490).

3-Phenyl-6-hydrazino-s-triazolo-(4,3-b)-pyridazine (V, R = C_6H_5, R_1 = $NHNH_2$)

To a solution of III (R = C_6H_5; 2·3 g) in EtOH (15 ml) hydrazine hydrate (2·0 g of 80%) was added. The mixture was heated under reflux for 3 hr, most of the solvent evaporated *in vacuo*, the residue filtered off and washed with a little water. The dried crude product (1·9 g) was crystallized from water and afforded colourless needles, m.p. 261–262°. (Found: C, 58·20; H, 4·25; N, 36·99. $C_{11}H_{10}N_6$ requires: C, 58·39; H, 4·46; N, 37·15%), λ_{max}^{EtOH} 270 mμ (ε 18,600).

3-Phenyl-(bis-s-triazolo-(4,3-b, 3',4'-f)-pyridazine) (VIII, R = H, R_1 = C_6H_5)

a. *Benzylidene s-triazolo-(4,3-b)-pyridazine-6-hydrazone* (VII, R = H, R_1 = C_6H_5). To a solution of 6-hydrazino-s-triazolo-(4,3-b)-pyridazine[18] in hot EtOH (20 ml) freshly distilled benzaldehyde (1·1 g) was added. The mixture was heated under reflux for 20 min, cooled, filtered and the product washed with EtOH. The crude product was crystallized from a mixture of toluene and N,N-dimethylformamide giving rise to colourless crystals, m.p. 303–304°, yield 2·0 g (83%). (Found: C, 60·70; H, 4·26; N, 35·09. $C_{13}H_{10}N_6$ requires: C, 60·49; H, 4·23; N, 35·28%), λ_{max}^{EtOH} 230 and 303 mμ (ε 17,590 and 20,450).

b. *Cyclization of the hydrazone with bromine in glacial acetic acid.* To a suspension of the above hydrazone (1·2 g) and anhydrous AcONa (1·25 g) in glacial AcOH (15 ml) a solution of 0·25 ml Br_2 in glacial AcOH (3 ml) was added dropwise. Some heat is evolved and a clear solution resulted. The reaction mixture was left for 30 min then 30 ml water was added and the solution neutralized with $NaHCO_3$. The precipitated crude bis-s-triazolopyridazine was dried and crystallized from EtOH as colourless plates (0·7 g, 58%), m.p. 242–243°. (Found: C, 60·70; H, 3·50; N, 35·68. $C_{13}H_8N_6$ requires: C, 61·00; H, 3·41; N, 35·59%), λ_{max}^{EtOH} 290 mμ (ε 8,100).

c. *Cyclization of the hydrazone with lead tetraacetate.* A stirred suspension of the above hydrazone (1·2 g) in glacial AcOH (15 ml) was treated with $Pb(AcO)_4$ (2·3 g). During the exothermic reaction the hydrazone dissolved and the reaction mixture was left for 30 min. After the addition of 30 ml water, $NaHCO_3$ was added to neutralize the solution. A reddish precipitate was formed and was separated by filtration, washed with little water and crystallized from water, yield 0·75 g (62%). A mixed m.p. with the compound obtained according to the procedure under (b) showed no depression and IR spectra were identical.

3-Methyl-6-phenyl-(bis-s-triazolo-(4,3-b, 3',4'-f)-pyridazine) (VIII, R = C_6H_5, R_1 = CH_3)

a. *3-Methyl-6-hydrazino-s-triazolo-(4,3-b)-pyridazine* (VI, R = CH_3). A mixture of III (R = CH_3; 3·4 g), hydrazine hydrate (3·7 ml of 80%) and EtOH (5 ml) was refluxed for 1 hr. The solvent was evaporated to dryness and the residue diluted with 10 ml iced water. The brown precipitate was washed with some iced water and dried *in vacuo* over KOH. The product (2·0 g, 60%) was purified from water–MeOH (3:1) giving rise to almost colourless crystals, m.p. 235–236°. (Found: C, 43·48; H, 5·02; N, 51·79. $C_6H_8N_6$ requires: 43·89; H, 4·91; N, 51·90%), λ_{max}^{EtOH} 228 and 286 mμ (ε 21,000 and 4,780).

b. *Benzylidene derivative* (VII, R = CH_3, R_1 = C_6H_5). This was prepared from the above hydrazino compound (1·6 g) and a solution of benzaldehyde (1·1 g) in EtOH (20 ml). After 30 min of heating under reflux the product was separated and crystallized from N,N-dimethylformamide–toluene (1:2) to afford colourless crystals, m.p. 292–293°, yield 2.0 g (79%), (Found: C, 62·25; H, 4·99; N, 33·14. $C_{13}H_{12}N_6$ requires: C, 61·89; H, 4·79; N, 33·32%), λ_{max}^{EtOH} 230 and 308 mμ (ε 19,500 and 26,200).

c. *Cyclization of the benzylidene derivative.* Cyclization was accomplished with Br_2 in glacial AcOH in essentially the same manner as described in the case of compound III. The product (0·8 g, 65%) was crystallized from EtOH–N,N-dimethylformamide (2:1) as colourless plates, m.p. 295–296°. (Found: C, 62·28; H, 4·13; N, 33·24. $C_{13}H_{10}N_6$ requires: C, 62·39; H, 4·03; N, 33·58%), λ_{max}^{EtOH} 296 mμ (ε 7,760).

3,6-*Diphenyl-(bis-s-triazolo-*(4,3-b,3′,4′-f)-*pyridazine*) (VIII, R = R_1 = C_6H_5)

a. *Bis-benzylidene derivative of* X (R = C_6H_5). A solution of 3,6-dihydrazinopyridazine[31] (0·7 g) in 90% EtOH (30 ml) was heated to boiling and freshly distilled benzaldehyde (3·2 g) was added. Refluxing was continued for 15 min, the product washed with EtOH and crystallized from toluene–N,N-dimethylformamide as colourless crystals (1·4 g, 88%), m.p. 261–262°. (Found: C, 68·08; H, 5·38; N, 26·86. $C_{18}H_{16}N_6$ requires: C, 68·33; H, 5·10; N, 26·57%), λ_{max}^{THF} 358 mμ (ε 42,400).

b. *Cyclization* of the above bis-benzylidene derivative was accomplished as described in the case of VIII (R = H, R_1 = C_6H_5), using Br_2 in glacial AcOH. The crude product (0·6 g, 77%) was crystallized from AcOEt as colourless needles, m.p. 277–278°. (Found: C, 68·99; H, 4·65; N, 26·51. $C_{18}H_{12}N_6$ requires: C, 68·77; H, 4·49; N, 26·74%), $\lambda_{max}^{cyclohexane}$ 245 mμ (ε 30,100).

c. *Cyclization with* $Pb(AcO)_4$. The above bis-benzylidene derivative (0·8 g) was dissolved in glacial AcOH (10 ml) and $Pb(AcO)_4$ (2·2 g) was added. Some heat was evolved and the reaction mixture was left at room temp for 30 min, diluted with 50 ml water and $NaHCO_3$ added portionwise until pH 7. The resulting precipitate crystallized from AcOEt as colourless needles, m.p. 277–278° (0·63 g, 70%). A mixed m.p. with the compound, prepared under (b) showed no depression.

3,6-*Di-*(p-*methoxyphenyl)-(bis-s-triazolo-*(4,3-b,3′,4′-f)-*pyridazine*) (VIII, R = R_1 = *p*-CH_3O—C_6H_4)

a. The condensation product between 3,6-dihydrazinopyridazine and *p*-methoxybenzaldehyde (X, R = *p*-$CH_3OC_6H_4$) was prepared in the manner described for the bis-benzylidene derivative. The product was crystallized from toluene–N,N-dimethylformamide as pale yellow needles, m.p. 225–226°. (Found: C, 63·76; H, 5·22; N, 22·24. $C_{20}H_{20}N_6O_2$ requires; C, 63·82; H, 5·36; N, 22·33%), λ_{max}^{EtOH} 250 and 347 mμ (ε 13,000 and 41,300).

b. This compound was cyclized with Br_2 in glacial AcOH in the manner described for VIII (R = H, R_1 = C_6H_5). The crude product was purified from a EtOH–N,N-dimethylformamide (1:2) yielding (68%) of colourless plates, m.p. 278–279°. (Found: C, 64·05; H, 4·50; N, 22·23. $C_{20}H_{16}N_6O_2$ requires: C, 64·16; H, 4·85; N, 22·45%), λ_{max}^{EtOH} 268 mμ (ε 24,650).

3,6-*Dimethyl-(bis-s-triazolo-*(4,3-b,3′,4′-f)-*pyridazine*) (VIII, R = R_1 = CH_3)

a. *Ethylidene 3-methyl-s-triazolo-*(4,3-b)-*pyridazine-6-hydrazone* (VII, R = R_1 = CH_3). A mixture of 3-methyl-6-hydrazino-s-triazolo-pyridazine (3·3 g), 90% EtOH (30 ml) and glacial AcOH (0·5 ml) was heated to boiling and a solution of acetaldehyde (2·0 g) in EtOH (10 ml) was added dropwise. The reaction mixture was refluxed for 1/2 hr, the precipitate washed with EtOH, dried and crystallized from toluene–N,N-dimethylformamide (2:1) as colourless needles, m.p. 260–261°, yield 2·8 g (78%). (Found: C, 50·80; H, 5·47; N, 44·45. $C_8H_{10}N_6$ requires: C, 50·51; H, 5·30; N, 44·19%), λ_{max}^{EtOH} 254 and 300 mμ (ε 25,950 and 5,370).

b. *Cyclization of the hydrazone.* The above hydrazone (1·9 g) was dissolved in glacial AcOH (15 ml) and anhydrous AcONa (2·8 g) was added. A solution of Br_2 (0·5 ml) in glacial AcOH (5 ml) was added dropwise during external cooling. If the temp was allowed to reach room temp, evolution of N_2 was observed and the yield was markedly affected. After standing for ½ hr the mixture was diluted with 40 ml water and neutralized with $NaHCO_3$ to pH 7. After standing at 0° for 24 hr the violet coloured precipitate was washed with water, dried and crystallized from 50% AcOH as colourless plates, m.p. 271–272°, yield 0·6 g (32%). (Found: C, 51·01: H, 4·26; N, 44·51. $C_8H_8N_6$ requires: C, 51·06; H, 4·28; N, 44·66%), λ_{max}^{EtOH} 294 mμ (ε 8,260). NMR ($(CF_3CO)_2O$, cyclohexane as internal standard): two singlets at τ_{CH_3} = 8·17 and $\tau_{H_9,H_{10}}$ = 3.45 in ratio 3:1.

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[31] J. Druey, K. Meier and K. Eichenberger, *Helv. Chim. Acta* **37**, 121 (1954).