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SYNTHESIS OF PYRIDAZINE DERIVATIVES—VIII

IMIDAZO(1,2,-b)PYRIDAZINES AND SOME TRICYCLIC AZA ANALOGS

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Abstract—6-Substituted and 3,6-disubstituted imidazo(1,2-b)pyridazines have been prepared. Some of these derivatives were used for convenient syntheses of a new azaheterocycle, imidazo(1,2-b)s-triazolo(3,4-f)pyridazine (V) and its derivatives. Another new heterocyclic system, imidazo(1,2-b)-tetrazolo-(5,1-f)pyridazine (XVI) has also been prepared.

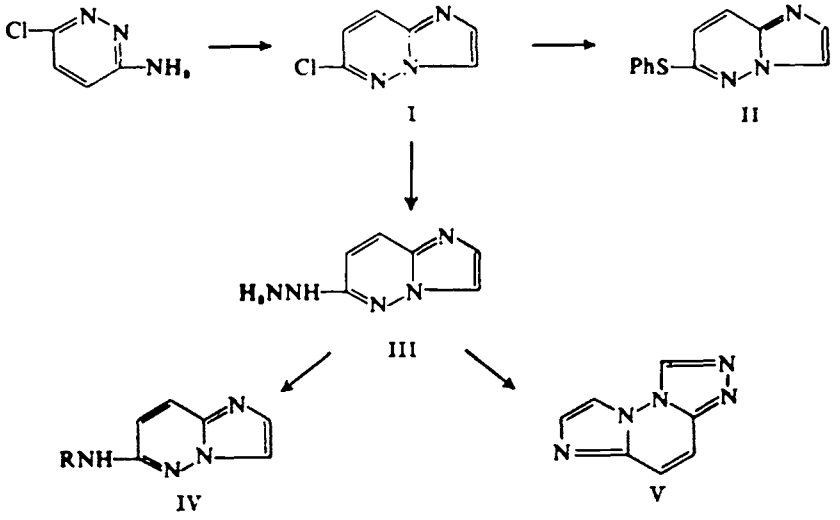
CONTINUING the investigations on some bicyclic and tricyclic systems based on pyridazine[1-3] we wish to report the synthesis and reactions of different imidazo(1, 2-b)pyridazines and some tricyclic aza analogs. Among different possible imidazo-pyridazines there are known imidazo(4,5-d)pyridazines[4-6] and some imidazo(1,2-b)-pyridazines were prepared only recently.[7-9]

The synthesis of the imidazo(1,2-b)pyridazine nucleus can be achieved most efficiently by starting with 3-amino-6-chloropyridazine and bringing about a ring closure with bromoacetaldehyde to form the 6-chloro derivative (I) in fairly good yield, rather than the reverse procedure of forming the pyridazine nucleus by a suitable cyclization reaction. Compound I formed crystalline salts with HX acids although it is considerably weaker base (pK_a 3·6 in water at 20°) than imidazole or benzim-idazole.[10] The 6-chloro group is sufficiently reactive to be replaced in nucleophilic reaction with thiophenol (II), but attempts to replace the halogen with an amino or thiol group by direct aminolysis or when using a KSH solution were unsuccessful. Likewise failure attended the attempted reaction with thiourea to give the 6-mercapto derivative. Subsequently, the 6-amino derivative (XVII) was obtained in a different way. The introduction of the hydrazino group, however, presented no difficulties and this compound (III) is a useful intermediate for the formation of another fused ring.

It is known that a fused triazole ring is formed when the corresponding heterocycle with the hydrazino group adjacent to the ring nitrogen is allowed to react

[1] A. Pollak and M. Tišler, *Tetrahedron* **21**, 1323 (1965).
[2] A. Pollak and M. Tišler, *Tetrahedron* **22**, 2073 (1966).
[3] B. Stanovnik and M. Tišler, *Tetrahedron Letters* No 22, 2403 (1966).
[4] R. N. Castle and W. S. Seese, *J. Org. Chem.* **23**, 1534 (1958).
[5] D. L. Aldous and R. N. Castle, *J. Heterocycl. Chem.* **2**, 321 (1965).
[6] G. A. Gerhardt, D. L. Aldous and R. N. Castle, *J. Heterocycl. Chem.* **2**, 247 (1965).
[7] F. Yoneda, T. Ohtaka and Y. Nitta, *Chem. Pharm. Bull. Japan* **12**, 1351 (1964).
[8] L. M. Werbel and M. L. Zamora, *J. Heterocycl. Chem.* **2**, 287 (1965).
[9] Japanese Patents 22,263, 22,265 and 22,267 (1965); *Chem. Abstr.* **64**, 3566, 3567 (1966).
[10] K. Hofmann, *Imidazole and Its Derivatives* Pt. I; pp. 15, 251. Interscience, New York (1953).

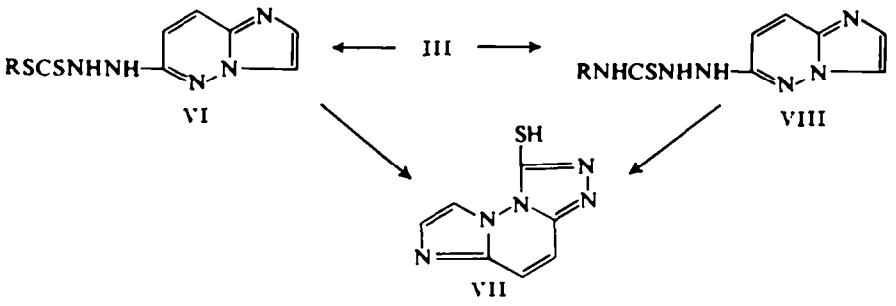
with formic acid or triethyl orthoformate.[11-13] If III was treated with these reagents, formylation occurred preferentially (IV, R = HCONH—) or the corresponding ethoxymethylene hydrazino compound (IV, R = C_2H_5OCH=N—) was obtained. Similarly, the benzoylated derivative (IV, R = C_6H_5CONH—) upon heating could not be transformed into the cyclic compound although this was possible to achieve with some similar ring systems.[8] With diethoxymethyl acetate,[14] however, the fused triazole ring is formed conveniently at room temperature to give the requisite imidazo(1,2-b)s-triazolo(3,4-f)pyridazine (V), the parent 14π electrons azaheterocycle.



Derivatives of this parent ring system could be obtained also through other synthetic approaches. Compound III, if reacted with CS_2 afforded the corresponding dithiocarbazinic acid (VI, R = H) of appreciable stability. The acid derivatives (VI, R = NH_4 or CH_3) upon heating underwent thermal cyclization to give 1-mercaptoimidazo(1,2-b)s-triazolo(3,4-f)pyridazine (VII). The potentially tautomeric mercapto group at position 1 could conceivably exist in the mercapto form or in the alternative thioamide form. Support for the proposed structure is found by examination of the IR spectrum (SH absorption band at 2410 cm^{-1}) and pK value corresponding to this group (pK- 5·2) is also in accord with such formulation.[15-18] The same compound can be prepared from different thiosemicarbazides (VIII) formed from III and the corresponding isothiocyanates or thiocyanic acid. Compounds of type VIII when heated at a temperature above their m.ps. or in glacial acetic acid lose the amine or ammonia to give VII. The alternative possible way of

[11] D. Libermann and R. Jaquier, *Bull. Soc. Chim. Fr.* 355 (1962).
[12] N. Takahayashi, *J. Pharm. Soc., Japan* **75**, 1245 (1955).
[13] T. Kuraishi and R. N. Castle, *J. Heterocycl. Chem.* **1**, 42 (1964).
[14] H. W. Post and E. R. Erickson, *J. Org. Chem.* **2**, 261 (1938).
[15] B. Stanovnik and M. Tišler, *Croat. Chem. Acta* **36**, 81 (1964).
[16] B. Stanovnik and M. Tišler, *Croat. Chem. Acta* **37**, 17 (1965).
[17] B. Stanovnik and M. Tišler, *Arzneimittelforsch.* **14**, 1004 (1964).
[18] C. Ainsworth, *J. Amer. Chem. Soc.* **78**, 4475 (1956).

cyclization to give the corresponding substituted amino instead of mercapto derivatives, known in some cases,[19,20] was not observed during cyclization of our compounds.

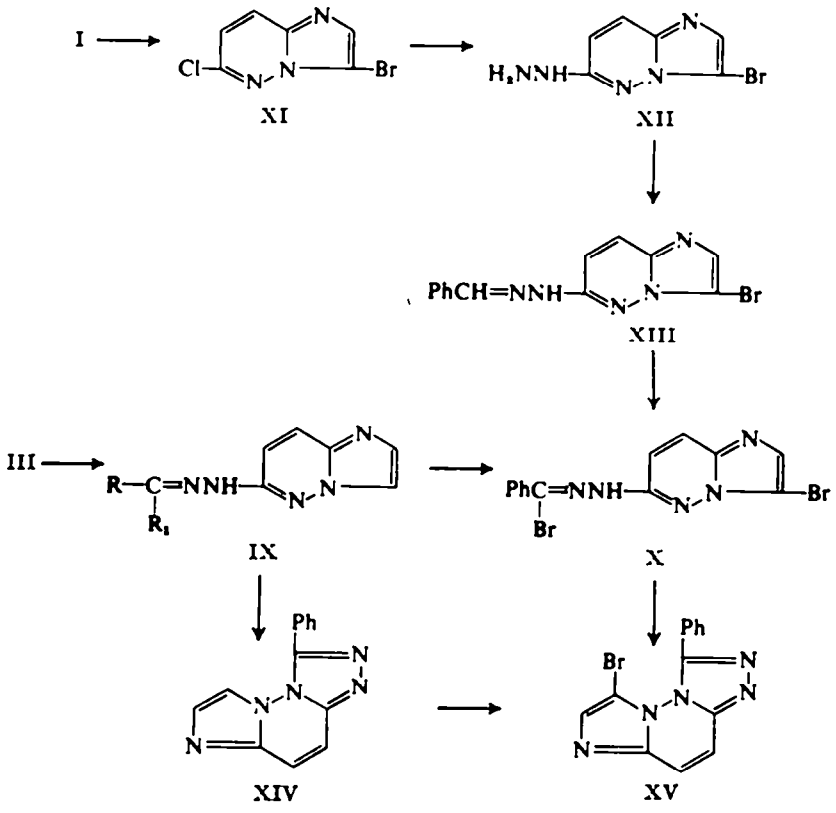


A third route, the dehydrogenative cyclization of alkylidene or arylidene hydrazones which was successfully applied for the preparation of s-triazolo(4,3-b)pyridazines[2] presented here different results. With bromine in glacial acetic acid the benzylidene hydrazone (IX, R = C_6H_5—, R_1 = H) prepared from III afforded the corresponding brominated hydrazone (X) and besides this the imidazole ring was brominated. The relative easiness for electrophilic substitution of the imidazole nucleus of imidazo-(1,2-b)pyridazine was observed also in further experiments. The formation of hydrazidic bromides was observed in the case of arylidene hydrazones[21] and kinetics of this reaction has been studied recently,[22] although addition to the double bond followed by cyclization is also known.[23]

The proof for the structure of X was accomplished in two different ways. In the first, bromine was introduced in the imidazole ring (XI) after bromination of I. In the reaction with hydrazine hydrate the 6-chloro group is more readily displaced than the 3-bromo group and thus the 6-hydrazino derivative (XII) was formed. The corresponding benzylidene derivative (XIII) upon bromination afforded an identical brominated hydrazone (X). Furthermore, IX (R = Ph—, R_1 = H) could be cyclized by means of $Pb(Ac)_4$ to 1-phenylimidazo(1,2-b)s-triazolo(3,4-f)pyridazine (XIV) which upon bromination afforded the same 8-bromo derivative (XV) as obtained from X by treatment with base.

The reaction of heterocycles, containing a hydrazino group adjacent to the ring nitrogen, with nitrous acid to give a fused tetrazole ring and known to proceed also in the case of some pyridazines[12,13] was accomplished similarly with III. It should be mentioned that in the case of related ring systems the formation of a second fused tetrazole ring is usually difficult to achieve and a substituted azide is formed.[24,25] We have obtained as reaction product a stable but photochromic compound (XVI) which did not decompose at its m.p. and the compound was obtained unchanged from its melt whereas most organic azides are sensitive to heat and light.[26] The IR

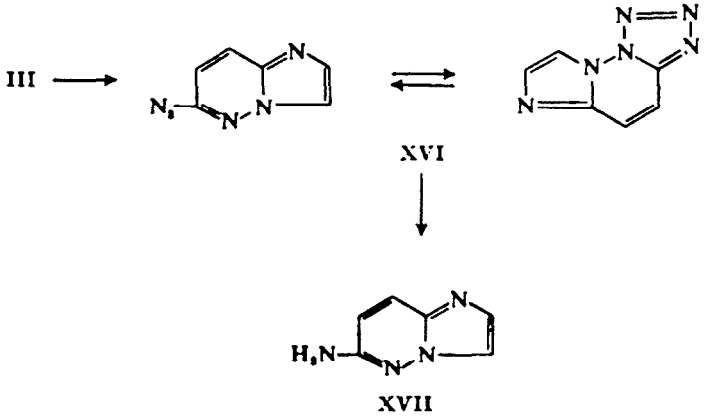
[19] W. Marckwald and E. Meyer, *Ber. Dtsch. Chem. Ges.* 33, 1885 (1900).
[20] I. Zugravescu, M. Petrovanu, E. Rucinschi and M. Caprosu, *Rev. Chim. Roumaine* 10, 641 (1965).
[21] F. D. Chattaway and A. J. Walker, *J. Chem. Soc.* 975 (1925).
[22] A. F. Hegarty and F. L. Scott, *Tetrahedron Letters* No 42, 3801 (1965).
[23] M. S. Gibson, *Tetrahedron* 19, 1587 (1963).
[24] T. Itai and S. Kamiya, *Chem. Pharm. Bull. Japan* 11, 348 (1963).
[25] R. Stolle and H. Storch, *J. Prakt. Chem.* 135, 128 (1932).
[26] J. H. Boyer and F. C. Canter, *Chem. Revs.* 54, 1 (1954).



spectra examined in solid state and in solution revealed that we had an example of azidoazomethine-tetrazole equilibrium, known already for other similar ring systems.[27–31] Since the infrared spectrum of XVI in solution (N,N-dimethylformamide) showed an almost complete disappearance of a band at 2120 cm^{-1} characteristic for the azido group[32,33] and which is present if the IR spectrum is examined in solid state the presence of the azido form should be taken into account. In the solid state besides this band bands at 1072, 970 and 735 cm^{-1} due to the presence of the tetrazole ring[28,34] are present. This easy tautomerization is quite possible, since it is known that similar systems do not require much energy for such interconversions.[27] Thus, the overall result can be well explained by assuming the equilibrium of both forms which must lie at room temperature more in the direction of the tetrazole form. Tautomerisation is consistent also with the observation on other related systems, particularly tricyclic, where a second fused tetrazole ring is usually not present in the cyclized form[24,25] and this tetrazole destabilization through fusion appears to

[27] C. Temple and J. A. Montgomery, *J. Amer. Chem. Soc.* **86**, 2946 (1964).
[28] J. H. Boyer and E. J. Miller, *J. Amer. Chem. Soc.* **81**, 4671 (1959).
[29] J. H. Boyer and H. W. Hyde, *J. Org. Chem.* **25**, 458 (1960).
[30] C. Temple, R. L. McKee and J. A. Montgomery, *J. Org. Chem.* **27**, 1671 (1962).
[31] C. Temple, M. C. Thorpe, W. C. Coburn and J. A. Montgomery, *J. Org. Chem.* **31**, 935 (1966).
[32] L. J. Bellamy, *Infrared Spectra of Complex Molecules* p. 230. Methuen, London (1954).
[33] E. Lieber, C. N. R. Rao, T. S. Chao and C. W. W. Hoffman, *Analyt. Chem.* **29**, 916 (1957).
[34] E. Lieber, D. Levering and L. Patterson, *Analyt. Chem.* **23**, 1594 (1951).

occur from electron withdrawal. On the other hand XVI reacted readily with hydrogen sulfide to form the 6-amino derivative (XVII) which was not accessible through aminolysis via I. Such conversions are usually taken as a proof for the exclusive presence of an azido group[35] but in the case of XVI this facile reducibility should be interpreted in terms of the above findings. Finally, an attempt to prepare the azide form from I with NaN_3 was, however, unsuccessful.



XVI

XVII

The UV spectra of imidazo(1,2-b)pyridazines exhibit a long wave-length band in the 3200–3370 Å region and with most compounds also a short wave-length band (below 2500 Å) was observed. These spectra are very similar to those of imidazo(1,2-a)-pyridines[36] whereas in the case of tricyclic compounds V, VII and XVI the long wave-length band is shifted to longer wave-length bands and this is consistent with the introduction of more nitrogens in these heterocyclic systems.[36–38] In the case of XVI the UV spectrum presented little evidence for the presence of any form. It is known that tetrazole itself does not absorb in the near UV region[39] although resonance interaction with this ring may have a significant influence. On the other hand UV spectra of organic azides were recorded[40] but data for heterocyclic azides are lacking.

The preparation of other substituted imidazo(1,2-b)pyridazines will be dealt with in later papers.

EXPERIMENTAL

UV spectra: Beckman Model DU Spectrophotometer; IR spectra: Perkin–Elmer Model 21 Spectrophotometer as KBr discs or Nujol mulls; M.ps: Kofler m.p. apparatus and are corrected.

6-Chloroimidazo(1,2-b)*pyridazine* (I)

A mixture of bromoacetaldehyde diethylacetal (20 g), HBr (5 ml, $d = 1{\cdot}38$) and water (5 ml) was heated under reflux for 2 hr. The reaction mixture was poured into 200 ml 1,2-dimethoxyethane (instead of this solvent 50 ml 2-methoxyethanol or 50 ml EtOH can be used, without significantly

[35] E. Lieber, E. Sherman, R. A. Henry and J. Cohen, *J. Amer. Chem. Soc.* **37**, 2327 (1961).
[36] J. D. Bower, *J. Chem. Soc.* 4510 (1957).
[37] A. I. Scott, *Interpretation of the Ultraviolet Spectra of Natural Products* p. 191. Macmillan, New York (1964).
[38] S. F. Mason, *Quart. Revs.* **15**, 287 (1961).
[39] F. W. Schneler, S. C. Wang, R. M. Featherstone and E. G. Gross, *J. Pharm. Exptl. Therapeutics* **97**, 266 (1949).
[40] E. Lieber, C. N. R. Rao, T. S. Chao and W. H. Wahl, *J. Sci. & Ind. Res.* **16B**, 95 (1957).

affecting the yield) and to the stirred soln solid $NaHCO_3$ was added portionwise until the evolution of CO_2 stopped and the soln had pH 8–9. To the filtered soln 3-amino-6-chloropyridazine (7 g) was added and the mixture was stirred for 4 hr at room temp. The crude product separated as the hydrochloride, was filtered off, dissolved in water and the free base obtained after the addition of $NaHCO_3$. After standing overnight on ice, the product was filtered off and crystallized from water with the addition of charcoal to yield 3·6 g (45%) of crystals, m.p. 115°. (Found: C, 46·82; H, 3·05; N, 26·87; $C_4H_4ClN_3$ requires: C, 46·92; H, 2·61; N, 27·36%.) λ_{max}^{EtOH} 3320 Å (ε 4,070): $\lambda_{max}^{H_2O}$ 2120, 3170 and 3300 Å (ε 19,300, 1,370 and 4,290).

The hydrochloride was obtained by dissolving the base (100 mg) in EtOH (3 ml), then adding conc. HCl and the mixture evaporating to dryness *in vacuo*. After crystallization from EtOH the hydrochloride had m.p. 240°. (Found: C, 37·80; H, 2·85; N, 21·86; $C_4H_5Cl_2N_3$ requires: C, 37·92; H, 2·65; N, 22·10%.)

Hydrobromide was similarly prepared and does not melt up to 320°, but it sublimed strongly. (Found: N, 17·85; $C_4H_4BrClN_3$ requires: N, 17·92%.)

6-Phenylthioimidazo(1,2-b)*pyridazine* (II)

Sodium (0·23 g) was allowed to react in abs. EtOH (15 ml) and thereafter thiophenol (1·1 g) and I (1·53 g) were added. The reaction mixture was heated under reflux for 40 min, cooled on ice and diluted with iced water (80 ml). The ppt was filtered off and air dried. For purification it was dissolved in cooled EtOH (15 ml), charcoal added, filtered, cooled on ice and under stirring iced water (150 ml) was added dropwise, yield 1·85 g (83%), m.p. 100°. (Found: C, 63·23; H, 3·59; N, 18·23; S, 14·45; $C_{12}H_9N_3S$ requires: C, 63·43; H, 3·99; N, 18·49; S, 14·08%.) λ_{max}^{EtOH} 2300 and 3350 Å (ε 21,900 and 4,700).

6-Hydrazinoimidazo(1,2-b)*pyridazine* (III)

Compound I (1·0 g) was treated with hydrazine hydrate (5 ml of 80%) and the mixture heated on a water bath for 1 hr until the product separated. After cooling on ice the ppt was filtered, washed with cold water and crystallized first from water and thereafter from EtOH to yield 90% of the pure compound, m.p. 225°. (Found: C, 48·34; H, 4·91; N, 47·03; $C_6H_7N_5$ requires: C, 48·32; H, 4·73; N, 46·95%.) λ_{max}^{EtOH} 2280 and 3200 Å (ε 21,600 and 6,090); $\lambda_{max}^{H_2O}$ 2240 and 3170 Å (ε 20,150 and 6,180).

The compound formed a dihydrochloride (with ethanolic HCl), m.p. 261–262° (EtOH). (Found: C, 32·94; H, 4·34; N, 31·63; $C_6H_9Cl_2N_5$ requires: C, 32·44; H, 4·08; N, 31·53%.)

6-Ethoxymethylene-hydrazino-imidazo(1,2-b)*pyridazine* (IV, R = $EtOCH{=}N{-}$)

To III (1·49 g) triethyl orthoformate (10 ml) was added and the mixture was heated under reflux for 3 hr. After evaporation of the solvent *in vacuo* until crystals began to separate and cooling on ice, the product was filtered off and crystallized twice from AcOEt giving 0·9 g, m.p. 137–138°. (Found: C, 53·00; H, 5·74; $C_9H_{11}N_5O$ requires: C, 52·68; H, 5·40%.) λ_{max}^{EtOH} 2520 and 3370 Å (ε 29,950 and 8,430).

6-Formylhydrazino-imidazo(1,2-b)*pyridazine* (IV, R = $HCONH{-}$)

Compound III (0·75 g) was heated with formic acid (5 ml of 98%) under reflux for 3 hr. Evaporation *in vacuo* gave an oily residue to which AcOEt (5 ml) was added. After standing on ice, a ppt was formed, collected and upon crystallization from water colourless crystals (0·65 g, 37%) were obtained, m.p. 218° (sublimes). (Found: 47·32; H, 4·08; N, 39·40; $C_7H_7N_5O$ requires: C, 47·46; H, 3·98; N, 39·53%.)

6-Benzoylhydrazino-imidazo(1,2-b)*pyridazine* (IV, R = $C_6H_5CONH{-}$)

a. To a stirred soln of III (1·49 g) in dry pyridine (25 ml) benzoyl chloride (1·41 g) was added dropwise. The mixture was maintained overnight at room temp and thereafter ice (100 g) was added. The ppt was collected, washed with water and crystallized from AcOEt–EtOH (1:2) to give colourless crystals (1·86 g, 74%), m.p. 258°. (Found: C, 61·52; H, 4·47; N, 27·40; $C_{13}H_{11}N_5O$ requires: C, 61·65; H, 4·38; N, 27·65%.)

b. An equimolar mixture of III and benzoic acid was heated to melt and thereafter at 180–190° for 2 hr. Upon cooling EtOH was added, the crystalline material filtered and crystallized from AcOEt–EtOH (1:2). The compound thus obtained was shown by its m.p. 258° and mixed m.p. to be identical to the compound prepared by method a.

Imidazo(1,2-b)*s-triazolo*(3,4-f)*pyridazine* (V)

A mixture of III (149 mg) and diethoxymethyl acetate (1 ml) was left at room temp for 2 days. The separated cyclized product was filtered off and crystallized from N,N-dimethylformamide, yield 113 mg (71%) colourless crystals, m.p. 283–285°. (Found: C, 52·60; H, 3·45; N, 43·68; $C_7H_6N_6$ requires: C, 52·83; H, 3·17; N, 44·00%.)

Imidazo(1,2-b)*pyridazinyl-6-dithiocarbazic acid and derivatives* (VI)

a. Compound III (0·75 g) was dissolved in EtOH (20 ml) and CS_2 (0·42 g) was added. The mixture was shaken vigorously and after some time VI (R = H) separated. After filtration it was washed thoroughly with EtOH. Attempts to purify the acid with crystallization failed since on heating the acid is transformed back into III.

b. Into a mixture of III (1·49 g) in EtOH (5 ml) and CS_2 (0·86 g) NH_3 gas was bubbled and the ammonium salt of VI (R = NH_4) began to separate. Water was added until a clear soln resulted, thereafter MeI (1·45 g) added and the mixture shaken vigorously. The solid which separated was filtered off and crystallized from EtOH–water (1:1) affording 0·5 g (21%) pale yellow crystals of VI (R = Me), m.p. 170°. (Found: C, 39·88; H, 3·44; N, 29·69; S, 27·08; $C_6H_6N_4S_2$ requires: C, 40·17; H, 3·79; N, 29·28; S, 26·76%.)

Similarly with 5% NaOH aq the Na-salt was prepared and after treatment with MeI the identical methyl ester was obtained in practically the same yield.

6(4′-*Phenylthiosemicarbazido*)*imidazo*(1,2-b)*pyridazine* (VIII, R = Ph—)

Compound III (1·49 g) was dissolved in the minimum amount of EtOH at 65° and at this temp a soln of phenyl isothiocyanate (1·35 g) in EtOH (5 ml) was added dropwise. After addition was complete the mixture was left aside and after standing on ice the separated product was filtered off and crystallized from EtOH (2·45 g, 86%), m.p. 179°. (Found: C, 54·80; H, 4·53; N, 29·94; S, 11·04; $C_{12}H_{11}N_6S$ requires: C, 54·92; H, 4·26; N, 29·57; S, 11·26%.)

In the same way the following compounds were prepared:

(i) 6(4′-*p*-Ethoxyphenyl-thiosemicarbazido)imidazo(1,2-b)pyridazine (VIII, R = *p*-C_2H_5O—C_6H_4—) in 86% yield, m.p. 120° (EtOH). (Found: C, 54·84; H, 4·76; N, 25·53; S, 9·94; $C_{16}H_{16}N_6OS$ requires: C, 54·87; H, 4·91; N, 25·60; S, 9·75%.)

(ii) 6(4′-*n-Buthylthiosemicarbazido*)*imidazo*(1,2-b)*pyridazine* (VIII, R = n-C_4H_9—) obtained in 52% yield, m.p. 190° (EtOH). (Found: C, 50·00; H, 6·28; N, 32·09; $C_{11}H_{16}N_6S$ requires: C, 49·99; H, 6·10; N, 31·80%.)

(iii) 6(4′-*Thiosemicarbazido*)*imidazo*(1,2-b)*pyridazine dihydrochloride* (VIII, R = H). To a soln of III (1·49 g) in water (10 ml), KSCN (0·98 g) and conc. HCl (1 ml) were added. The mixture was heated on water bath for 2 hr, concentrated *in vacuo* to ⅓ of its original volume and the residue crystallized from EtOH (yield 34%). The compound has no definite m.p. since upon heating it is transformed into the VII. (Found: C, 30·37; H, 3·56; N, 29·90; $C_7H_{10}Cl_2N_6S$ requires: C, 29·90; H, 3·58; N, 29·89%.)

1-*Mercaptoimidazo*(1,2-b)*s-triazolo*(3,4-f)*pyridazine* (VII)

a. *From thiosemicarbazides.* Compound VIII (R = Ph—) when heated at a temp higher than its m.p. (over 183–185°) decomposes into aniline and from the melt after some time crystals began to separate. The crude product was dissolved in 10% NaOHaq, filtered and acidified with HCl, yield 35%, m.p. about 340° (dec). A better, almost quantitative yield of the same compound could be obtained upon heating the starting compound (1·42 g) in ethylene glycol (15 ml) under reflux for 25 min. (Found: C, 44·25; H, 2·98; N, 36·61; S, 16·74; $C_7H_6N_6$ requires: C, 43·99; H, 2·64; N, 36·64; S, 16·74%.) $\lambda_{max}^{H_2O(pH7)}$ 2540 and 3500 Å (*ε* 19,120 and 4,460); $\lambda_{max}^{H_2O(pH6)}$ 2590 and 3450 Å (*ε* 15,200 and 4,360). IR Nujol: max (cm^{-1}) at 2410 (SH).

The same compound was obtained also after heating other substituted or unsubstituted thiosemicarbazides over their m.p. or in glacial AcOH soln.

b. *From the corresponding thiocarbazidic acid derivatives* (VI). If the ammonium salt of VI (R = NH_4) was heated at about 245°, or the ester (R = Me) at about 230°, from the melt the tricyclic mercapto compound separated and after purification as under a the compound was found identical with the above obtained product.

Ethylidene derivative of 6-hydrazinoimidazo(1,2-b)pyridazine (IX, R = Me, R_1 = H)

To a suspension of III (1·49 g) in EtOH (15 ml) a soln of acetaldehyde (0·44 g) in EtOH (5 ml) and 2 drops of glacial AcOH were added. The resulting soln was heated under reflux for 10 min, the solvent evaporated *in vacuo* and the residue crystallized from AcOEt to give 0·8 g (46%) of the pure compound, m.p. 172°. (Found: C, 54·76; H, 5·35; N, 39·92. $C_8H_9N_5$ requires: C, 54·85; H, 5·18; N, 39·97%.)

In an analogous way the following derivatives were prepared:

(i) Isopropylidene derivative IX (R = R_1 = Me) in 34% yield, m.p. 162° (acetone). (Found: C, 57·33; H, 6·00; N, 36·92. $C_9H_{11}N_5$ requires: C, 57·13; H, 5·86; N, 37·01%.)

(ii) Benzylidene derivative IX (R = Ph, R_1 = H), m.p. 224° (from N,N-dimethylformamide–toluene, 1:4). (Found: C, 65·67; H, 4·81; N, 29·46. $C_{13}H_{11}N_5$ requires: C, 65·81; H, 4·67; N, 29·52%.)

(iii) *p*-Nitrobenzylidene derivative IX (R = *p*-NO_2—C_6H_4—, R_1 = H), m.p. 307–309° (N,N-dimethylformamide–toluene, 1:4). (Found: C, 55·40; H, 3·76; N, 29·85. $C_{13}H_{10}N_6O_2$ requires: C, 55·31; H, 3·57; N, 29·78%.)

(iv) *p*-Bromobenzylidene derivative IX (R = *p*-Br—C_6H_4—, R_1 = H), m.p. 270–271° (N,N-dimethylformamide–toluene, 1:3). (Found: C, 49·23; H, 3·48; N, 22·17. $C_{13}H_{10}BrN_5$ requires: C, 49·38; H, 3·19; N, 22·15%.)

(v) *p*-Hydroxybenzylidene derivative IX (R = *p*-HO–C_6H_4—, R_1 = H), m.p. 310–311° (N,N-dimethylformamide–EtOH, 1:4). (Found: C, 61·54; H, 4·74; N, 27·23. $C_{13}H_{11}N_5O$ requires: C, 61·65; H, 4·38; N, 27·65%.)

N-α-*Bromobenzylidene*-N'(3-*bromoimidazo*[1,2-b]*pyridazinyl*-6)*hydrazine* (X)

a. The above IX (R = Ph—, R_1 = H, 1·07 g) was dissolved in glacial AcOH (15 ml), anhydrous AcONa added and during stirring a soln of Br (1 g) in glacial AcOH (5 ml) added dropwise. After standing on ice for 1 hr the mixture was poured on 50 ml iced water. The ppt was filtered and crystallized from N,N-dimethylformamide–toluene (1:4), yield 1·3 g (65%) X, m.p. 154°. (Found: C, 39·82; H, 2·62; N, 17·60. $C_{13}H_9Br_2N_5$ requires: C, 39·51; H, 2·30; N, 17·73%.)

b. Compound XIII (1·58 g) was suspended in glacial AcOH (10 ml), anhydrous AcONa (0·41) and a soln of Br (1 g) in glacial AcOH (3 ml) added. The mixture was left on ice for ½ hr and filtered. After crystallization from N,N-dimethylformamide–toluene (1:4) the product (1·2 g, 60%) had m.p. 154°, undepressed in a mixed m.p. with the compound prepared under a.

3-*Bromo-6-chloroimidazo*(1,2-b)*pyridazine* (XI)

To a soln of I (1·53 g) in glacial AcOH (7 ml) Br was added dropwise until the soln remained coloured. After standing at room temp for 15 min, the product which separated was filtered and washed with glacial AcOH. The crude product was purified by sublimation at 160°/1 mm (yield 92%), m.p. 156°. (Found: C, 30·59; H, 1·80; N, 18·16. $C_6H_3BrClN_3$ requires: C, 30·99; H, 1·30; N, 18·08%.)

The compound obtained (100 mg) when suspended in abs. EtOH (5 ml), conc. HCl added and the soln evaporated *in vacuo* afforded the hydrochloride (EtOH), m.p. 233–235°. (Found: C, 27·01; H, 1·39; N, 15·43. $C_6H_4BrCl_2N_3$ requires: C, 26·80; H, 1·50; N, 15·63%.)

3-*Bromo-6-hydrazinoimidazo*(1,2-b)*pyridazine* (XII)

The above XI (2·32 g) was suspended in hydrazine hydrate (6 ml of 80%) and the mixture heated under reflux for 15 min, cooled and filtered (yield 85%). After crystallization from water the compound melted at 236°. (Found: C, 31·42; H, 2·62; N, 30·42. $C_6H_6BrN_5$ requires: C, 31·60; H, 2·65; N, 30·71%.)

The derivative XIII was prepared from benzaldehyde and XII in the usual way. After crystallization from a mixture of N,N-dimethylformamide and toluene (1:2) the compound had m.p. 241°. (Found: C, 49·57; H, 2·76; N, 22·35. $C_{13}H_{10}BrN_5$ requires: C, 49·38; H, 3·19; N, 22·15%.)

1-*Phenylimidazo*(1,2-b)*s-triazolo*(3,4-f)*pyridazine* (XIV)

To a soln of IX (R = Ph—, R_1 = H; 2·39 g) in glacial AcOH (15 ml) $Pb(Ac)_4$ (4·43 g) was added and the mixture left for 24 hr at room temp. The mixture was cooled on ice, filtered, the filtrate evaporated *in vacuo* to an oily residue, made alkaline with 10% NaOHaq (10–15 ml) and heated on water bath with stirring at 50° for 1 hr. After extraction with chf and separation of the layers the chf soln was washed with water, dried over $MgSO_4$ and concentrated to dryness. The residue was crystallized from EtOH giving rise to 0·25 g (11%) of the pure product with m.p. 188°. (Found: C, 66·54; H, 3·77; N, 30·05. $C_{10}H_6N_6$ requires: C, 66·37; H, 3·86; N, 29·77%.)

1-*Phenyl*-8-*bromoimidazo*(1,2-b)*s-triazolo*(3,4-f)*pyridazine* (XV)

a. *From* X. Compound X (1 g) was heated with 10% NaOHaq (10 ml) at 40–50° with stirring for 1 hr, filtered and washed with cold water until neutral reaction. A sample of the crude product (0·5 g, 62%) was for analysis sublimed at 240–250°/1 mm to afford the pure compound of m.p. 274°. (Found: C, 49·52; H, 2·44; N, 22·35. $C_{10}H_5BrN_6$ requires: C, 49·64; H, 2·56; N, 22·27%.)

b. *From* XIV *by bromination.* Compound XIV (47 mg) was dissolved in glacial AcOH (1 ml) and 0·25 ml of a molar soln of Br in glacial AcOH was added. Immediately a product separated (55 mg, 88%) which was collected and sublimed *in vacuo* (240–250°/1 mm), m.p. 274–276°, mixed m.p. with the compound under a was undepressed.

Imidazo(1,2-b)*tetrazolo*(5,1-f)*pyridazine* (XVI)

A soln of III (1·49 g) in 2N HCl (25 ml) was cooled on ice and a conc. $NaNO_2$aq was added dropwise until the reaction on starch-KI paper was positive. After standing on ice for ½ hr solid $NaHCO_3$ was added to neutralize the acid and the separated product was collected, washed with cold water and dried (1·05 g, 65%). For analysis a sample was dissolved in benzene, charcoaled, filtered and during stirring a fivefold quantity of n-hexane added dropwise. The separated crystals were thereafter crystallized from benzene, m.p. 108°. The compound is photochromic, it is yellow, but exposed to sunlight crystals become purple. (Found: C, 45·04; H, 2·78; N, 52·94. $C_5H_4N_6$ requires: C, 45·00; H, 2·52; N, 52·48%.) λ_{max}^{EtOH} 2370 and 3330 Å (*e* 20,950 and 5,160).

6-*Aminoimidazo*(1,2-b)*pyridazine* (XVII)

Compound XVI (100 mg) was dissolved in EtOH (2 ml) and water (2 ml) and thereafter for ½ hr a stream of H_2S was bubbled into the soln. The soln was heated to boiling, the colloidal S filtered off and the filtrate evaporated under red press to dryness. The crude residue was crystallized from water and charcoaled (57 mg, 67%), m.p. 196°. (Found: C, 53·59; H, 4·79; N, 41·59. $C_6H_6N_4$ requires: C, 53·72; H, 4·51; N, 41·77%.)

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