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SYNTHESIS OF IMIDAZO/1,2-b/-s-TRIAZOLO/3',4'-f/PYRIDAZINE A NEW TRICYCLIC AZAHETEROCYCLE

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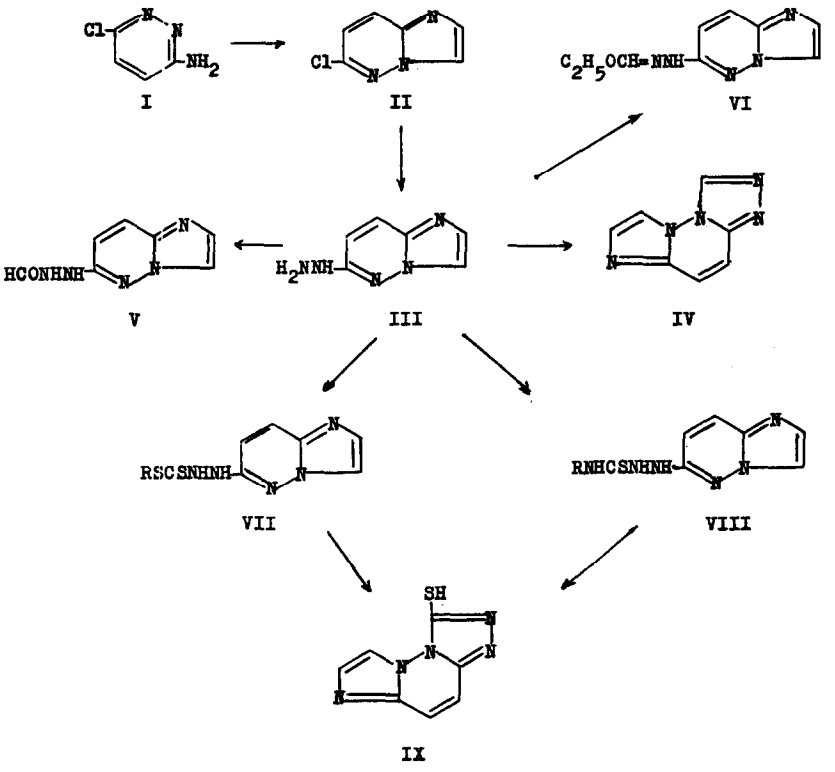
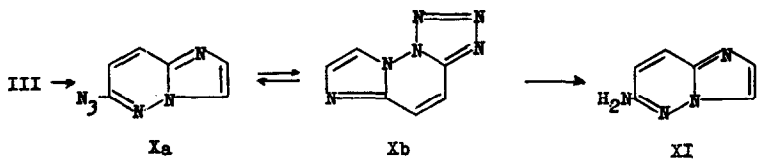
Recently we have described the preparation of some bicyclic and tricyclic systems based on pyridazine (1,2). In connection with the newly described bis-s-triazolo/4,3-b, 3',4'-f/pyridazines we wish to report different synthetic routes for a new azaheterocycle, e.g. imidazo/1,2-b/-s-triazolo/3',4'-f/pyridazine.

The starting compound for all syntheses was 6-hydrazino-imidazo-/1,2-b/pyridazine (III; m.p. 225°). Derivatives of this ring system were prepared only recently (3,4). The synthesis of 6-chloro-imidazo-/1,2-b/pyridazine (II; m.p. 115°) was accomplished utilizing 6-chloro-3-amino-pyridazine (I) as starting material and this reacted with bromoacetaldehyde to form the fused imidazole ring. The halogen at the position 6 was successfully replaced with different nucleophiles and the reaction with hydrazine hydrate afforded the corresponding hydrazino compound (III) in 90% yield.

Attempts to effect further cyclization with formic acid or triethyl orthoformate were unsuccessful, although simple hydrazino-pyridazines could be transformed with these reagents into the s-triazolo/4,3-b/-pyridazines (5,6,7). When III was treated with formic acid the formyl derivative was isolated (V; m.p. 218°). Similarly, with triethyl orthoformate the ethoxymethylene hydrazino compound (VI; m.p. 137-8°) was formed. A convenient synthesis of the parent tricyclic azaheterocycle (IV; m.p. 283-5°) has been accomplished from III and diethoxymethyl acetate (8) in 71% yield.

In another way the 1-mercapto derivative of this tricyclic system (IX; m.p. about 340°, dec.) was obtained in the following manner. III was transformed with carbon disulfide in the dithiocarbazic acid or its


Cl
NH2
I
Cl
II
C2H5OCH=NNH
VI
HCONHNH
V
H2NNH
III
IV
RSCSNHNH
VII
RNHCSNHNH
VIII
SH
IX


III
N3
Xa
Xb
H2N
XI

derivatives (VII; R = H, NH_4 or CH_3) which upon heating underwent cyclization into IX. The same procedure was effective also in the case of the corresponding thiosemicarbazides (VIII), obtained from III and isothiocyanates. It is conceivable that ring closure could take place to give either IX or an amino derivative as this second type of ring closure is also known to take place with similar compounds (9,10). In our case such compounds were not formed. The potentially tautomeric mercapto group at position 1 exists in the mercapto form as evident from the infrared spectrum exhibiting an absorption at 2410 cm^{-1}.

Furthermore, the known reaction of heterocyclic hydrazines with nitrous acid to form fused tetrazoles has been applied to III. It is noteworthy that such reaction can lead to tetrazolo derivatives as in the case of simple pyridazines (6,7) but in the case where two fused tetrazole rings should be formed, one is present in the uncyclized form, e.g. as an substituted azide (11,12). The obtained compound X is perfectly stable and does not decompose at its m.p. (108°), but is photochromic. In solid state the IR spectrum revealed an azide absorption band at 2120 cm^{-1}, indicating the presence of the azido derivative Xa, but also presence of the tetrazole ring is indicated by bands at 1072, 970 and 735 cm^{-1} (13,14). In solution (N,N-dimethylformamide), however, the azide absorption band almost disappears indicating the preponderance of Xb. This fused tetrazolo system represents also a new azaheterocycle, e.g. imidazo/1,2-b/tetrazolo/5',1'-f/pyridazine. Since azidomethine-tetrazole tautomerization, demonstrated on other heterocyclic systems, does not require much energy (15), forms Xa and Xb could be in equilibrium and at room temperature the equilibrium must lie more in the direction of the tetrazole. Although X reacted readily in solution at room temperature with hydrogen sulfide to form 6-amino-imidazo/1,2-b/pyridazine (XI; m.p. 196°), this facile reducibility should not be taken as a proof for the exclusive presence of an azido group (16). Finally, it should be mentioned that II did not react with sodium azide in order to obtain X on a different way.

Different derivatives of the above mentioned new system were also prepared and satisfactory elemental analyses have been obtained on every recrystallized product. Full details of this research will be reported elsewhere.

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