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STRUCTURE AND REACTIVITY CORRELATION OF BICYCLIC 10-π ELECTRON SYSTEMS WITH BRIDGEHEAD NITROGEN

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Abstract - A survey is made of the present knowledge of the chemistry of azaindolizines, covering the experimental and theoretical results and significance of their reactivity. Some generalizations which can be drawn are presented.

INTRODUCTION

Azaindolizines represent a group of heterocyclic compounds, which are structurally related to purines and are isoelectronic with naphthalene, indene monoanion, indole, etc. The chemistry rapidly developed in the last decades because of biological interest and since many derivatives have found applications. A large number of investigations were devoted to theoretical aspects and their reactivity.

The indolizine and azaindolizine skeletons are incorporated in many natural compounds and alkaloids. Perhydroindolizine is the alkaloid δ-coniceine and the reduced azaindolizine nucleus contain alkaloids alchornine, arenaine, oxaline, septicine, ipalbidine, elaeocarpine, slaframine, pluviine, lycornine, the vinca alkaloids, the bioluminiscent compounds cypridina luciferin and renilla luciferin, the trail pheromone of the Pharaoh ant, etc. The imidazopyrimidine skeleton is incorporated also in the fluorescent Y-base from yeast phenylalanin transfer RNA (1). Related ethenoadenosines were synthesized as fluorescent probes in biochemical systems (2). The structural similarity of azaindolizines with purine nucleosides stimulated the research on several nucleoside analogs.

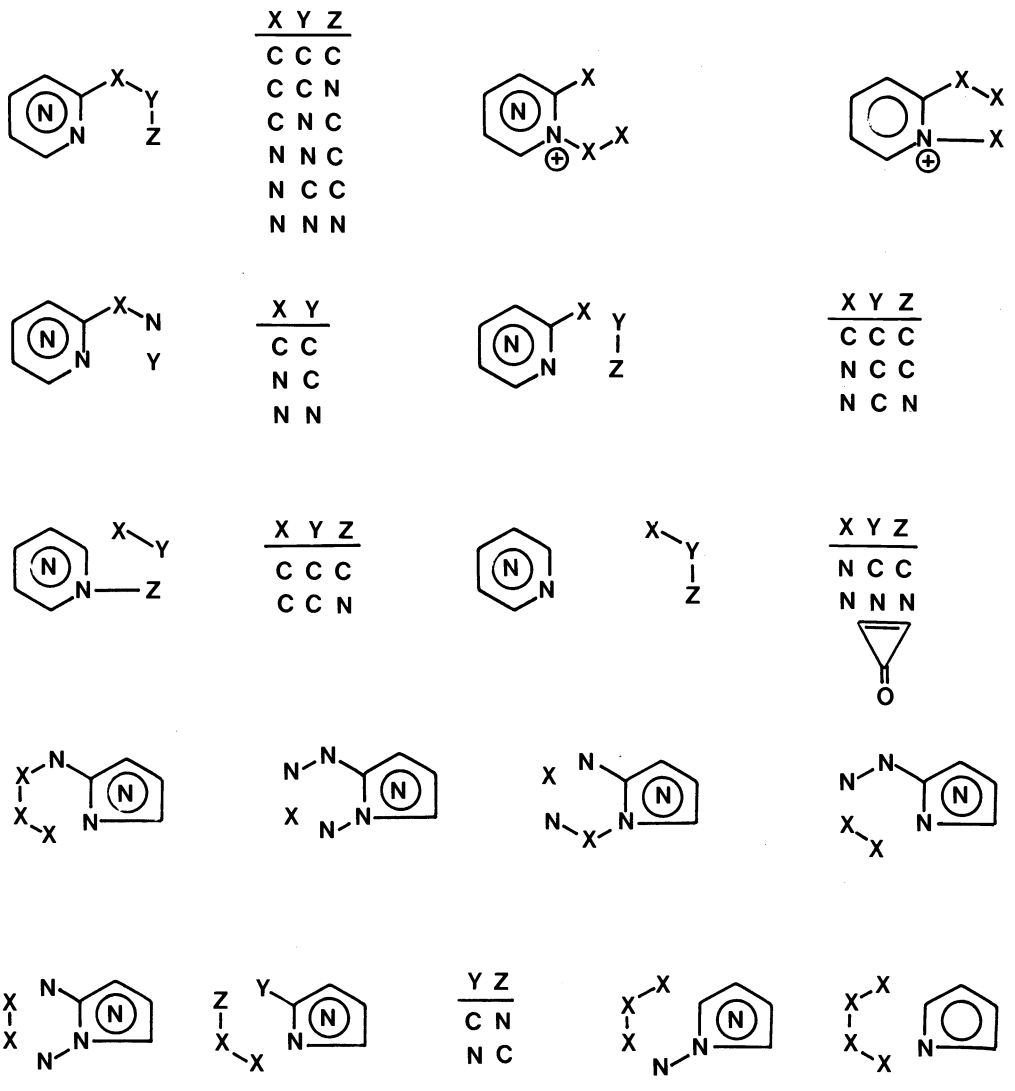
In a formal sense indolizine and azaindolizines can be regarded as 10-π electron systems, thus obeying the Hückel's rule (3,4) and being aromatic. The term aromatic, which was adopted long ago to summarize the chemical behaviour of a certain group of organic compounds remains not unequivocally defined and is used with different meanings (5-10). Moreover, according to another topological approach (11) we can define azaindolizines as being a combination of a π-excessive and π-deficient ring. The nomenclature of some most important and investigated systems is presented in Appendix I.

The number of possible aza analogs of indolizine is quite large, 128, but less then half of them are known and still less were investigated in detail. We shall consider here only those analogs with one nitrogen in the ring junction and which are fully conjugated. Different aspects of the chemistry of indolizine and of some of its aza analogs have been discussed in several articles and reviews (12-26). Here, we like to present some less common aspects of azaindolizine reactivity and to correlate experimental evidence with structural features.

SYNTHESES

For indolizine and its aza analogs, numerous syntheses were developed, some being generally applicable to several bicyclic systems. From the structural standpoint, two general synthetic approaches have been developed. The first one uses as starting synthons functionalized azines and in the second one the six-membered part is annelated to five-membered synthons. According to the reaction type all these reactions can be classified as condensations, oxidative cyclizations or cycloadditions. In minor extent azaindolizines were prepared from other heterocycles and by ring relocations or ring contractions. A schematic representation of the most important synthetic possibilities is given in Scheme 1.

Scheme 1



STRUCTURE

Based on chemical reactivity and nmr spectroscopy, several authors have suggested that azaindolizines are planar and possess a high degree of aromatic character. Also from ^{13}C-NMR evidence the bridgehead nitrogen lone pair is considerably delocalized, thus contributing to the aromatic stability of azaindolizines (27). Until recently, there were no X-ray data available. X-ray examinations of derivatives of imidazo(1,2-a)pyridine (28,29), s-triazolo(1,5-c)pyrimidine (30), and in particular of the parent azolopyridizines (s-triazolo(4,3-b)-, s-triazolo(1,5-b)- and tetrazolo(1,5-b)pyridazine)(31), has shown that these molecules are essentially planar and that most of the bond lengths and angles are within the normal ranges for aromatic heterocyclic systems. However, the bond lengths N_5-C_6 and C_7-C_8 in s-triazolo(4,3-b)- and tetrazolo(1,5-b)pyridazine demonstrate a considerable double-bond character and thus considerable bond localization in the six-membered ring. This is revealed also in some chemical transformations such as hydrogenation, opening of the six-membered ring by nucleophiles, photochemical and cycloaddition reactions or epoxidation. These chemical transformations will be discussed later. The double bond character of the C_7-C_8 bond is also indicated by the magnitude of the coupling constant ($J_{7,8}$ = 8.9-9.5 Hz (32-34).

In contrast to purines, no annular tautomerism exists with azaindolizines. However, suitably substituted hydroxy or mercapto compounds possess delocalizable protons and can exist in the corresponding oxo or thioxo forms. In general, it is anticipated that the oxo or thioxo form prevails as established

for simple azines (35,36). However, there are some exceptions (37-39). An X-ray examination of 6-hydroxy-s-triazolo(4,3-b)pyridazine, for which formerly the lactam form was proposed on hand of ir spectroscopic evidence, revealed that the compound exists in solid state in the hydroxy form (40). Also ^{13}C-NMR data on several 6- or 8-hydroxytriazolo- or tetrazolopyridazines, when correlated with their methylated and protonated derivatives, demonstrate that the neutral oxo derivatives exist in solution predominantly in the hydroxy form (41). A reasonable explanation for this phenomenon is that in the lactam form there should be two adjacent pyridazine ring nitrogens, each of them contributing the electron pair to the π-system and this is energetically less favourable.

REACTIVITY

The reactivity of azaindolizines can be reasonably well interpreted on hand of experimental data as well as on theoretical grounds.

The aromaticity, according to the Hückel´s rule is the property of a conjugated cyclic compound in the ground state. Chemical reactivity depends on the difference in free energy between that of the ground state and that of the transition state in a certain reaction.

In general, one can consider qualitatively a certain compound to possess the aromatic character if:

- it has a certain stability and reactivity of conjugated systems reflecting in high resonance energy and substitution rather then addition reactions,
- it has an electronic structure corresponding Hückel´s 4n+2 π-electron rule,
- it has the ability to sustain an induced ring current of π-electrons.

We must take into consideration that replacement of a CH group in a cyclic conjugated system by N (or more CH groups by more N) leads to disturbance of the symmetry of the π-electron system. This reflects in nonequivalence of bonds and nonuniform electron distribution of electric charge. With increasing number of nitrogens the polarity of C=N bonds increases because of enhancing charge density at nitrogen atoms and diminishing electron density at the neighbouring carbon atoms. This results in decrease of stabilization energy and renders the heterocycle more susceptible for nucleophilic attack.

The difficulty arises if we attempt to give the aromaticity a quantitative value, in particular with heterocyclic compounds. This implies a certain classification of analogs as being "more or less aromatic". It is well known, that we have an enormous interval in partial rate factors for electrophilic substitution between the two extremes, i.e. for the most reactive pyrrole and the least reactive pyridinium ion - a difference of 10^{42} - and yet both compounds are considered to be aromatic.

It is certain that we cannot consider azaindolizines as aromatic as the superaromatic benzene and a better and more founded correlation would be to regard them as aza analogs of a delocalized 10 π-electron system, representing a combination of a fused π-excessive part (five-membered ring) and π-deficient part (six-membered ring). As pointed out, azaindolizines show a great number of reactions which fit in the accepted pattern of aromatic substitution reactions, but they undergo also a great number of reactions, which can be explained on hand of appreciable bond localization. Besides, there are some reactions, as azido-tetrazolo isomerization, which are immanent only to compounds with special structural features. One of the main characteristics of aromatic stability is the tendency to revert to type, i.e. temporarily lost aromatic stability of a reactive intermediate is regained in the reaction product. Many reactions of this type are typical for azaindolizines. Finally, it should be mentioned that perturbing the aromatic stability in a bicyclic system requires less energy then in a monocyclic system like benzene or azines.

ELECTROPHILIC REACTIONS

A number of theoretical calculations were performed and the results are in accord with the observed pattern of electrophilic, nucleophilic or radical substitutions. The reactivity assignments are based mainly on examination of the electronic distribution in the ground state although some models for transition state have been studied too.

System	Calculations of π-electron densities[a]		Wheland model[a]	
	E^+	Nu^-	E^+	Nu^-
Pyrrolo(1,2-a)pyridine	3~1>5>7	5>8>7>6	1>3>5>7	5>8>7>6
Imidazo(1,2-a)pyridine	3>5>8	5>8>7	3>8≃5	5>7>8
Imidazo(1,2-a)pyrimidine	3>5>7	5>7>2	3>5>2	5>7>6
Imidazo(1,2-a)pyrazine	3>5>6≃8	8>5>2	3>5>2	5>8>6
Imidazo(1,2-c)pyrimidine	3>5>7	5>8>7	3>8>5	5>8>7

a) Ref. 127, 128

Protonation and N-quaternization. Protonation of a nitrogen containing heterocyclic system normally occurs at nitrogen rather than carbon atom. In indolizine the nitrogen atom is common to both rings and the free electron pair contributes toward the total number of 10 π-electrons of the conjugated bicylic system. Indolizine is therefore protonated at C_3 (42-45), but 3-substituted derivatives preferentially at C_1. This is similar to pyrrole, indole, isoindole, etc. Other heteroaromatic systems which contain both a pyrrole-type and a pyridine-type ring nitrogen protonate at the last mentioned one. The basic strength of azaindolizines depends both on the number and position of ring nitrogens. In general, protonation occurs at the five-membered ring on nitrogen (if there is an additional one to the bridgehead one), but never at N_4 which is common to both rings. If an additional nitrogen is only in the six-membered ring, protonation may occur there, as for example with pyrrolo(1,2-a)pyrazine. If the additional nitrogen is in the six-membered ring adjacent to the bridgehead one, protonation occurs at C_3 and C_1 as explified with pyrrolo(1,2-b)pyridazine (46,47). Tetrazolopyridazine is such a weak base that no protonation or quaternization occurs.

N-Alkylation follows practically the same pattern as protonation, except for s-triazolo(1,5-a)pyrimidine (48) where methylation occurs at N_3. s-Triazolo-(4,3-b)pyridazines and s-triazolo(4,3-a)pyridines, depending on the substituent present, form N_1 or N_2 quaternary salts (32,49). These can be interconverted at higher temperatures as in the case of s-triazolo(4,3-a)pyridine (50). That N_1 is the most nucleophilic site of azolopyridazines could be shown on hand of complexation with shift reagents, Eu(fod)$_3$ and Pr(fod)$_3$ (51). By using ^{13}C-NMR technique for the investigation of protonation and quaternization site of some azoloazines it could be established that in these processes the bridgehead nitrogen is not involved and that, of the possible tautomeric forms, the N_1 tautomer predominates (52). Thermal O→N alkyl or N→N_x alkyl rearrangements have also been observed and they may occur either in the same ring (53) (s-triazolo(4,3-a)-1,3,5-triazines), or in the adjacent one or in both rings (54,55).

N-Oxidation and N-amination. Until recently, several attempts to prepare azoloazine N-oxides by standard N-oxidation methods were unsuccessful. The first synthesis of an azoloazine N-oxide was reported in the s-triazolo(4,3-b)pyridazine series. The 5-N-oxide was prepared first by cyclization of the corresponding pyridazine N-oxide and later by direct N-oxidation (56,57). It is noteworthy that N-oxidation took place at N_5, i.e. at a different ring nitrogen than protonation and quaternization (N_1 or N_2). The 5-oxides are formed also in the imidazo(1,2-b)pyridazine series (57) whereas upon N-oxidation of tetrazolo(1,5-b)-pyridazine the fused tetrazolo ring is isomerized into azido group (58). This contrasts 8-cyano-tetrazolo(1,5-a)pyridine which afforded with an alkaline solution of hydrogen peroxide the corresponding cis-trans diepoxide, the addition taking place at C_5-C_6 and C_7-C_8 bonds (59). On the other hand, N-oxidation of s-triazolo(1,5-a)pyrazine and imidazo(1,5-a)pyrazine gives the corresponding 7-oxides (60,61). Azoloazines with no additional nitrogens in the six-membered ring are usually unstable towards oxidation and the six-membered ring is degraded into azolocarboxylic acid or derivatives.

So far, no direct introduction of a N-oxide function in the five-membered ring of azoloazines is known. The only known examples of 1- or 3-oxides have been prepared by cyclization of appropriate substituted azines (62-66).

N-Amination is reported for imidazo(1,5-a)pyridine and takes place at N_2 (67).

Electrophilic substitution at carbon atoms. Since azaindolizines can be regarded as a combination of π-excessive and π-deficient heterocyclic ring, it is not suprising that electrophilic substitutions proceed in general at carbon atoms in the five-membered ring. This is also in accord with molecular orbital calculations of varying degree of sophistication. There are also some exceptions, governed mainly by extra nitrogen atoms. For example, s-triazolo(1,5-a)pyrimidines are substituted at position 6 (68-71), and triazolopyrazines give 5-substituted derivatives (72).

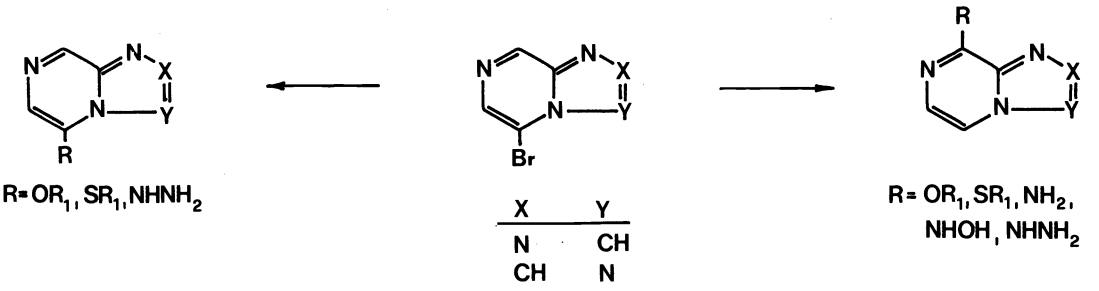
Unless an activating substituent is present, progressive aza substitution rapidly diminishes susceptibility for electrophilic atack at ring carbon atoms. For example, tetrazolopyridazines do not undergo electrophilic substitution under normal reaction conditions.

Deuterium exhange was studied under various conditions. In acid solution the deuterium exchange follows the pattern of electrophilic substitution, whereas under basic conditions the exchange takes place in general at positions ortho to ring nitrogens. As anticipated, the relative rates of deuterium exchange increase with the number of ring nitrogens.

REACTIONS WITH NUCLEOPHILES

On hand of MO calculations and experimental data, progressive aza substitution in indolizine enhances the ease for nucleophilic attack. There are many examples of azaindolizine functionalization via nucleophilic substitution, but there are also several examples of more sophisticated transformations. Under the influence of nucleophile ring opening and eventual recyclization may take place. Since the six-membered ring is most susceptible for nucleophilic attack, these reactions occur in general there. A ring opening of the five-membered ring was observed only with the corresponding N-methiodides (48,73,74). In acid solution v-triazoloazines behave similarly (75-77).

The ring opened products are azoles with an unsaturated side chain and usually cis-trans isomerization accompanies the process (78,79). The first step is most probably addition to double bond, similar to covalent hydration, but so far conclusive evidence is lacking. In a similar manner, from hydrazinolysis of several azoloazines aminoazoles have been isolated as degradation products (55,80-87). During hydrazinolysis of imidazo(1,2-a)-, s-triazolo(4,3-a)- and s-triazolo(1,5-a)pyrazine the six-membered ring is cleaved. In order to explain the formation of a mixture of azoles, an initial attack of hydrazine either at position 5 or 8 of the bicycle must be taken into consideration (82). This occurs also when 5-halo triazolopyrazines are treated with nucleophiles. Along with the normal substitution products (at C_5) 8-substituted derivatives were obtained and the reaction is best formulated as telesubstitution (72,88).

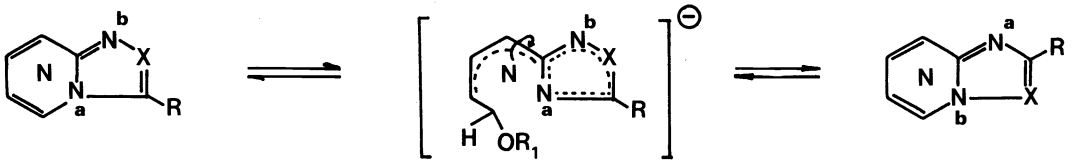


After this first example in the azaindolizine series, teleamination with metal amides at almost all positions of the pyridine part of imidazo(1,2-a)pyridine could be observed (89). The reaction is accompained by dimer formation.

Closely related are rearrangements of the Dimroth type. Many azaindolizines can be rearranged (Table I) and a nitrogen at position 1 is the condicio sine qua non. As a result of Dimroth rearrangement, positions 2 and 3 are exchanged in this process. The ease and course of rearrangement are influenced

Table I. Systems which undergo Dimroth rearrangement

System	Rearranged system	Ref.
Imidazo(1,2-a)pyridine		129
-(1,2-c)pyrimidine		90,130
-(1,2-a)pyrimidine		90
s-Triazolo(4,3-a)pyridine	-(1,5-a)-	131
-(4,3-c)pyrimidine	-(1,5-c)-	30,132
-(4,3-a)pyrazine	-(1,5-a)-	133
-(4,3-a)pyrimidine	-(1,5-a)-	91,94,98,134-138
-(4,3-b)-1,2,4-triazine	-(1,5-b)-	92
-(4,3-d)-1,2,4-triazine	-(2,3-d)-	92
-(4,3-a)-1,3,5-triazine	-(2,3-a)-	53,139
-(3,4-c)-1,2,4-triazine	-(3,2-c)-	140,141



by several factors. First of all, the rearrangement is facilitated with progressive aza substitution thus rendering position 5 of the bicycle more susceptible for nucleophilic attack. This is supported also from MO calculations (90). Substituents exhibit a similar effect, i.e. electron attracting groups facilitate the process. Rates of isomerization have been studied for s-triazolo(4,3-a)-

pyrimidines and a steep increase of the reaction rates in the range of pH 10-12,5 and pH 1.5-2.5 has been observed (91). The driving force for rearrangement of triazoloazines seems to be a greater thermodynamic stability of the 1,5-x systems when compared with the 4,3-x systems. It should be mentioned, however, that few cases of a retro-Dimroth rearrangement are known.

The potentiality of Dimroth rearrangement must be envisaged in synthetic paths leading to triazoloazines. For example, cyclization of 5-hydrazino-1,2,4-triazines with formic acid proceeds in the normal manner at 18°, whereas at elevated temperatures the isomeric system is formed (92). Similar observations have been frequent in the pyrimidine series (93-96) where oxo groups facilitate the cyclization, but render the isomerization more difficult (97,98). Recently, in aqueous buffers, the rearrangement could be stopped at the acylaminoalkenyltriazole stage (96).

Tetrazolo(1,5-c)pyrimidines, when cleaved in the manner as discussed above, are recyclized with the participation of either nitrogens adjacent to the side chain giving back the starting compound (99). A Dimroth-type rearrangement with participation of a side chain has been observed with certain pyrazolo(1,5-c)pyrimidines. Here, instead of a ring nitrogen an acetyl group was involved in the recyclization step (100).

REDUCTION

Catalytic hydrogenation of indolizine and azaindolizines in neutral solution leads to the corresponding 5,6,7,8-tetrahydro derivatives, whereas in the presence of acid the five-membered ring of indolizine is reduced selectively (101). Azolopyridazines give either the 7,8-dihydro or 5,6,7,8-tetrahydro derivatives, this being ascribed to appreciable bond localization (102).

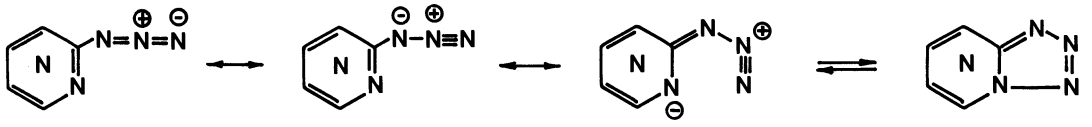
On the other hand, reduction of some azaindolizines with metal hydrides gives the 5,8-dihydro derivatives (103). The mechanism of $NaBH_4$ reduction was investigated with azolopyridazines which form first an immonium ion by protonation at N_5. Furthermore, it could be shown that reduction of the C_7-C_8 bond preceeds that of the N_5-C_6 bond unless substituents are present at C_7 and C_8, leading then to a 5,6-dihydro product (104,105). The later is obtained also from borohydride dehalogenation and reduction of perchloro s-triazolo(4,3-b)pyridazines (106).

CYCLOADDITION REACTIONS

Indolizines undergo cycloaddition reactions with dimethyl acetylenecarboxylate to give cyclazines (107,108). Only few other azoloazines form cycloadducts (109-113). Some react in two steps via the fumarate, as shown with pyrrolo(1,2-b)pyridazines. Polyazaindolizines do not react and this has been ascribed to a high degree of aromatic character of these systems.

AZIDO-TETRAZOLO ISOMERIZATIONS

Interconversion of an azine, having an azido group adjacent to the ring nitrogen, into a tetrazoloazine with a fused tetrazole ring can be defined and interpreted as azidomethine-tetrazolo equilibrium, or 1,5-dipolar cycloaddition or cyclization, and as valence isomerization. The last term is used in general in connection with fast, usually concerted rearrangements accompained by reorganization of electrons. Although the remaining two definitions fit with the description of the above isomerizations, we prefer the terminology of azido-tetrazolo isomerizations (for review see ref. 18,114).



Several factors influence this equilibrium. MO calculations indicate that there is a small energy difference between the linear and bent arrangement of the azido group. The electron density on the azine ring nitrogen which participates in ring closure is mainly responsible for the ease of cyclization and the stability of the tetrazolo form. The smaller the electron donating capacity of the azine, the weaker is the N-N bond and consequently less stable is the tetrazolo form. A greater delocalization of the negative charge in the azine (one or two additional nitrogens, particularly in m-position to the ring nitrogen) stabilizes the azide form. For example, 2-azido-1,3,5-triazine exists entirely in the azide form. In general, the conversion of the fused tetrazole into an azide is an endothermic process and substituents may exert a stabilizing or destabilizing effect. As with other equilibria, azido-tetrazolo isomerizations are influenced by the solvent, temperature or blocking an adjacent

ring nitrogen. The later holds for pyridazines with a N-oxide function or when fused to another ring. Thus, 6-azidotetrazolo(1,5-b)pyridazine exists only in this form and an interplay of the azido group and tetrazole ring is best evidenced in the 7-methyl analog, being thermally converted in the 8-methyl isomer (115).

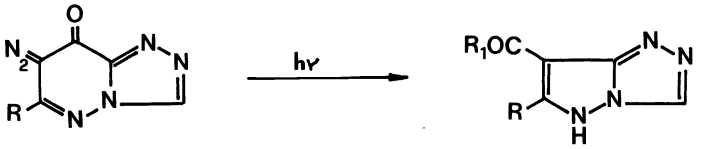
PHOTOCHEMICAL TRANSFORMATIONS

Several aspects of the photochemistry of azoloazines have been investigated. Photolysis of tetrazolo(1,5-b)pyridazines causes ring opening to give 3-cyanocyclopropenes and traces of 3-cyanopyrazoles (116,117).

s-Triazolo(4,3-b)- and imidazo(1,2-b)pyridazines are photochemically alkylated in the presence of alcohols to give 7- and 8-substituted products (118). It is anticipated that mixtures of the corresponding hydroxyalkyl-7,8-dihydro derivatives are formed first and upon thermal dehydration these are converted into alkylated azoloazines.

s-Triazolo(4,3-b)- and s-triazolo(1,5-b)pyridazines when irradiated in the presence of alkenes or cycloalkenes give a mixture of products. For their formation a mechanism which involves addition with subsequent ring opening of the bicycle has been forwarded (119-123).

Upon irradiation, diazoketones of the s-triazolo(4,3-b)pyridazine series undergo ring contraction to pyrazolo(3,2-c)-s-triazoles (124-126).



SUMMARY AND CONCLUSIONS

In this review it has not been possible to give more than a brief survey of the most important transformations and reactivity of azaindolizines. Although much additional work would be needed to fully understand and explain many transformations in this field, it is nevertheless possible to make some conclusions on hand of existing data. The relative stability and reactivity of particular azaindolizine is governed primarily by the dual character of the bicycle (π-excessive and π-deficient part) and secondly by the number and position of additional ring nitrogens. If these effects are understood properly, this is of enormous help in rationalizing their chemical reactivity.

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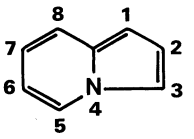
Appendix I



Additional N at positions	Name[a)]
-	pyrrolo(1,2-a)pyridine (indolizine)
1	imidazo(1,2-a)pyridine
2	imidazo(1,5-a)pyridine
3	pyrazolo(1,5-a)pyridine
5	pyrrolo(1,2-b)pyridazine
6	pyrrolo(1,2-c)pyrimidine
7	pyrrolo(1,2-a)pyrazine
8	pyrrolo(1,2-a)pyrimidine
1,2	s-triazolo(4,3-a)pyridine
1,3	s-triazolo(1,5-a)pyridine
1,5	imidazo(1,2-b)pyridazine
1,6	imidazo(1,2-c)pyrimidine
1,7	imidazo(1,2-a)pyrazine
1,8	imidazo(1,2-a)pyrimidine
2,3	v-triazolo(1,5-a)pyridine
2,7	imidazo(1,5-a)pyrazine
2,8	imidazo(1,5-a)pyrimidine
3,5	pyrazolo(1,5-b)pyridazine
3,6	pyrazolo(1,5-c)pyrimidine
3,7	pyrazolo(1,5-a)pyrazine
3,8	pyrazolo(2,3-a)pyrimidine
1,2,5	s-triazolo(4,3-b)pyridazine
1,2,6	s-triazolo(4,3-c)pyrimidine
1,2,7	s-triazolo(4,3-a)pyrazine
1,2,8	s-triazolo(4,3-a)pyrimidine
1,2,3	tetrazolo(1,5-a)pyridine
1,3,5	s-triazolo(1,5-b)pyridazine
1,3,6	s-triazolo(1,5-c)pyrimidine
1,3,7	s-triazolo(1,5-a)pyrazine
1,3,8	s-triazolo(1,5-a)pyrimidine
1,6,7	imidazo(1,2-d)-1,2,4-triazine
1,6,8	imidazo(1,2-a)-1,3,5-triazine
2,3,8	v-triazolo(1,5-a)pyrimidine
2,6,7	imidazo(1,5-d)-1,2,4-triazine
1,2,3,5	tetrazolo(1,5-b)pyridazine
1,2,3,6	tetrazolo(1,5-c)pyrimidine
1,2,3,7	tetrazolo(1,5-a)pyrazine
1,2,3,8	tetrazolo(1,5-a)pyrimidine
1,2,5,8	s-triazolo(4,3-b)-1,2,4-triazine
1,2,6,8	s-triazolo(4,3-a)-1,3,5-triazine
1,2,7,8	s-triazolo(3,4-c)-1,2,4-triazine
1,2,6,7	s-triazolo(4,3-d)-1,2,4-triazine
1,3,5,8	s-triazolo(1,5-b)-1,2,4-triazine
1,3,6,8	s-triazolo(2,3-a)-1,3,5-triazine
1,3,6,7	s-triazolo(2,3-d)-1,2,4-triazine
1,3,7,8	s-triazolo(3,2-c)-1,2,4-triazine
2,3,7,8	v-triazolo(5,1-c)-1,2,4-triazine

a) Nomenclature according to Chemical Abstracts and Revised Ring Index