A New Ring Transformation of 3-Halo-2-azidopyridine 1-Oxides. A Novel Synthesis of 1,2-Oxazin-6-ones.

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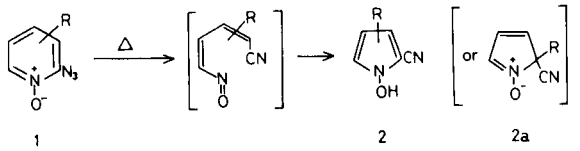
The course of the thermal ring-opening and recyclization of 2-azidopyridine 1-oxides is radically altered by the presence of a 3-halo substituent. Provided the 6-position is blocked, recyclization leads to a 6-cyano-6-halo-1,2-oxazine which hydrolyzes very readily to the 6*H*-1,2-oxazin-6-one. The structure of 4-bromo-3-methyl-6*H*-1,2-oxazin-6-one so obtained was confirmed by single crystal X-ray analysis. If the 6-position is not blocked, the product undergoes a further ring opening to give (*Z*)-β-cyanoacrylates.

J. Heterocyclic Chem., **13**, 415 (1976).

Sir:

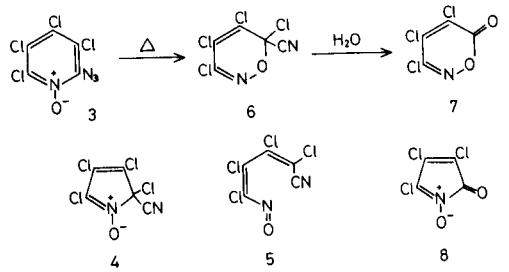
The thermal decomposition of 2-azidopyridine 1-oxides (**1**; R = H) resulted in an interesting ring contraction leading to 2-cyano-1-hydroxypyrroles (**2**) (1). The corresponding 2-azidoquinoline (2), -pyrazine (1), and quinoxaline 1-oxides (2) gave the 2-cyanoindoles, -imidazoles, and -benzimidazoles, respectively. A mechanism involving a concerted ring-opening nitrogen-elimination followed by recyclization was proposed (1), and the suggested ring-opened products could be trapped by nucleophilic solvents. Thermolysis of 3-azidopyridazine 2-oxides led to the isolation of the ring-opened products (3). When a methyl group was present at the 3-position of the pyridine ring (**1**; R = CH_3) ring-opening and recyclization led to 2*H*-pyrrole 1-oxides (4). We now report the remarkable effect of a halogen atom at the 3-position of the pyridine ring (**1**; R = 3-Cl or -Br) which leads to a complete change in the mode of recyclization.

Thermolysis of 2-azido-3,4,5,6,-tetrachloropyridine 1-oxide (**3**) (5,6) in dry toluene under completely anhydrous conditions gave a product, $C_5Cl_4N_2O$, (A), b.p. 47-49°



1 2 2a

at 1μ (70.8%). Two possible structures **4**, and **5**, were initially considered for this product but had to be rejected on the basis of the product's spectral and chemical properties. Thus, the mass spectrum did not show an



3 6 7

4 5 8

M^+ -16 or an M^+-17 peak (*e.g.*, **2** and **2a**) but did show an M^+ - NO peak. Treatment of the compound with wet hexane gave a compound $C_4Cl_3NO_2$, (B) (5), m.p. 53-54°, initially thought to be **8** (ν C=O 1730 cm^{-1}) which also did not exhibit an M^+ -O peak in the mass spectrum as would have been expected for **8**. (A) did not give a cycloadduct (7) with phenyl isocyanate, only 1,3-diphenylurea (67.4%) being isolated. Similarly, no reaction occurred between (A) and cyclopentadiene, or 2,3-dimethyl-2-butene (8), or diethylamino-1-propyne (in the latter case only *N,N*-diethylpropionamide was isolated). This ruled out structures **4** and **5** and left only **6** for consideration. Support for the 6*H*-1,2-oxazine structure comes from the uv spectrum of (A) (λ max (ethanol) 262 nm, log ε 3.96). Compounds having the nitrone function $>C=\overset{+}{N}-\underset{O^-}{|}$ are reported to absorb at 311 nm (log ε 4.20), while those having a >C=N-O function absorb at 266 nm (log ε 4.13) (9). Both (A) and (B) exhibit an N-O stretching band at 950 and 920 cm^{-1}, respectively. (B) is thus the oxazinone **7**.

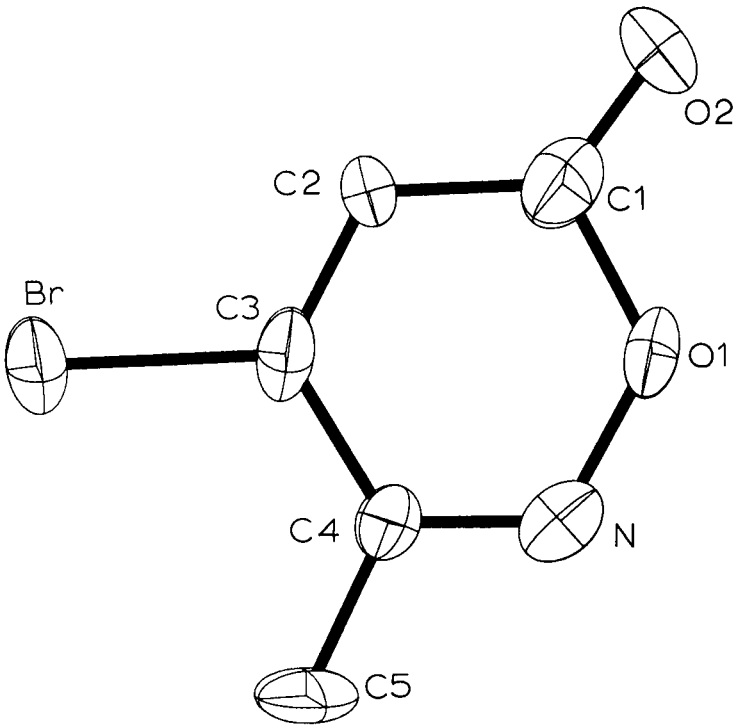
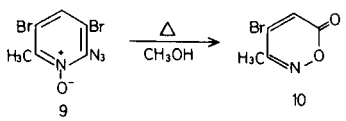
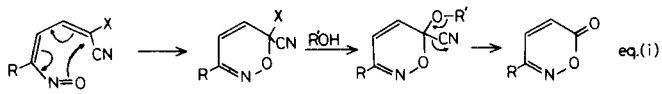


Figure 1. Molecuar structure of **10** with the atoms represented by their 50% probability ellipsoids for thermal motion. Important bond distances are: C1-C2, 1.43(2); C2-C3, 1.36(2); C3-C4, 1.47(2); C4-N, 1.29(2); N-O1, 1.42(1); O1-C1, 1.42(2); C1-O2, 1.19(2); C3-Br, 1.87(1); C4-C5, 1.44(2). The closest intermolecular approach is 3.004(9)Å between Br and O2. The six-membered ring is planar to within 0.015Å.

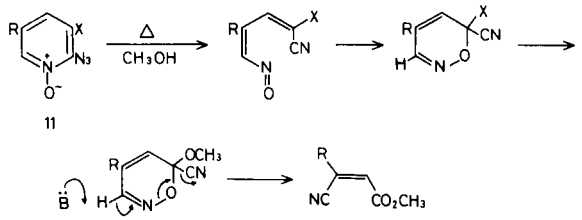
Definitive evidence for the oxazine structure came from a study of the decomposition of 2-azido-3,5-dibromo-6-methylpyridine 1-oxide (**9**), m.p. 99-100°, in methanol, ethanol, or wet benzene to give, in every case, 6*H*-4-bromo-3-methyl-1,2-oxazin-6-one (**10**), m.p. 67-68° (74%, methanol; 36%, wet benzene). The mass spectrum of **10** showed no M^+-O or M^+-OH peak but did show M^+-NO and M^+-NO-CO peaks. It exhibited the expected infrared and nmr spectra. The single crystal X-ray structure analysis (10) gave the strucural parameters and archistructure depicted in Figure 1. Thus, the presence of a 3-halogen atom in **1** diverts the recyclization from its normal route, probably as in equation (i), provided C-6 is blocked (11).



9 10



If C-6 is not blocked, a further ring-opening reaction is observed. Thus, thermolysis of 2-azido-3-chloropyridine 1-oxide (**11**; X = Cl, R = H), m.p. 71-72° dec., (5), in methanol gave methyl *cis*-β-cyanoacrylate (**12**); R = H), m.p. 30-31° (72%), identical with an authentic sample (3,14). Similarly, thermolysis of 2-azido-3-bromo-5-methylpyridine 1-oxide (**11**; X = Br, R = CH_3) (5) in degassed methanol at 105° gave methyl β-methyl-(*Z*)-β-cyanoacrylate (**12**; R = CH_3), b.p. 46-48° at 30μ (60%) (5), also identical with authentic material (14). Proton-abstraction from C-3 of the intermediate would account for the results.



11 12

There has been relatively little work published on 6*H*-1,2-oxazin-6-ones (15) or on the parent 1-2-oxazine system itself so that the above convenient synthesis stimulates us to study the scope of this reaction and the properties of this relatively simple but interesting molecule.

Acknowledgements.

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(5) All new compounds analyzed correctly and exhibited the expected spectral (ir, nmr, and mass) properties.

(6) This azide, m.p. 103-105° dec., (5), was prepared from pentachloropyridine 1-oxide and sodium azide in hot ethanol,

and was obtained as a mixture with two diazidotrichloropyridine 1-oxides (5) (probably the 2,4- and 2,6-diazido derivatives), m.p. 119-121° dec., and m.p. 116-118° dec. These azides could be separated by preparative thin layer chromatography. It was obtained more conveniently, and uncontaminated by starting *N*-oxide or diazides, in 58.9% yield by reaction of **3** with tetramethylguanidinium azide in methylene chloride at room temperature for 5 hours followed by chromatography on a column of silica gel.

(7) Compare the behavior of other nitrones related to **4** (4).

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(10) $C_5H_4BrNO_2$: monoclinic, $P2_1/n$; a = 5.934 (7), b = 7.845 (7), c = 14.455 (9) Å; β = 101.78 (5) °; ρ_{calcd} = 1.92 g. cm^{-3} for Z = 4 least-squares refinement gave R_1 (F) = 0.067 and R_2 (F) = 0.075 for 758 independent reflections collected on a CAD-4 diffractometer.

(11) There are two reports in the literature of cyclic nitrones isomerizing to 1,2-oxazines. The first (12) is an experimentally unsubstantiated isomerization of 2-methoxy-2,3,5-triphenyl-(2*H*)-pyrrole 1-oxide to 6-methoxy-3,5,6-triphenyl-1,2-(6*H*)oxazine at 215-220° which, if confirmed, may well involve preliminary ring-opening to the nitroso derivative followed by recyclization as proposed above [equation (i)]. The second (13) is an acid-catalyzed isomerization of a bicyclic nitrone. We have found no evidence for the intermediacy of a nitrone [**4** or **2a** (R = Br)] in our reactions and, indeed, nitrones **2a** do not isomerize to 1,2-oxazines under our reaction conditions (4). We therefore do not believe that a cyclic nitrone is an intermediate in the reactions reported here.

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