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Hiroshi Igeta: Syntheses of Pyridazine Derivatives. VI.[1] 3-Chloropyridazine 1-Oxide.

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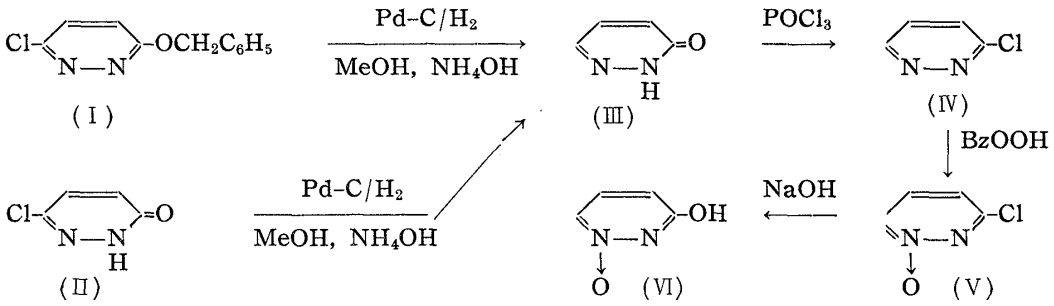
In Part III[2] of this series, it was shown that oxidation of 3-methoxypyridazine with hydrogen peroxide in glacial acetic acid gave 3-methoxypyridazine 1-oxide. The present paper describes the oxidation of 3-chloropyridazine with perbenzoic acid in a chloroform solution.



Catalytic hydrogenation of 3-benzyloxy-6-chloropyridazine[3] (I) and of 6-chloro-3-pyridazone[4] (II) with palladium-carbon in hydrous methanolic ammonia solution gave 3-pyridazone (III). 3-Pyridazone was treated with phosphoryl chloride by the usual way to form 3-chloropyridazine (IV). 3-Chloropyridazine is so labile that this, without further purification, was immediately submitted to oxidation with perbenzoic acid. 3-Chloropyridazine mono-N-oxide (V) so obtained was hydrolysed with 5% NaOH and a hydroxypyridazine N-oxide was obtained which was proved to be identical with 3-hydroxypyridazine 1-oxide (VI)[2] by admixture and also by comparing the infrared absorption spectra.

Thus the oxygen atom in 3-chloropyridazine N-oxide was proved, as in the case of 3-methoxypyridazine 1-oxide, to be attached to the nitrogen in 1-position.

Experimental

3-Pyridazone (III)—i) A mixture of a solution of 0.8 g. of (I) dissolved in 20 cc. of MeOH, 0.5 cc. of 28% NH_4OH, and Pd-C, prepared from 0.2 g. of charcoal and 5 cc. of 1% $PdCl_2$ solution, was hydrogenated. After 220 cc. (ca. 2 moles) of H_2 was absorbed, the catalyst was removed by filtration and MeOH was evaporated. The residue was extracted with dehyd. EtOH to remove NH_4Cl by filtration. After evaporation of EtOH, the residue was submitted to a low-pressure distillation, collecting the fraction of $b.p_{11}$ 160~165° (bath temp.) and 0.2 g. of the distillate obtained was recrystallized from benzene to white needles, m.p. 74°.

ii) A mixture of 5 g. of (II) dissolved in 30 cc. of MeOH, 5 cc. of 28% NH_4OH, and Pd-C, prepared from 0.5 g. of charcoal and 10 cc. of 1% $PdCl_2$ solution, was hydrogenated. After removal of the catalyst by filtration, MeOH was evaporated to dryness. The residue was extracted with benzene, which was filtered while hot and the filtrate was concentrated to a small volume. After cool, the deposited crystals were collected. Yield, 3.4 g. of m.p. 74°.

3-Chloropyridazine 1-Oxide (V)—A mixture of 5 g. of (III) and 20 cc. of $POCl_3$ was heated on a steam bath for 5 min. and excess of $POCl_3$ was removed under a reduced pressure below 70°. The reaction mixture was poured onto ice, neutralized with $NaHCO_3$, and extracted with Et_2O. The Et_2O

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1) Part V: This Bulletin, 8, 550(1960).
2) Part III: *Ibid.*, **7**, 938(1959).
3) Part I: Yakugaku Zasshi, **74**, 1195(1954).
4) T. Kuraishi: This Bulletin, **5**, 376(1957).

layer was dried over anhyd. K_2CO_3 and evaporated. Somewhat reddish solid, m.p. 35°, so obtained, was immediately dissolved in 20 cc. of $CHCl_3$ and 300 cc. of a $CHCl_3$ solution of perbenzoic acid (containing 0.0024 g. of active oxygen per cc.) was added. The solution was allowed to stand for 4 days at room temperature and $CHCl_3$ was removed under a reduced pressure. Water was added to the residue, neutralized with $NaHCO_3$, and then extracted with $CHCl_3$. The $CHCl_3$ layer was dried over $CaCl_2$ and $CHCl_3$ was evaporated. The residue was recrystallized from $(iso\text{-}Pr)_2O$ to white needles, m.p. 93°. Yield, 1.5 g. *Anal.* Calcd. for $C_4H_3ON_2Cl$: C, 36.80; H, 2.31; N, 21.46. Found: C, 36.78; H, 2.39; N, 21.96.

Hydrolysis of 3-Chloropyridazine 1-Oxide (V): Formation of 3-Hydroxypyridazine 1-Oxide (VI)—A solution of 200 mg. of (V) in 6 cc. of 5% NaOH was heated on a steam bath for 30 min. After acidification of the solution, water was evaporated under a reduced pressure and the residue was extracted with EtOH while hot, removing NaCl by filtration. The filtrate was concentrated to a small volume, the crystals that separated out were collected, and recrystallized from EtOH to white needles, m.p. 200~205° (decomp.), undepressed on admixture with an authentic specimen.

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Summary

The oxygen atom of 3-chloropyridazine N-oxide was, as in the case of 3-methoxypyridazine 1-oxide, proved to be in 1-position.

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