

Reactions with 2*H*-Pyrido[2,3-*e*]-1,3-oxazine-2,4(3*H*)-dione

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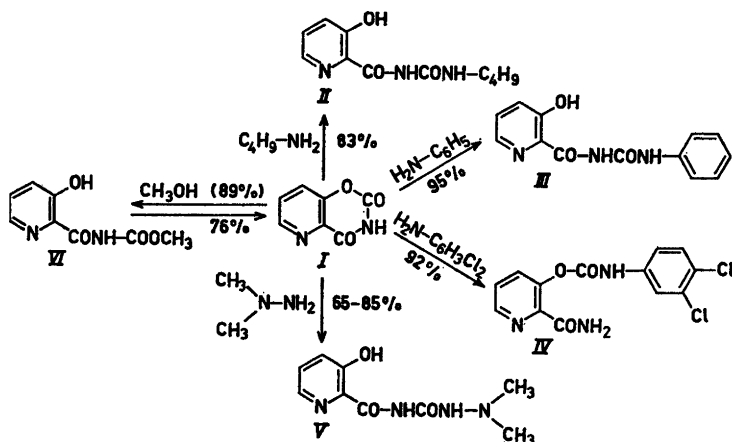
The recently described pyridoöxazine I lends itself to a number of reactions of preparative value. Representative examples of such reactions are shown below and described in the experimental part. All compounds prepared (II–VI) are new. Their structures follow from the syntheses, from analyses, and from the fact that they all, except the carbanilate IV, give a red ferric chloride reaction.

Experimental. *N*-Butyl-*N'*-(3-hydroxypicolyl)urea (II). I (1.00 g) and butylamine (5.0 ml) are mixed and heated under reflux (30 min). The resulting clear solution is evaporated to dryness from a water bath (95°), at last under 1 mm. The pasty residue is dissolved in methanol (12 ml). Water (4 ml) is added and the hot solution brought to pH 5–6 by addition of 3 N hydrochloric acid (2.5–3.0 ml). The solution is cooled, whereby crystals of II separate. The white crystals are isolated by filtration, washed with water (5 ml), and dried (1 h, 50°, 1 mm). The yield is 1.20 g (83 %) of II, m.p. 102–103° (Hershberg app., corr.). [Found: C 55.6; H 6.3; N 17.7. Calc. for C₁₁H₁₆N₃O₃ (237.3): C 55.7; H 6.4; N 17.7]. The product gives a red ferric chloride reaction in aqueous-ethanolic solution.

N-Phenyl-*N'*-(3-hydroxypicolyl)urea (III). I (1.00 g) is heated (100°) with aniline (5.0 ml) for a few minutes to give a clear solution. The solution is kept at 120° (30 min). After cooling, ether (40 ml) is added. The resulting white crystals of III are isolated by filtration, washed with ether, and dried (15 h, 90°, 1 mm). The yield is 1.49 g (95 %) of III, m.p. 191°. [Found: C 60.7; H 4.2; N 16.2. Calc. for C₁₃H₁₁N₃O₃ (257.2): C 60.7; H 4.3; N 16.3]. The product gives a red ferric chloride reaction in ethanolic solution.

3-(3,4-Dichlorophenylcarbamyloxy)picolinamide (IV). I (2.00 g, 0.0122 mole) and 3,4-dichloroaniline (2.00 g, 0.0123 mole) are mixed and kept at 140° for 75 min. The resulting crystalline mass is crystallized from dimethylformamide (100 ml) with carbon black. The wet crystals are washed with dimethylformamide (two 15 ml portions) and dried (90 min, 80°, 1 mm). The yield is 3.64 g (92 %) of IV, m.p. 237–238°. [Found: C 48.2; H 3.0; Cl 21.8; N 12.6. Calc. for C₁₃H₉Cl₂N₃O₃ (326.1): C 47.9; H 2.8; Cl 21.7; N 12.9]. The product gives no ferric chloride reaction.

N-Dimethylamino-*N'*-(3-hydroxypicolyl)urea (V). I (1.00 g) and dimethylhydrazine (5.0 ml) are mixed and heated under reflux (45 min). The resulting clear solution is evaporated to dryness from a water bath (80°) under 10 mm. The pasty residue is dissolved in hot methanol (2 ml). Ether (200 ml) is added in one portion. The almost clear solution is filtered through a sintered glass disk (G 4), whereby a small amount of a brownish-yellow, cloudy precipitate is removed. The filtrate is evaporated with stirring to 20–30 ml, whereby white crystals of V separate. The crystals are



isolated by filtration and dried overnight (20°, 1 mm). The yield is 0.88 g (64 %) of V. [Found: C 48.3; H 5.5; N 24.9. Calc. for $C_9H_{12}N_4O_3$ (224.2): C 48.2; H 5.4; N 25.0].

The products obtained in the above synthesis do not always behave in the same way, when heated in a tube. They may soften and melt completely at temperatures between 115° and 152°, depending upon the particular product, as well as upon the rate of heating. The yields obtained in the synthesis are also not reproducible, being either around 65 % or around 85 %. However, all products are always analytically pure, give a red ferric chloride reaction, and have identical infrared absorption spectra in a chloroform solution. It has not been investigated, whether the different products obtained in the crystalline state are polymorphic or isomeric (e.g. tautomeric).

3-Hydroxypicolylcarbamie acid methyl ester (VI). I (1.00 g) is added to a solution of sodium methoxide in methanol [from sodium (0.15 g) and methanol (5 ml)] and the mixture heated under reflux (5 min). The reaction mixture is cooled and acetic acid (0.37 ml) and then water (10 ml) added. The resulting suspension of white crystals is stirred for half an hour. The crystals are isolated by filtration, washed with water (10 ml) and dried (2 h, 50°, 1 mm). The yield is 1.07 g (89 %) of VI. [Found: C 48.8; H 4.2; N 14.7; OCH_3 15.1. Calc. for $C_8H_8N_2O_4$ (196.2): C 49.0; H 4.1; N 14.3; one OCH_3 15.8]. The product gives a red ferric chloride reaction.

The above analyses indicate, that the product contains about 4 % of pyridoöxazine as an impurity. Thin-layer chromatography also shows the presence of pyridoöxazine. We believe that the pyridoöxazine was not present in the wet crystals, but has been formed during drying.

When heated in a tube the product melts around 170° and resolidifies around 220° (formation of I). 1.00 g of the product was heated in an open tube to 190–210° for 7 min. During this time it first gave off methanol and then solidified. The resulting brown solid was crystallized from acetic acid (12 ml) with carbon black to give 0.64 g (76 %) of I, m.p. 265–270° with decomposition.¹ [Found: C 51.3; H 2.7; N 16.9. Calc. for $C_7H_4N_2O_3$ (164.1): C 51.2; H 2.5; N 17.1].

1. Clauson-Kaas, N., Brammer Petersen, J., Sørensen, G. O., Olsen, G. and Jansen, G. *Acta Chem. Scand.* **19** (1965) 1147.

Received August 30, 1966.

Acta Chem. Scand. **20** (1966) No. 7

Studies on Orchidaceae Alkaloids

V.* A New Alkaloid from *Phalaenopsis amabilis* Bl.

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A new alkaloid phalaenopsin (I) has been isolated from *Phalaenopsis amabilis* Bl., m.p. 99°–101°, elementary formula $C_{20}H_{27}NO_5$, MW 361 which was verified by its mass spectrum. Prominent peaks in the mass spectrum are m/e 361 (M^+), 330, 288, 124 (base peak), 83, and a metastable ion at m/e 230 corresponding to a breakdown of m/e 361 to m/e 288.

The hydrochloride of I ($C_{20}H_{28}ClNO_5$) had m.p. 155°–156°. The UV absorption of the base has maxima at 264, 258, 254, 248, and 243 $m\mu$, the IR spectrum shows a strong band at 1735 cm^{-1} , but no NH band. The molecule contains one O—CH₃ but no N—CH₃ or C—CH₃. The hydrochloride of I shows the following distinct bands in the NMR spectrum (DMSO d_6): $\tau = 2.55$ 5H singlet, $\tau = 4.3$ 1H singlet ($N^+ - H$), $\tau = 5.72$ 2H triplet ($J = 6$ cps), $\tau = 6.24$ 3H singlet, $\tau = 6.84$ 2H singlet, $\tau = 6.86$ and 7.33 2H A—B ($J = 16$ cps).

The data suggest that the alkaloid is an ester containing a *mono*-substituted benzene nucleus. All elementary analyses gave the correct values. The LD₅₀ of the hydrochloride of I in mice (intravenous) is 75 mg/kg. A full report on the isolation and structure of I will be published later.

The mass spectra were measured by Dr Ryhage and the NMR spectrum of the hydrochloride by Dr. Melera, Varian AG, Zürich, on a HA 100 spectrometer. The work has been supported by grants from the *Swedish Natural Science Research Council*.

Received September 7, 1966.

* Paper IV of this series: Lünig, B. *Phytochemistry*. *In press*.