Synthesis of Dipyrido[3, 2-*b*: 2′, 3′-*e*][1,4] oxazine (1,9-Diazapheno xazine)

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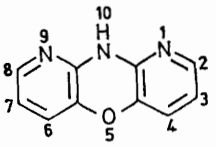
Summary Dipyrido[3,2-*b*: 2′,3′-*e*][1,4]oxazine has been synthesized from 2-aminopyridin-3-ol and 2-chloro-3-nitropyridine in Me_2SO.

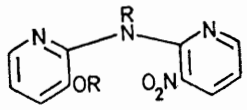
RECENT reports on the enhanced biological activities of aza-analogues of phenothiazine[1] have prompted similar studies on the structurally related phenoxazine;[2,3] so far 14 monoaza-, diaza-,[4] and triaza-phenothiazines[5] are known but only 4 monoaza-[6] and 1 diaza-phenoxazines[7] have been described. With the exception of 3-azaphenoxazine,[2] the

parent azaphenoxazines are also unknown. We therefore report here the synthesis of 1,9-diazaphenoxazine (**1**).†

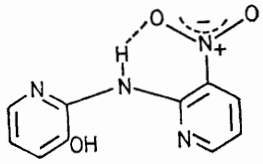
By using the acid-catalysed procedure already described and refluxing for 12 h, the reaction of 2-aminopyridin-3-ol with 2-chloro-3-nitropyridine gave a purple-red compound



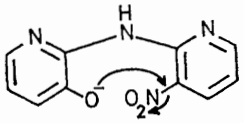
(1)



(2) R=H
(3) R=Ac



(4)



(5)

(45%), $C_{10}H_8N_4O_3$, m.p. 169°, which was identified as compound (**2**) by its i.r. (ν_{max} 3380, 3240, 1346, 1232, 747, and 772 cm^{-1}), n.m.r., and mass spectra. Acetylation (Ac_2O) of (**2**) gave the diacetyl derivative (**3**) [ν_{max} 1773 (ester) and 1695 (tertiary amide) cm^{-1}] which showed no phenolic OH or aromatic NH i.r. absorptions, thus ruling out the alternative oxygen-bridged structure 2-aminopyridin-3-yl 3-nitropyridin-2-yl ether.

Cyclization of compound (**2**) in aqueous or alcoholic base failed, probably owing to strong NHO hydrogen bonding [*i.e.* structure (**4**)] This chelation is supported by the i.r. spectrum in which the NH stretching frequency of compound (**2**) was shifted from 3400 to 3240 cm^{-1}, and confirmed by the shift in the N=O frequency from 1360 to 1346 cm^{-1}. Because of the strong hydrogen bonding we used Me_2SO as a solvent for the cyclization since the amino-hydrogen would preferentially form a hydrogen bond with it, and so free the nitro-group for cyclization *via* (**5**). Compound (**2**) was heated with NaOH (1 mol. equiv.) in refluxing Me_2SO for 9 h, to give a yellow solid, $C_{10}H_7N_3O$, m.p. 245°, λ_{max} (MeOH) 338 (log ϵ 4·12), 217 (4·30), and 210 (4·29) nm; ν_{max} 1297s, 1250, 747, and 772 cm^{-1}, which was assigned structure (**1**).‡ This structure was confirmed by its n.m.r. spectrum; τ 1·50 (s, 10-H) 2·76 (dd, 2- and 8-H), 2·94 (dd, 4- and 6-H), and 3·30 (dd, 3- and 7-H); $J_{2,3} = J_{7,8} = 6$ Hz; $J_{2,4} = J_{6,8} = 1$ Hz; $J_{3,4} = J_{6,7} = 8$ Hz, which confirms the symmetrical nature of the molecule (2-H ≡ 8-H, 3-H ≡ 7-4, 4-H ≡ 6-H) and rules out the alternative unsymmetrical 1,6-diaza-structure. Compound (**1**) was also obtained directly from 2-aminopyridin-3-ol and 2-chloro-3-nitropyridine in refluxing alkaline Me_2SO, but in only 8% yield.

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† Satisfactory microanalyses were obtained for all new compounds.

‡ Alkylaminoalkyl derivatives of compounds obtained by replacement of the ring oxygen in 1,9-diazaphenoxazine with sulphur and selenium have been reported [S. Rath, 1957, U.S.P. 2,789,978] but neither the method of preparation nor their chemical and physical properties were described.

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