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Studies on Heterocyclic Chemistry. XX.[1] Photo-reactions of 5-Benzylideneamino-3-arylisoxazoles in Trialkylamine

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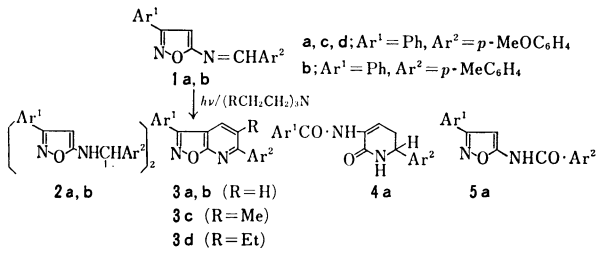
Synopsis. Irradiation of 5-benzylideneamino-3-arylisoxazoles at 254 nm in a mixture of trialkylamine and nitrile gives diaminoethanes (reduction), benzamides (oxidation), and isoxazolo[5,4-*b*]pyridine (cyclization).

From a growing interest in the photo-reactions of organic compounds in amines,[2] studies were carried out on 5-benzylideneamino-3-arylisoxazoles (**1**) which undergo photo-reduction, photo-oxidation, and photo-cyclization in trialkylamine.

Irradiation of **1a** in a mixture of triethylamine and benzonitrile (2:13) at 254 nm afforded *N,N'*-bis-(3-phenyl-5-isoxazolyl)-1,2-*p*-anisyl-1,2-ethanediamine (**2a**) and 3-phenyl-6-*p*-anisylisoxazolo[5,4-*b*]pyridine (**3a**) in low yields. The structure of **2a** was confirmed by synthesis, and that of **3a** rests on its spectral data. The high resolution mass spectrum displays M^+ as the base peak and the NMR spectrum two sets of one-proton doublets at δ 8.10 (J=8 Hz) and 8.67 ppm (J=8 Hz) besides methyl and phenyl protons. The β,γ-unsubstituted pyridine structure is established from their J value,[3] the lower-field doublet being assigned to the γ-proton by virtue of its remarkable downfield shift (0.46 ppm) in deuteriotrifluoroacetic acid. Absence of a benzoyl ion in its mass spectrum[4] rules out the corresponding oxazolo[5,4-*b*]pyridine structure. Photolysis of **1b** likewise produced the corresponding **2b** and **3b** in low yields.

Acetonitrile may be used as a solvent, but the reaction is far less clean. Thus, **1a** afforded 3-benzoylamino-6-*p*-anisyl-5,6-dihydro-2(1*H*)-pyridone (**4a**), *N*-(3-phenyl-5-isoxazolyl)-*p*-anisamide (**5a**), *p*-methoxybenzyl alcohol,[5] and 5-amino-3-phenylisoxazole in addition to **2a** and **3a**. The NMR spectrum (see Experimental) and mass spectral fragmentations [major ions: M^+, $Ar^2CH{=}NH_2^+$ (base peak), $Ar^1C{\equiv}O^+$, $(M\text{-}Ar^1CO)^+$, and $(M\text{-}Ar^2CH{=}NH)^+$] of **4a** are consistent with the assigned structure, whereas the structure of **5a** was confirmed by synthesis.



The two carbon fragment at positions 4 and 5 of the isoxazolopyridine ring arises from the amine, as supported by the regioselective formation of the 5-methyl and 5-ethyl derivatives (**3c**) and (**3d**) when **1a** was photolyzed in tripropylamine and tributyamine, respectively. It was found that **3c** and **3d** are obtained again in low yields by photolyzing **1a** in triethylamine in the presence of propionaldehyde and butyraldehyde, respectively.[6] This suggests the intermediacy of an aldehyde in the cyclization step leading to **3**, which may be formed by the photo-oxidation of the amine.[7] Isolation of butyric acid from the photolyzate in tributylamine supports the occurrence of the oxidation of amine.

Besides the occurrence of photo-reduction to **2** and photo-oxidation to **5**, photo-cyclization of **1** to **3**, which bears a marked resemblance to the photo-cyclization of some of the Schiff bases with ethanol,[8,9] is interesting because the related systems (*e.g.*, 5-benzylideneaminopyrazoles and *N*-benzylideneanilines) were photo-unreactive in amine[10] and relatively few studies[11] have been made on the isoxazolo[5,4-*b*] pyridine ring system. Attempts to obtain **3** in a moderate yield were unsuccessful. It may be relevant, however, to note some findings on the conditions to give **3**. Photolysis of a $(2\text{—}3)\times10^{-2}$ mol l^{-1} solution of **1** in a nitrile in the presence of *ca.* 50 molar excess of the amine was found to give **3** in 2—7% yield. Use of a solvent other than a nitrile (*e.g.*, ethanol and tetrahydrofuran) and >300 nm light was ineffective and use of dialkylamine (*e.g.*, diethylamine) slowed down the reaction

Experimental

NMR spectra were measured at 100 MHz using a Varian HA-100 spectrometer. The assignments were confirmed by decoupling techniques when necessary. The light source was a Riko low pressure mercury lamp (30 W) immersed in a quartz well.

*N,N'-Bis(3-aryl-5-isoxazolyl)-1,2-diaryl-1,2-ethanediamines (**2**).* The compounds were prepared in 20—48% yield as described[12] using wet tetrahydrofuran and crystallized from ethanol, for which satisfactory spectral data have been obtained. **2a**: mp 237—238 °C (dec). Found: C, 72.88; H, 5.13; N, 9.87%. Calcd for $C_{34}H_{30}N_4O_4$: C, 73.10; H, 5.41; N, 10.03%. **2b**: mp 260 °C (dec). Found: C, 77.34; H, 6.01; N, 10.75%. Calcd for $C_{34}H_{30}N_4O_2$: C, 77.54; H, 5.74; N, 10.64%.

*N-(3-Phenyl-5-isoxazolyl)-*p*-anisamide (**5a**).* The compound was prepared in 75% yield by the Schotten-Baumann procedure and crystallized from ethanol, mp 186—187 °C. Found: C, 69.20; H, 4.82%. Calcd for $C_{17}H_{14}N_2O_3$: C, 69.37; H, 4.80%.

Photolysis in Benzonitrile. A mixture of **1**, triethylamine (20 ml), and benzonitrile (130 ml) was irradiated under the conditions given in Table 1. Evaporation *in vacuo* and chromatography[5] of the residue with ether gave **3**, which crystallized from ethanol. **3a**: mp 170—171 °C, NMR (DMSO-d_6): δ 3.88 (s, 3H), 7.10 (d, J=9, 2H), 7.64 (m, 3H), 8.07 (m, 2H), 8.10 (d, J=8, 1H), 8.22 (d, J=9, 2H), 8.67 ppm (d, J=8, 1H); UV (EtOH) λ_{max} (log ε): 243 nm (4.12), 332

(4.43). Found: C, 75.75; H, 4.73; N, 9.42%. Calcd for $C_{19}H_{14}N_2O_2$: C, 75.48; H, 4.67; N, 9.27%. **3b**: mp 170—171 °C, NMR: δ 2.38 (s, 3H), 7.32 (d, J=9, 2H), 7.60 (m, 3H), 8.08 (m, 5H), 8.67 ppm (d, J=8, 1H); UV (EtOH) λ_{max} (log ε): 247 nm (3.96), 320 (4.12). Found: C, 79.56; H, 5.10; N, 9.64%. Calcd for $C_{19}H_{14}N_2O$: C, 79.70; H, 4.93; N, 9.78%. Elution with acetone gave **2**, identical with authentic specimens.

Table 1. Photolysis of **1** in benzonitrile

Compound	Irradiation time: Weight (g)	Irradiation time: h	Products Weights (g)
1a	(0.83)	20	**2a** (0.04) + **3a** (0.02)
2b	(1.00)	7	**2b** (0.12) + **3b** (0.01)

Photolysis in Acetonitrile. (a) A mixture of **1a** (2.78 g), triethylamine (40 ml), and acetonitrile (260 ml) was irradiated for 20 h. Evaporation *in vacuo* and chromatography of the residue with chloroform gave the starting material (0.57 g) and **3a** (0.01 g). GLC of the filtrate revealed the presence of *p*-methoxybenzyl alcohol. Elution with ether-ethyl acetate (5 : 1) gave an oil, which was triturated with ethanol to give an additional amount of **3a** (0.06 g). Evaporation of its filtrate and re-chromatography of the residue with ether-ethyl acetate (5 : 1) gave 5-amino-3-phenylisoxazole (0.10 g) and **5a** (0.10 g), identical with an authentic specimen. Elution with acetone gave **4a** (0.009 g), which was crystallized from ethanol, mp 199—200 °C, NMR: δ 2.70 (m, 2H), 3.72 (s, 3H), 4.64 (t, J=7, 1H), 6.88 (d, J=9, 2H), 7.11 (t, J=4, 1H), 7.28 (d, J=9, 2H), 7.52 (m, 3H), 7.81 (m, 2H), 8.28 (s, exchangeable, 1H), 9.04 ppm (s, exchangeable, 1H). Found: C, 70.97, H, 5.70; N, 8.76%. Calcd for $C_{19}H_{18}N_2O_3$: C, 70.79; H, 5.63; N, 8.69%. TLC of its filtrate revealed the presence of **2a**. (b) A mixture of **1a** (1.00 g), tripropylamine (or tributylamine) (20 ml), and acetonitrile (130 ml) was irradiated for 20 h and worked up as before. Elution with ether gave the corresponding 5-alkylisoxazolopyridines, which crystallized from ethanol. **3c**: mp 192—193 °C, NMR: δ 2.50 (s, 3H), 3.83 (s, 3H), 7.04 (d, J=9, 2H), 7.64 (m, 5H), 8.09 (m, 2H), 8.58 (s, 1H): UV (EtOH) λ_{max} (log ε): 236 nm (4.19), 321 (4.15). Found: C, 76.17; H, 4.96; N, 8.81%. Calcd for $C_{20}H_{16}N_2O_2$: C, 75.93; H, 5.10; N, 8.86%. **3d**: mp 144—145 °C, NMR: δ 1.16 (t, 3H), 2.84 (q, 2H), 3.83 (s, 3H), 7.04 (d, J=9, 2H), 7.53 (d, J=9, 2H), 7.62 (m, 3H), 8.08 (m, 2H), 8.57 ppm (s, 1H); UV (EtOH) λ_{max} (log ε) 234 nm (4.19), 318 (4.08). Found: C, 76.05; H, 5.51; N, 8.66%. Calcd for $C_{21}H_{18}N_2O_2$: C, 76.34; H, 5.49; N, 8.48%. (c) A mixture of **1a** (1.00 g), propionaldehyde (or butyraldehyde) (10 ml), triethylamine (10 ml), and acetonitrile (150 ml) was irradiated for 20 h. Work-up gave the corresponding 5-alkylisoxazolopyridines [**3c** (0.025 g); **3d** (0.046 g)].

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