

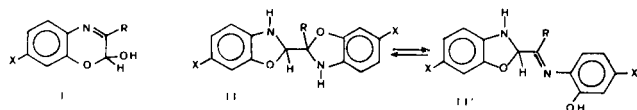
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A series of 1,4-benzoxazines (I) and 2,2'-dibenzoxazolines (II) were obtained by condensation of 2-aminophenol and 2-amino-5-nitrophenol with glyoxal derivatives of the heterocyclic series. The structure of compounds (I) was investigated by uv, pmr and mass spectroscopy.

J. Heterocyclic Chem., 17, 1625 (1980).

In previous papers (1,2) it was reported that from the condensation between 2-aminophenol and a series of phenylglyoxal derivatives two types of products, namely 2-hydroxy-3-aryl-(2*H*)-1,4-benzoxazines and 2'-aryl-2,2'-dibenzoxazolines were obtained. A further investigation of these reactions was carried out studying the condensation of 2-aminophenol and 2-amino-5-nitrophenol with glyoxal derivatives of the heterocyclic series (3,4,5). The same two types of compounds I and II were obtained employing either 1:1 or 2:1 molar ratios; a third product III was separated only from the reaction of 2-amino-5-nitrophenol with 2-furyl and 2-thienyl glyoxal. The 2-amino-5-nitrophenol was used to better understand the interesting tautomeric equilibrium of the dibenzoxazolines II and the related ketimine forms II'.



- I,II a: R = 2-furyl, X = H
 b: R = 2-thienyl, X = H
 c: R = 3-thienyl, X = H
 d: R = 2-furyl, X = NO₂
 e: R = 2-thienyl, X = NO₂
 f: R = 3-thienyl, X = NO₂
 g: R = phenyl, X = NO₂

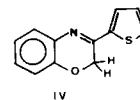
The relative amounts of the compounds I,IIa-c were determined through ultraviolet investigation after separation by thin layer chromatography. (Table 1).

Table 1
Relative percentages of I,IIa-c

Compound	Molar ratio 1:1	Molar ratio 2:1	R _f
Ia	48	15	0.47
IIa	52	85	0.55
Ib	52	19	0.56
IIb	48	81	0.61
Ic	31	9	0.56
IIc	69	91	0.66

In the case of the condensation of glyoxals with 2-amino-5-

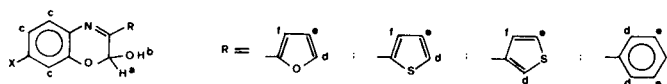
nitrophenol such a quantitative determination was not possible since together with compounds III d,e, unreacted nitroaminophenol and other unidentified by-products were always separated on the chromatographic plates. For the R_f of the compounds I,II d-g and III d,e see Experimental. This paper concerns the 1,4-benzoxazines I while the 2,2'-dibenzoxazolines II will be treated in the following paper. The structure I for the obtained benzoxazines was confirmed by uv and pmr spectroscopy. The ir spectra, in fact, give no useful indication because the broad band due to hydrogen bonds, in Nujol or in potassium bromide discs, overlaps the ν OH. On the other hand, it is impossible to obtain the spectra in chloroform or in carbon tetrachloride due to the very small solubility of Ia-g in these solvents. The ultraviolet spectra show a very high conjugation band with λ max 333 and 339 nm for Ia and Ib respectively, red-shifted with respect to the corresponding 3-phenyl derivatives for the greater dienic nature of the heterocyclic substituent, and with λ max 312 nm for the less conjugated Ic. The spectrum of Ib, moreover, in accord with the proposed structure, closely resembles the one of 3-(2-thienyl)(2*H*)-1,4-benzoxazine IV that was prepared by univocal synthesis.



The great red-shift of the conjugation band of the compounds Id-g is, naturally, due to the strong chromophore NO₂ group in position 7. The pmr spectra of Ia-c reveal, together with the other proton signals, two doublets (J = 6.5 Hz) due to coupling of H and OH in position 2, at about δ 6.40 and δ 7.80. The latter is sometimes superimposed by the protons of the substituent R in position 3. For the presence of the nitro group in position 7 in compounds Id-g such doublets (J = 7.5 Hz) result shifted to about δ 6.50 and δ 8.10, respectively. Upon addition of deuterium oxide, the OH signal disappears and the sharp singlet of the methine proton is observed (Table 2).

Table 2

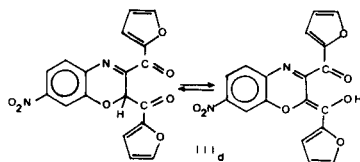
Analytical and Spectral Data of 1,4-Benzoxazines Ia-g and IV



Compound	M.p. °C Solvent	Formula	Analysis (a)			UV, nm (Log ε) (b)	PMR δ, ppm (c)
			C	H	N		
Ia	239-240 ethanol	C ₁₂ H ₉ NO ₃	66.69 (66.97)	4.21 4.21	6.41 6.51	239 (3.86), 333 (4.27)	6.30 (d, H ^a , J = 6.5), 6.78 (m, H ^a), 7.20 (m, H ^c), 7.50 (m, H ^f), 7.80 (d, H ^b , J = 6.5), 8.00 (m, H ^g)
Ib	238-239 ethanol	C ₁₂ H ₉ NO ₂ S	62.14 (62.32)	3.88 3.92	5.80 6.06	238 (3.87), 250 (3.83), 280 (3.89), 339 (4.23)	6.40 (d, H ^a , J = 6.5), 7.25 (m, H ^c + H ^f), 7.80 (m, H ^b + H ^d + H ^g)
Ic	238-239 ethanol	C ₁₂ H ₉ NO ₂ S	62.42 (62.32)	4.00 3.92	5.85 6.06	238 (4.10), 292 (4.20), 312 (4.18)	6.35 (d, H ^a , J = 6.5), 7.25 (m, H ^c), 7.70 (m, H ^b + H ^e + H ^g), 8.22 (m, H ^d)
Id	265-266 acetone	C ₁₂ H ₈ N ₂ O ₅	55.14 (55.39)	2.95 3.10	10.87 10.77	234 (4.04), 372 (4.38)	6.42 (d, H ^a , J = 7.5), 6.80 (m, H ^a), 7.70 (m, H ^c + H ^f), 8.10 (m, H ^b + H ^g)
Ie	265-266 acetone	C ₁₂ H ₈ N ₂ O ₄ S	52.24 (52.17)	2.90 2.92	10.06 10.14	232 (4.06), 290 (3.83), 376 (4.36)	6.58 (d, H ^a , J = 7.5), 7.30 (m, H ^a), 7.65 (m, H ^f), 7.90 (m, H ^c), 7.98 (m, H ^c), 8.18 (d, H ^b , J = 7.5)
If	262-263 acetonitrile	C ₁₂ H ₈ N ₂ O ₄ S	52.34 (52.17)	2.89 2.92	10.09 10.14	227 (4.23), 360 (4.30)	6.49 (d, H ^a , J = 7.5), 7.69 (m, H ^c), 7.85 (m, H ^e + H ^f), 8.05 (d, H ^b , J = 7.5), 8.35 (m, H ^d)
Ig	258-259 acetonitrile	C ₁₄ H ₁₀ N ₂ O ₄	62.54 (62.22)	3.61 3.73	10.14 10.37	228 (4.18), 317 (4.20), 357 (4.23)	6.52 (d, H ^a , J = 7.5), 7.52 (m, H ^a), 7.75 (m, H ^c), 8.02 (m, H ^b + H ^g)
IV	113-115 ethanol	C ₁₂ H ₉ NOS	66.82 (66.95)	4.08 4.21	6.50 6.51	240 sh, 257 (3.97), 275 sh, 348 (4.14)	5.15 (s, H ^a), 7.15 (m, H ^c + H ^f), 7.80 (m, H ^d + H ^g)

(a) Values in parentheses refer to the calculated percentages. (b) Solvent = methanol. (c) DMSO solution; TMS as internal reference; coupling constants are reported in Hz.; chemical shifts quoted in the case of multiplets were measured from the approximate center.

From the condensation of 2-amino-5-nitrophenol and 2-furyl glyoxal the related dibenzoxazine was never obtained but compound III_d that was identified by means of its spectroscopic and analytical properties as



The ir spectrum, in fact, shows bands at 3550 and 1630 cm⁻¹ (ν OH and ν CO modes respectively) in chloroform solution.

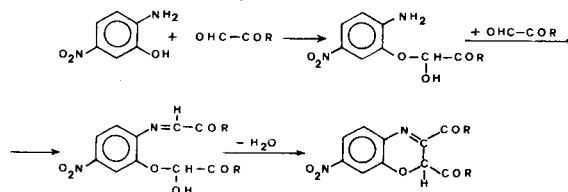
In the mass spectrum the M⁺ is m/e 367 (8.2%), while the base peak is m/e 95 (100%) corresponding to the furyl-C≡O⁺ ion. The other prominent peaks are m/e 351 (44.4%), 350 (44.2%), 321 (29.5%), 272 (50.1%), 255 (29.5%), 209 (14.7%).

The examination of its pmr spectrum reveals two singlets at δ 8.88 (broad) and δ 5.88 attributable respectively to the OH and to the CH₍₂₎ groups of the two tautomeric forms.

The other protons appear as multiplets centered at δ 7.75 and δ 6.95. The ultraviolet absorption spectrum agrees with such an extended conjugated system, especially of the tautomeric enol form, and exhibits the longest wavelength band with λ max 414 nm (Log ε 4.67). The

same structure as III_d can be attributed to III_e, which behaves identically. The formation of the compounds III_{d,e} is only explained by an initial attack of the OH on the glyoxal formyl group; the *p*-substitution by nitro, in fact, lowers the nucleophile power of the amino in addition to the decreased reactivity of the glyoxal keto carbonyl group due to the electron donor 2-furyl and 2-thienyl substituents.

In this case, therefore, the reaction mechanism would be



EXPERIMENTAL

The ir spectra were measured with a Perkin-Elmer model 417 spectrophotometer and pmr spectra on a Perkin-Elmer R 32 instrument at a probe temperature of about 38°. The uv spectra were recorded on a Cary model 14 spectrophotometer and Mass spectra on a Perkin-Elmer model 270 B with a system for direct injection of the sample into the ionization region at 80° with an ionization potential of 50 eV. Melting points are uncorrected.

1,4-Benzoxazines Ia-g.

The compounds Ia-g were obtained following the general procedure

of condensation between 2-aminophenol and α -dicarbonyl compounds and separated by thin layer chromatography under the conditions reported (2). For the compounds I, II d-g the corresponding Rf are: Id = 0.53, Ie = 0.56, If = 0.60, Ig = 0.59, Iie = 0.58, IIf = 0.55, IIg = 0.54.

3-(2-Thienyl)(2H)-1,4-benzoxazine IV.

Potassium hydroxide (2.3 g.) and 8.1 g. of bromomethyl (2-thienyl) ketone in ethanol solution were added to 6 g. of *N*-acetyl-2-aminophenol. The mixture was heated for 1 hour at 50°. The potassium bromide formed was filtered, the solvent was removed under reduced pressure and the 2-acetylaminophenoxymethyl (2-thienyl) ketone was obtained, white crystals from ethanol, m.p. 126-128°. The 2-acetylaminophenoxymethyl (2-thienyl) ketone (3.5 g.) dissolved in a solution of 12 g. of potassium hydroxide in 60 ml. of 20% ethanol were boiled for one hour. After cooling the precipitated 3-(2-thienyl)(2H)-1,4-benzoxazine IV was filtered and crystallized from ethanol, m.p. 113-115°.

2,3-Di(2-furoyl)(2H)-7-nitro-1,4-benzoxazine III d.

The product was obtained as yellow crystals from acetonitrile, m.p. 222-223°; Rf = 0.62; uv (methanol): 234 (4.04), 252 (3.94), 297 (3.88), 414

(4.67).

Anal. Calcd. for $C_{18}H_{10}N_2O_7$: C, 59.02; H, 2.75; N, 7.64. Found: C, 58.80; H, 2.87; N, 7.80.

2,3-Di(2-thenoyl)(2H)-7-nitro-1,4-benzoxazine III e.

This compound was separated by tlc on silica gel GF₂₅₄ plates using benzene/ethanol 95:5 as the mobile phase, yellow crystals from acetonitrile, m.p. 204-205°, Rf = 0.65; uv (methanol): 234 (4.20), 250 (4.12), 305 (3.90), 414 (4.63).

Anal. Calcd. for $C_{18}H_{10}N_2O_5S_2$: C, 54.26; H, 2.53; N, 7.03. Found: C, 54.40; H, 2.81; N, 7.25.

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