# Condensation of *o*-Aminophenol and α-Dicarbonyl Compounds.
## Part 2. Dibenzoxazolines

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The study of 2′-aryl-2,2′-dibenzoxazolines (II), obtained together with 2-hydroxy-(2*H*)-1,4-benzoxazines (I) by condensation of *o*-aminophenol with a series of phenylglyoxal derivatives, emphasized that these compounds are an equilibrium mixture of dibenzoxazolines and related tautomeric ketimine forms. This behaviour was widely investigated by ir, uv and pmr spectroscopy.

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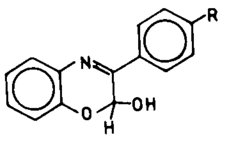
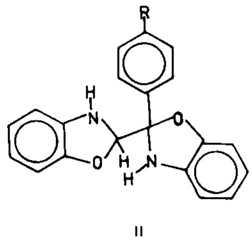
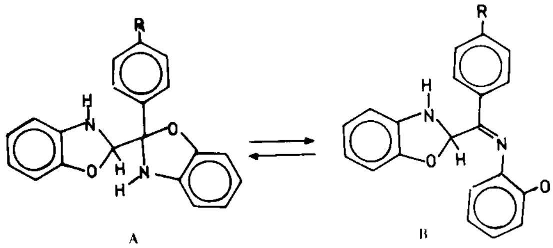
It has been reported in the previous paper (2) that, together with 3-aryl-2-hydroxy-(2*H*)-1,4-benzoxazines (I), whose structure were widely determined, 2′-aryl-2,2′-dibenzoxazolines (II) were formed by the condensation of *o*-aminophenol and arylglyoxal. The present investigation was undertaken in order to determine the properties and the structures of II; in fact, from spectroscopic evidence, these compounds appear to be an equilibrium mixture of dibenzoxazoline (A) and related tautomeric ketimine forms (B):



I



II



A B

The ir spectra (potassium bromide) show at 3400 $cm^{-1}$ the characteristic ν NH amino, the aromatic ring bands and, at about 1040 $cm^{-1}$, the C-O stretching band. In carbon tetrachloride the above mentioned tautomeric equilibrium is emphasized by the absorption bands of the amino and hydroxy groups. The compounds IIa→d show, in fact, at 3600 $cm^{-1}$ the ν OH (very weak for IIa) together with the ν NH at 3420 $cm^{-1}$ (See Figure 1). The ultraviolet spectra of 2′-aryl-2,2′-dibenzoxazolines are closely related to that of *o*-aminophenol itself, with a double absorptivity of course, and not effected by the 2′ substitution (see also the identity between the spectra of IIa and unsubstituted 2,2′-dibenzoxazoline (3), Figure 2); however, in the absorption spectra of the compounds IIb→e (solvent, methanol) a large shoulder arises at a wavelength higher than the characteristic absorption maximum (around 290 nm) (Figure 3). The B tautomeric structures of IIb→e, for the presence of a benzalaniline chromophore, should explain the observed shoulders, at the same time indicating that the 2′-aryl substituted benzoxazoline ring undergoes the opening reaction.

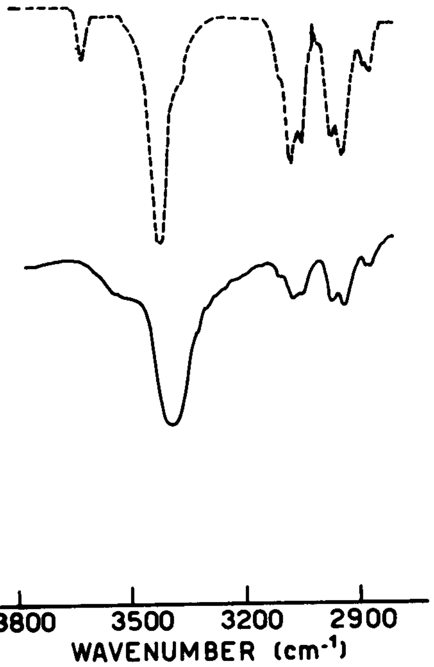


Figure 1: Infrared spectra of IIe: — —— potassium bromide, - - - - carbon tetrachloride.

It is known (4,5) that on addition of alkali, 2,2′-dibenzoxazolines give the corresponding glyoxaldianils, characterized by an absorption band in the visible region; no bathochromic shift of the conjugation band was found for IIa→e, so it seems reasonable to deduce that also in alkaline solution no opening occurs at the 2-unsubstituted benzoxazoline ring.

Analysing the spectra of IIa→e in sodium hydroxide 0.05 *N* (methanol/water) in every case we found two bands which may be attributed to the single isolated chromophores benzoxazoline-benzalaniline (Figure 4). Moreover, it was possible to calculate the approximative

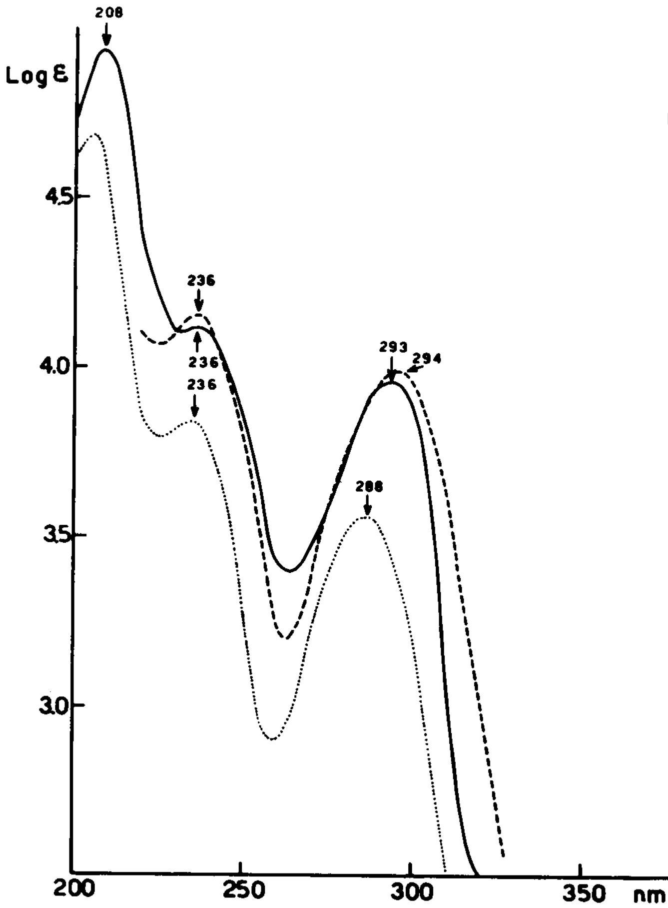


Figure 2: Ultraviolet spectra of: ——— IIa, – – – 2,2′-dibenzoxazoline, ......... o-aminophenol. Solvent, methanol.

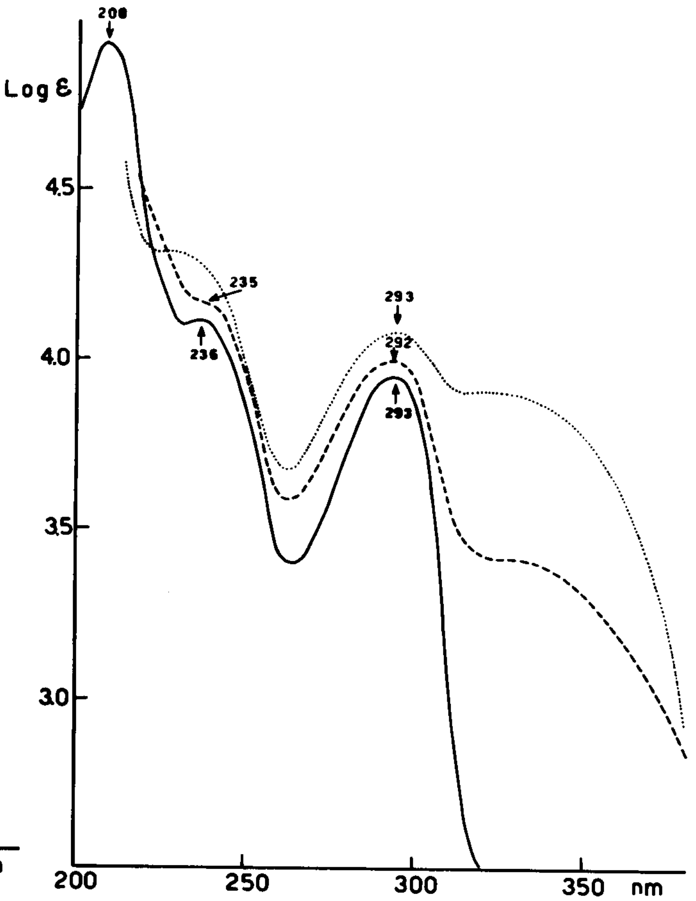


Figure 3: Ultraviolet spectra of: ——— IIa, – – – IIc, ........ IId. Solvent, methanol.

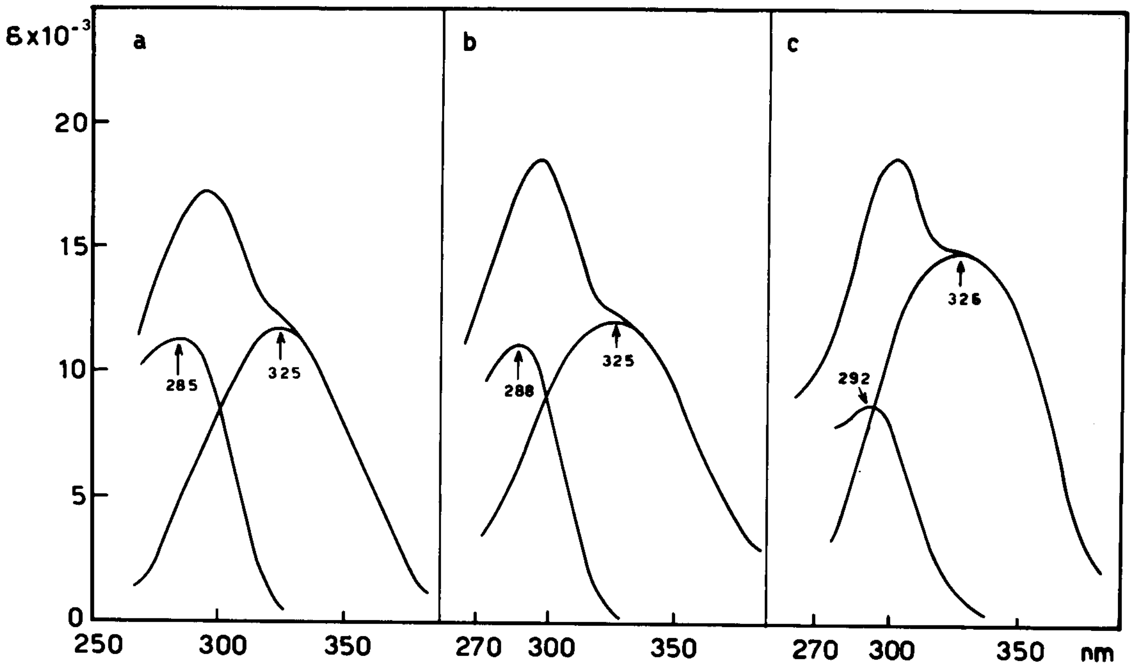


Figure 4: Ultraviolet spectra of: a) IIa, b) IIc, c) IId. Solvent, Sodium hydroxide, 0.05 *N* (methanol/water).

percentage of open chain compound in the equilibrium mixture in methanol and in dimethylsulfoxide. The latter solvent was chosen because a similar analysis was carried out also by pmr spectroscopy which offers the possibility of obtaining the absolute tautomeric values direct from the integration of the signal intensities.

The pmr spectra of II always show two doublets (J = 4.5 Hz) at 5.50 and 7.15 δ, due to the coupling between $H^a$ and $H^b$ (see the signature of hydrogen atoms in the formulas reported in Table II). From the integration it results that each doublet corresponds every time to one proton, this clearly means that such a benzoxazoline system does not tautomerize under these conditions. At 7.25 δ we can identify the singlet of the proton $H^e$. The spectra of the compounds IIa→d exhibit signals at about 8 δ (very weak for IIa) attributable to the *ortho* protons $H^{c'}$ of the N=C-phenyl system, which is characteristic of the tautomeric structure B. These signal intensities gave the percentages of such structure in the equilibrium mixture: these results, together with the data calculated by means of uv spectroscopy are summarized in Table I. For the compounds IIb→d it is possible to find the signal of $H^{e'}$ whose chemical shift is similar to the $H^a$ one.

Table I

Calculated Percentages of Tautomeric Structure B of Compounds II

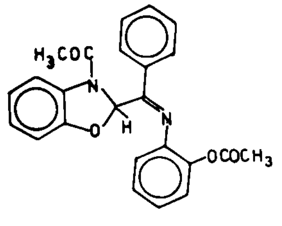
| | Uv (a) | | Pmr (b) |
|---|---|---|---|
| Compound | Methanol | Dimethylsulfoxide | Dimethylsulfoxide |
| IIa | 0.0 | 0.0 | 0.0 |
| IIb | 42.9 | 21.0 | 23.0 |
| IIc | 22.5 | 20.9 | 25.0 |
| IId | 55.0 | 50.0 | 48.0 |
| IIe | 35.5 | 0.0 | 0.0 |

(a) Concentration, 6 x $10^{-5}$ *M*; temperature, 20°. (b) Concentration, 14 x $10^{-2}$ *M*; temperature, 38°.

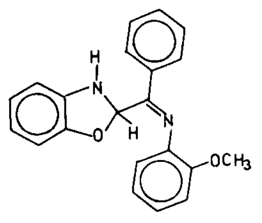
The A ⇌ B tautomerism is easier emphasized for the compounds IIb and IId considering the signals of the $CH_3$ groups. In fact the spectrum of IIb shows at 2.24 and 2.35 δ the singlets for the $CH_3$ (A) and $CH_3$ (B) respectively, and the spectrum of IId the singlets of $OCH_3$ (A) and $OCH_3$ (B) at 3.70 and 3.81 δ. The integration of $CH_3$ (A) versus $CH_3$ (B) gives, therefore, a further determination of tautomer ratios (Figure 5). Upon addition of deuterium oxide the NH and OH signals are no longer present while a singlet for the methine proton $H^a$ appears.

It must be noted that, in the polar basic solvent dimethylsulfoxide, the compound IIe exists in 100% dibenzoxazoline form (Table II).

By acetylation with acetic anhydride and by methylation with methyl iodide of compound IIa we obtained III and IV. These compounds confirm that 2-unsubstituted benzoxazoline undergoes no ring opening. The ir spectrum of III shows two well separated bands at 1765 and 1670 $cm^{-1}$ attributable, respectively, to *O*-acetyl and *N*-acetyl ν CO modes; the absorption band at 3420 $cm^{-1}$ indicates the presence of NH group for IV. The uv spectra of III and IV closely resemble the IIa one in alkaline solution (Figure 6).



III



IV

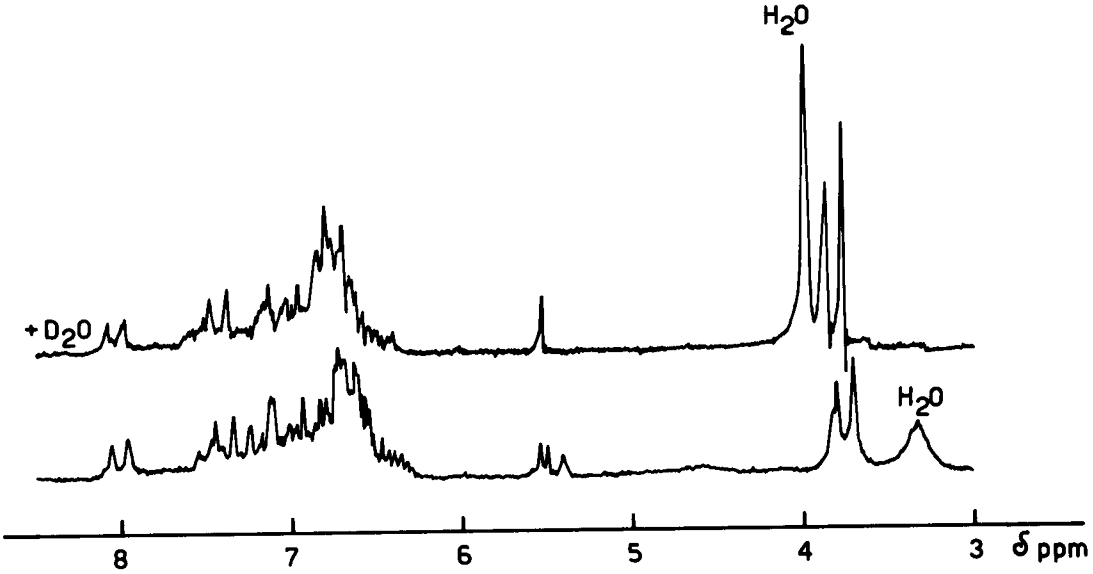
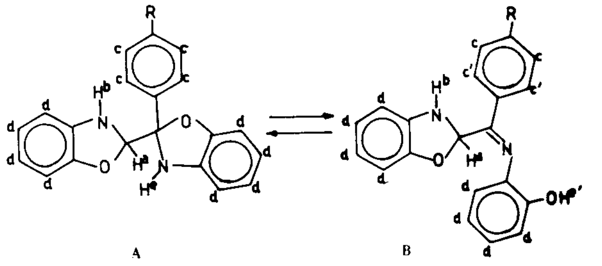


Figure 5: Proton magnetic resonance spectra of IId. Solvent, DMSO.

Table II

Analytical and Spectral Data of II



| Compounds | M.p. °C<br>Solvent | Formula | Analysis (a) C | H | N | Ir $\nu$ max, cm$^{-1}$ (b) | Pmr $\delta$, ppm (c) | Uv nm, (Log $\epsilon$) (d) |
|---|---|---|---|---|---|---|---|---|
| IIa | 155-157<br>benzene/ligroin<br>1:1 | $C_{20}H_{16}N_2O_2$ | 76.00<br>(75.93) | 5.18<br>(5.09) | 8.74<br>(8.85) | 3360, 1600, 1500, 1435, 1240, 1140, 1040, 940, 750, (3590 w, 3420) | 5.56 (d, $H^a$, J = 4.5), 6.70 (m, $H^d$), 7.12 (d, $H^b$, J = 4.5), 7.27 (s, $H^e$), 7.40 (m, $H^c$), 7.80 (m, $H^{c'}$) | 208 (4.94), 236 (4.12)<br>293 (3.97) |
| IIb | 89-90<br>*n*-hexane | $C_{21}H_{18}N_2O_2$ | 76.48<br>(76.34) | 5.55<br>(5.49) | 8.56<br>(8.48) | 3380, 1610, 1600, 1500, 1425, 1225, 1140, 1035, 860, 740, (3615, 3420) | 2.24 (s, $CH_3$) [A], 2.35 (s, $CH_3$) [B], 5.50 (s, $H^{e'}$), 5.52 (d, $H^a$, J = 4.5), 6.70 (m, $H^d$), 7.08 (d, $H^b$, J = 4.5), 7.16 (s, $H^e$), 7.30 (m, $H^c$), 7.95 (d, $H^{c'}$, J = 9) | 207 (4.90), 237 (4.24)<br>294 (4.11), 320 sh |
| IIc | 96-97<br>*n*-hexane | $C_{20}H_{15}ClN_2O_2$ | 68.61<br>(68.47) | 4.42<br>(4.31) | 8.05<br>(7.98) | 3390, 1615, 1600, 1500, 1430, 1230, 1145, 1040, 860, 750, (3615, 3420) | 5.58 (d, $H^a$, J = 4.5), 5.62 (s, $H^{e'}$), 6.70 (m, $H^d$), 7.20 (d, $H^b$, J = 4.5), 7.34 (s, $H^e$), 7.50 (m, $H^c$), 8.05 (d, $H^{c'}$, J = 9) | 207 (4.87), 230 (4.18)<br>292 (4.01), 320 sh |
| IId | 81-82<br>*n*-octane | $C_{21}H_{18}N_2O_3$ | . 72.69<br>(72.82) | 5.22<br>(5.24) | 7.96<br>(8.09) | 3380, 1610, 1500, 1310, 1260, 1180, 1040, 835, 750, (3610, 3410) | 3.70 (s, $OCH_3$) [A], 3.81 (s, $OCH_3$) [B], 5.40 (s, $H^{e'}$), 5.53 (d, $H^a$, J = 4.5), 6.70 (m, $H^d$), 7.12 (d, $H^b$, J = 4.5), 7.25 (s, $H^e$), 7.42 (m, $H^c$), 8.02 (d, $H^{c'}$, J = 9) | 206 (4.89), 226 (4.32)<br>293 (4.08), 320 sh |
| IIe | 170-172<br>dioxane/ligroin<br>1:10 | $C_{20}H_{15}N_3O_4$ | 66.37<br>(66.48) | 4.25<br>(4.18) | 11.63<br>(11.63) | 3400, 1600, 1500, 1440, 1230, 1150, 1040, 860, 750, (3410) | 5.70 (d, $H^a$, J = 4.5), 6.80 (m, $H^d$), 7.30 (d, $H^b$, J = 4.5), 7.55 (s, $H^e$), 7.80 (d, $H^c$, J = 8, *ortho*), 8.25 (d, $H^c$, J = 8, *meta*) | 206 (4.91), 236 (4.23)<br>260 sh, 288 (4.15)<br>352 (3.66) |

(a) Values in parentheses refer to the calculated percentages. (b) Potassium bromide; values in parentheses refer to chloroform solution. (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. (d) Solvent, methanol.

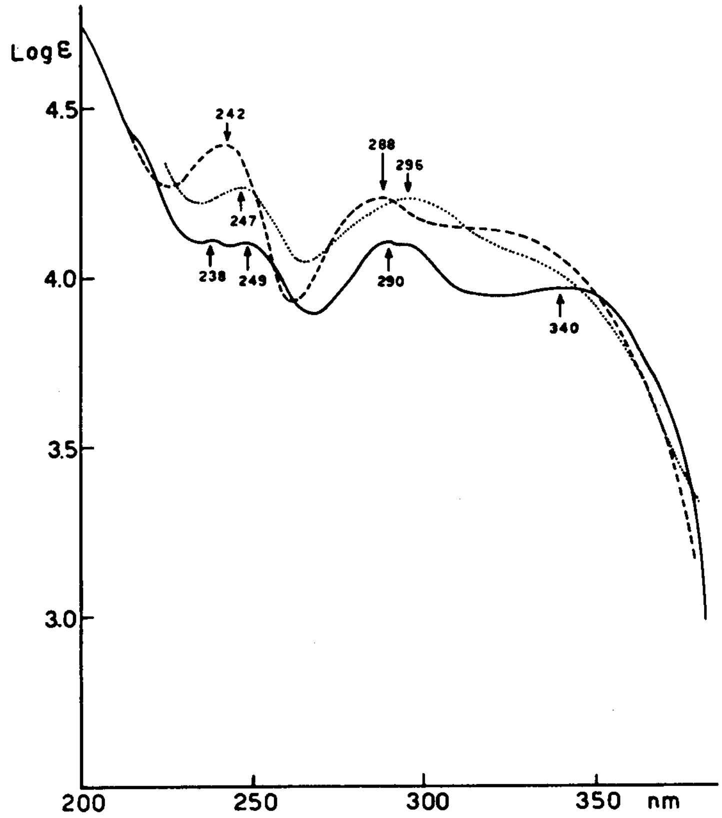


Figure 6: Ultraviolet spectra of: ——— III, – – – – IV solvent, methanol, ……. IIa solvent, sodium hydroxide 0.05 *N* (methanol/water).

In the pmr spectrum (deuteriochloroform solution) of III, together with the signals due to the aromatic protons, the following signals were found: two singlets at 1.75 and 2.32 δ for *N*-acetyl and *O*-acetyl, and at 8.20 δ the multiplet due to the *ortho* protons of the phenyl ring. The catalytic hydrogenation of III affords the dihydroderivative, one mole of hydrogen being absorbed on the C=N bond; in this case, of course, the signal at 8.20 δ disappears. For the compound IV the structure is confirmed, besides the signal at 3.60 δ of the methoxy group, by the coupling between the protons in positions 2 and 3.

The behaviour of 2′-phenyl-5,5′-dinitro-2,2′-dibenzoxazoline V is very interesting, for which, according to the pmr data, the uv spectrum reveals the sole tautomeric dibenzoxazoline form. An irrefutable proof is given by the comparison between the spectra of V and those of *p*-nitro-*o*-aminophenol and 5,5′-dinitro-2,2′-dibenzoxazoline, erroneously reported in literature (6) as an open chain compound glyoxal-bis(2-hydroxy-5-nitroanil) (Figure 7). Even for 2′-*p*-nitrophenyl-5,5′-dinitro-2,2′-dibenzoxazoline (VI), the tautomeric equilibrium is completely displaced towards the dibenzoxazoline structure. In alkaline solution, as expected, V and VI undergo, like compounds II, opening reaction exclusively at the 2′-aryl substituted benzoxazoline ring.

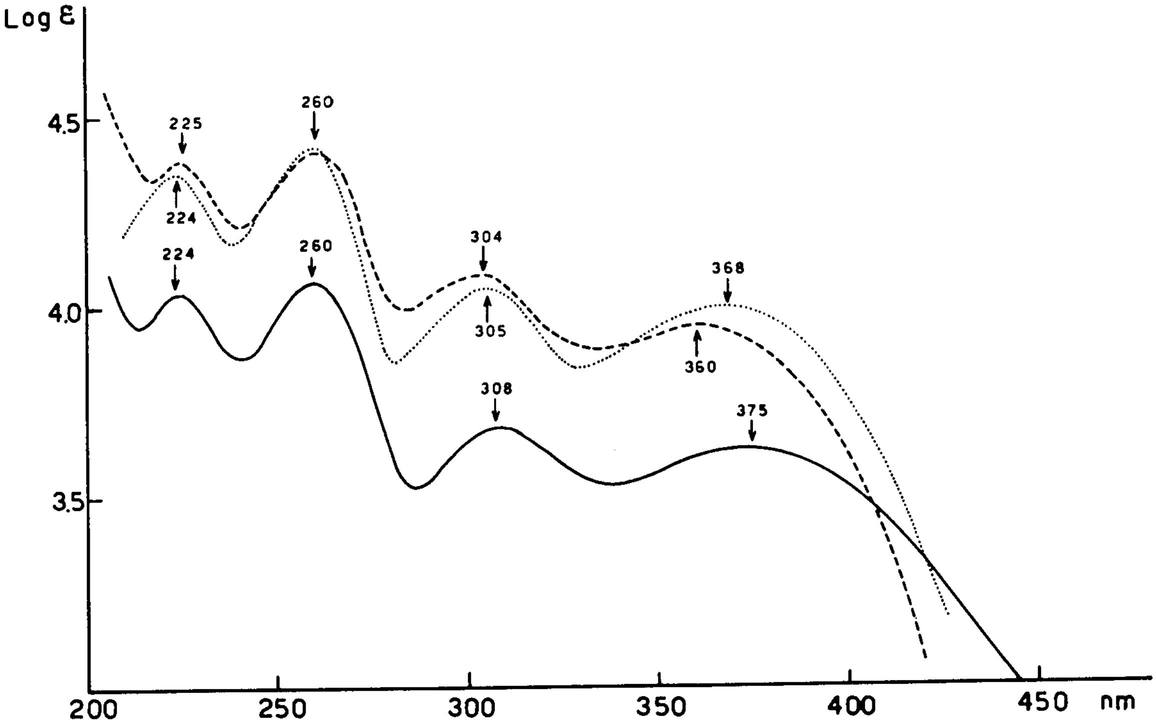
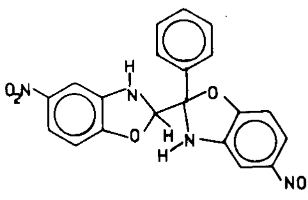
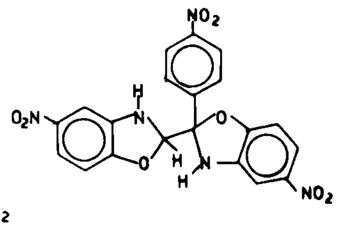


Figure 7: Ultraviolet spectra of: ——— *p*-nitro-*o*-aminophenol, – – – – V, solvent, methanol, ……. 5,5′-dinitro-2,2′-dibenzoxazoline, solvent, ethanol.



V



VI

## EXPERIMENTAL

Ir spectra were measured with a Perkin-Elmer model 417 spectrophotometer and pmr spectra on a Perkin-Elmer R 32 instrument at probe temperature of 38°. The uv spectra were recorded on a Cary model 14 spectrophotometer. Melting points are uncorrected.

Acetylation of Compound IIa to give III.

A solution of IIa (1 g.) in acetic anhydride (15 ml.) was boiled for 20 minutes. Upon cooling, the oily product solidified on standing overnight and was recrystallized from ethanol to give white crystals, m.p. 193-194°; ir (potassium bromide): 1765, 1670, 1615, 1500, 1370, 1280, 1210, 760 cm$^{-1}$; pmr (deuteriochloroform): 1.75 (s, 3H, $NCOCH_3$), 2.32 (s, 3H, $OCOCH_3$), 6.90 (m, 8H), 7.50 (m, 3H), 8.00 (s, 1H), 8.20 (m, 2H); uv (methanol): 238 (4.11), 248 (4.11), 288 (4.11), 340 (3.97).

*Anal.* Calcd. for $C_{24}H_{20}N_2O_4$: C, 71.99; H, 5.03; N, 7.00. Found: C, 72.07; H, 5.11; N, 6.97.

Hydrogenation of III.

A solution of III was hydrogenated at atmospheric pressure and room temperature using Adams catalyst. The reaction stopped after two hours when a slight excess of hydrogen was absorbed. The catalyst was filtered and the solvent removed under reduced pressure and the residue was recrystallized from ethanol, m.p. 151-152°; ir (potassium bromide): 3280, 1770, 1615, 1500, 1370, 1290, 1200, 750 cm$^{-1}$; pmr (deuteriochloroform + deuterium oxide): 1.65 (s, 3H, $NCOCH_3$), 2.22 (s, 3H, $OCOCH_3$), 5.15 (d, 1H, J = 3 Hz), 6.33 (d, 1H, J = 3 Hz), 6.95 (m, 13H); uv (methanol): 243 (3.85), 299 (3.63).

*Anal.* Calcd. for $C_{24}H_{22}N_2O_4$: C, 71.73; H, 5.51; N, 6.96. Found: C, 71.76; H, 5.56; N, 6.94.

Methylation of Compound IIa to Give IV.

A mixture of IIa (3.6 g.), potassium carbonate (1.8 g.) and methyl iodide (3 ml.) in methanol (75 ml.) was boiled for 10 hours. After cooling the precipitate was filtered and washed with cold methanol, yellow prisms from petroleum benzine (80-120°), m.p. 110-112°; ir (potassium bromide): 3420, 1615, 1600, 1515, 1250, 755, 740 cm$^{-1}$; pmr (deuteriochloroform): 3.60 (s, 3H, $OCH_3$), 5.15 (d, 1H, J = 8 Hz, NH), 6.48 (d, 1H, J = 8 Hz, methine), 7.15 (m, 11H), 7.98 (m, 2H); uv (methanol): 242 (4.39), 288 (4.23), 315 sh.

*Anal.* Calcd. for $C_{21}H_{18}N_2O_2$: C, 76.35; H, 5.49; N, 8.48. Found: C, 76.51: H, 5.52; N, 8.54. Zeisel Calcd. for $OCH_3$: 9.2. Found: 9.3.

## REFERENCES AND NOTES

(1) The authors are indicated in alphabetical order.
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