On the Structure of Condensation Products of o-Aminophenols with α-Dicarbonyl Compounds. I

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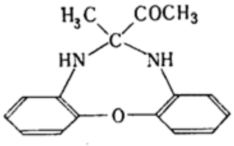
The condensation reaction between *o*-aminophenol and diacetyl was first carried out by Kehrmann in 1895, who tentatively suggested for the condensation product the eight-membered ring structure containing a diphenyl ether bond as shown in the formula A[1].



(A)

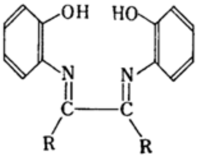
Recently, Bayer assigned Schiff base structures to the compounds obtained by the condensation of *o*-aminophenol with glyoxal and diacetyl and reported that glyoxal bis-(2-hydroxy anil) gave chelates with copper, nickel, cobalt, etc., but diacetyl bis-(2-hydroxy anil) did not form a metal chelate[2].

The present investigation was undertaken in order to confirm the structure of these condensation products.

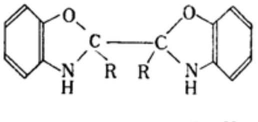
o-Aminophenol smoothly condensed with glyoxal and with diacetyl by heating the mixture in an aqueous or alcoholic solution. The product I from glyoxal was colorless needles, m. p. 210°C*, and the product II from diacetyl was colorless plates, m. p. 241°C**.

The Schiff base structure is represented as the formula B.

It was confirmed in some cases that condensation products of β-aminoalcohols and carbonyl compounds are oxazolidine or equilibrium mixtures of the Schiff base with the former[3]. Along with these facts, the alternative structure of I and II is bibenzoxazoline (C).



(B)



R : H (I)
R : CH_3 (II)

(C)

Only a few instances of benzoxazoline structure were reported concerning the condensation products of *o*-aminophenols and carbonyl compounds[4], but their structures were not always confirmed exactly. It has been accepted that the benzoxazole owes its formation to pyrolysis of the benzoxazoline primarily formed in the condensation of *o*-aminophenol with ketone[5].

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[1] F. Kehrmann, *Ber.*, **28**, 343 (1895).

[2] E. Bayer, *Ber.*, **90**, 2325 (1957).

* According to Bayer, the melting point of the product I is 204°C.

** The melting point of II is 227°C according to Bayer, but Kehrmann reported it as being 239~240°C.

[3] G. E. McCasland and C. Horswill, *J. Am. Chem. Soc.*, **73**, 3923 (1951); H. R. Nace and M. H. Gollis, ibid., **74**, 5189 (1952); J. Metzger and A. Pacault, *Rec. trav. chim.*, **71**, 259 (1952); E. P. Goldberg and H. R. Nace, *J. Am. Chem. Soc.*, **75**, 6260 (1953); E. D. Bergmann, E. Gil-Av and S. Pinchas, *Rec. trav. chim.*, **71**, 168 (1952); *J. Am. Chem. Soc.*, **75**, 358 (1953); H. R. Nace and E. P. Goldberg, ibid., **75**, 3646 (1953).

[4] A. Hantzsch, *Ber.*, **16**, 1948 (1883); Schroeter et al., *Ann.*, **426**, 83 (1922); F. Sachs and W. Brunetti, *Ber.*, **40**, 3234 (1907); L. Calatis, ibid., **66**, 1774 (1933).

[5] Elderfield, "Heterocyclic Compound", Vol. 5, John Wiley & Sons, Inc., New York, (1957), p. 431.

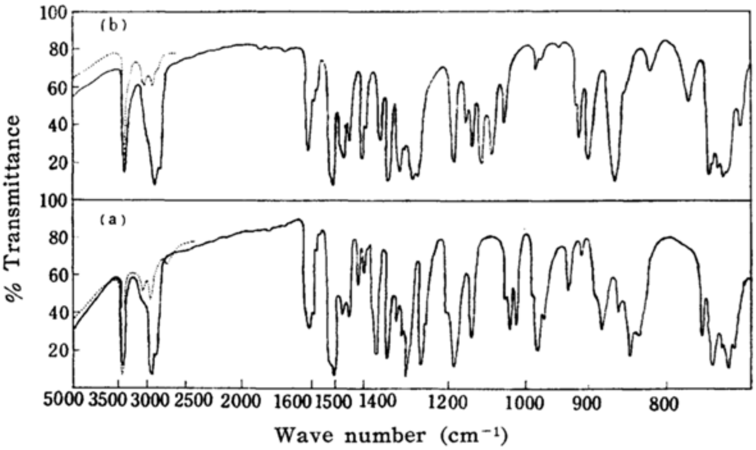

Fig. 1. Infrared spectra of the compounds. I : a and II : b, —— Nujol mull, ······ hexachlorobutadiene mull.

TABLE I. INFRARED ABSORPTION SPECTRA OF I, II AND RELATED SCHIFF BASES NEAR 3000 cm^{-1} AND 1600 cm^{-1} REGION

I	II	Diacetyl dianil	Glyoxal bis-(4-hydroxy anil)	Glyoxal bis-(4-dimethyl-amino anil)	Salicylidene o-amino-phenol	Bissalicylaldehyde ethylene-diimine	Assignment
3378	3358						NH stretching
		1631	1610	1605	1631	1631	Conjugated C=N
1613	1613						
1600	1587	1587	1595		1619	1613	Phenyl ring
1585	1580	1577	1580	1567	1597	1582	
1499	1497	1490	1513	1517	1531	1506	

Eventually, a Schiff base structure or an oxazoline structure will be the only choice offered for the determination of the structure of the condensation products of *o*-aminophenol with glyoxal and diacetyl. The following investigations led to the conclusion that the structures of these are not so much a Schiff base type as an oxazoline type.

Behaviors to Mineral Acid and Aqueous Alkali.—I and II are insoluble in dilute mineral acids and stable to such an extent that they are not hydrolyzed after standing overnight at room temperature with 3 N hydrochloric acid, but hydrolyzed by heating with 6 N hydrochloric acid; thus they were gradually hydrolyzed and *o*-aminophenol hydrochloride was obtained quantitatively. I and II were not only insoluble in dilute aqueous alkali, but also stable at room temperature. On heating them with a ten per cent aqueous sodium hydroxide solution, *o*-aminophenol was obtained and identified as the *N*-acetyl derivative.

Spectroscopic Investigation. — Infrared and ultraviolet absorption spectra of I and II are shown In Figs. 1 and 2 respectively***. The assignment of the infrared absorption bands and the ultraviolet absorption maxima are summarized and compared with those of the related Schiff bases in Tables I and II, respectively.

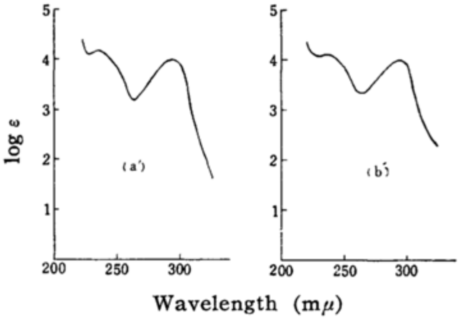

Fig. 2. Absorption curve of the compounds I (a') and II (b'), (ethanol solution).

*** The infrared spectra were obtained with a Perkin-Elmer Model 21 and an Oyōkōken D-201 spectrometer using NaCl prism. Ultraviolet spectra were obtained with a Beckman Model DK-2 spectrometer.

TABLE II. THE ULTRAVIOLET ABSORPTION SPECTRA OF I, II AND RELATED SCHIFF BASES IN ETHANOL

Compound	λ (mμ)	ε	λ (mμ)	ε	λ (mμ)	ε
I	236	14340	294	9880		
II	236	13200	293	9880		
Diacetyl dianil	227	40700			332	4360
Glyoxal bis-(4-hydroxy anil)	244	13200	296	8300	383	23980
Glyoxal bis-(4-dimethyl-amino anil)	253	15760	318	5700	450	37200

If the Schiff base structure (B) is adopted, the bands in the 3000 cm^{-1} region of infrared are assigned to OH vibration, 1613 cm^{-1} being a C=N vibration shifted by the strong conjugation in the same manner as in the case of the Schiff bases quoted.

Intermolecular hydrogen bondings, however, should be present in this case; a hydrogen bonding causes a shift of the OH stretching band to the lower frequency and broadening of the band[6]. From these circumstances, the shape and the position of these bands (Fig. 1) are more plausibly explained to correspond to the NH vibration. Furthermore, the ultraviolet absorption spectra of I and II (Fig. 2) are closely related to that of *o*-aminophenol itself (λ_{max} 232 mμ, ε_{max} 7240; λ_{max} 286 mμ, ε_{max} 4270)[7], thus the presence of the chromophore, such as conjugated azomethine linkages which cause a bathochromic effect, should be discounted.

It is well known that a compound having an anilino structure has an infrared absorption band near 1600 cm^{-1} region[8]. From the investigations of indolenine derivatives, Witkop and Patrick[9] have quoted a band at 1613 cm^{-1} as being typical of the structure $C_6H_5{-}NH{-}\overset{|}{\underset{|}{C}}{-}$. Since the structure of bibenzoxazoline (C) resembles that of indolenine and an absorption similar to that of the latter is present at 1613 cm^{-1}, the author concluded the absorption to be caused by the same structural element, and at least shouldered bands are regarded as phenyl ring vibrations; it is not completely clear whether this absorption arises from an NH deformation or from a phenyl ring.

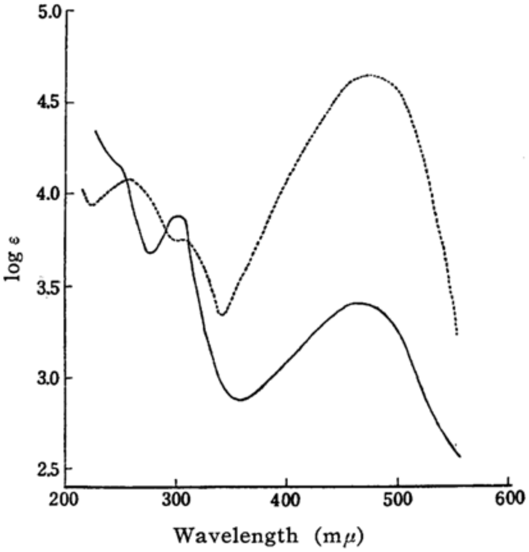

Fig. 3. Absorption curve of the compound I+KOH: —— and glyoxal bis-(4-hydroxy anil)+KOH: …….

Although compound I was insoluble in aqueous alkali, a reddish yellow color was produced when an excess of potassium hydroxide was added to its ethanol solution, and another absorption maximum was observed at 467 mμ (ε, 2445) as shown in Fig. 3.

In the case of glyoxal bis-(4-hydroxy anil), the absorption maximum shifted from 367 mμ to 470 mμ when potassium hydroxide was added. The explanation of this phenomenon is that when a proton acceptor such as a hydroxyl ion is present in the ethanol solution, bibenzoxazoline (C′) tautomerizes to Schiff base B′ under ring opening. The above consideration is tenable in view of the fact that oxazolidine tautomerizes to Schiff base resulting in an equilibrium mixture of the two structures[3].

The curve in Fig. 4 means that the Schiff base is produced as a result of tautomerism and the solution reaches an equilibrium. The curve comes up again after standing for a long time, because hydrolysis sets in.

The formation of a metal chelate I is also explained by the tautomeric change.

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[6] L. J. Bellamy, "The Infrared Spectra of Complex Molecules", John Wiley & Sons, Inc., New York, (1954), p. 86.

[7] R. A. Friedel, M. Orchin, "Ultraviolet Spectra of Aromatic Compounds", John Wiley & Sons, Inc., New York, (1951).

[8] Reference 6, p. 219.

[9] B. Witrop and J. B. Patrick, *J. Am. Chem. Soc.*, 73, 713 (1951).

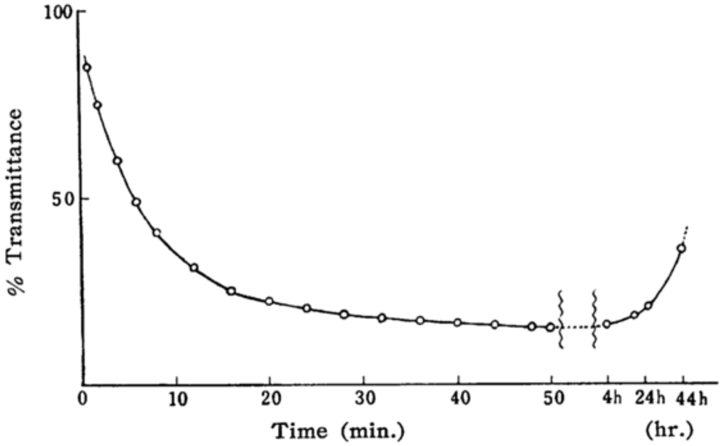

Fig. 4. Variation of the transmittance of the absorption maximum of I in ethanol (about 1/2000 mol.) at 470 mμ after the addition of potassium hydroxide.

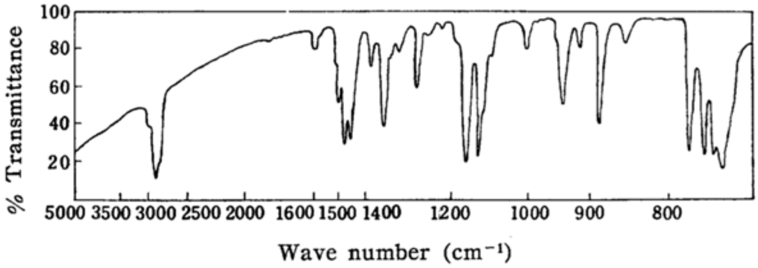

Fig. 5. Infrared spectrum of 2,2′-bibenzoxazole (Nujol mull).

When metal acetate has been added to the solution, an acetate ion acts as a proton acceptor and an anion of Schiff base is produced in the same manner as in the case of potassium hydroxide. The structure of a metal chelate thus formed, has been represented by Bayer as an ionic one of glyoxal bis-(2-hydroxy anil).

Compound II failed to give a new absorption band at a visible region on addition of potassium hydroxide to its ethanol solution. Accordingly, II lacks the feature of tautomerism in contrast with I, and the inability to form a metal chelate is well understood.

Chemical Properties.—Methylation of I and II was attempted using sodium amide and methyl iodide in dioxane or diazomethane in ether, but only an unchanged material was recovered.

By the acetylation of I with acetic anhydride, a crystalline diacetyl derivative was obtained, m. p. 263~265°C. It was not hydrolyzed by acid or alkali and the infrared spectrum showed absorptions at 1670 cm^{-1} (C=O stretching) and 1587 cm^{-1} (phenyl ring) and no absorption was observed in the 3000 cm^{-1} region. Thus, the diacetyl derivative proved to be *N,N′*-diacetyl-2,2′-bibenzoxazoline(D).

When the dilute solution of I in acetone was carefully treated with potassium permanganate, a dehydrogenation product was obtained in pale yellow prisms, m. p. 257°C. It was confirmed to be 2,2′-bibenzoxazole (E) from mixed melting point test with the authentic sample[10] prepared by the oxidative condensation of benzoxazole with copper acetate. 2,2′-Bibenzoxazole was also obtained by the oxidation of I with lead dioxide in benzene. The infrared absorption pattern (Fig. 5) of the dehydrogenation product was quite identical with that of the authentic sample.

Similar oxidation did not proceed in the case of II under the same conditions.

By the nitrosation of I, yellow dinitroso derivative (F) was obtained. It has no absorption band near 3000 cm^{-1} of infrared; the substitution of nitroso group occurred at imino hydrogen in the bibenzoxazoline (C′). By the catalytic hydrogenation of

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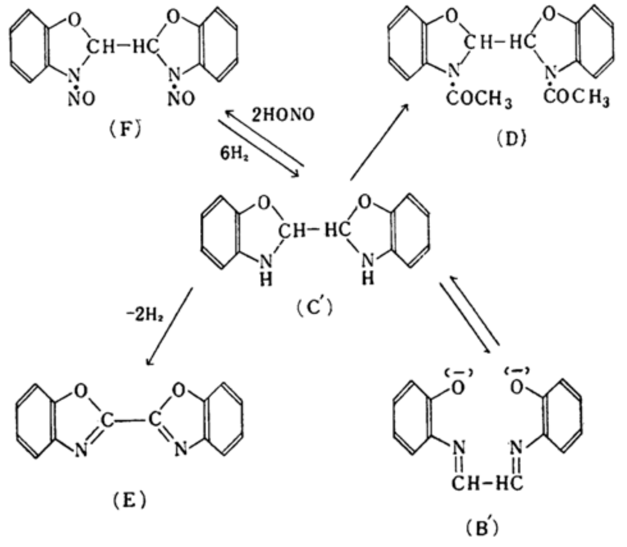
[10] D. R. Pat., 650,050 (1936); *Chem. Zentr.*, **1937**, II, 4395.



F, six moles of hydrogen were absorbed and I was reproduced.

The above reactions are summarized in the following schema.

Thus, the most reasonable conclusion to be drawn from the available data is that the condensation product of *o*-aminophenol with glyoxal is 2,2′-bibenzoxazoline and with diacetyl is 2,2′-dimethyl-2,2′-bibenzoxazoline as shown in the formula C. Bayer's investigation concerning the structure of metal chelates would be supported along with the consideration that 2,2′-bibenzoxazoline tautomerizes to glyoxal bis-(2-hydroxy anil).

Condensation products of many other α-dicarbonyl compounds with *o*-aminophenol derivatives and their structures will be reported in the subsequent paper.

Experimeatal

2, 2′-Dimethyl-2, 2′-bibenzoxazoline. — Prepared from *o*-aminophenol and diacetyl according to Kehrmann's method. Colorless plates, m. p. 241°C. The substance afforded a deep reddish violet color when dissolved in concentrated sulfuric acid. The aqueous alcoholic solution did not show the color reaction with ferric chloride.

Anal. Found: C, 71.97; H, 6.22; N, 10.52. Calcd. for $C_{16}H_{16}N_2O_2$: C, 71.67; H, 6.01; N, 10.44%.

2, 2′-Bibenzoxazoline.—To a solution of 10 g. of *o*-aminophenol in 90 ml. of hot ethanol, 15 g. of 30% aqueous glyoxal was added and gently refluxed for thirty minutes. The mixture became dark brown and the crystals separated out. The crystals collected after being cooled were washed with ethanol to give almost colorless ones. Recrystallization from ethanol using a Norit gave colorless needles, m. p. 210°C. Yield, 6 g.

2,2′-Bibenzoxazoline is soluble in methanol, benzene and dioxane and insoluble in water and chloroform. The substance afforded a deep green color when dissolved in concentrated sulfuric acid.

Anal. Found: C, 70.34; H, 4.86; N, 11.30. Calcd. for $C_{14}H_{12}N_2O_2$: C, 69.99; H, 5.03; N, 11.66%.

Acetylation of 2, 2′-Bibenzoxazoline : *N, N′*-Diacetyl-2-2′-bibenzoxazoline. — A solution of 0.5 g. of 2,2′-bibenzoxazoline in 20 ml. of acetic anhydride was gently refluxed for ca. 2 hr. The reaction mixture became dark brown. The solvent was removed under reduced pressure, and the resulting dark brown tarrish residue was treated with a small amount of benzene, filtered, and the remaining crystals were washed with benzene and methanol, and recrystallized from dilute acetic acid. Colorless crystals, m. p. 263~265°C, were obtained in a poor yield.

This diacetyl derivative is slightly soluble in benzene and soluble in dioxane and afforded a red color in warm concentrated sulfuric acid.

Anal. Found: C, 66.17; H, 4.97; N, 8.67. Calcd. for $C_{18}H_{16}N_2O_4$: C, 66.65; H, 4.97; N, 8.67%.

Potassium Permanganate Oxidation of 2, 2′-Bibenzoxazoline : 2, 2′-Bibenzoxazole.—To a solution of 0.5 g. of 2,2′-bibenzoxazoline in a mixture of 250 ml. of pure acetone and 50 ml. of water, 0.5 g. of potassium permanganate in 100 ml. of acetone was added dropwise with stirring and gentle boiling. The addition required ca. 3 hr. and the reaction mixture was boiled for an additional 1 hr. After being kept overnight, the reaction mixture was filtered and the filtrate was concentrated under reduced pressure. The yellowish brown residue was recrystallized twice from dioxane and then from chlorobenzene to give pale yellow prisms, m. p. 257°C.

Anal. Found: C, 71.27; H, 3.52; N, 11.60. Calcd. for $C_{14}H_8N_2O_2$: C, 71.18; H, 3.41; N, 11.86%.

Lead Dioxide Oxidation of 2,2′-Bibenzoxazoline: 2,2′-Bibenzoxazole. — To a solution of 2,2′-bibenzoxazoline in 80 ml. of hot benzene, was added 20 g. of lead dioxide. The mixture was refluxed for ca. 6 hr. and turned dark brown. The hot mixture was filtered and the solvent was distilled off. The reddish brown residue was treated with alcohol, dried and dissolved in 20 ml. of benzene. The benzene solution was chromatographed over commercial activated alumina and developed with the same solvent. The first fraction which was obtained almost unabsorbed amounted to ca. 100 ml.; the solvent was removed by evaporation, the pale yellow residue was treated with hot alcohol and recrystallized twice from dioxane to give pale yellow crystals, m. p. 256°C. Mixed melting point with the authentic sample showed no depression.

Nitrosation of 2,2′-Bibenzoxazoline. — A mixture of 1 g. of 2,2′-bibenzoxazoline in 130 ml. of benzene and 1.1 g. of sodium nitrite in 20 ml. of water was warmed at 50°C and stirred vigorously. To the mixture, 10 ml. of 1 N hydrochloric acid was gradually added; then the benzene layer became yellow. The benzene layer which separated was washed with water and dried over anhydrous sodium sulfate. The solvent was distilled off under reduced pressure and the residue was recrystallized from ca. 150 ml. of alcohol to yield yellow needles, m. p. 157°C (decomp.).

This dinitroso derivative was not hydrolyzed even by boiling with dilute mineral acid or aqueous alkali, but dissolved in concentrated sulfuric acid with a green color and evolution of nitrogen monoxide (potassium iodide starch paper test).

Anal. Found: C, 56.36; H, 3.47; N, 18.13; mol. wt. (cryoscopic method, benzene), 301. Calcd. for $C_{14}H_{10}N_4O_4$: C, 56.39; H, 3.36; N, 18.77%; mol. wt., 298.27.

Hydrogenation of *N,N′*-Dinitroso-2,2′-bibenzoxazoline. — A solution of 0.1 g. of the dinitroso compound in ca. 50 ml. of alcohol was hydrogenated using Adams catalyst at atmospheric pressure and room temperature. The yellow solution became colorless on absorption of a slight excess of hydrogen. The catalyst was filtered and the filtrate was evaporated under reduced pressure. The remaining crystals were recrystallized from alcohol, colorless plates, m. p. 209°C (decomp.). The substance was identical with 2,2′-bibenzoxazoline. From the gas in the hydrogenation vessel, ammonia was detected (Nessler's reagent).

Glyoxal Bis-(4-hydroxy anil).—To a solution of 1 g. of freshly recrystallized *p*-aminophenol in a small amount of 80% alcohol, was added 1.2 g. of 30% aqueous glyoxal, and the mixture was heated on a water bath for several minutes. Then, crystals were separated out and the mixture was cooled and filtered. Recrystallization from a large amount of alcohol gave yellow needles, m. p. 212~213°C (decomp.).

Anal. Found: C, 70.04; H, 5.10; N, 11.47. Calcd. for $C_{14}H_{12}N_2O_2$: C, 69.99; H, 5.03; N, 11.66%.

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