

## Metal Complexes of Gossypol

The magnetic and spectral properties of copper(II) gossypol and its Schiff's base complexes, are reported. A concurrent investigation has been made of the 2-hydroxy-1-naphthaldehydes which contain the functional groups most probably associated with the reactive sites of gossypol. The infrared data on 2-hydroxy-1-naphthaldehyde-anthranilic acid indicates that carbonyl groups are involved in a salt-

type linkage (dimer) with copper atoms. Electronic absorption spectra of several Schiff base complexes of 2-hydroxy-1-naphthaldehyde are also investigated. These and other spectroscopic data, in conjunction with magnetic susceptibility data, are evaluated to draw conclusions on the structure of gossypol complexes.

**G**ossypol (Figure 1) is a troublesome cottonseed pigment causing color problems in the extracted oil and, owing to its toxicity, restricting the use of the meal, especially as a source of protein concentrate. Furthermore, a chemical reaction between gossypol and protein results in a reduction in the availability of lysine, consequently reducing protein quality.

The addition of ferrous salts to cottonseed meal has been shown to produce beneficial effects in the animal feed (Withers and Brewster, 1913). The role of the ferrous ion in decreasing the toxicity is believed to be due to formation of a gossypol-iron complex (Phelps, 1966).

As part of a program to investigate the properties of gossypol complexes, the preparation and properties of several metal complexes of gossypol have been reported, including detailed studies of their stoichiometry and stability constants (Ramaswamy and O'Connor, 1968). In this paper the magnetic and spectral properties of copper(II) gossypol and its Schiff's base complexes, are reported. A concurrent investigation has been made of the 2-hydroxy-1-naphthaldehydes which contain the functional groups most probably associated with the reactive sites of gossypol.

### EXPERIMENTAL

Schiff's bases were prepared by condensing gossypol or 2-hydroxy-1-naphthaldehyde with methylamine, *n*-propylamine, aniline, anthranilic acid, and *o*-aminophenol, in absolute ethanol. The resulting Schiff's bases were treated with copper(II) acetate, in 1:1 and 1:2 molar ratio. Immediate green precipitates were obtained in all cases. These were filtered, washed, and dried overnight in a desiccator. Analytical data are shown in Table I. Previously, copper(II) chloride salt had been added to gossypol in sodium hydroxide. The precipitate obtained from this reaction, however, turned dark on drying. From this dark product, it was difficult to prepare analytically pure compounds.

Visible and ultraviolet spectra of the complexes in solution were obtained with a recording spectrophotometer, Cary Model No. 14. Reflectance spectra of solid samples were insoluble in organic solvents and were obtained on a recording General Electric Spectrophotometer. The effective magnetic moment was calculated from the expression  $\mu_{\text{eff}} = 2.86(X_M T)^{1/2}$  (Table II).

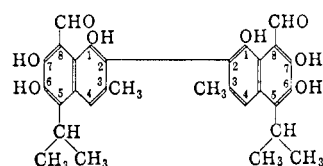


Figure 1. Gossypol structure

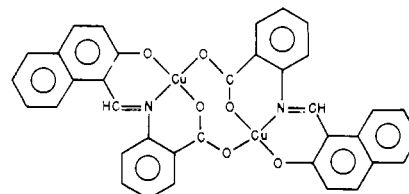


Figure 2. Dimeric structure for 2-hydroxy-1-naphthaldehyde anthranilic acid copper(II) complex

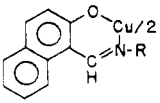
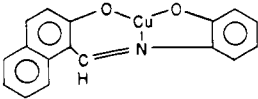
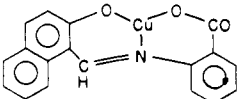
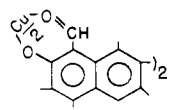
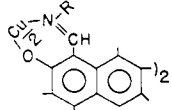
Table I. Analytical Data

Complex	Calculated			Found		
	C	H	N	C	H	N
(C <sub>12</sub> H <sub>10</sub> ON) <sub>2</sub> Cu	66.69	4.61	6.48	66.61	4.50	6.38
(C <sub>14</sub> H <sub>14</sub> ON) <sub>2</sub> Cu	68.85	5.73	5.73	68.85	6.01	6.15
(C <sub>17</sub> H <sub>12</sub> ON) <sub>2</sub> Cu	73.20	4.32	5.03	73.32	4.46	4.98
(C <sub>17</sub> H <sub>11</sub> O <sub>2</sub> N)Cu	61.65	3.36	4.29	62.33	3.44	4.24
(C <sub>18</sub> H <sub>11</sub> O <sub>3</sub> N)Cu	61.00	3.10	3.95	60.89	3.63	4.10
(C <sub>15</sub> H <sub>14</sub> O <sub>4</sub> ) <sub>2</sub> Cu	62.09	4.82	...	61.31	4.66	...
(C <sub>21</sub> H <sub>18</sub> O <sub>4</sub> NCu) <sub>2</sub>	61.16	4.37	3.39	60.13	4.34	3.29
(C <sub>18</sub> H <sub>21</sub> O <sub>3</sub> N) <sub>2</sub> Cu	...	6.34	4.23	...	6.12	3.99

### RESULTS AND DISCUSSION

The ligand field spectra of Schiff's base complexes of the type (R:NR')<sub>2</sub> Cu(R = 2-hydroxy-1-naphthaldehyde, R' = CH<sub>3</sub>, C<sub>6</sub>H<sub>7</sub>, C<sub>6</sub>H<sub>5</sub>) exhibit (other than the ligand absorption above 22,000 cm.<sup>-1</sup> where all compounds exhibit a multi-component band in the range 31,000–22,000 cm.<sup>-1</sup>), only one weak band around 16,000 cm.<sup>-1</sup>. This single band is very similar to that observed in known square planar copper(II) complexes (Holm *et al.*, 1966). The observed magnetic moment for these complexes (1.7–2.0 B.M.) is consistent with the square-planar stereochemistry. Although the spectra of *cis* and *trans* square planar copper(II) complexes are the

Table II. Spectral and Magnetic Properties

COMPLEX	$\chi_g$	$\chi_M$	$\mu_{eff}$	ABSORPTION MAXIMA $cm^{-1}$
$R$ $CH_3$	3.441	1709	1.95	31,750, 26,670, 25,310, 16,130 (Sh)
 $n-C_3H_7$	2.616	1479	1.88	32,680, 26,310, 25,000, 16,400 (Sh)
$C_6H_5$	2.725	1791	2.06	30,960, 24,390, 23,530 (Sh), 16,400
	2.010	775	1.39	32,780, 23,810, 22,220, 18,190 (Sh)
	4.22	1653	1.99	31,250, 24,390, 22,470, 18,190, 16,940
	1.837	1315	1.80	24,690 (Sh), 23,810 18,190, 16,930
	2.474	2150	2.25	26,310 (Sh), 23,530, 17,840
$R = C_6H_5$				

same (Holm *et al.*, 1966), *cis*-quadridentate complexes, being accentric, are characterized by a high intensity band in the 18,000  $cm^{-1}$  region. A *trans*-planar configuration has been assigned to these complexes on the basis of the low intensity of the observed band.

The infrared absorption spectrum of 2-hydroxy-1-naphthaldehyde anthranilic acid copper(II) complex exhibits a strong band at 1590  $cm^{-1}$ . The corresponding free acid (ligand) absorbs at 1708  $cm^{-1}$ . It is known (Bellamy 1958) that carbonyl absorptions fall in the range of 1690–1725  $cm^{-1}$ , C=O stretching, whereas the salt of organic acids give rise to an absorption between 1550 and 1610  $cm^{-1}$ , assigned to an antisymmetric  $COO^-$  stretching vibration. The infrared spectra of these complexes do not reveal any bands between 2400 and 4000  $cm^{-1}$ , representing coordination of water. These observations indicate that the carbonyl groups are involved in a salt-type linkage with copper atoms. If the complex had a monomeric structure with a coordination number three, the C=O stretching frequency would have been close to the free carbonyl stretching vibration. Furthermore, the existence of copper(II) complexes with coordination number three has been critically questioned (Holm *et al.*, 1966). In the absence of the localized  $-C=O-O-Cu$  structure, a binuclear structure (Figure 2) in which a copper atom is involved in an eight-membered ring, with two six-membered rings adjacent, is assigned to this complex. Spin interaction is negligible in this case, hence it exhibits a normal magnetic moment. This is essentially the structure proposed by Kubo (Kubo *et al.*, 1963) for 5-nitrosalicylalanthranilic acid copper complex.

The absorption spectra of the complex in chloroform shows two bands at 550 and 590  $m\mu$ . The corresponding gossypol complex has been reported previously (Ramaswamy and O'Connor, 1968).

**Gossypol Complexes.** The first and second acid dissociation constants (pK) of gossypol (determined by potentiometric titration with KOH) are 4.51 and 6.15. The average of the third and fourth dissociation constants is 12.61. This indicates that the dissociation of the first pair of protons of the  $-OH$  groups on the naphthaldehyde rings causes an inductive effect into the aromatic ring system. This in turn reduces the acidity of the other  $-OH$  groups. Thus the probability of forming the 1-to-1 complex with divalent metal ions is very high. This has been shown to occur with various metal ions (Ramaswamy and O'Connor, 1968). The copper(II) complex prepared here by the addition of copper(II) acetate to gossypol in acetone is green in color and is crystalline. The analytical data indicate a 1-to-1 composition (Table I). The insolubility of this complex and large heat of reaction involved in this formation of this complex when compared with those forming monomer species (Ramaswamy, Evans, and O'Connor, 1969) indicate possible polymerization in this case. The observed magnetic moment (1.80 B.M.) and a very weak absorption at 550 and 590  $m\mu$  is consistent with a planar configuration. Copper complexes with four oxygen donor atoms are generally characterized by low intensity spectrum with two broad bands in the range of 530 to 660  $m\mu$  [e.g., bis-(acetylacetonato)copper(II)]. The calculated stability constant (Ramaswamy and O'Connor, 1968) is in line with those reported for 2-hydroxy-1-naphthaldehyde and

salicylaldehyde, [Cu-gossypol 7.26; Cu-2-OH-1-naphthaldehyde 7.1] (Calvin and Wilson, 1945); Cu-salicylaldehyde 6.50 (Mellor and Maley, 1947).

**Gossypol-Schiff Base Copper(II) Complexes.** Schiff bases of gossypol of the formula Gossypol: $X_2$ , where  $X = o$ -aminophenol,  $n$ -propylamine, and aniline were prepared. The products from these reactions give complexes, when reacted with copper(II) acetate. Chemical analyses indicate a metal to ligand ratio of 1-to-1 when  $X =$  propylamine and aniline but a 2-to-1 ratio when  $X =$  aminophenol. The calculated magnetic moment is indicative of one unpaired electron and electronic absorption spectra show a band about  $17,000 \text{ cm}^{-1}$  which is expected for tetracoordinated copper (II) complexes.

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