Interaction of Copper(II) with Pyrimidine Bases

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EICHHORN *et al.*[1] reported recently that there is a reaction between polcyctidylic acid and Cu^{II} in which the data (given in terms of the increase in absorbance of polyC solutions at varying mole percentages of Cu^{II}) reveal that complexes are formed with a polyC/Cu^{II} ratio of more than one. The exact stiocheiometry, however, could not be revealed by the data. In the same Paper, these authors report they could obtain no evidence of interaction between Cu^{II} and polyuridylic acid.

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In an earlier work, Eichhorn[2] reports that there is an uptake of 1—2 Cu^{II} ions per nucleotide (on titration of DNA with Cu^{II}) and that n.m.r. data reveal binding of Cu^{II} to adenine, guanine, and cytosine, but not to thymine, nucleotides. Further evidence of Eichhorn and Clark[3] showing profound effects on DNA melting points caused by added Cu^{II} also suggested formation of base–Cu–base complexes. Chromatographic behaviour of nucleotides in the presence of Cu^{II} also showed that cytosine behaves differently from uracil.[4]

In line with these studies by Eichhorn and his co-workers, this report covers experiments wherein cupric chloride was allowed to react with an equimolar amount of cytosine in boiling methanol for 3 hr. (experiment I) and in unbuffered water (pH *ca.* 5·5) at 80° for 30 min. (experiment II). In experiment I, two complexes were obtained: a 2 : 1 cyt–Cu complex (A) obtained in 71% yield and a 1 : 1 cyt–Cu complex (B) obtained in 5% yield. Experiment II yielded 13% (A), 11% (B) [(A) and (B) were identified in experiment II by their i.r. spectra which differed markedly from each other and from that of cytosine] and, on concentrating mother-liquors, *ca.* 15% of a material (C) tentatively identified as a cytosine chlorocuprate. (Chlorocuprates have been reported to form on concentrating solutions of cupric chloride.)[5] Treatment of uracil with cupric chloride in equimolar amounts in hot water for 2·5 hr. gave a total 80% recovery of starting materials, no other materials being observed.

Thus, while from cytosine two discrete complexes were isolated (on treatment with $CuCl_2$), uracil gave no evidence of reaction. These results confirm and shed added light on the results of Eichhorn mentioned above. While much of the treatment of DNA with Cu^{II} involves bindings between two purines (1 : 1 purine–Cu complexes have also been suggested[6,7]) and between one purine and one pyrimidine (*i.e.*, pur–Cu–pyr) it would seem that the findings herein reported (*i.e.*, the isolation of a 2 : 1 cyt–Cu^{II} complex) might suggest the additional possibility of cytosine–Cu–cytosine cross-linkages. These results also help to explain the nature of the very stable linking of Cu^{II} to nucleic acid found by Wacher and Vallee.[8]

TABLE

Materials obtained on treatment of cytosine with cupric chloride

Material	M.p.	U.v. spectra[a] Max	Min	Max / Min
Cytosine		268 mμ	246 mμ	1·64
(A)	255—257° dec.	269	249	1·45
(B)	247—249° dec.	270	250	

a Determined in unbuffered water.

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