

## I. GENERAL REVIEW

### A. Biguanide and the related compounds :

Biguanides and guanyl ureas have been found to give rise to numerous complex compounds with bivalent and trivalent metals of the transitional series. A detailed account of the chemistry of biguanides and guanyl ureas has been given in a review article by P. Rây (71).

The complex forming properties of the ligands are related closely to their behaviour as bases, acids, zwitter ions or polar molecules. Biguanides and guanyl ureas are moderately strong bases and form well defined salts with acids. Many so called acid salts of biguanides are known whose formation can presumably be attributed to a comparatively weak character of biguanide as a diacid base (28, 72).

Guanyl urea generally behaves as a monoacid base and except for its acid sulphate, forms in most cases normal salts with one equivalent of acid. A quantitative measure of the basic character of these ligands is given by the value of the dissociation constants of their conjugate acids, the protonated ligands  $\text{BigH}_2^+$  or  $\text{BigH}_3^{++}$  as the case may be ( $\text{BigH}$  = a molecule of any biguanide).

The dissociation constants,  $K_a$  and  $K_a''$  of the first and second protonated biguanide and its several substituted products-

have been determined by the usual pH method and also from their ultra violet spectra within a certain pH range (71).

A consideration of the dissociation constants  $K_a$  values of the first protonated biguanides and their substituted products indicates that their basic strengths do not differ greatly from one another except in the case of a few mono and disubstituted biguanides containing aromatic system such as phenyl and naphthyl groups. Biguanides are in general much stronger bases ( $pK_a = 10 - 12.8$ ,  $pK_{a''} = 2 - 3.3$ ) than ammonia ( $pK_a = 9.2$ ), the  $pK$  values approaching those of alkyl amines ( $pK_a = 10.5 - 11.0$ ). Compared to ethylenediamine and propylenediamine with  $pK_a$  and  $pK_{a''}$  values of the order of 10.0 and 7.0 respectively, biguanides are stronger as mono acid bases, but considerably weaker as diacid ones, and in the latter capacity, they are even weaker than aniline ( $pK_a = 4.4$ ). This is possibly related to their ampholytic character, which enables them to form inner-metallic complexes with many metal ions (24).

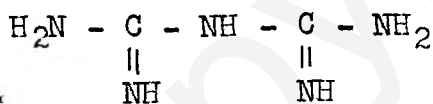
The  $pK_a$  values of guanyl ureas indicate that the unsubstituted simple guanyl urea is a weaker base than ammonia whereas guanyl-urea-O-alkyl ethers are much stronger bases resembling biguanides in this respect (25).

The degree of dissociation of the base  $BH_3(OH)_2 \rightleftharpoons BH_3(OH)^+ + OH^-$  was calculated from the conductivity of the free biguanide base and its nitrate in aqueous solution (83). The second

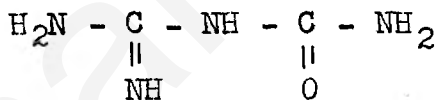
dissociation constant of the base has also been determined by conductometric and potentiometric titration of the aqueous solution by strong acids.

B. Structure of biguanide and guanyl urea :

Biguanide and guanyl urea are closely related compounds. The replacement of = O group in guanyl urea by = NH group will give rise to biguanide molecule. The close resemblance between these two substances may be attributed to their derivation from the same parent source, i.e. carbonic acid or its amide carbamic acid and guanidine. Guanyl urea may thus be regarded as the guaneide of carbamic acid and similarly biguanide may be viewed as guaneide of pseudo-urea  $\text{HN} = \text{C}(\text{OH})\text{NH}_2$ .

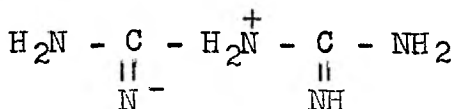
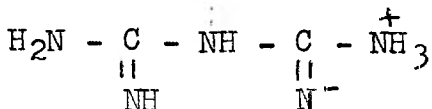
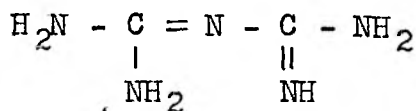
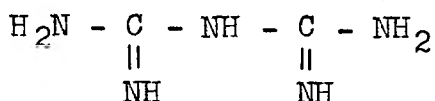


Biguanide

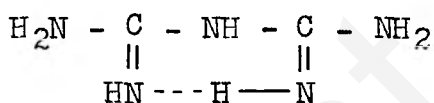


guanyl urea

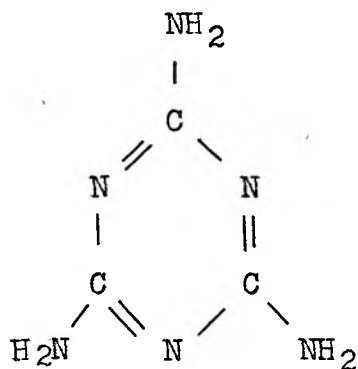
In view of the remarkable complex forming capacity of biguanides and guanyl ureas, their structures are of special interest. These two compounds may be represented satisfactorily as resonance hybrid of several tautomeric configurations including some zwitter ions. Owing to prototropy, the biguanide molecule may occur in the form of following tautomers.



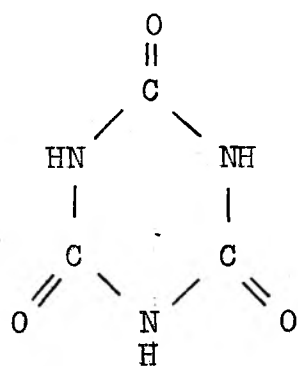
The molecule may be further modified by hydrogen bonding giving rise to cyclic structure.



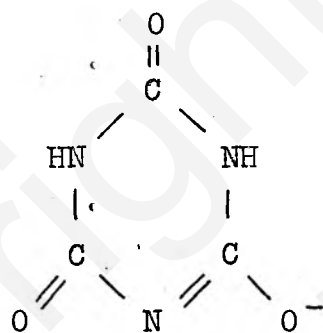
Hirt and Schmitt (32) have studied the ultraviolet absorption spectra of the oxygen containing symmetric triazines, their ions and their acyclic analogues. The spectra are correlated with their molecular structures in terms of conjugated single and double bonds between carbon and nitrogen atoms of the heterocyclic ring and exocyclic nitrogen and oxygen atoms. The spectra, structures and ionization constants of the oxygen containing triazine derivatives : ammeline, ammelide and cynuric acid, and their acyclic analogues : biguanide, guanyl urea and biuret, were discussed. Hirt and Shalley (33) investigated the ultraviolet spectra of malamine in the unionized form. The authors assigned the weak transition occurring at 42,500 K or 2350 A to a symmetry forbidden  $\pi$ -electron transition. The structure of malamine in the solid state and in neutral solutions have been studied and it has been found to exist in the symmetrical triamino form (33, 34, 26).



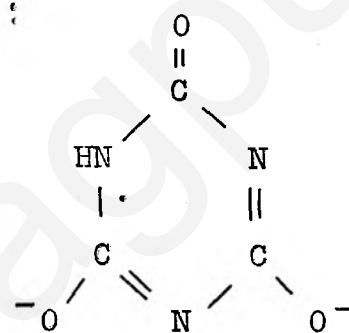
The ultraviolet absorption spectra and its pH dependence studies indicated the presence of three distinct forms of cynuric



pH = 1

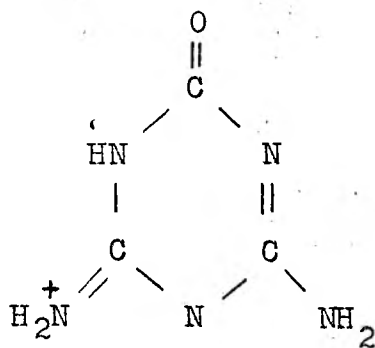
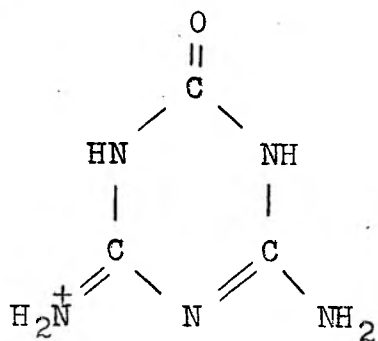


pH = 9



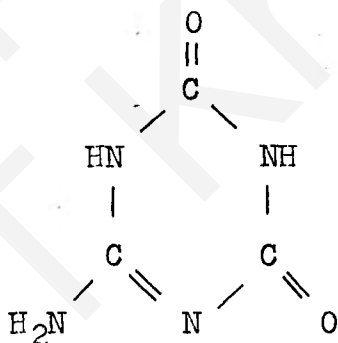
pH = 12

acid in the pH range from 1 to 14. It seems reasonable to assume that ammeline and ammelide should have molecular structures which are intermediate between those of malamine and cynuric acid. There are two possible structures for the positive ion of ammeline,



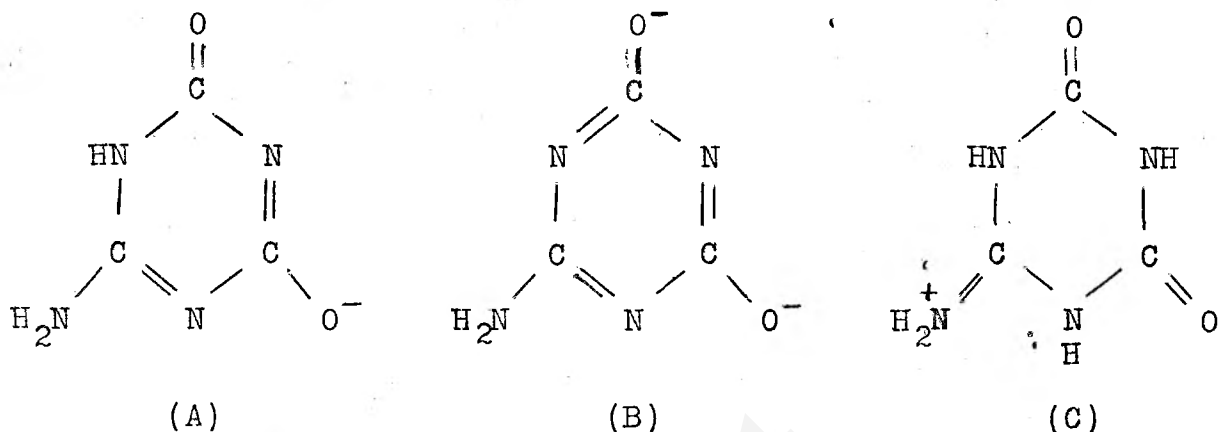
By comparing the wave length maxima at pH = 1 with that of its acyclic analogues : guanyl urea and biguanide, it becomes apparent that the first structure with its  $>\text{C} = \text{N} - \text{C} = \text{N} -$  conjugated system is the more likely choice. Both the positive ion of ammeline and positive ion of biguanide have their maximum absorption at identical energies (43,500 K or 23,000 Å), whereas the neutral form of guanyl urea with its  $>\text{C} = \text{N} - \text{C} = \text{O}$  conjugated system absorbs at 2180 Å.

Ammelide is reported to have a neutral form



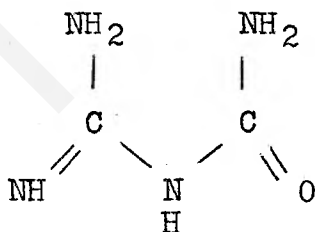
and a singly ionized negative ion form (A). The existence of two other forms have been shown in strong sodium hydroxide (B) and

hydrochloric acid (C) solution.



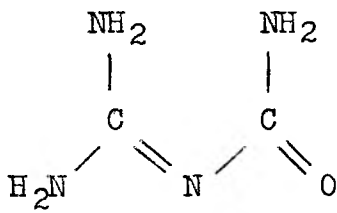
The nonconjugated forms of ammelide and cynuric acid did not display bands in the ultra-violet region above 2000 Å. The compound with analogous structures, biguanide and ammeline, guanyl urea and ammelide having the same arrangement of C, N and O atoms and their connecting bonds, on examination showed the same sort of spectral behaviour.

Guanyl urea, which shows no bands in acid solution must be written in a nonconjugated form, analogous to ammelide. If the conventional structure

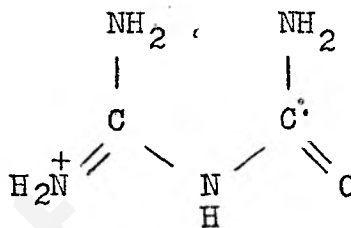


is written for guanyl urea, then in alkaline solution where the absorption at 45,870 K or 2180 Å is observed, it should be written

as (D) as in a solution of free base, considering the strong basic character of guanyl group in the compound. In acid solution, where it forms a salt, it should therefore, be represented by the protonated conventional structure (E).

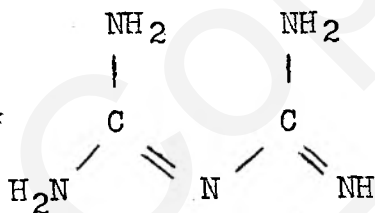


(D)

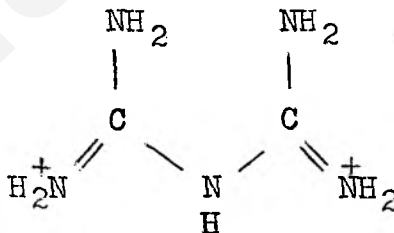


(E)

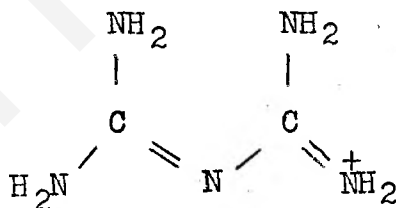
Biguanide which is likely to have a conjugated system as  $-\text{C}=\text{N}-\text{C}=\text{N}-$ , should show absorption at lower energy as in ammeline positive ion. It was found to absorb at 43,500 K or 230  $m\mu$ .



base



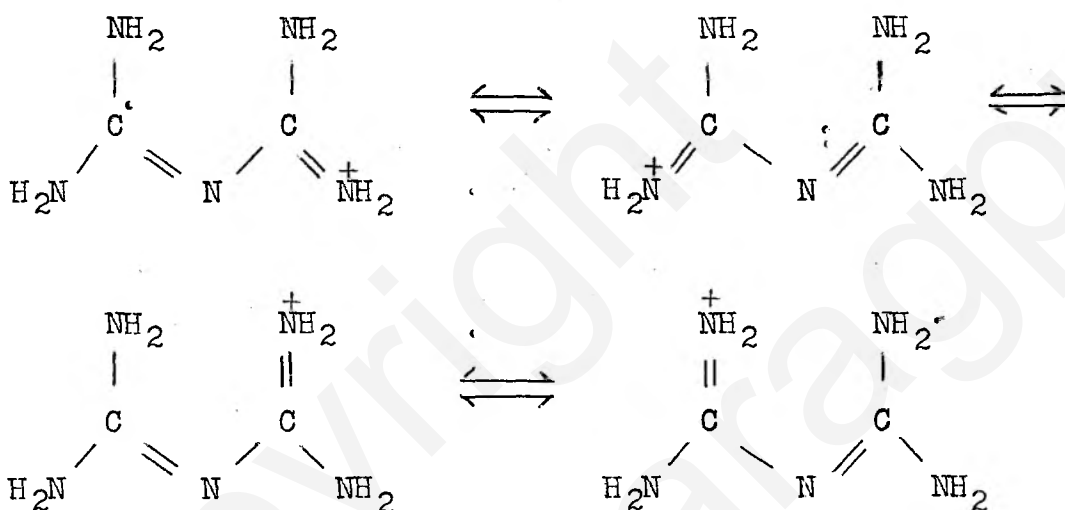
acid salt



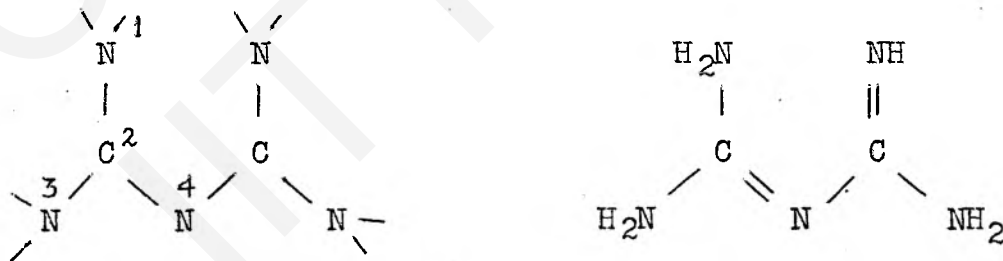
normal salt



However, the addition of a single proton to biguanide base does not shift the position of the absorption band, but only decreases its intensity. The addition of another proton makes the absorption band disappear altogether (32) indicating the formation of a nonconjugated structure. However, for the normal biguanide salts several resonance structures are possible;



A simple LCAO - Huckel calculation has been done first for the skeleton (88)



to ascertain the nature of the 43 kK transition in biguanide assuming it to be planar. The following general conclusions

arrived at are not very sensitive to the choice of parameter for N.

The bond order of the various bonds are as follows :

$$N_1 - C_2 = 0.50 , \quad C_2 - N_3 = 0.69 , \quad C_2 - N_4 = 0.45$$

The bond lengths were calculated using bond-order bond length relationship (65) and were found to be

$$N_1 - C_2 = 1.37\text{A}, \quad C_2 - N_3 = 1.33\text{A}, \quad C_2 - N_4 = 1.38\text{A} .$$

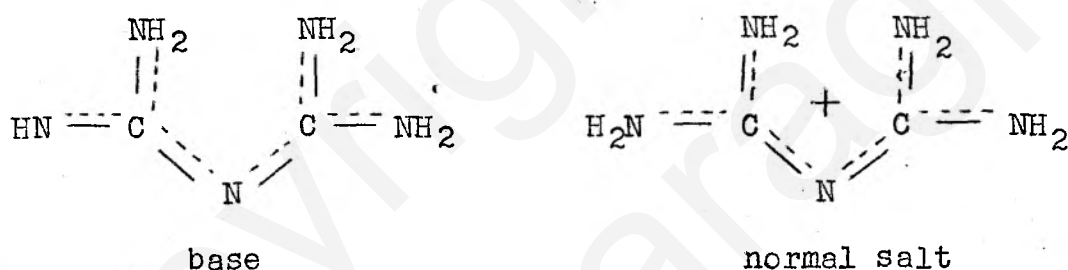
The experimental data corresponding to free biguanide is not known. However, the above values may be compared with those of the copper (II) complex of ethylenedibiguanide, as determined by Kunchur and Mathew (41).

C - N bond lengths in the biguanide molecule varies to some extent and are given below :

$$N_1 - C_2 = 1.29 - 1.35\text{A}, \quad C_2 - N_3 = 1.35 - 1.39\text{A}, \quad C_2 - N_4 = 1.39 - 1.43\text{A}$$

In the findings of Kunchur and Mathew (41) it is to be observed that the N - C bond connecting  $N_4$  to carbon are somewhat longer than the other C - N bonds. The carbon nitrogen bond length of biguanide has been estimated as 1.36A. This represents a shortening by 0.11 A when compared with the normal carbon nitrogen bond of 1.47A. This contraction is due partly to the shortening of the atomic radii of the carbon and nitrogen atoms, owing to their state of hybridization and partly due to  $\pi$  bond character of the carbon nitrogen bond.

It is reasonable to conclude that the base and the mono-protonated biguanide molecule has a planar structure affording the maximum opportunity for the formation of delocalized  $\pi$ -bonding in the whole molecule. The disappearance of the 43 kK transition in diprotonated biguanide may reasonably be attributed to the pyramidal distribution of the  $N_4$  valence bonds destroying the planarity of the molecule. All the above considerations led the author to suggest the following structure of the biguanide base and normal salt having the delocalized  $\pi$ -electron system over the whole molecule (88).



### C. Metal complexes of biguanide and related compounds :

The biguanide molecule behaves as a bidentate chelating ligand, giving rise to complexes of inner metallic type satisfying primary as well as secondary valency of the central metal atom. This has been proved by the preparation of several complexes such as anhydrous biguanides of chromium (III) (73), cobalt (III), copper (II), cobalt (II), palladium (II) and Ni(II) (74). These complex metal biguanidines form hydrated bases in aqueous solution and their corresponding salts in acids. The charge on the complex

cation is determined by the number of biguanide molecules, bound to the metal atom, each ligand molecule enabling the complex to imbibe one unit of positive charge in combination with a hydrogen ion of a water or an acid molecule to give a (hydrated) base or a salt. Thus the planar four coordinated complexes with bivalent metals form bipoisitive cations and the octahedral six co-ordinated complexes with tervalent or quadrivalent metals form tripositive or tetrapositive cations respectively..

The metal complexes of biguanides are comparatively more stable than those of guanyl ureas. In most cases the solubility of the complexes of biguanides is less than those of the corresponding complexes of guanyl ureas (71).

The magnetic properties of the metal complexes of all these ligands are in keeping with their nature as inner-metallic penetration or inner-orbital complexes except in the case of Mn(IV) and Re(V) biguanide complexes which show rather anomalous magnetic behaviour. The magnetic moments of all other metal atoms in these complexes agree well with what might be expected theoretically on the basis of Pauling's valence bond theory.

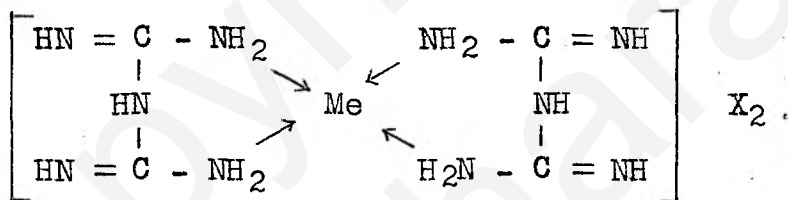
Besides the metal complexes, a large number of complexes of biguanide with nonmetals, viz. boron, silicon etc. have been prepared. A boron heterocycle was prepared by the interaction of biguanide and amino boranes or boric acids (47). A large number of boron and silicon heterocycles has also been synthesised by the

interaction of biguanides, guanylureas and related compounds and trimethoxy borate and silicon tetraiodide respectively (53).

The action of biguanide base with silicon tetraiodide yields the biguanide complexes of Si(IV) atom (53).

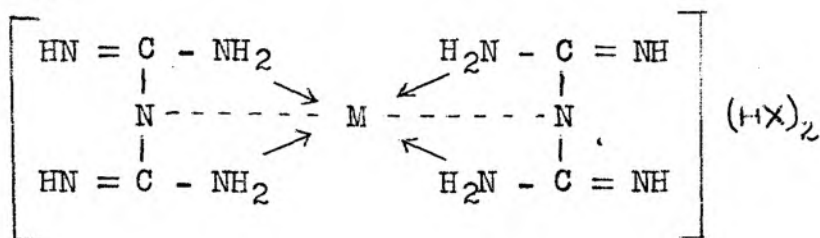
D. Structure of metal complexes of biguanide and related compounds :

The structure of the metal complexes of biguanide and guanylurea was a subject of controversy for a long time. From a consideration of the complex forming behaviour of acid imides and related compounds, Tschugaeff (89) represented the metal biguanide complex salt as



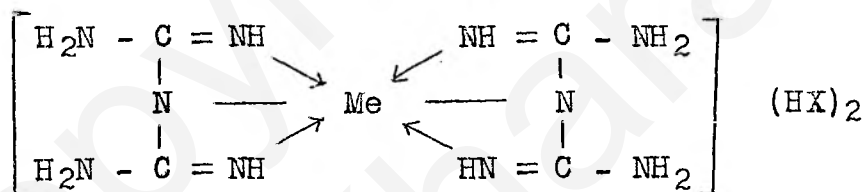
This structure, however, fails to explain the formation of complex anhydrobases  $\text{M(III)}(\text{C}_2\text{H}_6\text{N}_5)_3$  and  $\text{M(II)}(\text{C}_2\text{H}_6\text{N}_5)_2$  and does not represent the compound as an inner-metallic salt.

Ley and Muller (45) formulated the biguanide complexes as inner-metallic salts where the hydrogen of the central imino group of biguanide has been replaced by the metal atom.



In this structure, biguanide was shown to act as a tridentate ligand which, however, could not be confirmed by the latter workers.

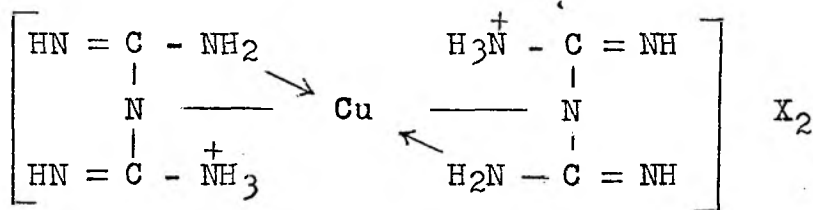
Slotta and Tschesche (44) suggested a similar structure considering the fact that the complex forming capacity of the biguanide is not affected by substitution in position 1 or 5, but is completely inhibited by the simultaneous substitution in position 1, 2, or 3 of the molecule.



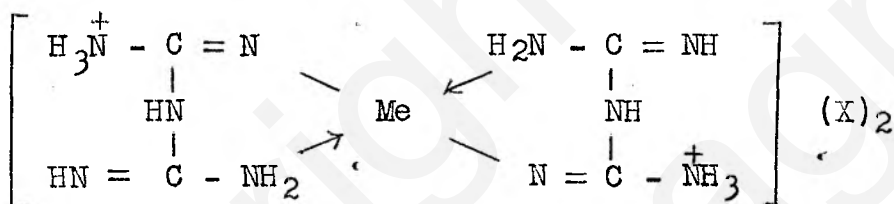
The authors were of the opinion that the hydrogen atom of the central imino group have been replaced by the metal atom with the formation of inner-metallic complexes. But this structure also suffers from the same disadvantage as former. The molecule according to this structure behaves as a cation of valency higher than that observed.

Traube and Glaubitt (90) suggested a structure of copper biguanide with four membered ring. It is doubtful whether a four

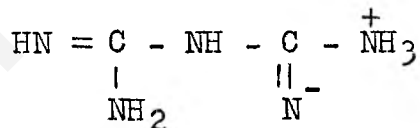
membered ring complex will have the stability like Cu(II) biguanide.



Rây and Saha (73) from a study of the preparation and properties of chromium tris(biguanide) complexes suggested the following structure for metal biguanides.



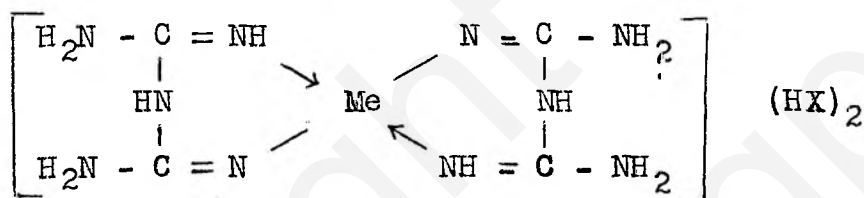
where Me = a bivalent metal atom. In this structure, the hydrogen atom of imino group (=NH) in each biguanide molecule is replaced by the metal atom and one of the two amino groups is linked to the metal atom by a co-ordinate bond, thus forming a six membered ring. The other amino group of the biguanide molecule acts as a base. It might also be assumed that the biguanide molecule reacts in its tautomeric zwitter ion form (24) with the metal ion.



The cationic complexes of such chelating ligands have been termed inner metallic salts of the third order (75).

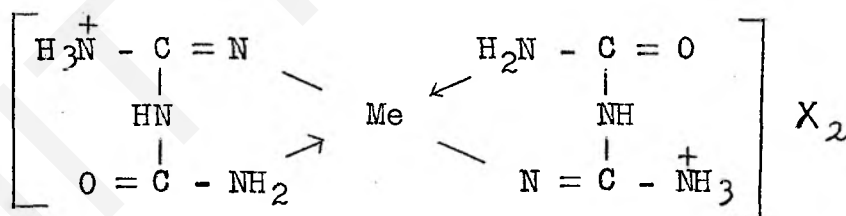
This structure can explain almost all the experimental facts except the observation of Slotta and Tschesche (84) that the simultaneous substitution at 1, 2, and 3 positions of the biguanide inhibits the complex formation with metal atoms.

An alternative structure has been suggested by Card and Rose (5) on the basis of symmetrical disposition of the biguanide molecule in a planar structure in its copper (II) complexes.



However, this structure would make the complex cation with four free amino groups and therefore should show a higher valency than that what is actually observed in the biguanide complexes.

Rây and Bandopadhyya (76) suggested the following structure for the metal guanylureas analogous to that of metal biguanides (73).



A study of ultra-violet spectra of the metal complexes of biguanide was done by Sen (88) to determine the particular form of the ligand molecule capable of complex formation with the

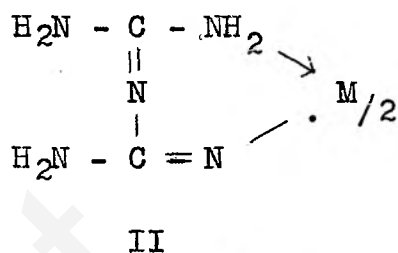
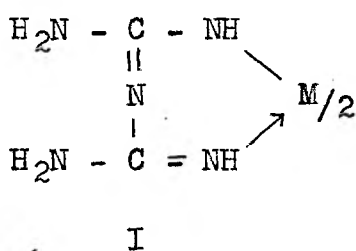


transition metal ions. It has been observed that the acid salt of biguanide, normal salt of guanylurea form complexes with copper only on the addition of sufficient quantity of alkali. The normal salt of biguanide i.e. monoprotanated biguanide can form complexes with many transition metals including copper directly without the addition of either alkali or ammonia. It, therefore, seemed likely that the main criterion of metal complex formation with the ligand lies in the attainment of suitable configuration for the production of appropriate ligand field around the metal ion.

It was observed (85) that the metal complexes of biguanide and guanylurea- $\theta$ -alkyl ether produce almost identical ultra-violet absorption spectra as given by biguanide base and its normal salt with absorption peak at about 2300A. However, an acid salt of biguanide does not have any peak in this region. It is therefore, inferred that the biguanide residue in a metal complex essentially retains this structure of biguanide as base or its normal salt with the conjugate - C = N - C = N - system. Similar studies with the metal complexes of simple guanylurea were not possible due to the nonavailability of complex salts in the pure state.

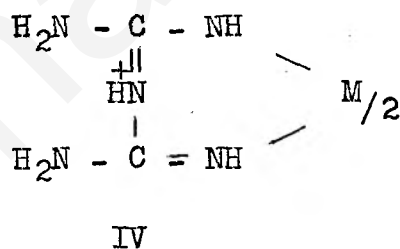
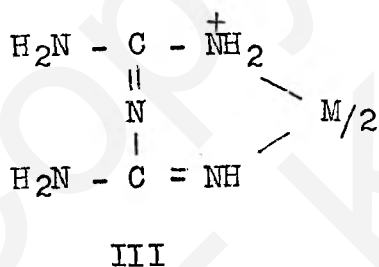
The evidence, obtained from the study of ultra-violet absorption spectra, points to the fact that the prerequisite for the metal complex formation with biguanide, guanylurea- $\theta$ -alkyl ether and guanylurea is the prior prototropic arrangement in the respective ligands resulting in the formation of a conjugated

system like  $-C=N-C=N-$ . Considering the fact that only biguanide and the monoprotonated biguanide molecules are capable of complex formation, while the diprotonated molecule is not, the complex metal biguanidines may be represented by the structures.



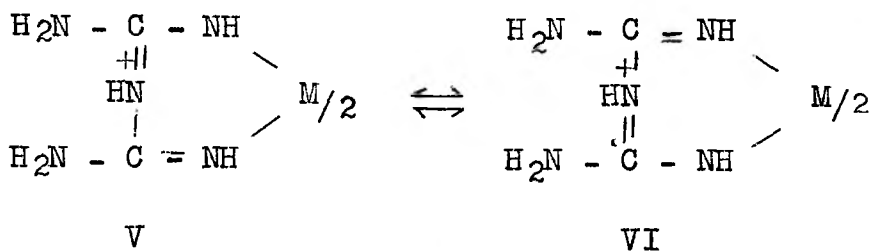
But the structure (I) is preferred as  $=\text{NH}$  group is more basic than  $-\text{NH}_2$ .

The hydrated complex base or its salt may, therefore be given the structure

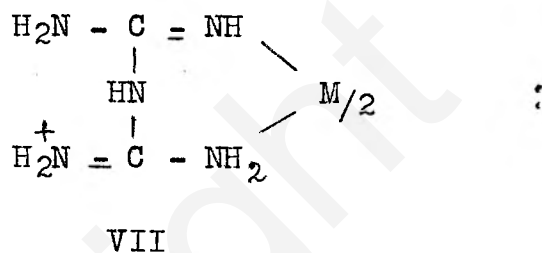


Among these two ~~the~~ structures, (IV) is more likely as it is more symmetrical than the structure (III).

Again in this form, the molecule may further be stabilized by resonance due to shifting of the double bonds.



There may be a third possibility with the configuration as in the biguanide acid sulphate.



In this form biguanide will form ammine type complexes rather than inner-metallic complex compounds.

The suggested structure of the metal biguanide complexes can satisfactorily explain all the properties of the metal biguanides. For example it is known that  $\text{N}^1$  (p-chlorophenyl) $\text{N}^5, \text{N}^5$ -diethyl  $\text{N}^1$  methylbiguanide gives beautiful rose red copper (II) complex showing that the  $\text{N}^1$  and  $\text{N}^5$  atoms do not apparently take part in the complex formation (6,77).

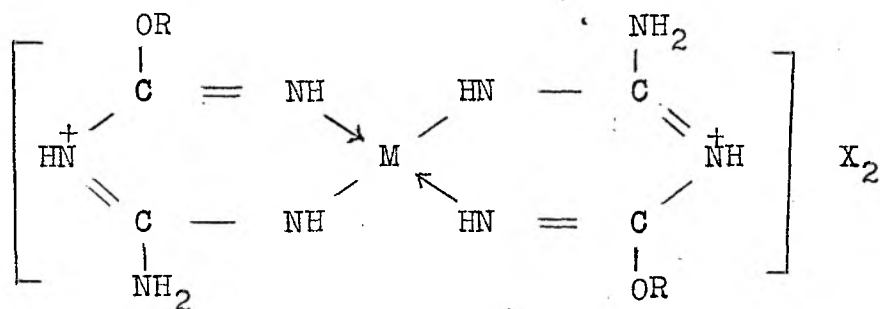
The reaction of chromium (III) and cobalt (III) biguanide bases with mercury (II) chloride in aqueous solution with the formation of water insoluble complex indicates the presence of one free amino group in biguanide molecule as it gives compound .

of composition  $\text{Cr(III) (BigHgCl)}_3$  and  $\text{Co(III) (BigHgCl)}_3\text{HgCl}_2$  (78). This can be explained on the assumption that the protonation of the = N - group leads to the formation of a strong hydrogen bond with one of the adjacent -  $\text{NH}_2$  groups, leaving only the other -  $\text{NH}_2$  group for reaction with mercury (II) chloride. The inertness of the bound -  $\text{NH}_2$  group has been demonstrated by the failure of  $\text{Co(III)}$  trisethylenediamine to react with mercury (II) chloride.

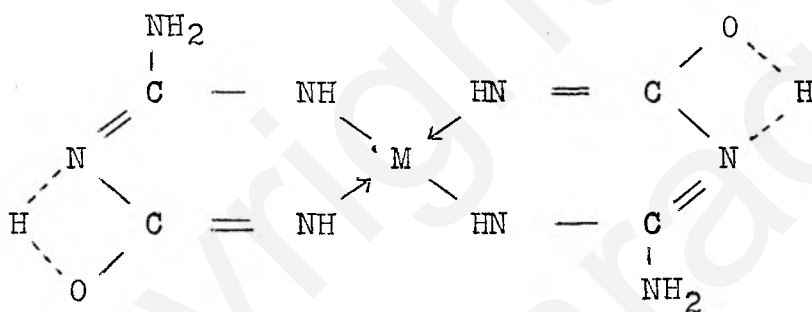
That the central nitrogen plays a very important role in the formation of metal biguanide complexes has been indicated by many earlier workers (84, 90). Some of them even went as far as to suggest a structure for metal biguanides with a metal ligand bond with the middle nitrogen atom making a four membered ring compound. Slotta and Tschesche (84) have shown that, when the hydrogen atom in position 3 of the biguanide molecule is substituted by an alkyl group, the molecule then ceases to act as a complexing ligand, whereas substitution in position 1 and 5 does not hinder the complex formation. Nevertheless, they have pointed out that copper hydroxide is not precipitated from a solution containing 3,alkyl-biguanide which may be attributed to cuprammine type of complex formation as given by the structure (VII) of the metal biguanides. Substitution in position 3 of the biguanide molecule inhibits the resonance between structures (V) and (VI) for the metal biguanides.

By analogy with the metal biguanide complexes, the metal complexes of guanylurea- $\theta$ -alkyl ether may be represented as

follows :



The anhydro-base of metal guanyluarea may as well be represented as (85)

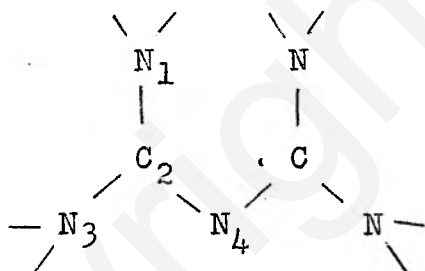


Experimentally it has been observed that biguanide and guanyluarea-*O*-alkyl ether metal complexes form very stable salts with ease by digestion of the complex base with ammonium salts. On the other hand, though the Cu(II) guanyluarea base can be prepared very easily by the addition of alkali to a metal salt and guanyluarea, the preparation of the salt from this base presents considerable difficulty.

From the observations made above, it seems reasonable to assume that the occurrence of the chromophoric group  
 $-\text{C}=\text{N}-\text{C}=\text{N}-$  is the most important requirement for the

formation of inner-metallic complexes of biguanides, guanylurea and guanylurea-O-alkyl ethers. The experimental conditions for the preparation of complexes varied as much as necessary for the formation of the above chromophoric group in the ligand concerned.

Sen (88) attempted to explain the shift of the ultra-violet spectra of the metal complexes of biguanide on the basis of a modified structure, taking into account the delocalised  $\pi$ -electron system in the ligand.



It was found (41) that in the Cu(II) complex, the  $C_2 - N_4$  bond length is somewhat greater than the other C - N bonds. This lengthening of the bonds between  $N_4$  and the two carbon atoms can be explained by the slight localization of the electron density towards the positive metal ion from an otherwise delocalized biguanide molecule. In this case the perturbation of the  $\pi$  levels of the ligand by the metal atom was taken into account in order to explain satisfactorily the experimental result. Only the 3d and 4p orbitals of the metal could interact with the ligand  $\pi$ -electrons. It has been observed by Sen (88) that the following sequence of levels in order of increasing energy is consistent

with the experimental result;  $d(M)$ , topmost filled  $\pi$ ,  $p(M)$ ,  $\pi^*$  (lowermost unfilled). In the case of Pt(II) and Pd(II) the  $d(M)$  has to be placed above topmost  $\pi$ . This is reasonable in view of the fact that the 4d electrons are more loosely bound to the metal than 3d. The metal d orbitals of interest here are  $d_{xz}$  and  $d_{yz}$  in case of square planar complexes and  $d_{xz}$ ,  $d_{xy}$ , and  $p_x$ ,  $p_y$ ,  $p_z$  in case of octahedral complexes.

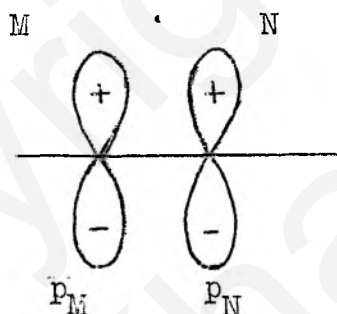
The antisymmetric  $\pi^*$  level will not interact with p. One combination of the ligands  $\pi_1^* + \pi_2^*$  will not interact with d either, the other ( $\pi_1^* - \pi_2^*$ ) will be raised. The lower  $\pi$  level will be shifted in both directions. The interaction with p will lower the energy of  $\pi_1 + \pi_2$ , (if the d orbitals is lower than  $\pi$ ) and will stabilize  $\pi_1 - \pi_2$ , if d orbitals is higher in energy than  $\pi$ . The bands because of their width will probably not be resolved, and the net shift will depend upon the relative magnitude of interaction with the p orbitals and with the d orbitals. In case of Pt(II) and Pd(II), only one band is obtained that is blue shifted which is understandable on the basis of the above scheme. In these cases, the d orbitals could be above the  $\pi$  orbitals and then both  $\pi_1 - \pi_2$  and  $\pi_1 + \pi_2$  will be stabilized by the interaction and the 43 kK band will show a blue shift.

$\pi_1$ ,  $\pi_2$ ,  $\pi_3$  represent symmetric orbitals of ligands 1, 2 and 3 while  $\pi_1^*$ ,  $\pi_2^*$  and  $\pi_3^*$  represent antisymmetric orbitals. According to group theory, functions belonging to the same representation can interact with each other. It was realised (88)

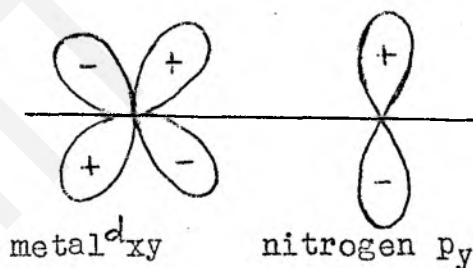
that interaction with certain metal orbitals with ligand  $\bar{\pi}$  orbitals will be important. In particular it was shown that the anti-symmetric orbitals will not interact with p, but will interact with d only, while the symmetric wave function will interact mainly with p. It should be noted that there will also be a  $\sigma - \bar{\pi}$  interaction in octahedral complexes which may add to the complication.

The following type of interaction of the metal p or d orbitals with the nitrogen p orbitals are shown in the figure.

$p_M / p_N$  = overlap integrals involving metal orbitals ( $p_M$ ) and nitrogen p orbitals ( $p_N$ )



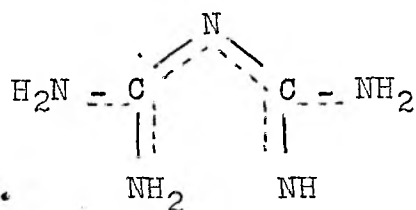
$d_M / p_N$  = overlap integral involving metal d orbitals of type  $xy$  with nitrogen p orbitals.



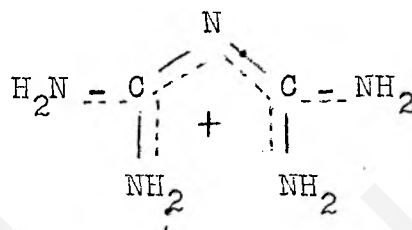
$d_M / p_N$  and  $p_M / p_N$  are of the same order of magnitude ( $\approx 0.2$ ) for chromium (III) and cobalt (III).



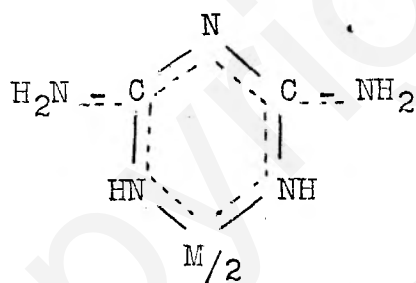
From the above consideration, the biguanide, monoprotonated biguanide, anhydrous metal biguanide complexes and their salts may be represented by the structures (I), (II), (III) and (IV) respectively, taking into account the  $\pi$  electron delocalization in the molecule (88).



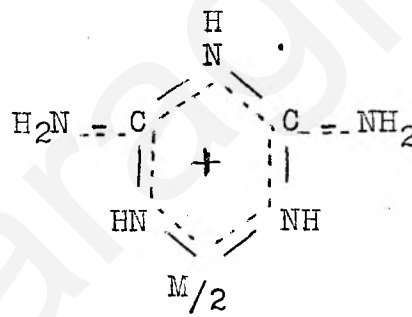
I



II



III



IV

The proton addition in structure (IV) does not disturb the planarity of the metal biguanide ring, though it is destroyed in case of diprotonated biguanide as observed by the disappearance of the 43 kK band. The proton in structure (IV) is quite loosely bound as can be experimentally verified by the preparation of anhydrous metal biguandines from their hydrated bases just by

heating at  $110^{\circ}\text{C}$  or below. The X-ray investigation (41) also indicates the lengthening of the C - N bond lengths containing protonated N from other C - N bonds in the biguanide molecule. However, those bonds retain some double bond character, and do not attain the C - N single bond length.

The suggested structures (III and IV) of the metal biguanides can explain all the chemical properties of this series of compounds like Ray and Saha's (73) formula. These structures have, however, the additional advantage of explaining the observed fact that  $\text{N}^3$  substituted biguanides are incapable of complex formation.

All the above considerations point to the fact that there is every possibility of the mixing of the ligand  $\pi$  orbitals with the d or p orbitals of the metal atom whenever symmetry permits. The X-ray crystal structure determination of copper ethylenedi-biguanide complex (41) indicates the planarity of the metal chelate ring which may contribute to the development of the aromaticity in the complexes. The presence of ring currents in these complexes shorten the C - N bond lengths from that of a single bond.

It is generally known that double bonds between metals and donor systems may be of the  $d\pi - p\pi$  or  $d\pi - d\pi$  type. The first being exemplified by  $\text{M} - \text{CN}$  and the second by  $\text{M} - \text{PX}_3$  type of bonds. The  $d\pi - d\pi$  and  $d\pi - p\pi$  bonding in such cases help in dissipating the accumulated negative charge on the metal atom due to  $\sigma$  bond resulting in the increase of bond strength.

The bonding involved in these cases may be symbolized as  $M \begin{array}{c} \leftarrow \\ \rightleftarrows \\ \rightarrow \end{array} X$ . Metal-nitrogen  $\pi$  bonding, if any, in metal biguanides may be represented as  $M \begin{array}{c} \leftarrow \\ \rightleftarrows \\ \rightarrow \end{array} N$ . This is due to the fact that though biguanide molecule does not have any vacant bonding orbital of  $\pi$  type symmetry, certain metal ions have vacant  $d\pi$  and  $p\pi$  orbitals to which the electrons from the filled  $p\pi$  orbitals of the ligand can swim over. This type of delocalization may be considered unique in metal complexes with acetylacetonate and biguanides and differs in kinds from those with cyanides, carbonyls and phosphines. Electron flow from the filled ligand  $\pi$  orbitals to the vacant metal  $d$  or  $p$  orbitals in metal biguanides is supported by the fact that biguanide is capable of stabilising the higher oxidation states of many transition metals (85). Although extensive  $Np\pi - Md\pi$  or  $Mp\pi$  bonding may not appear likely with many metals, some mixing of the  $Np\pi$  and  $Md\pi$  or  $Mp\pi$  orbitals will doubtless occur where permitted by symmetry and is likely to have some effect on the electronic structures of the metal chelates.

The ultra-violet spectral study supports the proposed scheme to a great extent (88). The overlap ( $Np\pi - Md\pi$  or  $Mp\pi$ ) must vary from metal to metal atom ranging from zero to a maximum value. In this connection, it appears worthwhile to tabulate the  $\pi$  bonding possibilities as determined by the methods of group theory. The ligand has only one type of orbitals designated as  $\pi_z$ . This occurs on the nitrogen atoms and on all carbon and nitrogen atoms in the ring, its nodal plane being the plane of the chelate ring. This orbital may easily overlap with the vacant

metal orbitals which are perpendicular to the metal ligand plane. The  $\pi$  bonding possibilities in metal biguanides are given below:

Type of complex	Point group symmetry	Metal orbitals available for $\pi$ bonding
$MA_2$ (planar)	$D_{2h}$ ( $dsp^2$ )	$d_{xz}$ , $d_{yz}$ , $p_z$
$MA_2$ (tetrahedral)	$D_{2d}$ ( $sp^3$ )	$d_{x^2-y^2}$ , $d_{xz}$ , $d_{yz}$
	$D_{2d}$ ( $sd^3$ )	$d_{x^2-y^2}$ , $p_x$ , $p_y$
$MA_3$ (octahedral)	$D_3$ ( $d^2sp^3$ )	$d_{xz}$ , $d_{yz}$ , $d_{xy}$

It has been pointed out that the metal d or p orbitals remain just above and below the topmost filled  $\pi$  orbital of the ligand (88) and hence the energy difference between these orbitals will not be too high to prevent their mixing. It should be noted that the greater stability of the metal nitrogen bond in metal biguanide chelate can be explained assuming the presence of  $\pi$  bonding. This exceptional co-ordinating capacity of the biguanide molecule makes it a powerful and versatile complexing agent. There is strong  $\sigma$ -bond (  $L \rightarrow M$  ) in the complex due to amine co-ordination, in which both the electrons come from the lone pair orbital of the ligand. The conjugate double bond and single bond system and the presence of  $-N=$  group in the molecule having filled p - orbitals with  $\pi$  electrons and the resultant delocalization of these  $\pi$  electrons over the chelate ring contribute mainly to the stability of the metal biguanide complexes.

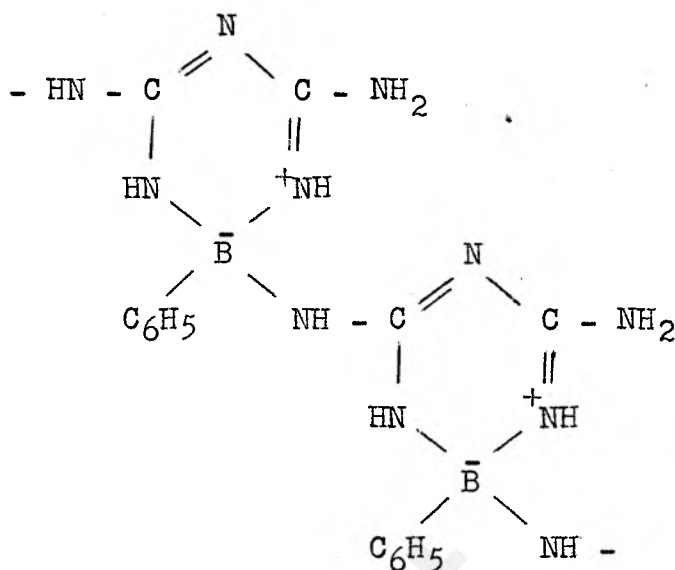
It is evident from the experimental facts that dipyridyl and phenanthroline, with one nitrogen p orbital already involved in a delocalised  $\pi$ -orbital of the aromatic ring have superior co-ordinating power than ethylenediamine which can only form ligand to metal  $\sigma$  bond.

Further proof of the proposed structure of metal biguanide complexes is revealed by the tendency of the biguanide molecule to stabilize higher valency states of the transition metals. No biguanide metal complexes with metal atom in its abnormal lower valency state has yet been made, though extremely stable complexes with Co(III), Cr(III), Ag(III), Au(III), Pt(IV), Pd(IV), Ru(III) and Fe(III) have been described (87, 85). It has been observed by Chatt (7) that ligands having lone pairs of electrons in addition to those forming  $\pi$  bonds with the metal atom and with no vacant orbitals in the valency shell will be most effective in stabilizing the higher valency states of the metal atom. When the p orbitals of the ligand atoms are filled and contain unshared lone pairs which can be utilised for  $\pi$  bonding with the vacant d or p orbitals of the metal atom, the electrons from the antibonding levels of the latter are powerfully repelled and they can be easily removed from the antibonding molecular orbital rather than from pure d orbital of the metal atom. The lone pairs of ligand electrons will be attracted towards the metal through the bonding  $\pi$  molecular orbital especially if the metal atom carries a large positive charge. The lone pair will, however, remain

associated with the ligand due to electronegativity of the ligand atom and the antibonding orbital, mainly singly occupied by the electron, will largely be on the metal atom.

The stabilization of higher valency state, therefore, be regarded as a result of lone pair repulsion. The electrons in the lone pairs of the ligand repelling the electrons in the  $d_{xy}$ ,  $d_{yz}$  and  $d_{xz}$  orbitals of the metals and so making their removal more easy. The extra stabilization of the higher valent metal complexes must be due to  $\pi$  bonding capacity of the biguanide molecule with the delocalized  $\pi$ -electron system capable of extending the delocalization through vacant d or p orbitals of the highly oxidized metal atom, thus decreasing the electronegativity to a great extent. The delocalized  $\pi$  electrons envelope over the metal ion and thus partially prevent the capture of any electron from outside by the highly charged positive metal atom to reduce its oxidation state.

Some experimental evidences indicating the possibility of the ring currents in metal biguanides may be discussed here. The reaction between biguanide base and bis (dimethylamine)-phenyl borane (53) in hot pyridine gave a solid product insoluble in organic solvents other than dimethylformamide and infusible below  $400^{\circ}\text{C}$ . The compound may be represented as follows :



Synthesis of monocyclic system was accomplished by the reaction between diethylamino-diphenyl borane with biguanide base in hot pyridine. On the basis of ultra-violet absorption spectra and hydrolysis studies, these compounds have been shown to possess aromaticity (53). The relative high stabilities of these compounds compared to other B - N compounds are of importance and indicated the participation of the ligand  $\pi$  orbitals for delocalized  $\pi$  bonding. The stability of these borinide rings towards solvolysis is undoubtedly influenced by electron releasing or withdrawing substituents on boron and the consequent effect of the ease of dissociation of the B - N bond. The cleavage of the B - N bond takes place readily with the addition of acids. The splitting of the bond can be explained by taking into account the fact that the initial protonation on the B - N ring withdraws the  $\pi$  electrons from the delocalized bond destroying aromaticity. The B - N bond is then prone to hydrolytic attack.

Similarly in silicon, the d orbitals are completely vacant. Biguanide having filled  $\pi$  orbitals forms very strong silicon heterocycles in which the ligand  $\pi$  electrons easily swim through the vacant hybridized orbitals of silicon (IV) (53). Overlapping of the filled  $\pi$  orbitals of the ligand with the vacant d orbitals of silicon is also indicated by the infrared spectral study of silicon compounds. The extensive conjugation in the  $\pi$  system of the silicon heterocycles has brought about a decrease in bond order of C - N stretching in the ring, which has been shown experimentally from the splitting of C - N stretching bands in the silicon biguanide complexes.

The ultra-violet spectra of biguanide, substituted biguanides, and their metal complexes were studied in aqueous solution (63). In cases of metal biguanides two  $\lambda$  max's were obtained : one denoted by  $\lambda$  max<sub>1</sub>, observed at the far ultra-violet region<sup>at</sup> about 200 m $\mu$  and the other, denoted by  $\lambda$  max<sub>2</sub>, obtained near about 230 m $\mu$  region. Biguanide and substituted biguanides show only one peak near  $\lambda$  max<sub>2</sub> (at about 230 m $\mu$ ). It was concluded that the absorption peak ( $\lambda$  max<sub>1</sub>) which is completely different from that of the ligand and of the hydrated metal ion, may be due to some new chromophore containing the biguanide and the metal atom. The other peak  $\lambda$  max<sub>2</sub> is most probably due to ligand biguanide. The new chromophore giving rise to  $\lambda$  max<sub>1</sub> was suggested to be due to a heterocyclic ring containing carbon, nitrogen and the metal atom having a conjugated system. Thus the



metal biguanide may be considered as a pseudo-aromatic ring. This aromaticity as denoted by the value of  $\epsilon$  ( molar absorptivity), varies from metal to metal. In the case of the substituted biguanide metal complexes, both the peaks are shifted somewhat towards longer wave lengths. The shift of  $\lambda_{\max_2}$ , which is assumed to be due to biguanide molecule of metal chelates is very small and is comparable to shifts due to substitution. The shift of  $\lambda_{\max_1}$  is comparatively large and compares well with the shift on alkyl substitution in amino groups attached to aromatic rings viz. aniline, aminopyrimidine etc. From these indications it is reasonable to assume the presence of aromatic ring currents in the metal biguanide chelates.

That the metal complexes of guanylurea-O-alkyl ethers are more stable than those of the simple metal guanylureas can be explained on the basis of the existence of aromatic ring currents in metal guanyl-ureas. In simple metal guanylureas, the hydrogen of the hydroxyl group is strongly held due to hydrogen bond between two strong electronegative atoms, i.e. oxygen and nitrogen. The oxygen atom involved in hydrogen bonding attracts the electrons from the ring, thus decreasing the extent of delocalization, thus lowering the stability of the metal chelates. In the case of guanylurea-O-alkyl ether metal complexes, the hydrogen bonding is totally absent. On the other hand the electronegativity of the oxygen atom is reduced due to electron releasing capacity

of the alkyl groups, which in turn reduces its electron withdrawing tendency from the ring. This helps considerably in electron delocalization in the metal chelate ring resulting in the increasing stability of the metal guanylurea-O-alkyl ethers.

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