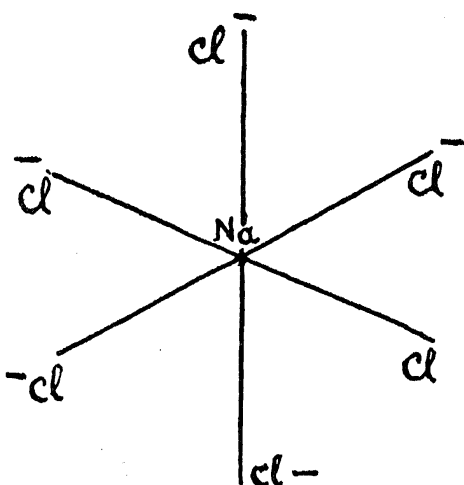


Pauling without reference to his electro-negativity theory. If we consider a six bonded unit NaCl_6 or ClNa_6



and that only one bond of the six, is covalent and the remaining *fully* ionic, the dipole moment due to four mutually perpendicular ionic bonds will cancel as they oppose in pairs

the remaining $\overset{-}{\text{Cl}}\overset{+}{\text{Na}}:\overset{-}{\text{Cl}}$ will give 0.5 ionic character for a total of six NaCl bonds. If we assume that the influence of surrounding bonds is given by Madelung constant A just as in the case of bond energy, the effective ionic character for six NaCl bonds will be $6 \times A$ times the apparent ionic character of each bond. The results in the last column for a range of the alkali halides are in agreement with the theoretical value 0.5.

The above concept that only one bond out of six is covalent in character gives $5/6$ or 83% as the value of the ionic character of alkali halides which is supported by the data on crystal energy, magneto optic anomaly, &c., as will be shown in a separate note.

Indian Inst. of Sci., S. K. K. JATKAR.
Bangalore 3, (Miss) S. B. KULKARNI.
February, 17, 1949.

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ON THE PREPARATION OF PALUDRINE (PROGUANIL)

FOLLOWING the discovery of Paludrine,¹ sufficient interest has been developed in the field of substituted biguanides as potential antimalarials. For the chemical synthesis of substituted biguanide derivatives, a number of methods¹⁻⁶ are available,

the simplest being the condensation of a substituted cyanoguanidine with an amine. For the synthesis of N^1 -aryl- N^5 -alkylbiguanides the reaction between arylcyanoguanidine and alkylamine has been successfully conducted in the presence of copper sulphate or by fusion (using salt of the amine) but the desired products are not formed when the reactants are refluxed with alcohol.

During the course of investigations of N^1 -aryl- N^5 -heterocyclic biguanides,⁴ we were unable to condense certain substituted amino-heterocyclics (using hydrochloride salts) with arylcyanoguanidines in boiling alcohol. Considering that this reaction temperature may not be sufficient for reaction, iso-amyl alcohol was used instead in order to give reaction temperature of about 140°C . Although, no success was encountered in the above cases, the same procedure has been successfully employed for the preparation of paludrine as follows:

p-Chlorophenylcyanoguanidine (5 g.) and isopropylamine hydrochloride (3 g.) were refluxed together in isoamyl alcohol (15 c.c.) in an oil-bath maintained at 150°C . for 14 hours. The reaction mixture was extracted with boiling water and the aqueous portion was concentrated and chilled. Paludrine hydrochloride was collected by filtration and dried. Yield 1.5 g.; m.p. 244° .

Curd, *et al.*² have also recently prepared N^1 -*p*-fluorophenyl- N^5 -isopropylbiguanide hydrochloride by a similar procedure, using nitrobenzene as solvent. In my experiment, replacement of iso-amyl-alcohol by nitrobenzene gave paludrine hydrochloride (3 g.), m.p. 244° .

Attempts are being made to improve the yield still further by varying the solvent and the experimental conditions.

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Organic Chem. Lab., H. L. BAMJ,
Indian Institute of Science,
Bangalore,
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