and each individual is classified according to the single attribute 'cold', and another world, in which people go without XYZ and again are classified by 'cold'. In case (2) we wish to decide which of these two possible worlds should be made the real one.

Now suppose all our experimental subjects catch colds. In case (1) we might say we learn nothing. But in case (2) we do learn—in fact it would seem not worth while to give people XYZ, since they seem to catch colds anyway. Of course, the evidence may not be conclusive; but such as it is, it is surely relevant.

Other points will, I hope, become clear in a forthcoming paper.

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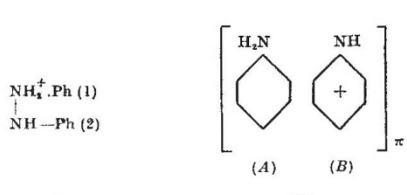
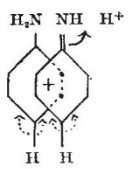
Mechanism of the Benzidine and Related Rearrangements

Two electronic theories have been proposed for the benzidine rearrangement[1,2], but both are open to criticism. The present theory is an elaboration of the Robinson[2] mechanism in terms of the quantum theory[3] of aromatic structure.

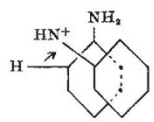
It is suggested that, in the initial hydrazobenzene salt (I), a non-localized π-electron migrates from ring 2 to ring 1 with consequent fission of the N–N bond to produce the complex molecule (II), composed of the aniline derivative A and the ion-radical B. Since the electron levels of the latter are incompletely filled, and since the π-orbitals of the rings will overlap, exchange forces should hold A and B together. The product will be called a π-complex. The 'π–π' bond in it will be of novel type, joining aromatic systems and not a pair of atoms, but it will be otherwise analogous to the bond in the helium molecule ion He_2^+. Rotation about the bond will be possible, but three positions of stability with intermediate energy-hills will be defined by the alternating polarities round the rings; in them the nitrogens will be opposite each other or 120° apart. The rings in the π-complex will be parallel and co-axial.



(I) (II)



(X)



(Y)

If the p-substituents in the π-complex can be eliminated as positive ions, process X will be possible (dotted arrows indicate displacements of single electrons), leading to a benzidine. If reaction is delayed, rotation to a 120° position will allow the formation of a diphenyline by a type X process. Thirdly, process Y, involving a 60° or 180° orientation of the π-complex, will lead to a semidine; this involves a configuration corresponding to an energy-hill and should be less facile than X. If we assume that process X is in fact easier than Y only if it involves a p-position of component A, all the data[4] on the benzidine rearrangement can be interpreted in detail.

The products formed will depend not on the 'migratory aptitudes' of the groups but on the point of attack of the proton catalyst; thus in Y the more basic ring will function as component A and carry the free amino-group in the product. A diphenyline can form only if the more basic ring has a free *para* position. These conclusions are confirmed in detail by the existing evidence. Moreover, in naphthalene derivatives, where rotation of the π-complex should be inhibited since the rings are not symmetrical, diphenylines and p-semidines are in fact never formed.

Similar π-complex intermediates can be written for other analogous rearrangements (for example, N-bromacetanilide, *para* Claisen, Hofmann, etc.).

The theory will be investigated and full details published elsewhere in due course.

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Properties of Optically Isomeric Mepacrines

IN a recent communication, Hammick and Chambers[1] report that whereas the racemic form of the well-known antimalarial drug mepacrine is given to human patients, only the lævo isomer of this drug is excreted in their urine. It seems appropriate to record here that the problem of biological relations of optically isomeric mepacrines has been dealt with in a number of Russian publications during the last few years. After the resolution of racemic mepacrine into its isomers by Chelintsev and Osetrova[2] in 1940, Gause and Alpatov[3] noticed that both isomers of this drug are equally effective against malaria, whereas the dextro isomer is about twice less toxic than the lævo form for mammals and birds. Further, Gause[4] recorded that the dextro isomer differs from the lævo form in the mechanism of its permeability into the living cell. Finally, extensive clinical studies made under the supervision of Prof. Tareev in the clinical department of this Institute confirmed the observations of Gause and Alpatov and showed that the pure dextro form of mepacrine is less toxic for human patients than the usual racemic form, but the strength of antimalarial action in both forms is the same. It is hence clear that the dextro isomer of mepacrine is very interesting from the therapeutic point of view.

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