methane dye) has been related in a foregoing note.[1] The lability of these derivatives, however, makes it difficult to draw definitive conclusions concerning the relation between chemical structure and bacteriostatic activity.

We have now repeated these experiments with the diphenylmethane homologs of the above-mentioned derivatives. Although tetramethyl-diamino-diphenyl-methane dyes have a much weaker bacteriostatic activity than their triphenyl-methane homologs,[2] they offer, nevertheless, the advantage of forming more and stabler leucoderivatives, thus enabling the realization of more complete and more reliable comparative assays.

We have now found that the quinoid dye salts of tetramethyl-diamino-diphenylmethane (*i.e.,* dye salt of Michler's hydrol) and of tetramethyl-diamino-diphenyl (amino) methane (*i.e.,* auramine dye) are bacteriostatically active against *Staphylococcus aureus*, both of them practically at the same concentration (1:40,000).

The leucobases of both compounds, without quinoid structure, were inactive (to 1:5,000).

The methane-sulphonic derivative of Michler's hydrol, also a substance without quinoid structure, was equally inactive. This fact contrasts with our earlier observation according to which the triphenyl-methane homolog of the mentioned substance, *i.e.,* the bisulphite derivative of malachite green, showed a strong bacteriostatic activity in spite of its non-quinoid structure.[1] This bisulphite derivative is, however, an unstable substance ("vat dye"[3]), which transforms easily into the quinoid-structured dye salt, whereas its inactive diphenylmethane homolog has a stable non-quinoid character.[4]

Michler's ketone or tetramethyl-diamino-benzophenone, a non-quinoid substance, was inactive, and so was a series of other leucoderivatives of auramine and of Michler's hydrol (aminoethane nitril, aminoethanoilamide, hydroxyethanoilamide, aminoethanoic acid and hydroxyethanoic acid.[5]

Summary: Among various derivatives of tetramethyl-diamino-diphenylmethane only the quinoid-structured dye salts had bacteriostatic activity in our experiments, while the leucoderivatives were inactive.

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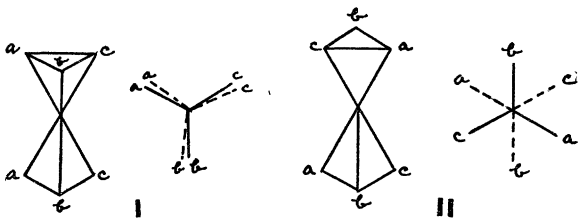
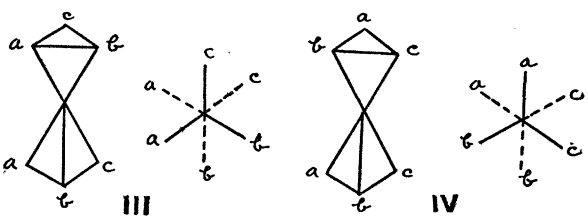
THE LACK OF MEANING OF THE PHRASE "INACTIVE BY INTERNAL COMPENSATION" AS APPLIED TO MESO COMPOUNDS

THE usual explanation of the inactivity of meso compounds given in both elementary and advanced texts is that the molecule consists of two asymmetric halves which are mirror images and hence rotate the plane of polarization equal amounts in opposite directions. The resulting compound is said to be "optically inactive by internal compensation." It frequently is recognized that the individual molecules would be inactive only when the groups occupy certain specified positions. For example, in the simplest case, the molecule Cabc Cabc is inactive only when the groups are in the positions corresponding to Figs. I and II and the molecules have, respectively, a



plane and a center of symmetry. In each case the mirror images are superimposable. In all other positions, however, for example, those illustrated by Figs. III and IV, there is no plane or center of sym-



metry, and the mirror image of the molecule is not superimposable. The explanation given for the non-existence of forms corresponding to III and IV is the same as that given for the non-existence of isomers of ethane and of 1,2-dichloroethane, namely, the assumption of "free rotation" about the single carbon-carbon bond. It is known, however, that in compounds such as 1,2-dichloroethane[1] and 1,2-dibromoethane,[2] rotation is not free, and that the mean

[1] Debye, *Physik. Z.*, 31: 142, 1930; Beach and Palmer, *Jour. Chem. Phys.*, 6: 639, 1938.
[2] Smyth and Kamerling, *Jour. Am. Chem. Soc.*, 53: 2988, 1931; Beach and Turkevitch, *ibid.*, 61: 303, 1939.

position of the atoms attached to the carbon atom is one in which they are staggered with respect to each other.

If II is the favored configuration, the molecule is inactive because it possesses a center of symmetry. Molecules corresponding to III and IV are active, and if IV is inverted, it becomes the mirror image of III; that is, they are enantiomorphs. Accordingly if III and IV should happen to be the most stable configurations, equal amounts of each would lead to a racemic mixture. One would not expect to be able to resolve it into the active components, however, because the barrier preventing free rotation usually would be low, and a molecule having configuration III and passing through configuration I would have an equal chance of returning to its original configuration or to that of its enantiomorph.

From chemical evidence in solution, it appears, in the case of meso 1,2-diaminosuccinic acid,[3] and meso dihydrobenzoin,[4] that the configuration corresponds to that of Fig. II, that is, the staggered position in which like groups are at the greatest possible distance from each other. On the other hand, the dipole moments of meso and racemic stilbene dichloride are 1.27 and 2.75, respectively, and those of meso and racemic dihydrobenzoin are 2.0 and 2.6. If free rotation existed, both meso and racemic forms should have identical moments. Moreover, if the meso stilbene dichloride molecule had a completely trans configuration analogous to Fig. II, the calculated moment is 0.52, while for free rotation it is 2.31.[5] Hence not only is rotation restricted somewhat but a considerable proportion of the molecules must have the unsymmetrical configurations of III and IV.

In the solid state the results of an x-ray investigation of meso erythritol are interpreted as indicating that this molecule has a center of symmetry.[6] However, in the case of anhydrous meso tartaric acid and of the dihydrate of its potassium salt, double molecules are present and the individual molecules are considered to be unsymmetrical.[7]

Therefore it may be concluded that the fact that the molecule has two similar asymmetric carbon atoms of opposite configuration has nothing whatever to do with the inactivity of meso compounds; that is, they are not inactive because of "internal compensation." They are inactive either because the molecules have a center of symmetry as in Fig. II, or because the enantiomorphs corresponding to Figs. III and IV are readily interconvertible, that is, readily racemized.

In the light of the above considerations, it immediately becomes obvious that if the groups on the ethane carbon atoms were large enough, rotation should be restricted sufficiently to permit the isolation of stable forms having configurations III and IV as well as configuration II. An examination of Stuart-type models indicates that such might be the case for α,β-dibromo-α,β-diiodosuccinic acid. Hence when the ethane carbon atoms of this compound have opposite configurations, it should exist in one resolvable racemic form and one meso form having a center of symmetry. In addition there should be three racemic modifications, instead of the usual one, when the ethane carbon atoms have like configurations. Moreover, tetraiodosuccinic acid should exist in a racemic as well as a meso modification. The possibility that these compounds would be chemically stable, however, is remote. Space relationships appear to prevent α,β-di-*ter*-butylsuccinic acid from existing in any configuration except that having a center of symmetry. There is a possibility that the chemical stability of α,α-dibromo-β,β-diiodosuccinic acid may be greater than that of α,β-dibromo-α,β-diiodosuccinic acid, and while the restriction of rotation appears to be less in the first compound, it may be sufficient to permit resolution.

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[6] Burgers, *Phil. Mag.*, [7] 1: 289, 1926.
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SCIENTIFIC APPARATUS AND LABORATORY METHODS

A GLUTAMINE-RICH PEPTONE FOR CULTIVATION OF HEMOLYTIC STREPTOCOCCI

GLUTAMINE has been shown by McIlwain *et al.*[1] and by Bernheimer and Pappenheimer[2] to be a growth factor for various strains of hemolytic streptococci. Lankford and Snell[3] have found glutamine to be of importance also for the cultivation of fastidious strains of gonococci.

Since glutamine is costly and its preparation rather cumbersome, a convenient substitute for this material is desirable. Such a substitute has been found in a peptone prepared by tryptic digestion of gliadin, a protein rich in glutamine. The process is as follows: 2 g of pancreatin (Parke, Davis and Co.) is suspended in 30 cc of water, kept at 37° for 1½ hours,

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[3] Ch. E. Lankford and E. E. Snell, *Jour. Bact.*, 45: 410, 1943.