627. *Polarisation in Conjugated Systems.   Part VI.   Interaction Moments and Related Topics.*

By K. B. EVERARD and L. E. SUTTON.

The interaction moments of a given pair of groups are smaller in stilbene and diphenyl than in benzene derivatives; possible reasons are given.

From the dipole moment of *cis*-4-bromo-4'-nitrostilbene, in which there is shown to be considerable steric inhibition of conjugation, it is calculated that the $C\overset{\frown}{=}C\text{-}C$ valency angle at the ethylene bridge in the molecule is 131°.

The discrepancy between the observed and calculated moments of 2-chloro-4'-dimethylaminostilbene suggests that the central $C=C$ bond may be unusually polar, which can be correlated with the pronounced nucleotoxic properties of the compound.

THE term " interaction moment " has been used by Marsden and Sutton (*J.*, 1936, 599) to mean the difference between the observed moment of a *para*-disubstituted benzene derivative and the algebraic sum of the moments of the two corresponding monosubstituted compounds.

In the case of angular substituents like NH_2, however, a vector treatment has to be employed, and it is assumed that the interaction moment acts along the 1 : 4 diagonal of the ring.

These authors and Leonard and Sutton (*J. Amer. Chem. Soc.*, 1948, **70**, 1564) have published tables of interaction moments in benzene derivatives, but few other systems have been studied. For certain compounds, no reliable moment value exists; therefore those interaction moments which have been based on unreliable values need correction.

Although relatively few of the compounds examined in the present work (Part I) are relevant to this topic, they suffice to demonstrate one important point. The available values are collected in Table II, and are based on the dipole moments listed in Table I.

TABLE I.

Dipole moments of p-disubstituted compounds.

	NMe$_2$. Cl.	NH$_2$. Br.	NO$_2$. Br.	NO$_2$. NMe$_2$.	NO$_2$. NH$_2$.
Benzene	3·32 [a]	2·87 [b]	2·68 [c]	6·87 [a]	6·35 [b]
Diphenyl	—	3·30 [b]	—	—	6·49 [b]
Stilbene	4·02 [d]	3·56 [d]	3·11 [d]	7·42 [d]	—

TABLE II.[e]

Interaction moments in p-disubstituted compounds.

Benzene	0·22	0·05	0·24	1·41	1·22
Diphenyl	—	0·01	—	—	0·54
Stilbene	0·01 [f]	—0·02	0·22	0·54	—

[a] Marsden and Sutton (*loc. cit.*), recalculated. [b] Le Fèvre and Le Fèvre (*J.*, 1936, 1130), recalculated. [c] Saxby, private communication. [d] Part I. [e] See Table I for headings. [f] Mesomeric moment of 4-chlorostilbene estimated to be 0·34 (by extrapolation of Fig. 1, Part IV).

It is clear that interaction moments in diphenyl and stilbene derivatives are usually much less than those in benzene derivatives. Kumler and Halverstadt remarked on the same thing when they measured the dipole moments of sulphanilamide and 4-*p*-aminophenylbenzene-sulphonamide (*J. Amer. Chem. Soc.*, 1941, **63**, 2182). Calculation shows that mutual electrostatic induction of moments in each substituent must be small ($\rightarrow \sim 0·1$) and sometimes opposed;

so evidently structures such as (I.) contribute less to the resonance hybrids of stilbene (and similarly for diphenyl) derivatives than those such as (II.) to the hybrids of benzene derivatives. The phenomenon is the more marked, because structure (I) has about twice the moment of (II). In the case of stilbene, this seems to be another example of the " insulating " effect of the bond between the β-carbon atom and the second benzene ring, which shows up in the electron-distribution diagram given in Part IV (Fig. 2). In the case of diphenyl, it might be a result of the partial suppression of conjugation across the central C–C bond by twisting of the phenyl groups with respect to one another; Bastiansen claims to have shown that the ring planes in certain diphenyl derivatives are inclined at an angle of *ca.* 50° (*Acta Chem. Scand.*, 1949, **3**, 408).

4-Bromo-4'-nitrostilbene.—The interaction moment in *trans*-4-bromo-4'-nitrostilbene is not very large (0·22); but it is curious. The reason for its equality to that in the benzene compound is not clear.

In the *cis*-isomer, the optical evidence reported in Part I shows that conjugation is suppressed; the molar exaltations of the two isomers are 7·4 and 1·8 c.c., respectively, each value having been based on the refraction of the appropriate stilbene isomer. This can be ascribed to steric hindrance (for a photograph of a model, see Wooster, McGowan, and Moore, *J. Sci. Instr.*, 1949, **26**, 140).

Presumably, therefore, any calculation of the moment of the *cis*-isomer should be made with values appropriate for *cis*-bromo- and -nitro-stilbene. If conjugation were inhibited completely, and if there were no interaction, the dipole moments of bromo- and nitro-benzene might be regarded as reasonable estimates. When these are taken, in order to obtain the observed dipole moment of 4·52 for *cis*-4-bromo-4'-nitrostilbene, a value of 82° has to be assumed for the angle between the 1 : 4 and 1' : 4' diagonals. This corresponds to a C–Ĉ=C

valency angle at the ethylene bridge of 131°. Had the normal trigonal angle of 120° been taken, the calculated moment would have been 0·5 too large. Any increase in the individual Br or NO_2 group moments over the values chosen above (*i.e.*, use of values nearer to those of the *trans*-compounds) would give an even larger angle.

This estimate of 131° may be compared with the 128—133° found by X-ray diffraction investigation of the structure of *trans*-stilbene (Robertson and Woodward, *Proc. Roy. Soc.*, 1937, *A*, **162**, 568); *cis*-stilbene itself appears not to have been examined. The prising open of the valencies may be ascribed to steric causes.

2-Chloro-4'-dimethylaminostilbene.—This compound was examined partly to test the assumptions which have to be made in calculating vectorially its moment (hereafter denoted as μ_1) from those of 4-dimethylaminostilbene (μ_2) and 2-chlorostilbene (μ_3). They are : (i) that the rotational orientation of the NMe_2 group is unaffected by the presence of the chlorine atom, (ii) that the direction of μ_2 is correctly determined by the procedure outlined in Part IV, (iii) that μ_3 (which has not been measured) may be correctly estimated from the table in Part III (p. 2817) to lie between 1·45 and 1·60, and (iv) that μ_3 acts along the C—Cl bond.

The result of the calculation is 2·16—2·18, which disagrees with the observed value of 2·65. It is unlikely that the discrepancy arises from an interaction moment, because the insulating effect evident in 4-chloro-4'-dimethylaminostilbene (see Table II) probably extends to its 2-chloro-isomer. Neither could it arise from steric interference by the chlorine atom, which is in any case shown to be absent by the optical evidence (Part II). Since it is also very unlikely that assumptions (i) and (iii) are seriously invalid, we shall confine our attention to (ii) and (iv) which, furthermore, are of particular relevance and importance to the discussion in earlier Parts of this series.

There are two possible ways in which (ii) could be wrong. (*a*) The rotating part of μ_2 (*i.e.*, the component of the NMe_2 group moment at right angles to the C—NMe_2 bond) may not have the value of 0·79 deduced by the method described in Part IV. However, variation of this between 0 and 1 only alters the calculated value of μ_1 by 0·07. (*b*) The non-rotating part of μ_2

NMe_2

(III.)

Cl

may not act along the direction of the C—NMe_2 bond, as has been assumed hitherto. However, it could not possibly be displaced from this direction by more than 9°, corresponding to a π-electron migration along the line joining the nitrogen to the β-carbon atom, and very probably the actual displacement is less than half this (deduced from Fig. 2, Part IV). Displacement through 9° would increase μ_1 only to 2·36 in the configuration shown in (III), corresponding to maximum conjugation energy and minimum steric interference. The increase would be less in other configurations. Clearly, therefore, invalidity of (ii) could not itself account for the difference from μ_1 (observed), though it would help.

The other possibility is that the direction of μ_3 is not along the C—Cl bond. A displacement of *ca.* 20° would be necessary to raise the calculated moment of configuration (III) to 2·65. Classical polarisation could not account for this; but non-classical inductive polarisation of the ethylene bridge by the chlorine atom (as shown in III) could do so. It would enhance the polarisation of the bridge caused by the dimethylamino-group.

Summarising Remarks.—Butler has recently suggested that nucleotoxic properties may arise from the presence of a highly polar C≡C bond in a molecule (*Nature*, 1950, **166**, 18) ; and, while due caution must be observed in any attempts to correlate pharmacological action with structure, it may be remarked that our experimental results support the theoretical conclusions of A. Pullman and of Coulson and Jacobs (see Part IV) that such a bond exists in the nucleo-toxic 4-dimethylaminostilbene and its derivatives. For lack of suitable material, we have not been able to show that this polarity vanishes when the ethylene bridge is twisted out of the plane of the substituted benzene ring ; but we have been able to confirm that conjugation with the second ring is inhibited to a greater or less degree by bulky 2'- or 6'-substituents.

Chlorine in the 2'-position appears to augment the polarity of the bridge bond, as we have seen ; and it is noteworthy that the compound is the sixth most potent growth-inhibitor in the large number (*ca.* 120) of compounds examined by Haddow, Harris, Kon, and Roe (*Phil. Trans.*, 1948, *A*, **241**, 147).