50. *The Infra-red Spectra of Carcinogens. Part I. Derivatives of Stilbene.*

By H. W. THOMPSON, EVA E. VAGO, M. C. CORFIELD, and S. F. D. ORR.

A survey has been made of the vibrational spectra of some carcinogens. This paper describes results for derivatives of stilbene. The spectra provide data which may be useful for analytical work, and correlations have been drawn up between important spectral features and the individual molecular structures. By use of such correlations it may be possible to identify the type of substitution in aromatic rings existing in such compounds.

THE main purposes of this investigation were (*a*) to begin a comprehensive survey of the infra-red absorption spectra of complex molecules which are important in the field of cancer research, and (*b*) to correlate spectral features with molecular structure in related series of molecules in which structural alterations are known to affect carcinogenic activity (Haddow, *Brit. Med. Bull.*, 1947, **4**, 331; Haddow, Harris, Kon, and Roe, *Phil. Trans.*, 1948, **241**, 147). We were stimulated to carry out this programme by discussions with the staff of the Chester Beatty Research Institute, from whom we have obtained most of the compounds examined. The compilation of the spectra of these compounds may well form a valuable basis for analytical work, such as has been developed for urinary keto-steroids by Dobriner, Liebermann, Rhoads, Williams, and Barnes (*J. Biol. Chem.*, 1948, **172**, 247). As regards structural diagnosis, much is now known about the correlation of certain absorption bands with particular atomic groupings (Thompson, *J.*, 1948, 328; Williams, *Rev. Sci. Instr.*, 1948, **19**, 135), and as more reference data have accumulated it has been found that the characteristic vibration frequencies of some groups may be affected by special electronic influences introduced by neighbouring substituents or structural factors. This has been illustrated clearly by the work on the steroids already mentioned (Jones, Williams, Whalen, and Dobriner, *J. Amer. Chem. Soc.*, 1948, **70**, 2024). The present paper summarises results for some derivatives of stilbene.

Experimental Method.

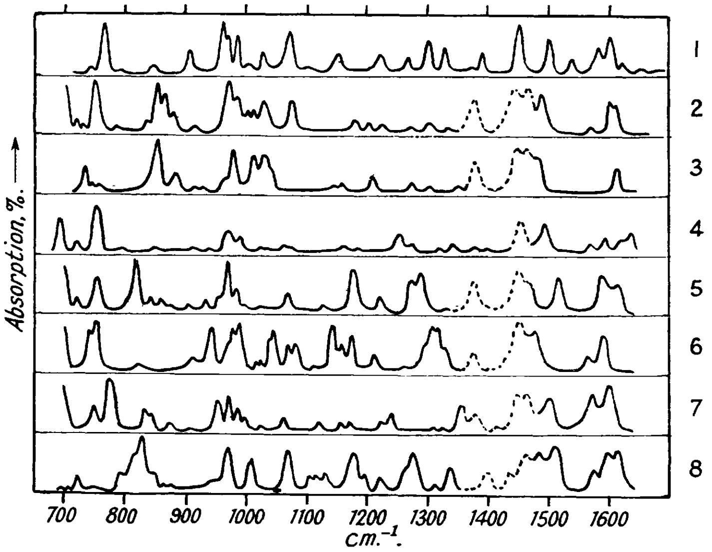
The spectra were measured between 5 and 15 μ. using the powdered solids ground to a paste with paraffin and pressed between rock-salt plates. Between 7 and 15 μ. a single-beam recording spectrometer was used with a rock-salt prism, and between 5 and 8 μ., where the absorption of atmospheric water vapour is strong, a double-beam recorder with a calcium fluoride prism was used. A few of the spectra were measured on a Perkin Elmer 12 C instrument with a rock-salt prism. The effective slit widths were about 5 cm.$^{-1}$ over the whole range. Unfortunately in the region 6·5—7·5 μ. there are paraffin absorption bands, and also, when the paste is used, scattering errors lead to inexact balancing of the double-beam recorder. For this reason some of the curves recorded over this range are uncertain, but no bands of major interest are to be expected here.

Results and Discussion.

The spectra are shown in Figs. 1—4. An experimental result of general interest was that with some of these compounds the Christiansen effect was observed as described recently for other slurries by Price and Tetlow (*J. Chem. Phys.*, 1948, **16**, 1157). This was clearly detectable by the very rapid changes of transmission coefficient near certain absorption bands. It may be significant that, in most cases of 4-dimethylaminostilbenes where it occurred, the phenomenon was particularly marked at about 1190 cm.$^{-1}$ (8·4 μ.), but several absorption bands in the same spectrum were usually affected.

FIG. 1.

Stilbene and derivatives.

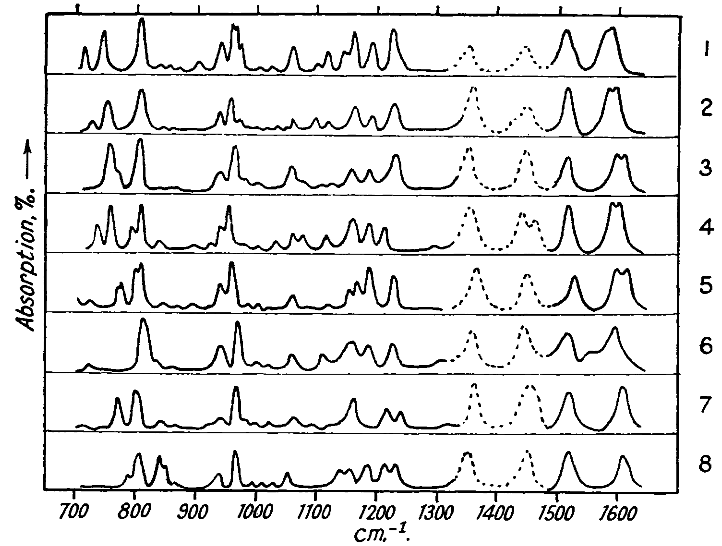


(1) *Stilbene.* (2) 2 : 4 : 6-*Trimethylstilbene.* (3) 2 : 4 : 6 : 2′ : 4′ : 6′-*Hexamethylstilbene.* (4) 2-*Aminostilbene.* (5) 4-*Aminostilbene.* (6) 2-*Dimethylaminostilbene.* (7) 3-*Dimethylaminostilbene.* (8) 4′-*Bromo*-4-*dimethylaminostilbene.*

The spectra shown in the figures reveal differences between the isomeric compounds and between related homologues which may be useful for analytical work.

FIG. 2.

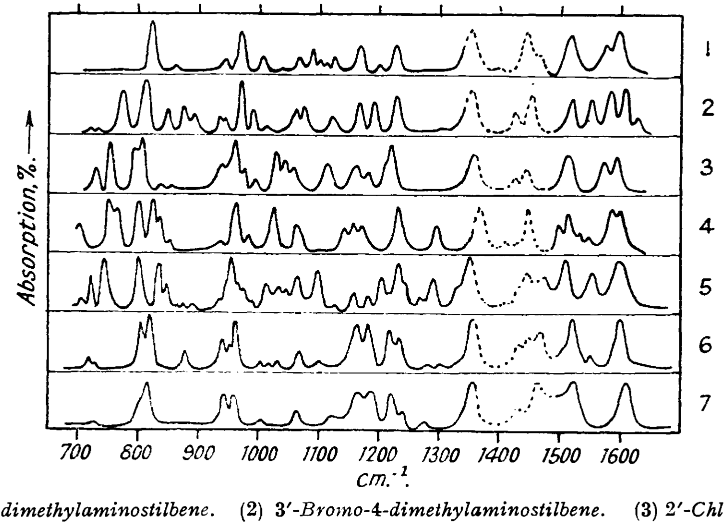
Stilbene derivatives.



(1) 4-*Dimethylaminostilbene.* (2) 4-*Dimethylamino*-2′-*methylstilbene.* (3) 4-*Dimethylamino*-2′-*ethylstilbene.* (4) 4-*Dimethylamino*-2′-iso*propylstilbene.* (5) 4-*Dimethylamino*-3′-*methylstilbene.* (6) 4-*Dimethylamino*-4′-*methylstilbene.* (7) 4-*Dimethylamino*-2′ : 6′-*dimethylstilbene.* (8) 4-*Dimethylamino*-2′ : 4′ : 6′-*trimethylstilbene.*

FIG. 3.

Stilbene derivatives.

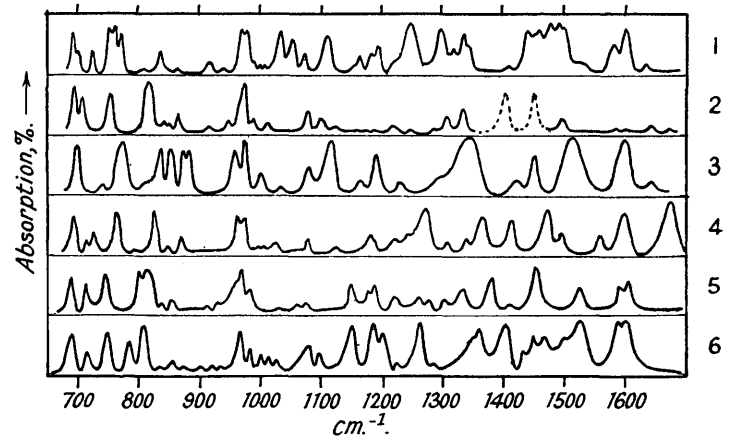


(1) 4′-*Chloro*-4-*dimethylaminostilbene.* (2) 3′-*Bromo*-4-*dimethylaminostilbene.* (3) 2′-*Chloro*-4-*dimethylaminostilbene.* (4) 2-*Chloro*-4-*dimethylaminostilbene.* (5) 4-*Dimethylamino*-2 : 2′-*dimethylstilbene.* (6) 4-*Dimethylamino*-2′ : 4′-*dimethylstilbene.* (7) 4 : 4′-*Bisdimethylaminostilbene.*

Characteristic spectral features are to be expected of (*a*) the substituted aromatic nuclei, and (*b*) the $-CH{=}CH-$ group. Of the former, perhaps the most striking is that which originates in the deformation of residual C–H bonds out of the plane of the substituted aromatic ring to which they are attached (Whiffen and Thompson, *J.*, 1945, 268; Thompson and Torkington, *Trans. Faraday Soc.*, 1945, **41**, 246; Bell, Thompson, and Vago, *Proc. Roy. Soc.*, 1948, *A*, **192**,

FIG. 4.

Stilbene derivatives.



(1) 2-*Methoxystilbene.* (2) 4-*Bromostilbene.* (3) 4-*Nitrostilbene.* (4) 4-*Acetylstilbene.* (5) 4-*Ethylaminostilbene.* (6) 4-*Diethylaminostilbene.*

TABLE I.

Characteristic vibration frequencies of different types of substituted stilbene derivatives.

Type of substitution,

		di.			tri.		tetra.
Stilbene derivative.	Mono.	*o.*	*m.*	*p.*	1 : 2 : 3.	1 : 2 : 4.	1 : 2 : 3 : 5.
2 : 4 : 6-Trimethyl	750	—	—	—	—	—	852
2 : 4 : 6 : 2′ : 4′ : 6′-Hexamethyl	—	—	—	—	—	—	851
2-Amino	752	752	—	—	—	—	—
4-Amino	750	—	—	818	—	—	—
2-Dimethylamino	740	752	—	—	—	—	—
3-Dimethylamino	750	—	775	—	—	—	—
4-Dimethylamino	747	—	—	810	—	—	—
4-Dimethylamino-2′-methyl	—	752	—	809	—	—	—
4-Dimethylamino-2′-ethyl	—	757	—	809	—	—	—
4-Dimethylamino-2′-*iso*propyl	—	757	—	809	—	—	—
4-Dimethylamino-3′-methyl	—	—	778	810	—	—	—
4-Dimethylamino-4′-methyl	—	—	—	816	—	—	—
4-Dimethylamino-2′ : 6′-dimethyl	—	—	—	805	772	—	—
4-Dimethylamino-2′ : 4′ : 6′-trimethyl	—	—	—	807	—	—	845
4′-Chloro-4-dimethylamino	—	—	—	822	—	—	—
3′-Bromo-4-dimethylamino	—	—	772	812	—	—	—
2′-Chloro-4-dimethylamino	—	755	—	809	—	—	—
2-Chloro-4-dimethylamino	755	—	—	—	—	802	—
4-Dimethylamino-2 : 2′-dimethyl	—	746	—	—	—	803	—
4-Dimethylamino-2′ : 4′-dimethyl	—	—	—	821	—	807	—
4 : 4′-Bisdimethylamino	—	—	—	816	—	—	—
2-Methoxy	755	755	—	—	—	—	—
4-Bromo	750	—	—	814	—	—	—
4′-Bromo-4-amino	—	—	—	830	—	—	—
4-Nitro	766	—	—	835	—	—	—
4-Acetyl	762	—	—	824	—	—	—
4-Ethylamino	750	—	—	810	—	—	—
4-Diethylamino	750	—	—	812	—	—	—

498). Intense bands occur in the region 700—900 cm.$^{-1}$ according to the number and position of substituents in the aromatic nucleus. Two other vibrations of the aromatic nucleus near 1500 cm.$^{-1}$ and 1600 cm.$^{-1}$ frequently occur, but their intensities, both absolute and relative to each other, are variable. The C–H out-of-plane vibrations in the present series of compounds fall into line well with the earlier deductions. Table I summarises the data, from which it is seen that with few exceptions the different substitution types have vibration frequencies lying close to fixed values, *e.g.*, *ortho*-derivatives near 755 cm.$^{-1}$, *meta* near 775 cm.$^{-1}$, *para* from 805 to 820 cm.$^{-1}$, 1 : 2 : 4-trisubstituted derivatives near 805 cm.$^{-1}$, and 1 : 2 : 3 : 5-

tetrasubstituted derivatives near 850 cm.$^{-1}$. The conjugation of highly polar groups such as NO_2 or $CO{\cdot}CH_3$, causes some displacement of frequencies, but this occurs also in simpler compounds when such groups are attached to single benzene nuclei. It therefore seems possible to use such correlation rules for diagnostic purposes with the stilbene derivatives. A further refinement may be added. The results of Table I suggest that an ambiguity may arise between monosubstituted and *ortho*-disubstituted rings, both having the strong band near 750 cm.$^{-1}$. It was found, however, by Whiffen (Thesis, Oxford, 1946) that a large variety of monosubstituted benzene derivatives have a strong band at 690—700 cm.$^{-1}$, whilst the *ortho*-disubstituted derivatives have no such band. This band, occurs similarly with monosubstituted rings in the stilbenes, but not with *ortho*-disubstituted rings. A similar band occurs with *meta*-disubstituted rings near 700 cm.$^{-1}$, but any ambiguity between monosubstituted and *meta*-disubstituted rings will as a rule be removed by consideration of their bands near 750 and 775 cm.$^{-1}$, respectively.

The spectra of olefins containing the $-CH{=}CH-$ group show a strong band near 965 cm.$^{-1}$ which arises from a vibration involving deformation of the C–H bonds. This occurs with all the stilbenes measured, although it is slightly displaced in the different cases. Any alteration in the electronic structure of this group caused by substituents in the phenyl nuclei might be expected to modify the frequency; alternatively, large groups in the *ortho*-positions might so affect the structure as to influence its vibration. There is some indication that the presence of blocking-groups in the *ortho*-positions raises the frequency, but it cannot be regarded as definite.

One question upon which the present results give no guide is the coplanarity or otherwise of the two phenyl nuclei. The possible connexion between this and carcinogenic activity has been discussed by Haddow, Harris, Kon, and Roe (*loc. cit.*). It seems possible that, by use of the rules given above for the identification of particular nuclei substituted in different ways, the study of single crystals with polarised radiation and the reflecting microscope (Barer, Cole, and Thompson, *Nature*, 1949, **163**, 198) may throw further light on this.

Another general matter is being examined, namely, the effect of the state of aggregation on the spectra. There are signs of small shifts in the positions of some bands on changing from solids to solutions, and this may to some extent affect the application of structural diagnosis.

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THE PHYSICAL CHEMISTRY LABORATORY, OXFORD. [*Received, June 30th*, 1949.]