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SHORT COMMUNICATIONS

On the electron donating properties of the major tranquilizers

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DURING the last few years several studies have pointed to the formation of charge transfer complexes between organic substances acting as acceptors on the one hand and phenothiazine and some of its derivatives acting as donors on the other hand.[1–6] However no systematic study of the major tranquilizers has been made so far. The present study on the derivatives of phenothiazine, butyrophenone and 2-phenylpent-2-ene has been undertaken with aim to find out whether there is a correlation between the characteristics of the complexes (association constant, thermodynamic properties, etc.) and their biological activity. Some preliminary results obtained therein are presented.

The charge transfer spectra of the complexes have been recorded with a Cary 14 spectrophotometer, in the temperature range of 120°–300°K, using an optical cell of path length 0·2 mm. Chloranil was used as the acceptor at concentrations varying between 5×10^{-3} M and 10^{-2} M in a solvent consisting of a 1:1 mixture of ethanol and acetone.

The wavelengths corresponding to the peaks of the charge transfer band of the tranquilizers investigated so far are presented in Table 1 while the same for the antihistaminic drugs are given in Table 2. Figures 1 and 2 show the appearance of the charge transfer bands at various temperatures in the dixyrazine–chloranil and triperidol–chloranil mixtures.

TABLE 1. λ_{max} OF THE CHARGE TRANSFER BANDS APPEARING IN THE CHLORANIL–MAJOR TRANQUILIZERS MIXTURES

	λ_{max}(nm)
Derivatives of phenothiazine	
chlorpromazine	690 (a)
thioridazine	685
triflupromazine	700
alimenazine	690
propericiazine	600
levomepromazine	—
thioproperazine	not soluble (b)
fluphenazine	not soluble (b)
mepazine	660
aminopromazine	not soluble (b)
dixyrazine	675
acepromazine	—
perphenazine	670
prochlorperazine	not soluble
promazine	not soluble (b)
Derivatives of butyrophenone	
triperidol	685
haloperidol	705
benperidol	685
spiroperidol	675
aceperone	660
droperidol	680
clofluperidol	680
fluanisone	685
azaperone	690
moperone	680

TABLE 1.—*cont.*

	λ_{max} (nm)
Derivatives of 2-phenylpent-2-ene	
isospirilene	670
fluspirilene	not soluble (b)
spiramide	not soluble

(a) In agreement with the value of Beukers and Szent-Györgyi (680 nm).

(b) In a 1:1 mixture of acetone and dichlormethane as solvent:

thioproperazine	—
fluphenazine	—
aminopromazine	670
promazine	700
fluspirilene	670

TABLE 2. λ_{max} OF THE CHARGE TRANSFER BANDS APPEARING IN THE CHLORANIL–ANTIHISTAMINIC DRUGS MIXTURES

	λ_{max} (nm)
antergan	705
mepyramine	695
captodiamine	690
histaphene	665
antistine	675
thenylene	690
pheniramine	695
thiazinamium methyl sulfate	670
pyribenzamine	700
benadryl	690
promethazine	745

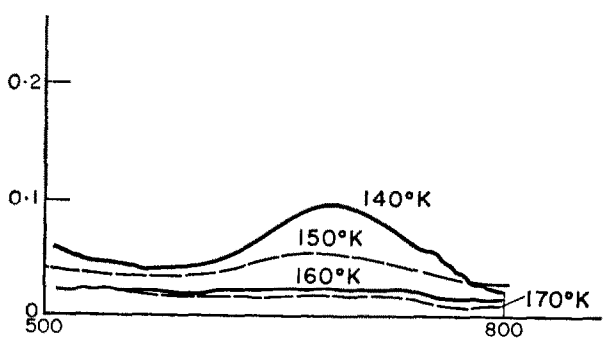

FIG. 1. Spectrum of the chloranil ($5 \cdot 10^{-3}$ M)–dixyrazine (10^{-1} M) mixture at various temperatures.

It appears that most of the tranquilizers which are sufficiently soluble form charge transfer complexes with chloranil. The general nature of the spectrum consists of a broad and asymmetrical band, which appears as the sample temperature is lowered and increases in intensity with decrease of temperature. The appearance and disappearance of the band as a result of the decrease and increase

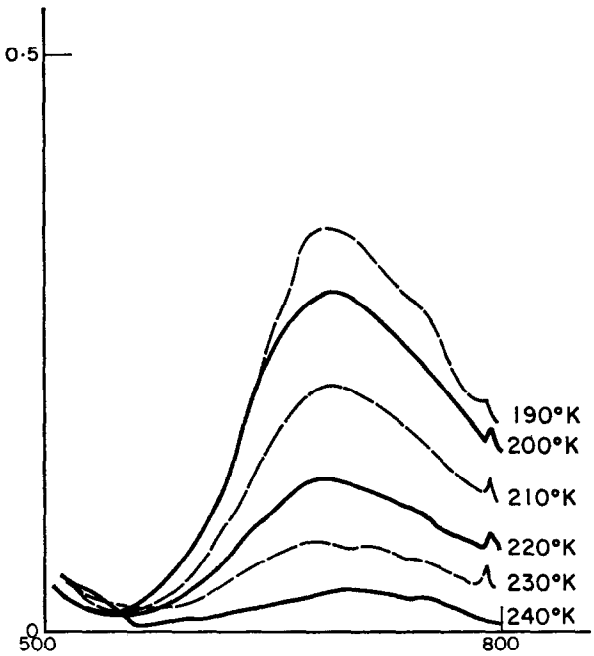

FIG. 2. Spectrum of the chloranil (10^{-2} M)–triperidol (10^{-1} M) mixture at various temperatures.

of temperature is completely reversible. Further at a particular temperature the intensity of the charge transfer band remains constant thus precluding the possibility of any chemical reaction. For both the tranquilizers and antihistaminic drugs the band appears only at temperatures lower than the room temperature. In certain cases (chlorpromazine among others)[2] they exist at room temperatures but can be seen only at higher concentrations of the solute or at larger path lengths of the cell.

The mechanism of action of tranquilizers has been reviewed recently.[7] In certain cases, the influence of the tranquilizers on the behavior of self stimulation has been expressed quantitatively. The results of the present experiment, namely the variation in the intensity of the charge transfer complexes of the eight compounds (viz. spiroperidol, isospirilene, benperidol, triperidol, haloperidol, chlorpromazine, dixyrazine, aceperone) indicate a similar behavior. The fact that these substances are very good electron donors could play a part in their mechanism of action. However it would be necessary to determine the thermodynamic constants of the complexes before a definite conclusion could be arrived at. The determination of these constants which would also confirm the theoretical predictions of Szent-Györgyi[1] are now in progress.

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