the antibody; 2. by a proper spatial distribution such that corresponding active points of antigen and antibody can come in apposition simultaneously; and 3. by the accessibility of the active points of the determinant groups to the antibody, owing to the absence of any large inactive group that would prevent or obstruct this approach. The introduction of polar groups into the less active parts of the determinant group affects the specificity of the immunological adsorption on account of 1. differences of electronic distribution; 2. differences in location of polar groups not fitting into receptors; and 3. production of spatial obstruction preventing combination with antibody (Marrack).

It is of significance and in support of the validity of the allergenic theory of cancerigenesis that similar chemical and stereo-chemical interrelations (composition, configuration, spatial arrangement, and size of side chains) seem to possess a decisive influence in determining the carcinogenic potency of the aromatic hydrocarbons (Bradley), as they are noted in connection with the chemo-immunity reactions of these and chemically related compounds. Investigations with various benzanthracene derivatives showed that compounds with substitutions in the 10., 9., 6., and 5. positions possess carcinogenic properties as long as the side chains are relatively short, while these specific qualities are greatly diminished or entirely absent in benzanthracene derivatives with substitutions in other positions (Cook and Kennaway). A similar reducing effect upon the carcinogenic potency of these compounds is elicited by too great an elaboration of an effective type of structure (Fieser, Fieser, Hershberg, Newman, Seligman and Shear; Kennaway; and Barry, Cook, Haslewood, Hewett, Hieger, and Kennaway).

In some of these hydrocarbons, such as methylcholanthrene, the molecule can be stripped of certain of its appendages without the loss of its carcinogenic potency. Similarly, one of the angular rings of 1.2.5.6-dibenzanthracene can be replaced by a cyclopenteno ring or by two methyl groups, respectively, with retention of the original potency (Fieser). The importance of stereochemical factors in determining the carcinogenic properties of these compounds is illustrated by the fact, that various heterocyclic isologues of the higher aromatic hydrocarbons (1.2.5.6-dibenzacridine and 3.4.5.6-dibenzacridine) are only feebly carcinogenic (Fieser), while the structural isomers of o-aminoazotoluol are not hepatocarcinogenic at all (Shear; and Kinosita). The influence of the character of the substituting groups upon the carcinogenic potency of these cyclic hydrocarbons is exemplified by the fact that the introduction of a hydroxy-group into the 3.4-benzpyrene molecule and into the methylcholanthrene molecule, respectively, destroys the carcinogenic quality of these compounds; but the substitution of a hydroxy-group for an amino-group in aminoazotoluol results in the loss of the carcinogenic organ specificity of this compound, which is shifted from the liver to the bladder (Nagao; and Kinosita).

The position of the substituting groups exerts an influence upon the relative