Certain members of the class of 5-phenyl-1,4-benzodiazepines possess a wide spectrum of psychotropic activity (anxiolytic, sedative/hypnotic, anticonvulsant, muscle relaxant). MNDO molecular orbital calculations have been made on twenty-five such compounds of known crystal structure and covering a wide range of biological activity as measured by their affinity for the specific benzodiazepine receptor in rat brain (Squires & Braestrup, Nature (1977) 266, 732). Electronic parameters including atomic $\pi$-electron charges, dipole moment components and molecular orbital energies derived from these calculations, together with geometrical parameters relating both to the overall conformation of the molecule and to bond length data derived from the X-ray analyses have been used in the structure-activity studies.

The results of statistical analysis of the data will be presented. Parameters which may be important in the correlation with affinity include HOMO energy (a measure of ionisation energy) LUMO energy (a measure of electron affinity), $E_{\text{HOMO}} + E_{\text{LUMO}}$ (a measure of molecular electronegativity) and dipole moment. Extension to multiple regression analysis has yielded some promising results based on 3-parameter equations.

The conformation of the acyclic fragment of the sugar moiety, have been found to contain not only all the atoms of the ribose moiety but also the aglycon fragment of DRB.

$$\text{E-PD}$$

$$\text{Z-PD}$$

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