- To modify specificity of action
- To improve duration of action
- To reduce toxicity
- To effect ease of application or administration or handling
- To improve stability
- To reduce cost of production

In order to obtain a therapeutically potent and better-tolerated drug there exists invariably an apparent conflict of pure scientific objectives and practical objectives. **This may be expatiated by citing the instance of an exceedingly toxic congener (say an anti-neoplastic agent) that possesses a very high degree of specificity and the researcher may have in mind to prepare still more toxic compounds so as to develop the highest possible specificity of action.** On the contrary, absolutely from the practical aspect, the proposed clue may not be pursued solely depending on the policy of the organization and not the individual or group of researchers.

In fact, there are a few generalized approaches utilizing the method of variation. In this particular context, the familiarity with the molecular structure is of the prime importance. The various possible approaches in designing newer drugs by applying variation of a prototype are quite numerous. Once the molecular structure of the compound in question is drawn on the drawing board, one takes into consideration such information as the following :

(a) study of the core nucleus of the hydro-carbon skeleton ;

(b) variation of functional groups and their proximity to one another ;

(c) various probable rotational and spatial configurations ;

(d) possibility of steric hindrance between various portions of the molecule in different configurations in space ; and

(e) probability of electronic interactions between various portions of the molecule including such matters as inductive and mesomeric effects, hyper-conjugation, ionizability, polarity, possibility of chelation, asymmetric centres and zwitterion formation.

The application of the method of variation, depending on the considerations enumerated above, is exploited in two different manners to evolve a better drug. The two main approaches for this goal can be indicated as :

(a) drug design through disjunction ; and

(b) drug design through conjunction.

6.1. Drug Design through Disjunction

Disjunction comes in where there is the systematic formulation of analogues of a prototype agent, in general, toward structurally simpler products, which may be viewed as partial or quasi-replica of the prototype agent.

The method of disjunction is usually employed in three *different* manners, namely :

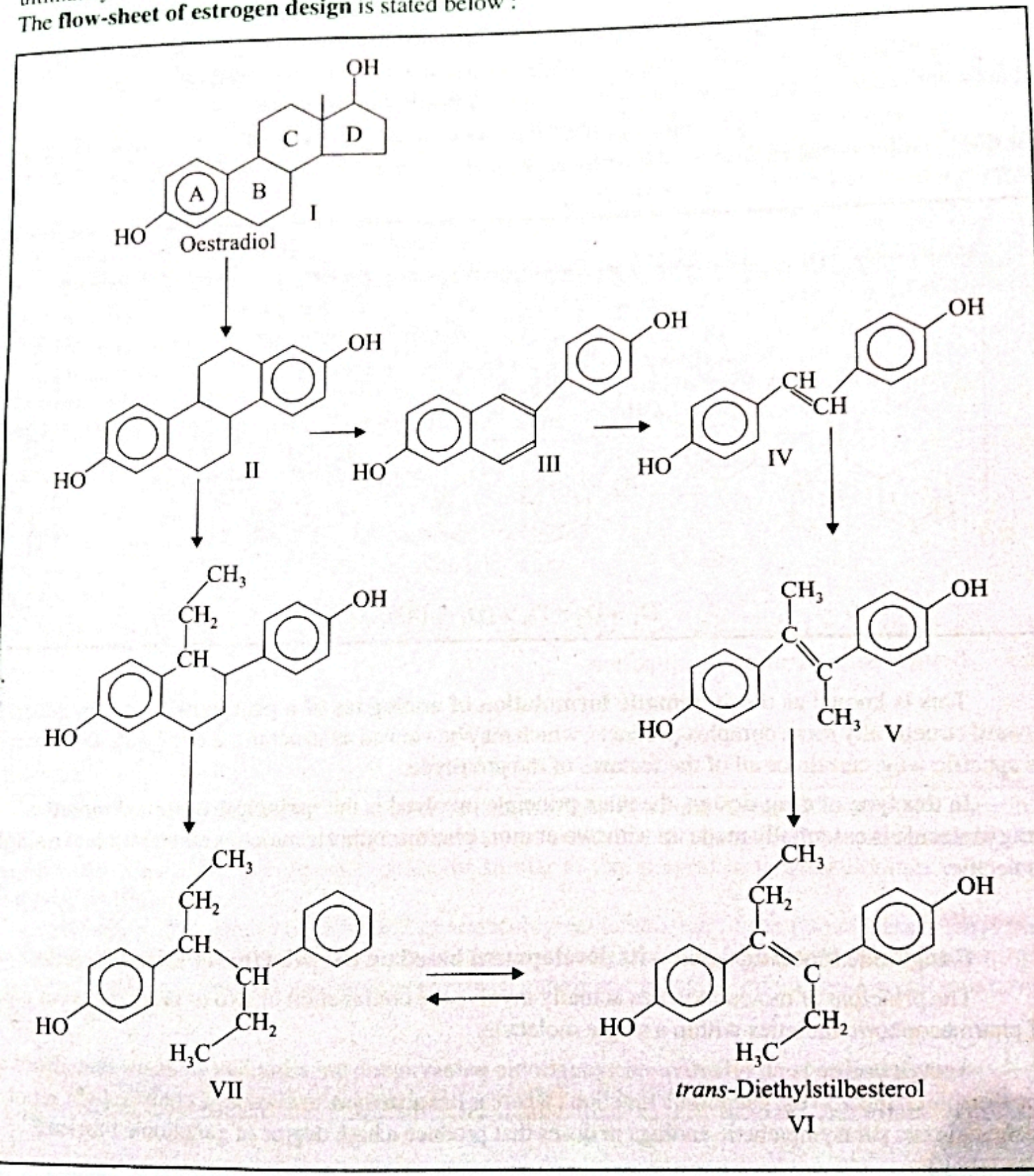
(i) unjoining of certain bonds ;

(ii) substitution of aromatic cyclic system for saturated bonds ; and

(iii) diminution of the size of the hydrocarbon portion of the parent molecule.

Example :

The extensive study on the estrogenic activity of oestradiol *via* drug design through disjunction ultimately rewarded in the crowning success of the synthesis and evaluation of *trans*-diethylstilbesterol. The **flow-sheet of estrogen design** is stated below :



Flow-sheet of Estrogen Design