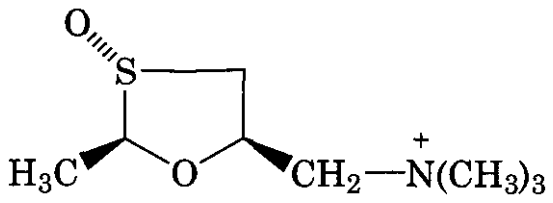
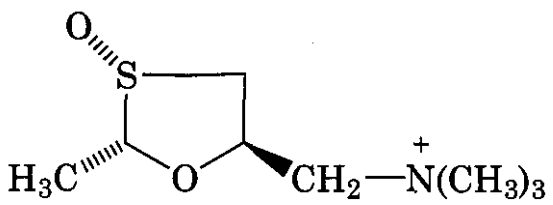
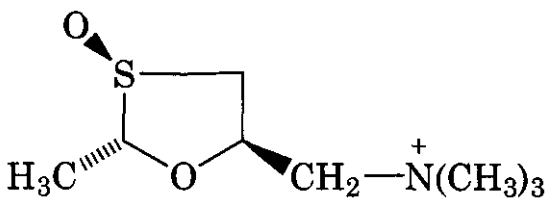


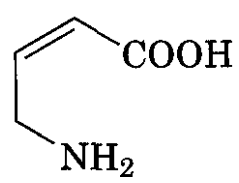
(97)



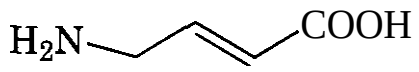
(98)



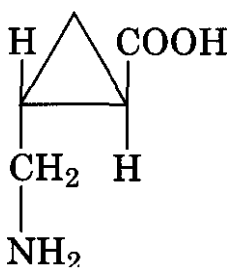
(99)



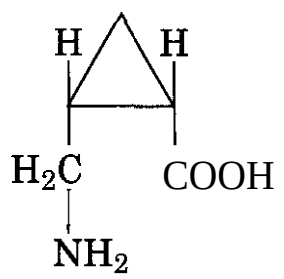
(100)



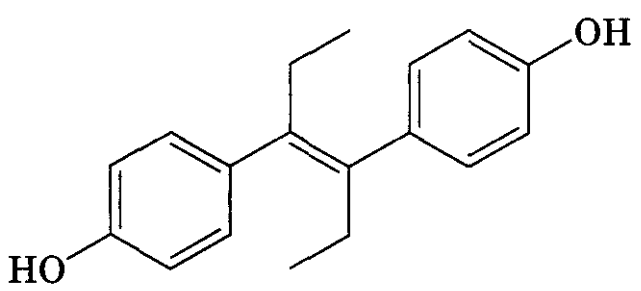
(101)



(102)



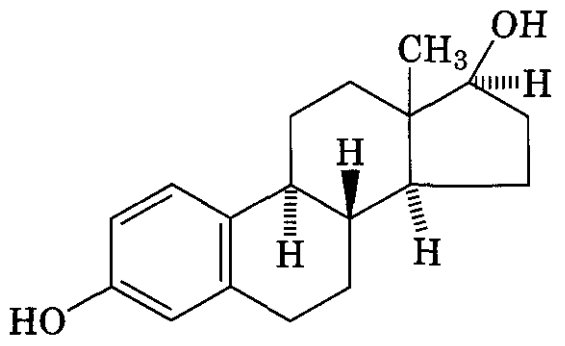
(103)



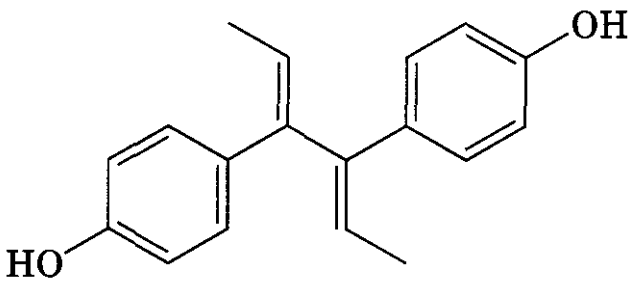
(104)

The folded 2-isomer (100) was inactive in assays for **GABA** agonism, whereas the extended E-isomer (101) was active. These data demonstrate biological differences of geometric isomers, which in turn involve a parameter discussed previously: imposition of a degree of structural rigidity on the molecule. **A** strategy analogous to this ***E/Z*** olefinic **GABA** congener design addressed cis- and ***trans*-1,2-disubstituted** cyclopropane derivatives (102) and (**103**), whose relative effects at **GABA** receptors paralleled those of the olefinic derivatives (65).

The E-isomer of the diethylstilbestrol structure (104) has 10 times the estrogenic potency of the ***Z*-isomer;** this effect has been rationalized from the conclusion that the E-geometric isomer is an open-chain analog of the natural estrogen estradiol (**105**) (66). In **dienestrol** (**106**), the geometric isomerism possible with olefinic moieties has been further



(105)



(106)