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THE ASYMMETRIC TOTAL SYNTHESIS OF ESTRADIOL BY AN INTRAMOLECULAR CYCLOADDITION REACTION OF o-QUINODIMETHANE

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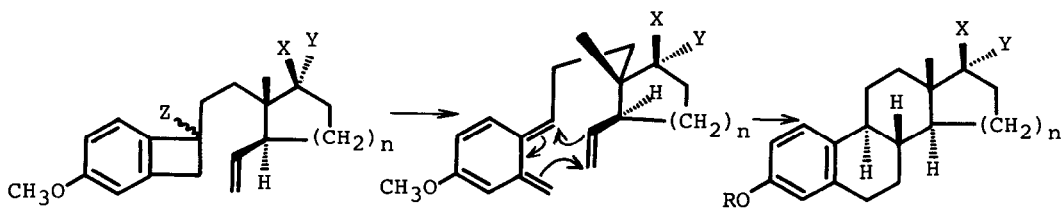
There are many reports on the synthesis of estrone and related compounds[1] and current interest on this field is focussed on an asymmetric[2] and biogenetic synthesis[3] of the above compounds. We have previously revealed[4] that the racemic form of the olefinic benzocyclobutene (1) could be induced to undergo a stereo- and regioselective intramolecular cycloaddition via o-quinodimethane (4)[5] to form O-methyl-D-homoestrone (5) in 95 % yield. In this communication we wish to report a new asymmetric synthesis of estradiol (8) by an asymmetric induction of the optically active cyclopentane derivative along our method.



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1 X + Y=O, Z=H, n=2
2 X=O$^{t}C_4H_9$, Y=Z=H, n=1
3 X=O$^{t}C_4H_9$, Y=H, Z=CN, n=1

5 R=CH_3, X + Y=O, n=2
6 R=CH_3, X=O$^{t}C_4H_9$, Y=H, n=1
7 R=CH_3, X=OH, Y=H, n=1
8 R=Y=H, X=OH, n=1

(1S,3aS,7aS)-1-tert-Butoxy-3a,4,7,7a-tetrahydro-7a-methyl-5(6H)indanone (9)[6] [$(\alpha)_D^{25}$ + 82.2° ($CHCl_3$)] was converted into the ketone thioketal (10) [mp 111 - 113°; 86 %; m/e 328 (M^+); $[\alpha]_D$ + 38.5°][7-9] by the usual way (1. HCO_2Et, NaH;