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AN EFFICIENT, STEREOSELECTIVE METHOD FOR THE CONSTRUCTION OF *ANTI-TRANS*-4,5-(4'-OXO-1',2',3',4'-TETRAHYDROBENZO)HYDRINDANE —— A POSSIBLE INTERMEDIATE TO ESTRADIOL AND CORTISONE

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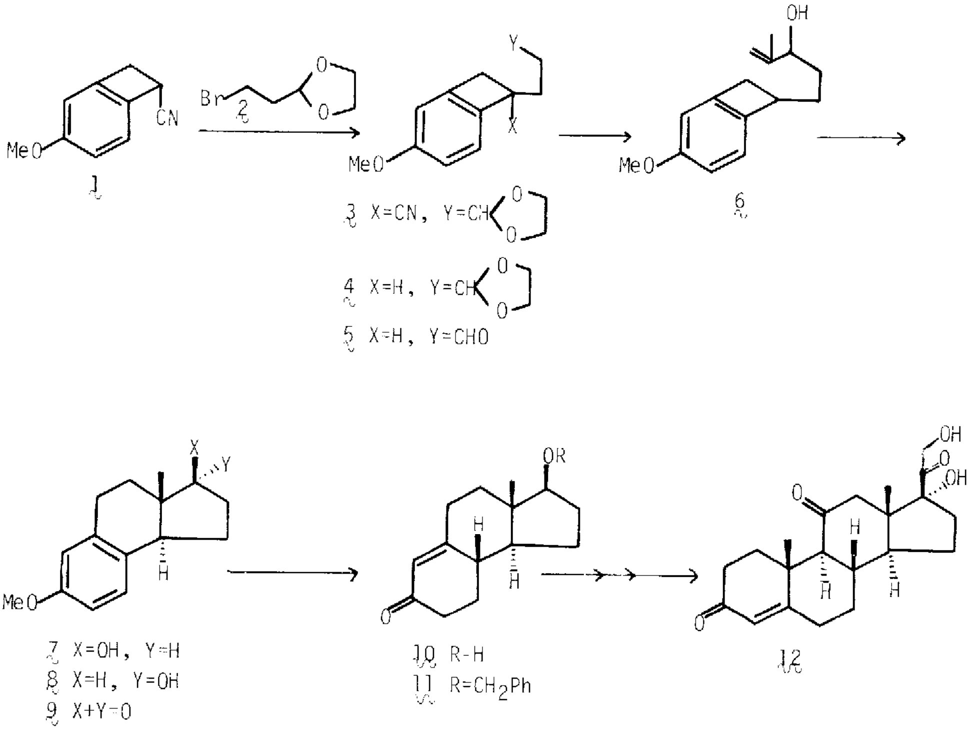
Summary: *anti-trans*-1β-Hydroxy-8β-methyl-4,5-(4'-oxo-1',2',3',4'-tetrahydrobenzo)-hydrindane, a possible intermediate to estradiol and cortisone, was synthesised stereoselectively by a thermolysis of benzocyclobutene as the key reaction.

Recently, benzocyclobutenes have been used as key compounds for total synthesis of A-ring aromatised steroids estrone and estradiol,[1,2] in which the estrane system is formed stereoselectively in one-step from benzocyclobutenes by an intramolecular cycloaddition. The finding of the stereoselective ring formation led us further to investigate an approach to nonaromatic steroids,[3] and here we describe a synthesis of *anti-trans*-13-hydroxy-8β-methyl-4,5-(4'-oxo-1',2',3',4'-tetrahydrobenzo)hydrindane (**10**) from the benzocyclobutene (**6**) *via* the *trans*-benzohydrindane (**7**) which has been correlated to cortisone (**12**) and estradiol.[4]

1-Cyano-4-methoxybenzocyclobutene (**1**)[5] was alkylated with the bromo-acetal (**2**) to give in 96 % yield the acetal (**3**),[6] which was decyanated reductively with sodium in liq. ammonia in the presence of ethanol to give **4** in 74 % yield. After treatment of **4**[6] with hydrochloric acid, the resulting aldehyde (**5**)[6] was treated with isopropenylmagnesium bromide to afford in 57 % yield the key material (**6**)[6] [$\nu_{max}^{CHCl_3}$ 3450 (OH) cm^{-1}; δ (CDCl$_3$) 1.70 (3H, s, Me-C=), 4.75 (1H, br s, $=C<^{H}_{H}$), 4.86 (1H, br s, $=C<^{H}_{H}$). Thermolysis of the benzocyclobutene (**6**) was carried out in a sealed tube at 180°C as a toluene solution for 16 h to furnish the expected cyclised product (**7**)[6,7] [mp 73 - 75°C (lit.,[8] 75°C); δ (CDCl$_3$) 0.63 (3H, s, >C-Me)] in addition to the its epimer (8)[6,7] as an oil [δ (CDCl$_3$) 0.50 (3H, s, >C-Me)] in a ratio of 1 : 1 and 81 % yield. The latter could be converted quantitatively into the former by successive treatment with chromic anhydride in sulphuric acid and sodium borohydride *via* ketone (**9**)[6,7] [mp 112 - 113°C (lit.,[8] 112 - 113°C)].

Finally, Birch reduction of **7** with lithium in liq. ammonia in the presence of ethanol gave the tricyclic enone (**10**)[6,7] in 58 % yield [mp 101 - 102°C; m/e 220 (M$^+$); $\nu_{max}^{CHCl_3}$ 1665 (C=O) cm^{-1}; δ (CDCl$_3$) 0.87 (3H, s, >C-Me) and 5.78 (1H, br s, =CH-)], whose benzylation afforded our desired compound (**11**) that had been transformed into cortisone (**12**) and estradiol.[4] The conversion of **10** to testosterone is now under progress in this laboratory.



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