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Conversion of Torgov's Synthesis of Estrone into a Highly Enantioselective and Efficient Process
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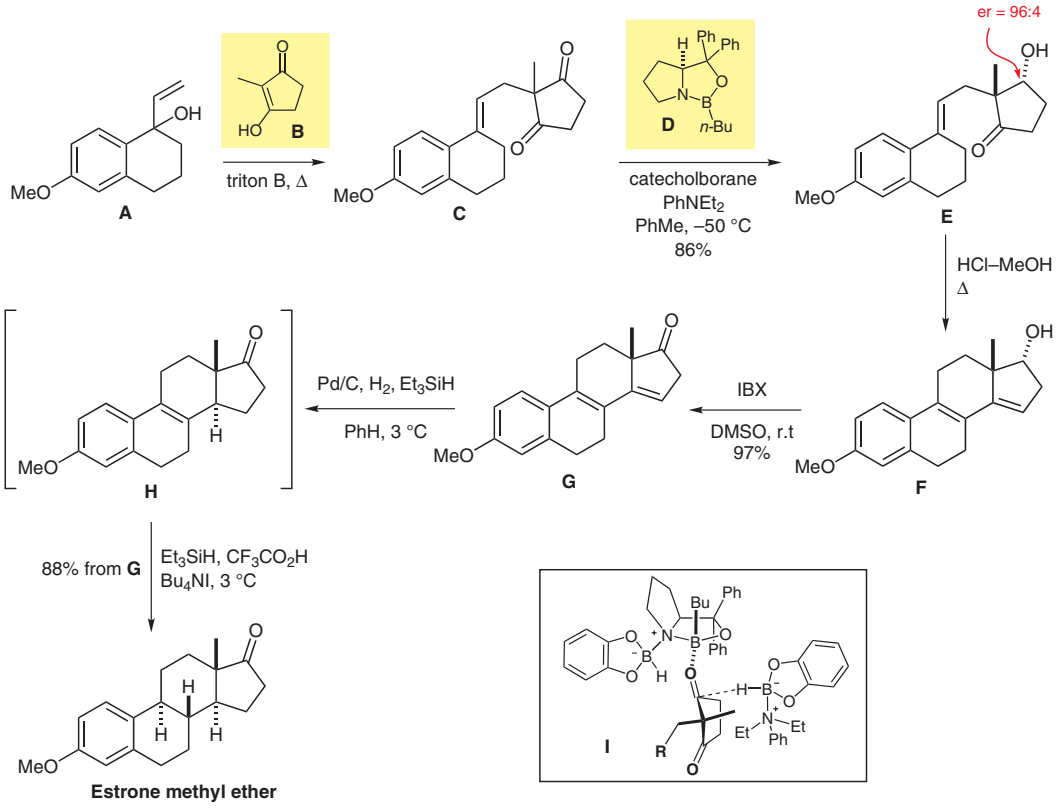
Synthesis of Estrone Methyl Ether



Significance: The short and efficient synthesis of estrone methyl ether reported here is a modified enantioselective version of the Torgov and Ananchenko synthesis (*Tetrahedron Lett*. **1963**, *4*, 1553). Although the key step in the synthesis involved an oxazaborolidine **D**, the reaction proceeded by a different pathway from the CBS reduction, via transition state **I** where the catecholborane-$PhNEt_2$ complex was a hydride donor rather than the oxazaborolidine-catecholborane complex. This method provides a practical alternative to the use of enzymes for reducing cyclic 1,3-diketones.

Comment: Reduction of ketone **C** proceeded with high stereoselectivity via transition state **I** and a single recrystallization afforded **E** in 99% ee. A similar reduction methodology was applied to five other cyclic 1,3-diketones with excellent enantioselectivity. Acidic treatment of alcohol **E** followed by oxidation and then reduction gave estrone methyl ether in good overall yield.

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