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DIENES AS CHIRAL TEMPLATES

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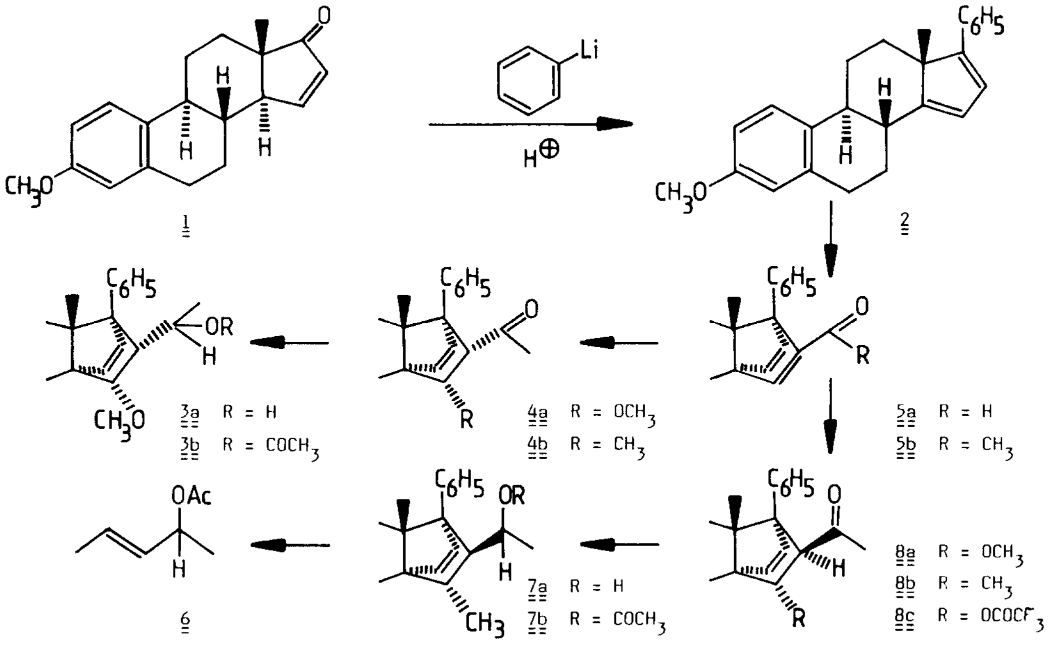
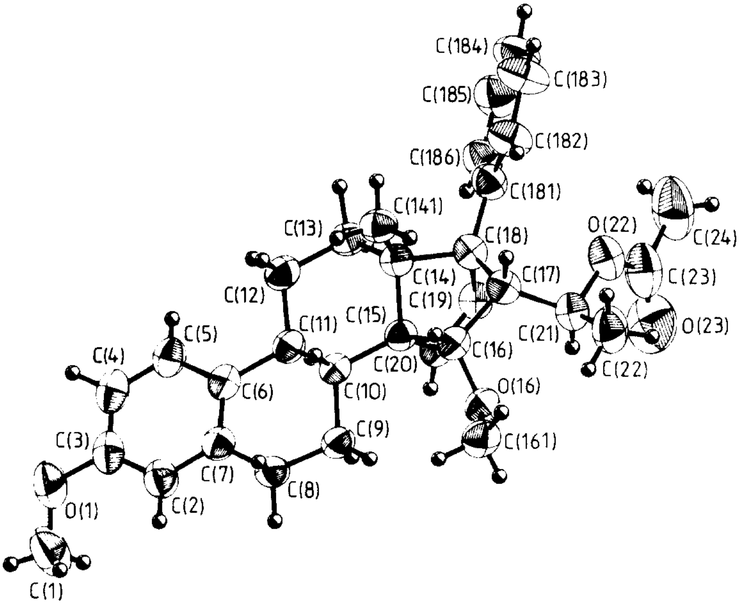
Abstract: Stereoselective and regioselective cycloadditions to the chiral cyclopentadiene 2 are reported. Diastereoselective transformations of the adducts followed by a thermal retroreaction yields pure enantiomers.

Chiral, natural products derived dienes hold good promise as templates for diastereoselective transformations of Diels-Alder adducts[1,2]. Followed by a later retro-Diels-Alder step they are expected to regenerate the diene and expel pure enantiomers. To test this concept we recently investigated ergosterin adducts. As these tended to form ansa-steroids under thermal conditions[1] we prepared the highly crystalline and also very stable diene 2 from dehydrooestrone-methylether 1[3,4] and were very pleased to note that Diels-Alder cycloadditions with propargylic-aldehyde as well as with butynone proceeded with very high yield (94%, 91%) and excellent regioselectivity and stereoselectivity (ß-attack)[5] to exclusively form the unsaturated ketones 5a or 5b (see structure determination of 3b)[6].



Conjugate additions take place under mild conditions and with high diastereoselectivity. A two-percent solution of sodium-methoxide in methanol at 0 °C gives rise mainly to the trans-addition product 4a (95 : 5, kinetic control).



Equilibration with methoxide generates a 1 : 1 mixture of 4a and 8a, while on selectride reduction of 4a one single carbinol (3a) is obtained in quantitative yield. The configuration of this compound - secured by an X-ray structure determination[7] of the corresponding acetate 3b (see plot) does not only prove the steric course of the reduction (Felkin-Anh model) but also details of the cycloaddition process (ß-attack, regioselectivity).

Accordingly the cuprate addition product 8b (thermodynamic control) should give rise to acetate 7b and indeed did a thermal retro-degration (200-220 °C) afford the optically pure acetate 6 which was proven to be >98% of one pure enantiomer by a chiral europium-shift reagent [Eu(tfc)$_3$][8] in comparison to a racemic mixture. Acid catalysed additions proved to be very efficient, too. A ten-percent solution of trifluoro acetic acid in dichloromethane gave rise to a quantitative yield of the pure cis-addition product 8c and methanol with a trace of sulfuric acid added in the same way to mainly yield 8a. Various other conjugate additions have been conducted in the meantime and will be discussed in a forthcoming full paper.

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[4] Thanks are due to Professor Dr. R.Wiechert and Dr. H.Laurent from the Schering Company, Berlin, for providing a generous amount of oestrone-methylether as starting material.
[5] A.J.Solo, B.Singh, E.Shefter, and A.Cooper, Steroids 11, 637 (1968).
[6] Recently Professor Dr. F.G.Klärner, Universität Bochum, succeeded in forming 5b under high pressure (7 kbar, 5 h, room temperature, quantitative yield).
[7] Atomic coordinates for this structure have been deposited with the Cambridge Crystallographic Data Centre. The coordinates can be obtained on request from The Director, Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, U.K.
[8] Thanks are due to Dr. E.Hofer[b)] for a series of shift-measurements.

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