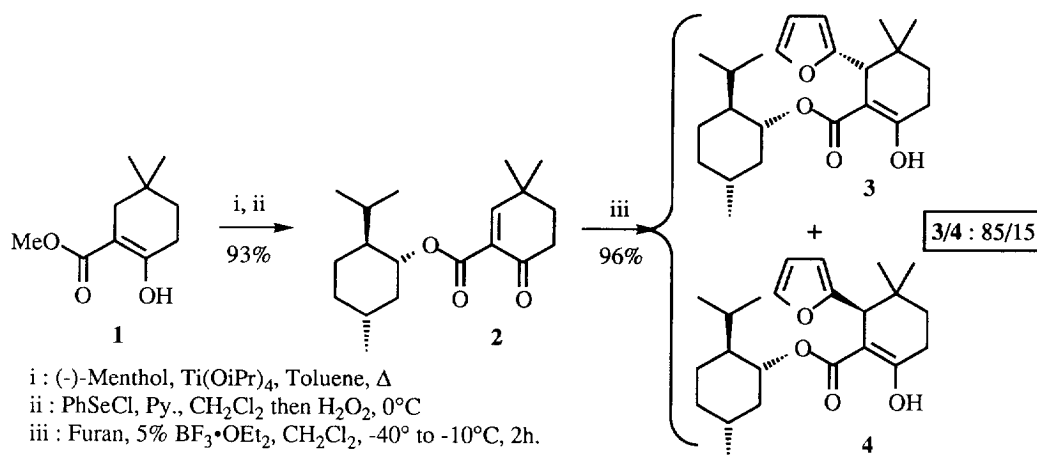


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Synthesis of Polyoxygenated Decalins : Part III^{1,2}**Pierre-Yves RENARD, Céline POIREL[†] and Jean-Yves LALLEMAND***Laboratoire de Synthèse Organique, Ecole Polytechnique
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CNRA, route de Saint-Cyr, 78000 Versailles, France.**Abstract:** Lewis acid catalysed addition of furan to an activated cyclohexenone bearing an optically active ester is described.

Following our interest in the development of new methods useful in the construction of functionalised decalins, we recently described the use of the acid catalysed addition of furan to an activated cyclohexenone,¹ and the stereocontrolled sequence involving oxidative furan ring opening and cyclisation.^{1,2} We want to report here our efforts towards the control of the enantioselectivity of this reaction.

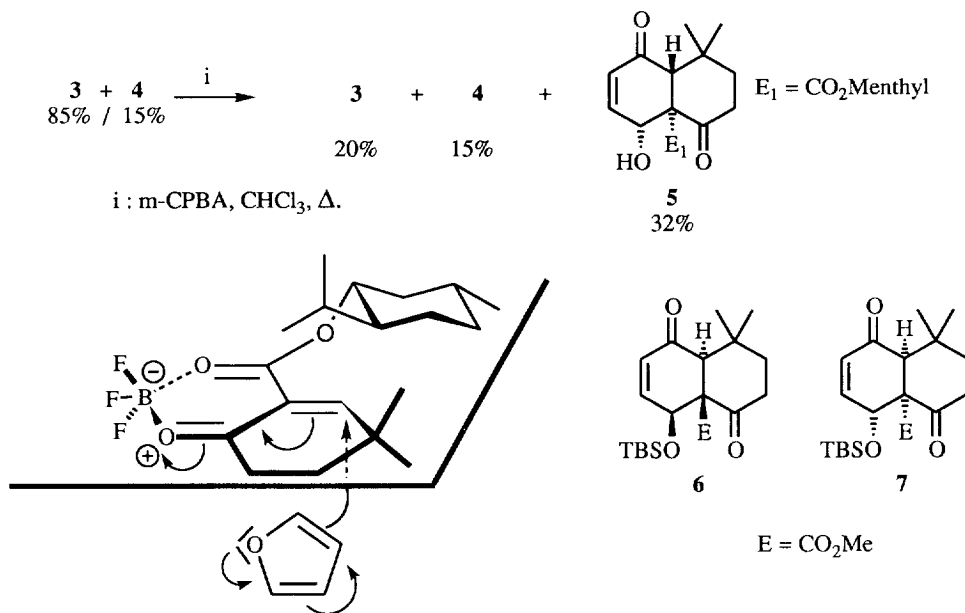
After various unsuccessful attempts to promote the addition step by the use of chiral Lewis acids,³ valuable results were obtained when a chiral auxiliary was introduced in the ester group. The menthyl ester **2** was prepared in two steps by Ti(OiPr)₄ catalysed transesterification⁴ of **1** with (-)-menthol,⁵ and synthesis of the conjugated enone **2** by well known selenium chemistry.^{1,2,6} BF₃·OEt₂ catalysed addition of furan to **2** then took place in high yield (96%). Two diastereoisomers **3** and **4** were isolated in a 85/15 ratio (Scheme 1). This diastereoselectivity is assumed to be due to the coordination of the boron atom to the dicarbonyl system, leading to a planar configuration of BF₃ complex with one face hindered by the menthyl ester bulkiness (Scheme 2).⁷ Attack of the furan is thus controlled and is expected to occur from the opposite face of the molecule with respect to the menthol residue.



Scheme 1

Assignment of the configuration of **3** and **4** was confirmed by the following observations : when the mixture of **3** and **4** was submitted to the oxidative furan ring opening in the conditions used to perform the reaction on the methyl ester (*m*-chloro peroxybenzoic acid (*m*-CPBA), MeOH, 5°C), no reaction was observed. This lack of reactivity can be accounted for by the steric hindrance of the menthyl ester group which prevents *m*-CPBA from reacting with the furan ring. When the mixture was submitted to more drastic conditions (*m*-CPBA, CHCl₃, 70°C), *trans*-decalin **5** ($[\alpha]_D^{25}$ (*c* = 0.1, CH₂Cl₂) = -78) was isolated as the only cyclised material. Diastereomer **4**, with a more sterically hindered furan ring did not react at all. From these observations, structure **3** was assigned to the "anti" isomer in which the menthyl ester residue is in an "anti" position relative to the furan. In addition, 400MHz NMR experiments with chiral europium shift reagent showed that the enantiomeric excess of **5** is >95%. Eu(III) ion is expected to bind to β keto-ester, inducing an important downfield shift from **5** of neighbouring protons.

Previously described controlled aldolisation reactions^{1,2} should allow us to reach enantiomerically pure decalins **6** and **7**.



Scheme 2

References and Notes

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- Ketoester **1** was prepared from 4,4-dimethylcyclohex-2-enone using the following sequence : 1) H₂, PtO₂, MeOH (88%); 2) NaH, CO(OMe)₂, refluxing DME (97%).
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