Tetrahedron Letters, Vol. 34, No. 33, pp. 5341-5342, 1993
Printed in Great Britain

0040-4039/93 $6.00 + .00
Pergamon Press Ltd

A Non-Enzymatic, Asymmetric Synthesis of Dicyclopentadienone

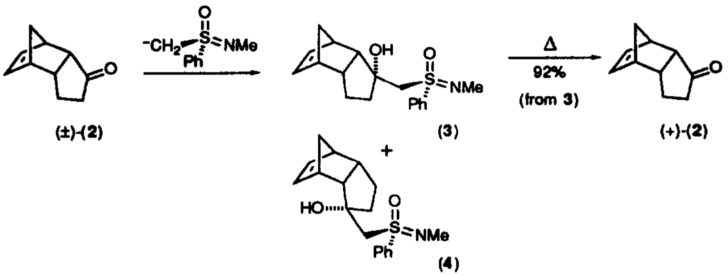
Bradley J. Childs and Gavin L. Edwards*

School of Chemistry, University of New South Wales, P.O. Box 1, Kensington, New South Wales, Australia, 2033

Abstract: A simple synthetic method for the preparation of optically active "dicyclopentadienone" is presented. The procedure involves the reaction of the magnesium enolate of the racemic ketone (2) with S_S-menthyl-*p*-toluenesulfinate, giving a β-ketosulfoxide as a single diastereoisomer. Conversions to enone (1) or saturated ketone (2) proceed with good optical and chemical yields.

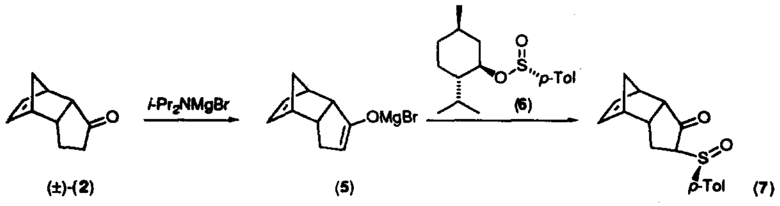
In connection with studies on asymmetric additions to chiral cyclopentenones, we sought to develop a new method for the preparation of enantiomerically pure "dicyclopentadienone"(**1**). This versatile compound has found widespread use in the synthesis of natural products, most notably in the work of Takano[1] and of Zwanenburg.[2] During the course of this work, an enzyme-mediated method for the resolution of ketone (**1**) was reported by Takano and coworkers,[3] however the preparation of the *exo*-alcohol precursor for kinetic enzymatic resolution requires use of selenium dioxide. We wish to report an alternative procedure for the preparation of enone (**1**) and the saturated ketone (**2**) in enantiomerically enriched form, without recourse to enzymatic methods or to highly toxic selenium reagents.

Racemic ketone (**2**) is readily accessible using the recently reported method of Little,[4] by the BF_3 catalysed Diels-Alder reaction of cyclopentadiene with 2-cyclopentenone. This method proved to be superior to $AlCl_3$ catalysed reactions[5] which gave variable outcomes. Initial attempts at resolution were based on Johnson's resolution procedure,[6] and reaction of racemic ketone (**2**) with the anion derived from (*S*)-(+)-*N*,*S*-dimethyl-*S*-phenylsulfoximine[7] gave a mixture of the two sulfoximine diastereoisomers (**3**)[8] and (**4**) as a 1:1 mixture. Although the mixture could only be partially separated by chromatography ($\Delta R_f \leq 0.03$), a small sample of one diastereoisomer (26% yield) was obtained and thermolysis in boiling toluene gave the optically active ketone (+)-(**2**) in 92% yield (ee 74%). However the incomplete separation of the sulfoximines caused us to investigate another approach.

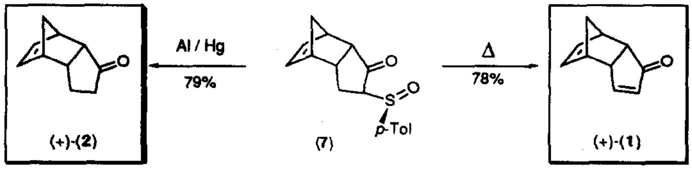


An alternative route centred on the synthesis of β-ketosulfoxide diastereoisomers, modelled on a novel asymmetric synthesis of 4-hydroxy-2-cyclohexenone reported by Carreño and coworkers.[9] Initial results were encouraging, where the reaction[10] of a three-fold excess of magnesium enolate (**5**) with S_S-(-)-menthyl-*p*-toluenesulfinate (**6**) gave the β-ketosulfoxide (**7**) as a ***single diastereoisomer*** in 56% yield.

There was no evidence for the formation of another isomer in the reaction; this result is a remarkable example of molecular recognition, where the rates of reaction of the (+)- and (-)-magnesium enolates (**5**) with the chiral sulfinate (**6**) differ markedly and hence only one isomer is apparently produced at this ratio of reactants. Reactions carried out with an equimolar ratio of (**5**) and (**6**) resulted in the formation of two diastereoisomers in a 3:1 ratio, which to date have not been satisfactorily separated by chromatography.



The parent ketone (**2**) was regenerated in optically active form by reductive desulfination[11] using aluminium amalgam in THF at 60°C for 90 min, giving (+)-(**2**) in 79% yield, $[\alpha]_{D}^{21}$ +226°(c 1.70, $CHCl_3$), with an enantiomeric excess of 84%.[12] Alternatively, thermal elimination[13] of toluenesulfenic acid by heating the sulfoxide in CCl_4 for 17 h gave the enone (**1**) in 78% yield, $[\alpha]_{D}^{21}$ +126°(c 1.27,MeOH). By comparison with the reported[14] rotation of +158.8°, this corresponds to an enantiomeric excess of 79%. We are currently investigating strategies for increasing the optical purities of the products, as well as the application of this method to other polycyclic ketones.



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Acknowledgement: We wish to thank the Australian Research Council for generously supporting this project.

(Received in UK 18 May 1993; accepted 25 June 1993)