Chiral Recognition during the Reaction of Dienyliron Complexes with Sulphoximine-stabilized Enolates

Anthony J. Pearson* and Jaeyon Yoon

Department of Chemistry, Case Western Reserve University, Cleveland, Ohio 44106, U.S.A.

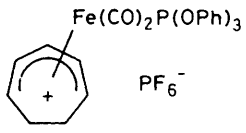
The first example is reported of chiral recognition during enolate nucleophile addition to dienyliron complexes; enantiomeric excesses of up to 50% were obtained by reaction of complex (**1**) with enolates derived from the sulphoximinyl ester derivatives (**8**) and a remarkable effect of the enolate countercation was observed, suggesting that nonco-ordinated enolate gives maximum enantioselectivity.

Current investigations in our laboratory[1] are aimed at using the cycloheptadienyliron complex (**1**) as a precursor for the synthesis of a wide range of macrolide antibiotics, such as tylosin (**2**) and carbomycin B (**3**). To this end, (**1**) has been converted by successive nucleophile additions, followed by demetallation, into the carboxylic acid (**4**), and this in turn has been converted into the acyclic molecules (**5**) and (**6**), representing right hand subunits of (**2**) and (**3**), respectively.[2] However, a major problem arises from this work: since (**1**) is a symmetrical molecule, the sequence employed unavoidably produces (**5**) and (**6**) in racemic form, so any attempt to couple these subunits to intermediates representing the left hand sections of (**2**) and (**3**) will lead to diastereoisomeric mixtures. A solution to this problem would be to produce (**5**) and (**6**) in optically active form and couple these to optically active left hand subunits. While this might be achieved by classical

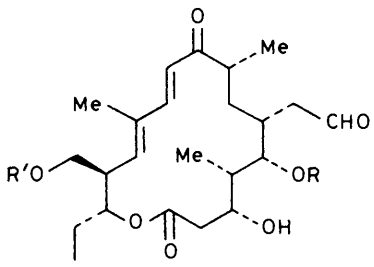
Table 1. Enantiomeric and diastereoisomeric excess observed during the reaction of complex (**1**) with enolates derived from (+)-(**8**).

Entry	Product isolated	Conditions used to generate (+)-(**8**) enolate	$[\alpha]_D^{20}$ of product	% Enantiomeric excess[a]	Diastereoisomer ratio[a]
1	(**12**)	Bu^nLi, THF	+2.6°	20	
2	(**12**)	NaH, THF	+5.6	25—30	
3	(**12**)	Bu^tOK, THF	+8.3	35—40	
4	(**12**)	Bu^tOK, THF, 18-crown-6	+10.1	50	
5	(**12**)	Bu^tOK, DME	+9.8	50	
6	(**12**)	NaH, THF, 18-crown-6	+9.6	50	
7	(**10**)	Bu^nLi, THF			1.5:1
8	(**10**)	NaH, THF			1.9:1
9	(**10**)	Bu^tOK, THF			2.5:1

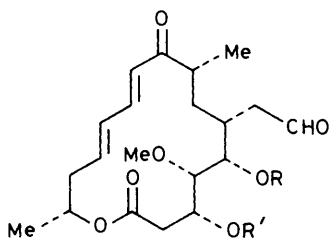
[a] Estimated from 200 MHz n.m.r. spectra (see text).



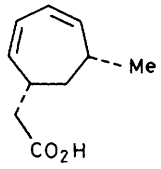
(1)



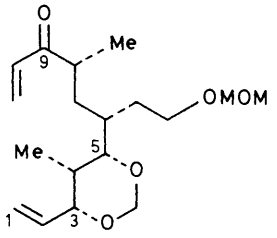
(2) R,R' = Sugar



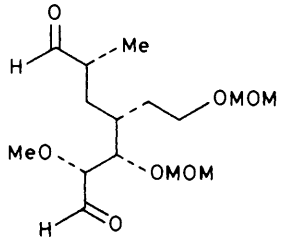
(3) R = Sugar



(4)

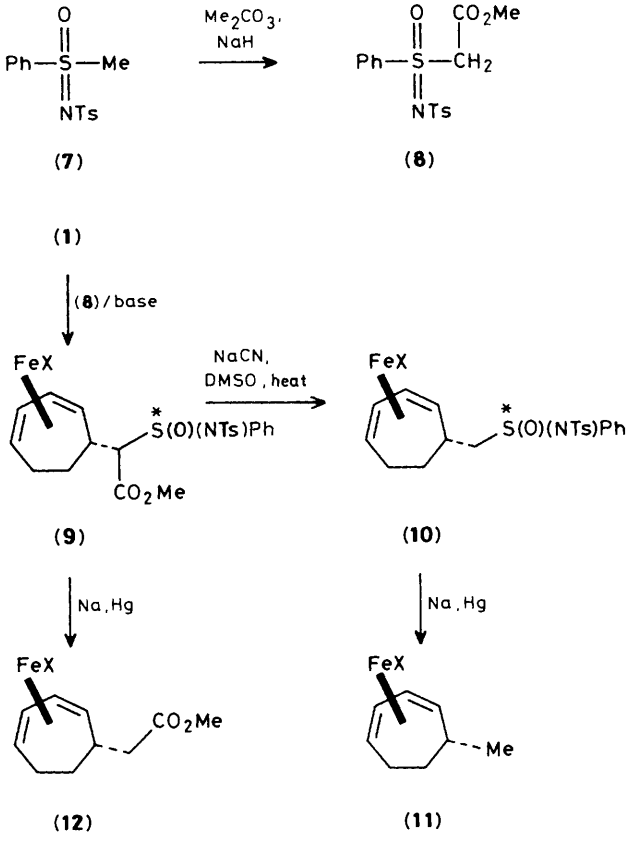


(5)



(6)

MOM = Methoxymethyl



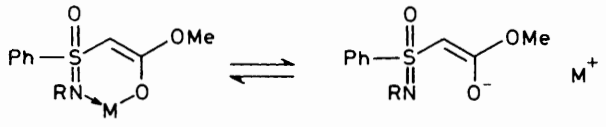
Ts = Tosyl
FeX = $Fe(CO)_2P(OPh)_3$

resolution of *e.g.*, (**4**), such operations are inelegant and rarely efficient. We report herein preliminary results of a study aimed at overcoming this problem, based on chiral recognition during the reaction of sulphoximine-stabilized enolates with dienyliron complexes.

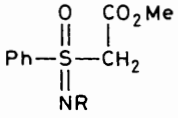
Both *S*- ($[\alpha]_D^{20} = +115°$) and *R*- ($[\alpha]_D^{20} = -117°$) enantiomers of the sulphoximine (**7**) were prepared in a state of high (>98%) optical purity by Johnson's method.[3] Since the carbanion produced by deprotonation of (**7**) did not react satisfactorily with complex (**1**), each enantiomer was converted into the ester derivative (**8**) (*S*: $[\alpha]_D^{20} = +42.1$, $c = 0.01$, acetone; *R*: $[\alpha]_D^{20} = -44.3°$, $c = 0.012$, acetone) by standard techniques [NaH, tetrahydrofuran (THF), dimethyl carbonate, reflux]. That no racemization occurs during this treatment was confirmed by n.m.r. spectroscopy, using the chiral lanthanide shift reagent tris(heptafluorobutyrylcamphorato)europium(III) [$Eu(hfbc)_3$]. At this point, it was established that decarboxylation of (**8**) to regenerate (**7**) using the Krapcho procedure[4] [NaCN, dimethyl sulphoxide (DMSO), 120 °C] proceeded without racemization, as expected.

The ester (**8**) was readily converted into its enolate anion using a variety of bases (Bu^nLi, NaH, or $KOBu^t$) and the enolate was allowed to react with complex (**1**) to give the diene complex (**9**) as a mixture of diastereoisomers (98—99% yield for all reactions studied). Several methods for the manipulation of (**9**) were examined. Decarboxylation (NaCN, DMSO, 80 °C, 48 h) gave the sulphoximine derivative (**10**) in 80% yield in which one of the two diastereoisomers was predominant as judged by 200 MHz n.m.r. spectroscopy. Desulphonylation of (**10**) (3% Na, Hg amalgam, THF–MeOH, Na_2HPO_4, 0 °C, 0.5 h) gave the methyl-substituted diene complex (**11**) in 60% yield, which was optically active. Conversion of (**9**) into the monoester (**12**), also optically active, was readily accomplished in 80—83% yield (3% Na, Hg amalgam as before) and the enantiomeric excess of this complex was estimated from the 200 MHz n.m.r. spectrum run in the presence of $Eu(hfbc)_3$ [δ 3.6 (CO_2Me)]. The enantiomeric excesses, together with diastereoisomer ratios for (**10**), are recorded in Table 1.

Perhaps the most striking feature of this study is the dependence of chiral recognition on the nature of the enolate–countercation pair used. When the cation is fairly strongly chelated, as in structure (**13**), M = Li (following the



(13) (14)



(15) R = Me

(16) R = $SiMe_3$

suggestion of Johnson[3]), the enantiomeric excess and diastereoisomeric excess observed is rather poor. When the anion is in the unco-ordinated form, as in structure (**14**) (M = K) the selectivity observed is much greater. The further enhancement of selectivity by using more strongly co-ordinating solvent [dimethoxyethane (DME)] or by using crown ether, supports this proposal, as do the reactions of the related sulphoximinyl esters (**15**) and (**16**). Reaction of the potassium enolate of (**15**) with complex (**1**), followed by desulphonylation afforded monoester (**12**) with an enantiomeric excess of only 5%, while similar reaction of (**16**) gave (**12**) with only slight (*ca.* 1%) enantiomeric excess. This is consistent with an enhanced ability of the enolate to co-ordinate the cation upon introducing a stronger electron donor onto the nitrogen atom, although at this point it is difficult to separate electronic effects from differences in steric properties of these molecules.

Clearly, there is considerable potential for asymmetric synthesis using the technique described herein. Future work will examine the generality of the procedure as well as its optimization, and will also determine the absolute stereochemistry of the major enantiomer in order to give a full understanding of the chiral recognition phenomenon.

We are grateful to the U.S. Public Health Service, National Institutes of Health for generous financial support of this work, and to the National Science Foundation and National Institutes of Health for grants toward the purchase of the Varian XL-200 n.m.r. spectrometers used.

Received, 10th June 1986; Com. 792

References

1 A. J. Pearson, S. L. Kole, and T. Ray, *J. Am. Chem. Soc.*, 1984, **106**, 6060; A. J. Pearson and T. Ray, *Tetrahedron*, 1985, **41**, 5765; A. J. Pearson and B. Chen, *J. Org. Chem.*, 1985, **50**, 2587.

2 A. J. Pearson and T. Ray, *Tetrahedron Lett.*, 1986, **27**, 3111. For a review describing previous total syntheses of tylonolide and carbonolide B, see: I. Paterson and M. M. Mansuri, *Tetrahedron*, 1985, **41**, 3569.

3 C. R. Johnson, *Acc. Chem. Res.*, 1973, **6**, 341; *Aldrichim. Acta*, 1985, **18**, 3.

4 A. P. Krapcho, *Synthesis*, 1982, 805; 893.