Tetrahedron Letters Vol. 21, pp 3355 - 3358
©Pergamon Press Ltd. 1980. Printed in Great Britain

0040-4039/80/0822-3355$02.00/0

BIOMIMETIC POLYENE CYCLIZATIONS - ASYMMETRIC INDUCTION IN THE CYCLIZATION OF A CHIRAL DIENIC IMINE

GILLES DEMAILLY AND GUY SOLLADIE*

Laboratoire de Chimie Organique de l'Ecole Nationale Supérieure de Chimie, ERA du CNRS n°687 - Université Louis Pasteur - B.P. 296/R8, 67008 STRASBOURG (France).

Abstract. The acid-catalyzed cyclization of the chiral aldimine prepared from trans-5,9 dimethyldeca-5,9-dienal and (-)S-α-phenyl-ethylamine affords diastereoisomeric amino-5 dimethyl-2,9 octalines, the asymmetric induction being 65% in the trans-trans series and 35% in the cis-trans series.

The work of W.S. Johnson (1) demonstrated that appropriably constructed polyolefinic allylic alcohols or acetals undergo non enzymic, acid-catalyzed cyclizations to give polycyclic substances possessing "natural" configuration. These cyclizations were stereospecific with respect to the relative configurations of the chiral centers produced at the bridge-heads ; however the products were racemic. In view of the fact that the enzymatic cyclization of squalene proceeds with total asymmetric induction to produce enantiomerically pure products, W.S. Johnson and al. (2) examined the cyclization of an optically active dienic acetal 2 which was shown indeed to proceed with a remarkbly high degree of asymmetric induction (scheme 2).

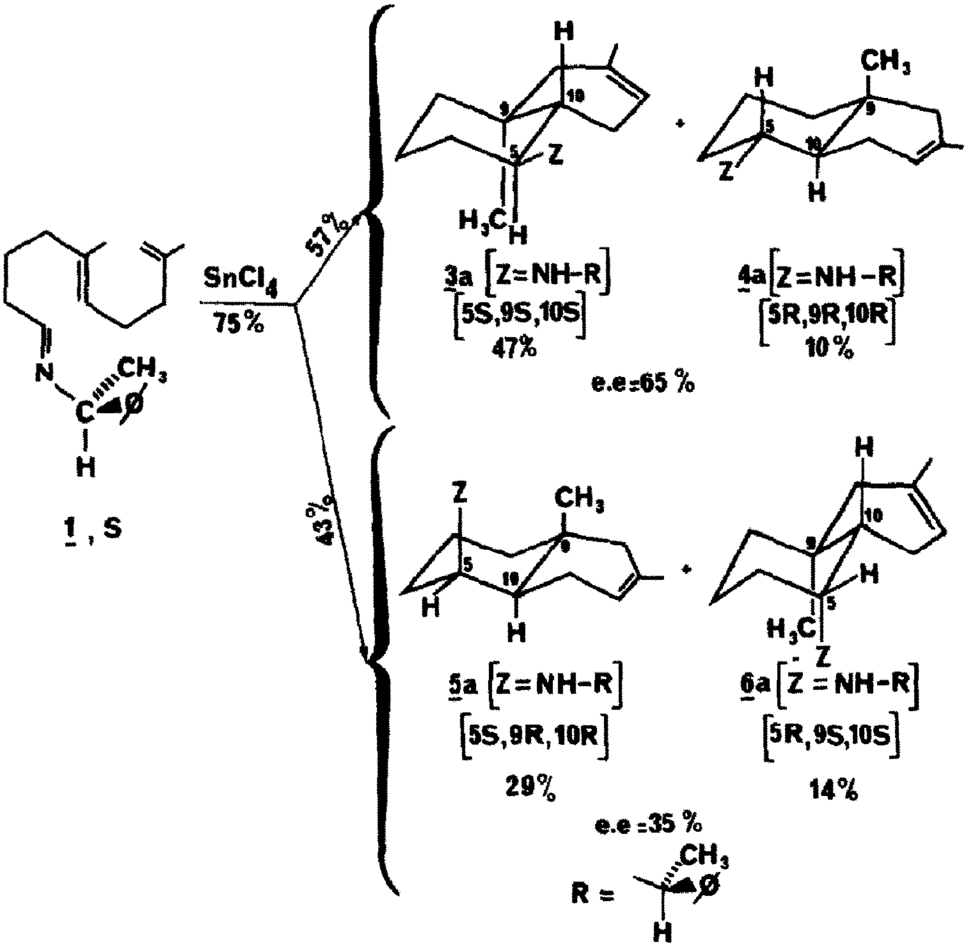
Previous work from our laboratory (3) has shown that a chiral imino-group is very efficient to initiate acid-catalyzed cyclizations of mono-olefinic substrates leading to high yields of monocyclic products with moderate extends of asymmetric induction.

The present paper describes the use of a chiral imino group to the acid-catalyzed cyclization of the dienic substrate already studied by Johnson in order to compare the advantages of this initiating group towards a chiral acetal group.

Imine 1 S was prepared in quantitative yield from trans-5,9- dimethyldeca-5,9-dienal(2), (-)S α-phenylethylamine in benzene in presence of molecular sieves at room temperature in 1 hour |IR : $\nu_{C=N}$ 1670 cm^{-1}|.

Then a solution of 4ml of $SnCl_4$ in 100ml of benzene was dropwise added, at room temperature, to a solution of 1.5g of imine 1 S in 1.5ml of anhydrous benzene under nitrogen and vigorous agitation. The resulting solution was stirred 24h in the dark. The usual work-up yielded 1.1g of secondary amines (75% yield).

This crude product was shown, by ^{1}H NMR at 250MHz, to be a mixture of 90% of amines 3a to 6a (4) having an endocyclic double bond |vinylic protons leading to a multiplet between 5.08 and 5.25 ppm| and 10% of amines having an exocyclic methylene group |characterized by a multiplet for the vinylic protons between 4.7 and 4.85 ppm (2)| which were easily separated by chromatography on silicagel.



- SCHEME 1 -

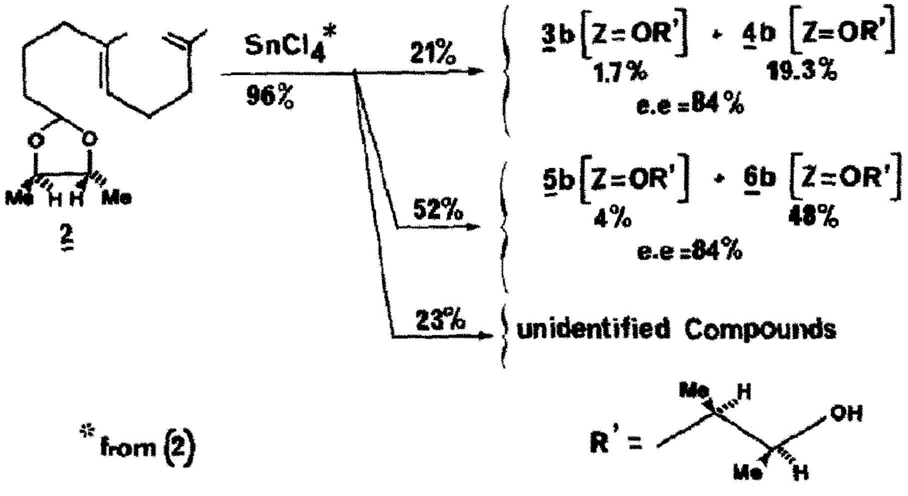
In the mixture of amines 3a to 6a (5), the diastereoisomers having an equatorial amino group, 3a and 4a (57%) and those having an axial amino group, 5a and 6a (43%) were easily distinguished by the relative positions of the NMR signals (and their intensities) for the angular methyl group which appeared at 0.78 (47%) and 0.83 (10%) in the case of an equatorial amino group and at 0.90 (14%) and 0.94 ppm (29%) in the case of an axial amino group (6).

Finally the diastereoisomeric series (3a+5a) and (4a+6a) were distinguished by the two quadruplets centered at 3.9 (76%) and 4.0 ppm (24%) corresponding to the benzylic proton.

It can be concluded from this NMR study that 76% of the reaction mixture has the same chirality on carbon C-5 (47% having an equatorial amino group and 29% an axial one) meanwhile 24% has the opposite chirality on C-5 (10% with an equatorial NHR and 14% with an axial one).

The absolute configuration of carbon C-5 in the major diastereoisomers was determined, after debenzylation on Pd-C, by using Horeau's method (7) : the formation of (-) α-phenylbutyric acid indicated that the C-5 absolute configuration in the predominant diastereoisomers was probably S (8).

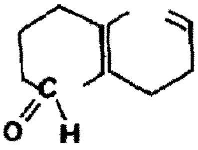
The composition of the products obtained by cyclization of imine 1 S is shown on scheme 1.



- SCHEME 2 -

The comparison of our results (scheme 1) and those of Johnson and al. (scheme 2) points out several comments :

1) The main diastereoisomer obtained from the chiral acetal 2 is the axial epimer 6b meanwhile the chiral aldimine 1 S leads mainly to the equatorial epimer 3a. Our result is similar to those obtained by Ireland (11) during the acid-catalyzed cyclization of aldehyde 7 which afforded mainly the racemic equatorial alcohol.



7

2) A striking difference between the two experiments is also observed in the extent of asymmetric induction. During the acetal cyclization a 84% enantiomeric excess is obtained in both diastereoisomeric series (cis-trans and trans-trans) meanwhile in the imine cyclization we observed a 65% enantiomeric excess in the trans-trans series but only a 35% in the cis-trans series, the optical purity of C-5 being 52% in our case and 84% in the acetal case.

A more detailed discussion of the origin of this chiral recognition as well as some additional results will be reported shortly in a full paper.

References

(1) *W.S. JOHNSON, Angew. Chem. Int. Ed. 1976, 15, 9 and references cited.*

(2) *W.S. JOHNSON, C.A. HARBERT, B.E. RATCLIFFE and R.E. STIPANOVIC, J. Am. Chem. Soc. 1968, 90, 5279 and 1976, 98, 6188.*

(3) *G. DEMAILLY and G. SOLLADIE, Tetrahedron Letters 1977, 1885.*

(4) *The endocyclic double bond in compounds 3a to 6a was located between carbons 2 and 3 by analogy with the results of Johnson (2) who has shown that less than 1% of the* Δ^{1-2} *isomer was present in the cyclization products from acetal 2.*

(5) *The absence in this mixture of isomers having an exocyclic double bond was confirmed by* ^{13}C *off-resonance NMR showing 4 doublets between 119 and 121,2 ppm corresponding to vinylic carbons bearing only one hydrogen atom.*

(6) *The position of NMR signal for an angular methyl group at C-9 in compounds having an axial substituent at C-5 is shifted downfield relative to the equatorial isomer as a result of 1,3-diaxial interactions |see R.F. Zurcher, Helv. Chim. Acta 46, 2054 (1963)|. In compounds 3b and 4b having an equatorial hydroxyether group the chemical shift of the angular methyl group is 0.80 ppm meanwhile in compounds 5b and 6b having an axial OR group this chemical shift is 0.92 ppm (2).*

(7) *a) A. HOREAU, Bull. Soc. Chim. 1964, 2673.*
b) R. WEIDMANN and A. HOREAU, Bull. Soc. Chim. Fr. 1967, 117.

(8) *Although this method was shown to present some exceptions in the case of primary amines (9) we have demonstrated by ORD in a very similar case (10) that the result was reliable.*

(9) *A. HOREAU in Stereochemistry, Vol.3, G. Thieme Publishers, Stuggart 1977.*

(10) *G. DEMAILLY and G. SOLLADIE, Bull. Soc. Chim. France, 1975, 2128.*

(11) *R.E. IRELAND, M.J. DAWSON, C.J. KOWALSKI, C.A. LIPINSKI, D.R. MARSHALL, J.W. WILEY and J. BORDNER, J. Org. Chem. 1975, 40, 973.*

(Received in France 9 May 1980)