Tetrahedron: Asymmetry Vol. 2, No. 12, pp. 1177-1180, 1991
Printed in Great Britain

0957-4166/91 $3.00+.00
Pergamon Press plc

Asymmetric Intramolecular Diels-Alder Reaction of a Sulphoximine-substituted Triene

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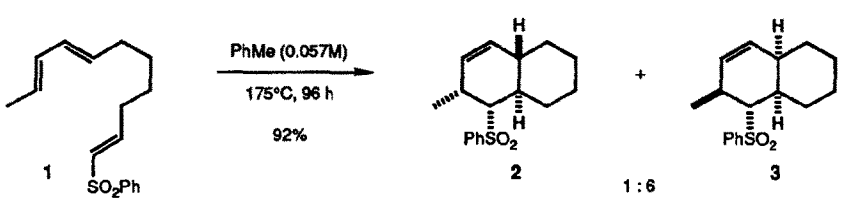
(*Received* 4 *October* 1991)

Key Words: Bicyclo[4.4.0]decene, intramolecular Diels-Alder, sulphoximine, triene

Abstract: The synthesis and thermally-induced intramolecular Diels-Alder (IMDA) reaction of $(S)_S$-(+)-*S*-[(1*E*,7*E*)-1,7,9-decatrienyl]-*S*-phenyl-*N*-(*p*-tolylsulphonyl)sulphoximine **4** is described. A model is proposed for the *cis*-selectivity of the cycloaddition based on previous results from the reactions of sulphonyl-substituted trienes. The stereochemistry of the major *cis*-fused cycloadduct is determined by single-crystal X-ray analysis of that obtained from reaction of racemic **4**.

Intramolecular Diels-Alder (IMDA) reactions are characterized by their usefulness for the assembly of bi- and polycyclic systems with high levels of regio- and stereocontrol.[1] Asymmetric IMDA reactions[2] offer opportunities for the synthesis of materials in which the absolute configuration of up to four stereocentres in the product is controlled by a single one in the enantiomerically pure triene substrate. We recently reported[3] the *cis*-selective IMDA reaction of (1*E*,7*E*,9*E*)-1-(phenylsulphonyl)-1,7,9-undecatriene **1**, which cyclized under thermal conditions to give a mixture of bicyclic products **2** and **3** in high yield (Scheme 1). We became

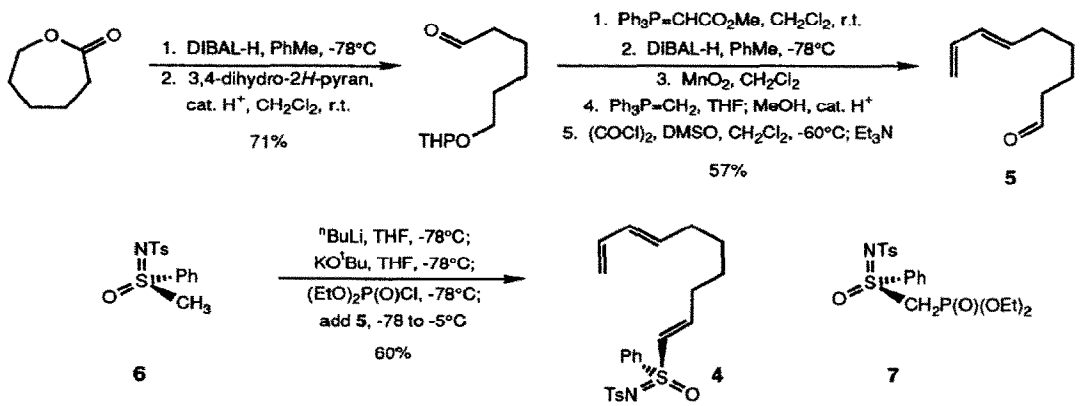


Scheme 1

interested in related IMDA reactions of trienes having dienophiles activated by electron-withdrawing groups possessing an asymmetric sulphur atom. Although vinylic sulphoxides have been reported[4] to undergo intermolecular Diels-Alder reactions with moderate to high diastereoselectivity, we felt that the elevated

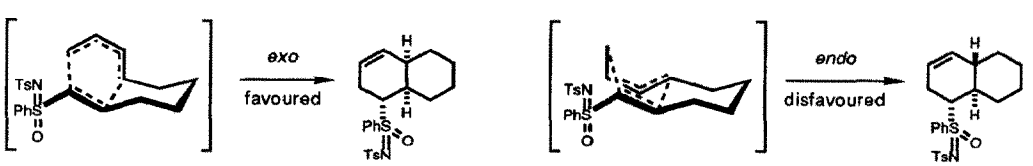
temperatures which were expected to be necessary for the intramolecular variant would cause undesired thermally-induced transformations[5] of the (arylsulphinyl)-substituted bicyclic products. Trienes substituted with a sulphoximine group[6] offered the prospects of (i) enhanced reactivity; (ii) increased *exo*-selectivity,[3] on account of the steric bulk associated with the sulphoximine group; (iii) access to both antipodes of IMDA products because of the ready availability of sulphoximine precursors in both enantiomeric series.

(+)-(S)$_S$-*S*-[(1*E*,7*E*)-1,7,9-Decatrienyl]-*S*-phenyl-*N*-(*p*-tolylsulphonyl)sulphoximine **4** was selected for our IMDA studies. It was anticipated that the absence of terminal substitution in the diene unit would enable the assembly of **4** with high geometric isomeric purity using Wittig reactions to establish the C7-C8 and C9-C10 double bonds. Triene **4** was prepared by modified Wadsworth-Emmons reaction[7] of key dienal **5**[8] with (+)-(S_S)-*S*-methyl-*S*-phenyl-*N*-(*p*-tolylsulphonyl)sulphoximine **6**.[9] In this efficient one-pot process the anion of the requisite sulphoximine-substituted phosphonate **7** was generated *in situ* prior to the addition of **5**. Triene **4** was obtained as a 94:6 mixture of *E* and *Z* isomers at the newly-formed double bond. Aldehyde **5** was prepared in high overall yield from ε-caprolactone. The synthetic route to **4** is depicted in Scheme 2.



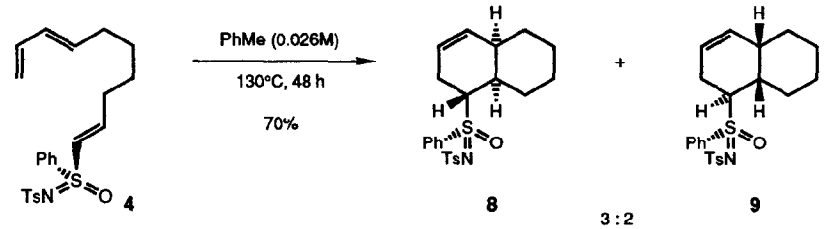
Scheme 2

Thermolysis of **4** was effected by heating a rigorously dried and degassed toluene solution in a resealable Carius tube under argon. ^{1}H Nmr analysis (300 MHz) of the crude product indicated the presence of two major cycloadducts in a 3:2 ratio. Strikingly, the the alkene protons appeared as slightly broadened singlets in the spectra of both components present in the crude mixture. By analogy with the IMDA reactions of sulphonyl-substituted trienes,[3] we initially assigned *cis*-ring junction stereochemistry to the cycloadducts. This is thought to be a consequence of unfavourable steric interactions between the diene and the bulky, sp^3-hybridized sulphur atom in the *endo* transition state for formation of the *trans*-fused product (Scheme 3).

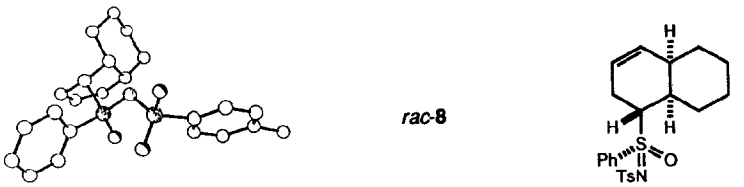


Scheme 3

Chromatography of the crude IMDA product gave a 3:2 mixture of the two major cycloadducts as a viscous, colourless oil in 70% yield from triene **4**. Trituration with toluene-petroleum ether gave the major isomer **8** as a crystalline solid in 29% yield from **4** (Scheme 4). The structure of **8** was assigned by X-ray crystallography. Thus, **8** exhibited ^{1}H nmr characteristics[11] identical with those of the major product of IMDA reaction of racemic **4**. The structure of *rac*-**8** is shown in the Figure.[12]



Scheme 4



Figure

In summary, we have demonstrated that the enantiomerically pure sulphoximine-substituted triene **4** undergoes asymmetric IMDA reaction to give a mixture of sulphoximine-substituted bicyclo[4.4.0]decenes **8** and **9** in 20% diastereomeric excess. We are currently investigating IMDA reactions of sulphoximine-substituted trienes bearing more electron-withdrawing *N*-substituents in an attempt to couple enhanced reactivity with increased diastereoselectivity. We are also looking at triene substrates possessing cyclic, more conformationally restricted sulphoximine groups as dienophile activators.

Acknowledgements

We thank Rhône-Poulenc Agriculture Limited for financial support of this research.

References and notes

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12. We thank Dr D. J. Williams and Ms A. M. Z. Slawin (Imperial College) for this determination.