Palladium-catalysed Intramolecular Asymmetric Ene Reactions of Chiral Allylic Sulphones *via* Chiral Allylic Sulphinate–Sulphone Rearrangements

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The chirality of the sulphinate sulphur atoms has been transferred to the carbon centres in chiral allylic sulphinate–sulphone rearrangements, followed by palladium-catalysed intramolecular ene reactions of the chiral allylic sulphones obtained, with high stereospecificity.

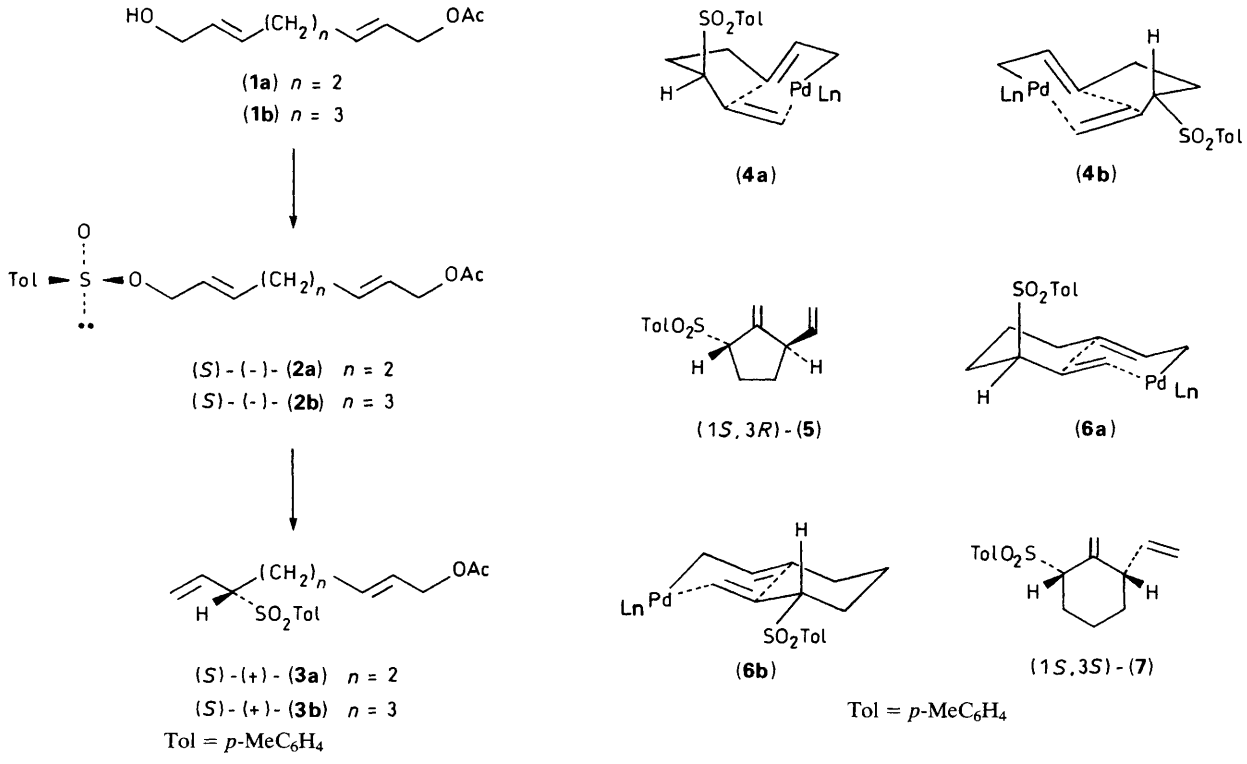
Ene reactions have received much attention as useful methods for construction of carbon–carbon bonds,[1] and intramolecular ene reactions have potential for stereoselective formation of cyclic frameworks. Hitherto ene reactions have usually been executed by means of thermolysis or acid catalysis; however, formal ene-type reactions could be achieved under palladium-catalysed conditions.[2]

We report here palladium-catalysed asymmetric ene reactions of chiral allylic sulphones obtained from optically active allylic sulphinates *via* thermal rearrangements.

Table 1. Stereochemical studies on the palladium-catalysed asymmetric ene reactions of (*S*)-(**3a,b**).[a]

(*S*)-(**3**) E.e.[b]/%	Catalyst	Reaction time/h	Product Yield/%	$[\alpha]_D^{20}$ (EtOH)	E.e./%[b]	Stereospecificity[c] in (**3**) → (**5**), (**7**)/%
(**3a**) 54	$Pd(dba)_2$	4	(**5**) 64	+42.6°	49	91
(**3a**) 44	$Pd(PPh_3)_4$	6	(**5**) 11	+14.6°	17	39
(**3b**) 44	$Pd(dba)_2$	4	(**7**) 56	+30.4°	31	70
(**3b**) 41	$Pd(PPh_3)_4$	6	(**7**) 18	+16.9°	17	41

[a] The reactions were carried out in acetic acid at 80 °C in the presence of $Pd(dba)_2$ (0.07 equiv.) or $Pd(PPh_3)_4$ (0.15 equiv.) with PPh_3 (0.66 equiv.). [b] The enantiomeric excess [e.e. (%)] was calculated by NMR analysis with the shift reagent [$Eu(hfc)_3$]. [c] Calculated based on e.e. (%) of the starting allylic sulphones (**3a,b**) and the products (**5**) and (**7**).



Scheme 1

Chiral sulphinates (*S*)-(−)-(**2a,b**) were prepared by boron trifluoride–ether-catalysed esterification of allylic alcohols (**1a,b**) with (*S*)-(+)-*N*,*N*-diethyltoluene-*p*-sulphinamide[3] (Scheme 1).

The stereochemistry of the sulphur atoms in the chiral sulphinates (**2a,b**) obtained was determined by conversion of the sulphinates (**2a,b**) into (*R*)-(+)-phenyl *p*-tolyl sulphoxide of known absolute configuration.[4]

Heating the sulphinates (*S*)-(−)-(**2a,b**) in *N*,*N*-dimethylformamide at 100 °C for 12 h gave chiral allylic sulphones (*S*)-(+)-(**3a,b**) in 76 and 68% yield with 91 and 80% enantiomeric excess (e.e.), respectively. The e.e. was determined by NMR spectral analysis of the sulphones produced with a shift reagent, tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorato]europium(III), [$Eu(hfc)_3$]. The absolute configuration of the allylic sulphones (**3a,b**) was assigned based on the mechanistic pathway for the rearrangement reported by us previously.[4]

Upon treatment of (*S*)-(+)-(**3a**) with bis(benzylideneacetone)palladium, [$Pd(dba)_2$], (0.07 equiv.) in acetic acid at 80 °C for 4 h, the allylic sulphone (**3a**) underwent a smooth intramolecular ene reaction to produce (1*S*,3*R*)-(+)-(**5**)[2] in 64% yield with 91% stereospecificity.

The same palladium-catalysed reaction of (*S*)-(+)-(**3b**) with $Pd(dba)_2$ under the same conditions gave (1*S*,3*S*)-(**7**)[2] in 56% yield with 70% stereospecificity. The above ene reactions with $Pd(dba)_2$ were more stereospecific than those with tetrakis(triphenylphosphine)palladium, [$Pd(PPh_3)_4$], which showed much lower stereospecificity (39 and 41%) in both cases. The products gave satisfactory IR, NMR, and mass spectral data. The results are summarized in Table 1.

The stereochemical pathway for this asymmetric induction could be rationalised in the following way. In the palladium-catalysed ene reaction of (*S*)-(**3a**), the more stable *cis* five–six-membered transition state (**4b**), possessing a tosyl substituent with less crowded *trans* orientation to the fused ring, would be formed to yield (1*S*,3*R*)-(**5**). Similarly, the ene reaction of (*S*)-(**3b**) proceeds *via* the more stable *trans*

six–six-membered transition state (**6b**) with an equatorial tosyl group to furnish (1*S*,3*S*)-(**7**). This is the first successful example of palladium-catalysed intramolecular asymmetric ene reactions of chiral allylic sulphones.

Other enantiomers of (**5**) and (**7**) could be obtained readily by the same reaction sequence employing the other stereoisomers of allylic sulphinates in the thermal rearrangement stages. Therefore, the present method provides a useful and convenient strategy for enantioselective construction of cyclic compounds, with the assistance of the chirality of the sulphinates.

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