Asymmetric Synthesis in Carbon-Carbon Bond Forming Reactions of a-Diazoketones catalysed by Homochiral Rhodium (11) Carboxylates

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Partial asymmetric synthesis has been observed in intramolecular **C-H** insertion, aromatic cycloaddition, and cyclopropanation reactions of α -diazoketones catalysed by homochiral rhodium(ii) mandelate and rhodium(ii) carboxylates derived from L-proline.

 $Rhodium(II)$ carboxylates are very efficient catalysts for the decomposition of α -diazocarbonyl compounds and their use has largely replaced copper-based catalysts in many characteristic reactions such as C-H insertion, cyclopropanation, aromatic cycloaddition, and electrophilic aromatic substitution.¹ Recently we added rhodium(II) mandelate to the range of useful, catalytically active rhodium(II) salts.² The introduction of rhodium(I1) mandelate for diazoketone decomposition raises the additional interesting prospect of asymmetric catalysis through its use in homochiral form. Although some success has been achieved with chiral copper catalysts for intermolecular cyclopropanation,3 they are not amenable to C-H insertion or aromatic cycloaddition reactions. We now report preliminary results of the first use of homochiral rhodium(II) catalysts in carbon-carbon bond forming reactions of α -diazocarbonyl precursors.

Three typical intramolecular diazocarbonyl reactions were chosen, *viz.* aromatic cycloaddition, C-H insertion, and alkene cyclopropanation. In addition to rhodium (II) (S)-mandelate **(l),4** two new carboxylates **(2)** and **(3)** were prepared by treating N-benzenesulphonyl-L-proline and N-l-napthalenesulphonyl-L-proline, respectively, with $Na_4Rh_2(CO_3)_4$.

Asymmetric synthesis in an aromatic cycloaddition reaction was probed with reference to the synthesis of trans-l-methylbicyclo[5.3 .O.]decan-2-one *(5) via* cyclisation of diazoketone **(6)** to bicyclic trienone **(7),** a reaction already known to be catalysed efficiently by rhodium (II) mandelate. Although some enantioselection was observed with rhodium(II) *(S)*mandelate, the extent (25%) was rather less than that obtained with proline carboxylate **(3).** Exposure of diazoketone **(6)** to catalyst **(3)** in hot dichloromethane furnished the optically active trienone **(7)** *(ca.* 80%) which did not respond well to NMR chiral shift reagents. However, reduction of **(7)** with lithium tri-t-butoxyaluminohydride in ether furnished alcohol **(8)**, $[\alpha]_D^{20}$ –9.44° (8.81, CH₂Cl₂), as a 3 : 1 mixture of epimers which was amenable to NMR analysis. The preponderant epimer was presumed to be that with the methyl and hydroxy group *cis* to each other on the basis of steric control of the direction of hydride addition. The epimers were not separated as such, but their IH NMR signals were clearly identifiable in the presence of $Eu(tc)_3$ [tris(trifluoroacetyl $camphorato)$ europium (u)], which produced a complete separation of the epimeric methyl groups and further resolution of the enantiomers of the *cis* isomer, indicating an

enantiomeric excess (e.e.) of 33%. Hydrogenation of **(7)** over palladium on carbon afforded **trans-1-methylbicyclo[5.3.0]** decan-2-one (5)⁵ (93%), $[\alpha]_D^{20}$ + 18.73° (2.59, CH₂Cl₂), also with 33% e.e. This short sequence represents an efficient partial asymmetric synthesis of this bicyclic ketone from a readily accessible precursor.

The reaction shown in equation (1) was chosen as an example of intramolecular C-H insertion of a ketocarbenoid for which rhodium (II) acetate was known to be catalytically active.6 For asymmetric synthesis, the rhodium salt of **N-benzenesulphonyl-L-proline (2)** proved to be the most

efficient, cyclising **(9)** in dichloromethane to a mixture of the *cis-* and trans-isomers of **(10)** in >90% yield. Dissolution of the isomer mixture in aqueous sodium hydroxide followed by acidification with ammonium chloride gave trans-(10) exclusively, $\lbrack \alpha \rbrack_{D}^{20}$ –19.1° (20.8, CH₂Cl₂). Recrystallisation of trans-(10) from ether removed racemic material as the less soluble fraction, thus enriching the enantiomer in the filtrate to $\lceil \alpha \rceil_D^{20} - 49.9^{\circ}$ (7.1, CH₂Cl₂). Desulphurisation of the latter with aluminium amalgam furnished the known (S) - $(-)$ -3methylcyclopentanone7 in **30%** e.e. Thus the e.e. achieved prior to enrichment by crystallisation was ca. 12%. Interestingly, the e.e. of *trans*- (10) could be further enriched by sodium borohydride reduction to a single crystalline alcohol (11), m.p. 82 -83 °C. Recrystallisation of (11) raised its e.e. to 60% as measured from $Eu(tfc)_{3}$ -resolved ¹H NMR spectra.

To complete this preliminary study of asymmetric synthesis in C-C bond forming reactions with homochiral rhodium catalysts, we examined the intramolecular cyclopropanation reaction shown in equation (2), a process also known to be amenable to rhodium (II) acetate catalysis.⁶ However, although rhodium(\mathbf{u}) (S)-mandelate brought about the conversion of (12) into **(13)** in 97% yield, the highest e.e. observed was ca. 12%. Clearly, catalyst design will be an important consideration in optimising these asymmetric reactions of α -diazoketone.

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