Acyclic Stereocontrol through the Metalla-Claisen rearrangement. Part II

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Abstract The metalla-Claisen rearrangement reported here, leads to 1,1-dimetallic compounds where three asymmetric centers are obtained with good diastereoselection

The development of new methodologies for achieving stereocontrol in the construction of acyclic systems is an important challenge in current synthesis¹ In this regard, the regio and stereochemically reliable Claisen rearrangement² has proven invaluable

However, Claisen or oxy-Cope rearrangements which transfer the asymmetry of a remote chiral center to the prochiral termini of the starting dienic system have been little investigated³, although they represent a fast access to linear systems bearing three contiguous asymmetric centers, in so far as the starting chiral diene is easily accessible. Thus, the Ireland-Claisen rearrangement of a β -hydroxy ester proceeds with excellent diastereoface selectivity (C α , C β stereocontrol), and moderate chair / boat selectivity (C α , C β stereocontrol)^{3e,3f}



In the preceding paper, we have reported⁴ that the metalla-Claisen rearrangement of an intermediate derived from (Z)- γ - lithic vinylic ethers and allyl zinc bromide affords the corresponding 1,1-dimetallic species with a very high diastereoselectivity





We now describe that this simple methodology can be extended to the elaboration of three contiguous asymetric centers (Z)- γ -10do allylic ethers are lithiated via metal halogen exchange Transmetallation with crotyl zinc bromide, leads to the intermediate crotyl vinyl zinc 3





Thus, 3 undergoes a [3,3] signatropic rearrangement to give the 1,1-dimetallic species 4 which is hydrolysed, to the ethylenic ether 5 The stereochemistry of 5 has been established unambiguously by the iodoalkoxylation of 6^5 As previously described, the dimetallic compound 4 reacts with organic substrates leading to useful transformations⁶, for example, addition of 1 eq of benzaldehyde furnishes after hydrolysis the 1,5-diene 6 in good yield and high stereomeric purity. In a similar fashion, treatment of 4 with D₃O⁺/D₂O gives the corresponding 1,1-dideuterated alkene 7 (100% deuteration). Subsequent reaction of the dimetallic reagent with one equivalent of isopropanol and one equivalent of iodine gives the unsaturated iodide 8, of excellent purity





The stereochemical relationships between all substituents of 6 was ascertained by transforming it into the tetrahydrofuran ring 9, by electrophilic cyclization of the $\delta_{,e}$ -unsaturated ether⁵ The Nuclear Overhauser Effect on this tetrasubstituted tetrahydrofuran clearly shows that all substituents are located on the same face¹¹





The stereochemical outcome implies that the crotyl moiety displays a pseudo axial methyl group in a chairlike transition state (see scheme 2) This puzzling result is in agreement with Oppolzer results⁷ concerning *magnesia*-ene reactions in these latter rearrangements, the Z isomer of crotyl-magnesium bromide is largely favoured over the E one⁸ (although NMR studies show a 60/40 ratio of these two Grignards)⁹

In conclusion, as far as the metalla-Claisen rearrangements reported here can be compared with the classical Claisen rearrangement, the diastereoselectivity obtained over three contiguous centers is much larger, and leads to (anti 3,4), (syn 4,5) 3,4-dimethyl-5 terbutoxy-1-alkenes, which prior to hydrolysis, behave as gem bismetallic reagents

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