Stereocontrolled Functionalization of Acyclic Molybdenum-η^3-Allyl Complexes: a New Approach to the Stereoselective Synthesis of 1,3-Diols

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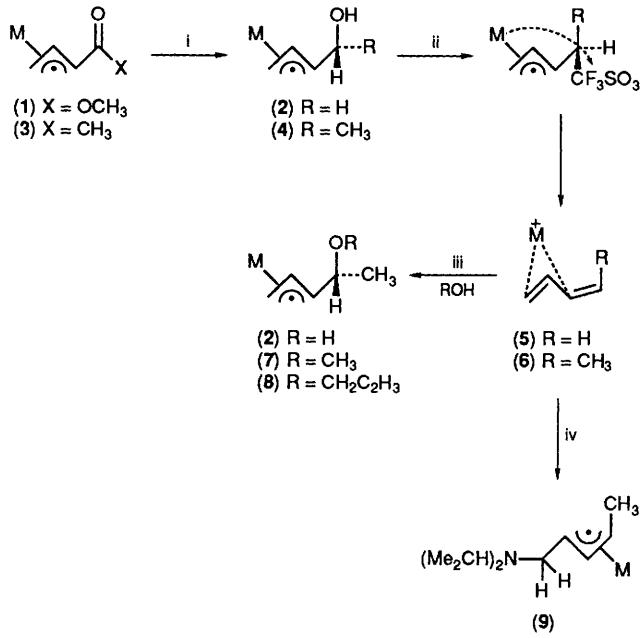
Functionalization of $[CpMo(CO)_2(\eta^3\text{-}syn\text{-}1\text{-}C_3H_4COCH_3)]$ proceeds in a highly stereospecific manner; the Mo-η^3-allyl unit is effective in directing asymmetric carbon induction in the course of *s-trans*-η^4-*cis*-pentadiene formation, aldol condensation and asymmetric 1,3-diol synthesis.

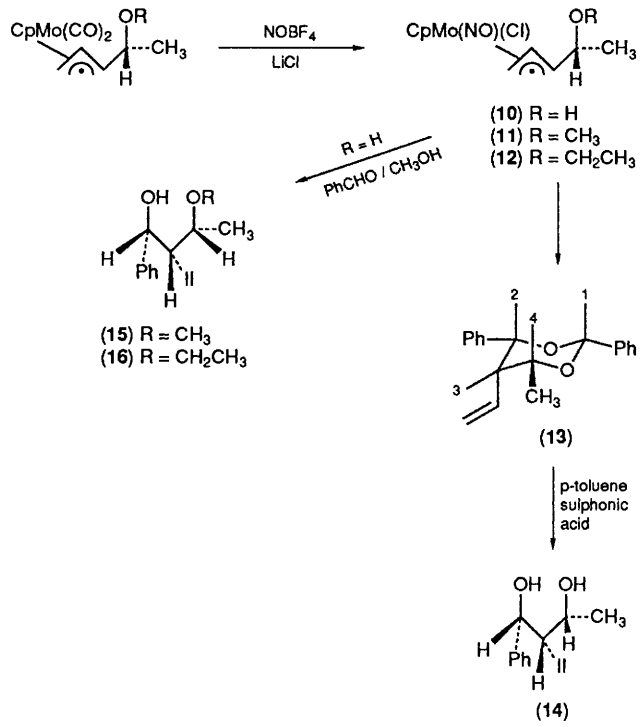
The control of stereochemistry during C–C bond formation is a central issue in modern synthetic chemistry. The use of a transition-metal moiety as a stereodirecting template has proven effective in the construction of subunits of natural products particularly in cyclic systems.[1,2] With an aim to achieve a highly stereocontrolled synthesis of complex acyclic molecules,[3,4] we have studied the stereochemistry of the functionalization of a ketone group adjacent to an asymmetric Mo-η^3-allyl fragment. We now report on the reaction of $[CpMo(CO)_2(syn\text{-}\eta^3\text{-}1\text{-}C_3H_4COCH_3)]$ which allows stereoselective synthesis of 1,3-diol and related 1,3-difunctional homoallylic alcohol. The acyclic 1,3-diol is a basic skeleton in natural product synthesis such as polyoxo ionophores, macrolides, and ansamycins and its asymmetric induction has been a subject of considerable interest.[5]

Treatment of (**1**) with DIBAL-H (2 equiv.) in CH_2Cl_2 at −78 °C afforded (**2**) in *ca.* 52% yield. The related alcohol (**4**) was obtained as a single isomer from reduction of (**3**) with $NaBH_4$ in CH_3OH at 23 °C. The *RR(SS)* configuration is assignable assuming that hydride adds to the carbonyl *trans* to the $CpMo(CO)_2$ fragment.† Treatment of (**2**) and (**4**) with one equiv. of $(CF_3SO_2)_2O$ in ether at −40 °C immediately produced an air-stable orange precipitate of the *s-trans*-η^4-diene cations[6] (**5**) and (**6**) of which the elemental analyses were satisfactory. Compound (**5**) has been characterized by a low-temperature NMR spectrum ($[^2H_6]$ acetone, −60 °C)

† Molecular structure of (**3**) has been determined by an *X*-ray diffraction study. The crystals belong to the triclinic system, space group, $P\bar{1}$, a = 7.0395(1) Å, b = 7.891(3) Å, c = 11.716(8) Å, α = 98.67(4)°, β = 92.50(4)°, γ = 112.93(3)°, V = 588.8(5) Å, Z = 2. Diffraction data were collected on an Enraf–Nonius CAD4 diffractometer using Mo-K_α radiation. A total of 2259 reflections were collected. Of the 2076 unique reflections, 2006 were considered observed having $I > 2\sigma(I)$. The position of the Mo atom was taken from a Patterson Map. The remainder of the non-hydrogen atoms were located in differences Fourier maps. Final R = 0.024 and R_w = 0.029. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.



Scheme 1. M=CpMO(CO)$_2$ i, X=OCH$_3$, DIBAL-H, CH_2Cl_2 (−78 °C), X=CH$_3$, NaBH$_4$/CH$_3$OH; ii, $(CF_3SO_2)_2O$, ether (−78 °C); iii, ROH = H_2O, CH_3OH, $C_2H_3CH_2OH$, ether (−46 °C); iv, $(Me_2CH)_2NH$, ether (−40 °C).



Scheme 2

which shows six inequivalent butadiene proton resonances within δ 4.00—5.00 ppm and four butadiene carbon resonances at δ 66.1, 67.1, 84.9, and 96.2 ppm. Attempts to obtain NMR spectra of (**6**) encountered difficulties because of its facile conversion to the more stable *s-cis*-η^4-pentadiene.[7]‡ The solid form of (**6**) showed remarkable reactivity in ether at −40 °C toward H_2O, CH_3OH and allyl alcohol and respectively yielded (**2**), (**7**), and (**8**) in *ca.* 52—68% yields. Treatment of (**6**) with $(Me_2CH)_2NH$ gave (**9**) in 51% yield. Compounds (**7**) and (**8**) retained the same configuration as that of (**4**) as hydrolysis of (**6**) regenerated (**4**). The formation of (**4**), (**7—9**) requires that (**6**) adopts a *s-trans*-η^4-*cis*-pentadiene configuration (Scheme 1). The stereospecific yield of (**6**) from (**4**) implies an intramolecular S_N2 substitution[8] during the ionization process. In this manner, $CpMo(CO)_2$ acts as a base to displace $CF_3SO_3^-$ in an opposite direction, and the resulting *s-trans*-diene is subsequently stabilized by the $CpMo(CO)_2$ fragment.

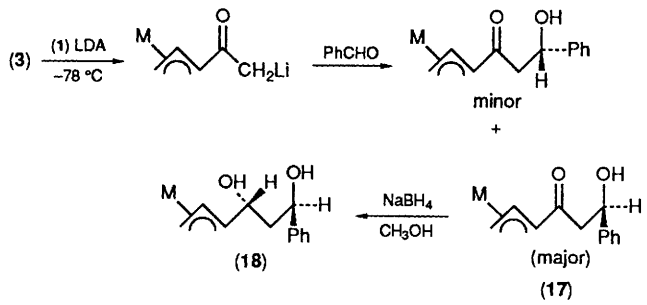
The availability of (**2**) and (**7–8**) can be utilized[4] for asymmetric synthesis of acyclic 1,3-diol and related analogues which contain three chiral carbons (Scheme 2). In a typical experiment, the dicarbonyl complexes were treated with $NOBF_4$ in CH_3CN. Further addition of LiCl to the NO-salt in acetone gave the chlorides (**10–12**) as air-stable complexes. Interestingly only one single diastereoisomer was observed for these chlorides in the ^{1}H NMR limit even though the molecules contain three chiral centres. Stirring of (**10**) with 2.5 equiv. of benzaldehyde in CH_2Cl_2 in the presence of CH_3OH, for a period of 2 days, stereospecifically produced the acetal (**13**) in 52% yield. The configuration of (**13**) was determined by ^{1}H NMR spectra and a NOE experiment.§ Hydrolysis of the acetal by *p*-$CH_3C_6H_4SO_3H$ gave 1,3-diol (**14**) in 60% yield. Similarly, stirring of (**11**) and (**12**) with benzaldehyde and CH_3OH in CH_2Cl_2, for a period of 2 days gave (**15**) and (**16**) as one single diastereoisomer in *ca.* 51—52% yield.

Of particular interest, the asymmetric [$CpMo(CO)_2$(η^3-1-C_3H_4R)] unit of (**3**) exhibits a pronounced effect in asymmetric carbon induction in aldol condensation. Treatment of (**1**) with LDA in THF at −78 °C generated the enolate which reacted with benzaldehyde to give a pair of diastereoisomers (**17**) in 87 : 13 ratio. The major isomer can be obtained in pure form after fractional recrystallization from ether. An *X*-ray diffraction study¶ revealed that the molecule adopts the *RR(SS)*-configuration. Reduction of (**17**) with $NaBH_4$ in CH_3OH gave 1,3-diol (**18**) as a single diastereoisomer (**18**) (81%). Following Scheme 2, this 1,3-diol (**18**) was converted to its chloride derivative (**19**) to give a single diastereoisomer (51% yield). Similarly stirring of (**19**) with benzaldehyde and CH_3OH stereoselectively produced the acetal (**20**) in 56% yield. Hydrolysis of the acetal by *p*-$CH_3C_6H_4SO_3H$ gave 1,3,5-triol(**21**) (53% yield).

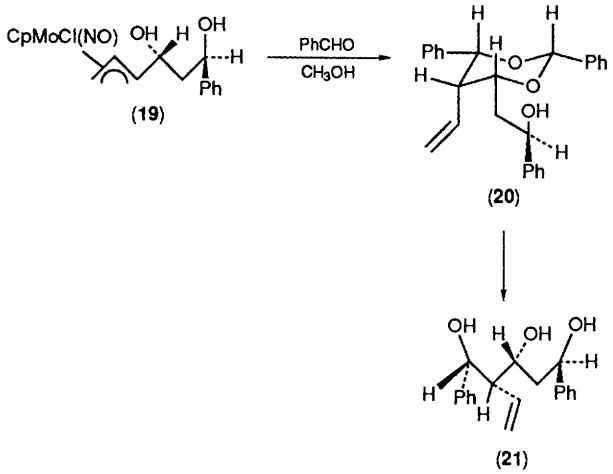
‡ The ^{1}H NMR spectra of (**6**) freshly dissolved in [$^2H_6$] acetone at −60 °C exhibited an ill-defined broad spectrum which nevertheless at −40 °C showed a well-resolved spectrum assignable to the *s-cis*-η^4-pentadiene containing both *anti*- and *syn*-methyl isomers. The two isomers are chemically exchangeable in a mechanism in which both *exo–endo* isomerization and butadiene-flipping processes are operative.[7]

§ In an NOE experiment, irradiation of the H^4 proton results in 6.2 and 3.2% increase in intensities of the H^1 and H^2 protons respectively. Moreover, the magnitudes of J_{23} 2.3 Hz and J_{34} 2.1 Hz are consistent with axial–equatorial coupling pattern.

¶ Molecular structure of the major isomer of (**17**) has been determined by an *X*-ray diffraction study. The crystals belong to the monoclinic system, space group $P2_1/C$, a = 14.901(7) Å, b = 8.611(4) Å, c = 13.830(6) Å, β = 104.57(3) °. Diffraction data were collected on a Nicolet R3m/V diffractometer using Mo–K_α radiation. A total of 2972 reflections were collected. Of the 2623 unique reflections, 1215 were considered observed having $I>3\sigma(I)$. The position of the Mo atom was taken from a Patterson Map. The remainder of the non-hydrogen atoms were located in differences Fourier maps. Final R = 0.035, R_w = 0.032. Supplementary crystallographic data have been deposited as for structure (**3**).†



Scheme 3



In summary, we have shown that functionalization of (**3**) proceeds in a highly stereospecific manner. The Mo-η^3-allyl unit is effective in directing asymmetric carbon induction, particularly in the course of *s-trans*-η^4-*cis* pentadiene formation, aldol condensation and asymmetric 1,3-diol synthesis. For extension of this chemistry, we are attempting to separate the racemic forms of (**3**) to achieve enantioselective synthesis of 1,3-diol.

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