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GENERATION AND ALDOL REACTION OF ENOLATE ANION ADJACENT TO A η^3-ALLYL-Mo(CO)$_2$Cp MOIETY. A NEW APPROACH TO THE STEREOSELECTIVE SYNTHESIS OF 1,3,5-TRIOL AND 2-VINYL-3-HYDROXYL-TETRAHYDROFURAN.

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Summary: The enolate of CpMo(CO)$_2$(syn-η^3-1-$C_3H_4COCH_3$) generated with lithium diisopropylamide in THF undergoes diastereoselective aldol reaction with benzaldehyde; the alcohol thus formed has been utilized for stereoselective synthesis of 1.5-diphenyl-2-vinyl-pentan-1,3,5-triol and 2-vinyl-3-hydroxyl-5-phenyl-tetrahydrofuran.

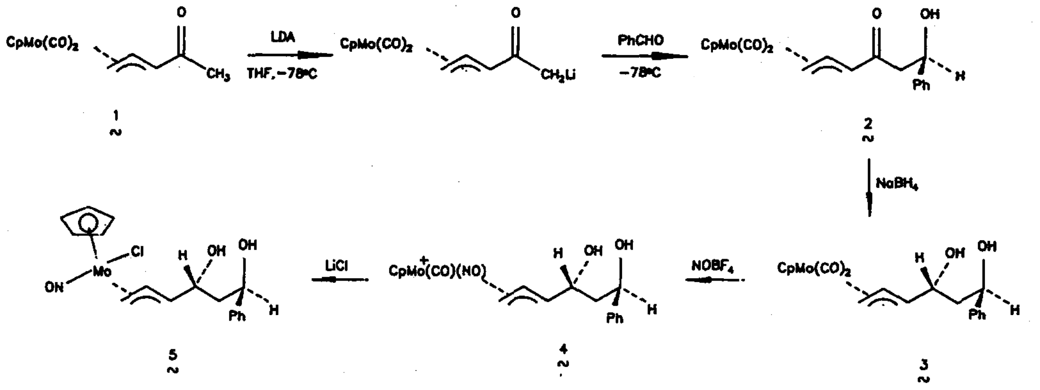
The control of stereochemistry during C-C bond formation is a central issue in modern synthetic chemistry. The use of a transition-metal moiety as a stereodirecting template has proven effective in the field of asymmetric organic synthesis, a prominent example is the iron-acyl enolate CpFe(CO)(PPh_3)($COCH_2Li$)[2] which has been utilized for stereoselective synthesis of lactones[2a]. lactams[2b], 1-hydroxyl-pyrrolizidin-3-one[2c] and threo-or erythro-α-methyl-β-hydroxyl-carboxylic acid[2d], Notably, because the acyl group of these iron complexes is chemically quite inert, their synthetic applications are somewhat limited.

Here we report generation and aldol chemistry of novel enolate CpMo(CO)$_2$(syn-η^3-1-$C_3H_4COCH_2Li$) and its synthetic approach for stereoselective synthesis of 1,3,5-triol and 2-vinyl-3-hydroxyl-tetrahydrofuran. The acyclic 1,3-diol is a basic skeleton of natural products such as polyoxo ionophores, macrolides and ansamycins, and its asymmetric synthesis has been a subject of considerable interest[3].

The complex CpMo(CO)$_2$(η^3-1-$C_3H_4COCH_3$)(1) was conveniently synthesized by reaction of CpMo(CO)$_3$Na with 5-chloro-3-penten-2-one (THF, 0°C) followed by decarbonylation with excess Me_3NO. The *syn* and *anti* isomers of 1 formed in a ratio of 6:1 are readily separable by silica-gel column chromatography. Deprotonation of the syn isomer of 1 with lithium diisopropylamide in THF at -78°C generated the enolate which upon treatment with benzaldehyde gave *exo*-2 [RR(SS):RS(SR)=88:12] exclusively. The pure RR form of 2 was obtained in 63% yield after a simple recrystallization from ether at -20°C. Its configuration has been clarified by an X-ray diffraction study[4]. An ORTEP drawing reveals that in this *exo* conformer, the allylic and ketone atoms are arranged in a sickle-shaped conformation. Reduction of 2 with $NaBH_4$ in CH_3OH/THF gave *exo-syn*-1,3-diol 3 (diastereomeric purity > 98%, 81% yield). The RRR(SSS) configuration is assignable to 3. ; presumably hydride adds to the ketone trans to the bulky CpMo(CO)$_2$ unit.

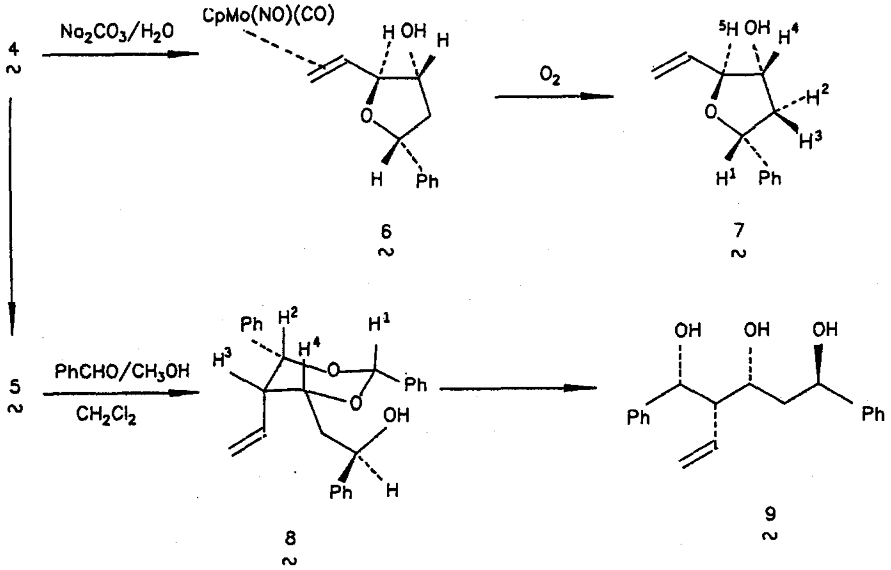
Allowing 3 to react with $NOBF_4$ in CH_3CN at 0°C produced the nitrosyl complex 4 in 71%. Only one isomer was detected which may have been either the exo or endo isomer[5]. According to the chemistry of related complexes[6], NO^+ replaces the trans carbonyl in the exo isomer and the cis carbonyl in the endo isomer relative to the CH-(OH)R substituent of 4. Adding LiCl to 4 in THF/acetone produced *exo*-5 in 56% yield. This chloride substitution proceeds via retention relative to stereochemistry of 4[6]. The exo-conformation is indicated by the magnitude of the geminal coupling constant J_{12}=1.8Hz[7,8].

Treatment of 4 with an aqueous Na_2CO_3 in ether at 0°C led to gradual dissolution of 4 and stereospecifica-



Scheme 1

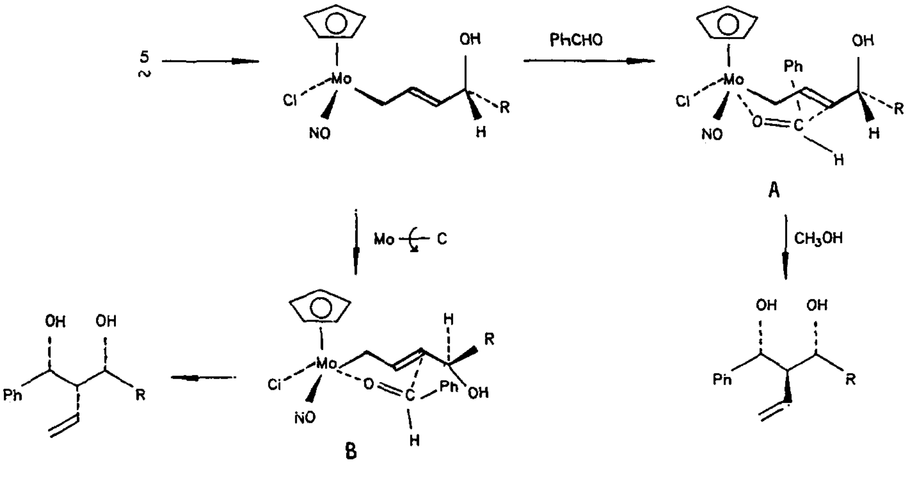
lly generated the tetrahydrofurans 6 and 7. 6 resulted from the intramolecular CHPhO⁻ addition at the C-3 allylic carbon opposite the metal fragment, and 7 was an air oxidation product of 6. Passing air through 6 in CH_2Cl_2 gave 7 in 73% yield. The specific proton positions on the ether ring of 7 were determined by a NOE experiment. The H^4 signal (δ 4.21) exerts an Overhauser enhancement of the H^1 and(CH_2=CH) signals whereas the H^5 signal is unaffected.



Scheme 2

Stirring of 5 with 2.5 equimolar amounts of benzaldehyde in CH_2Cl_2 in the presence of CH_3OH, during 2 days led to gradual deposition of precipitate. The acetal 8 was isolated in 52% yield from the CH_2Cl_2 phase. This metal decomposition proceeds in a highly stereospecific manner and no second acetal was found. For its structural elucidation we relied on ^{1}H-NMR spectroscopy. The magnitudes of the coupling constants J_{23}=2.3Hz and J_{34}=2.1Hz indicate axial-equatorial coupling. In a NOE experiment, the H^1 signal (δ5.97) exerts an Overhauser enhancement of the H^2 and H^4 signals ,whereas the *CH*(OH)PhCH$_2$ proton is unaffected. Hydrolysis of 8 with p-$CH_3C_6H_4SO_3H$ afforded 1,3,5-triol 9 in a single stereoisomer (51% yield).

It is of great interest to correlate the stereochemistry of 8 and 9 with that of 5. Based on Faller's concept[9], a mechanism is proposed in Scheme 3. In 5, the allyl carbon trans to NO dissociates to leave a vacant site for benzaldehyde. As a result of the interligand steric hindrance within the metal-coordination sphere after benzaldehyde becomes coordinated, two chair-like transition states are generated. The preferred aldehyde orientation is determined by decreased interaction with CpMo(NO)Cl fragment; thus the η^1-allyl adds to *re*-face of the aldehyde. The ultimate control of the diastereoselectivity is governed by the transition state B which places the bulky phenyl and CH(OH)R groups at the equatorial positions to minimize the interligand steric hindrance. In contrast, the insignificant role of state A is attributed to its axial phenyl which exerts increased steric interaction with the Cp group, and its addition product is thus not observed in the course of reaction.



Scheme 3

In conclusion, we have demonstrated stereoselective synthesis of 1,3,5-triol and 2-vinyl-3-hydroxyl-tetrahydrofuran derived from the Mo-η^3-allyl enolate. In synthetic applications, this enolate may have advantages over the iron acyl enolate in that its C=O group can be functionalized like a common ketone , and the Mo-η^3-allyl species thus formed can be decomplexed in a more versatile manner.

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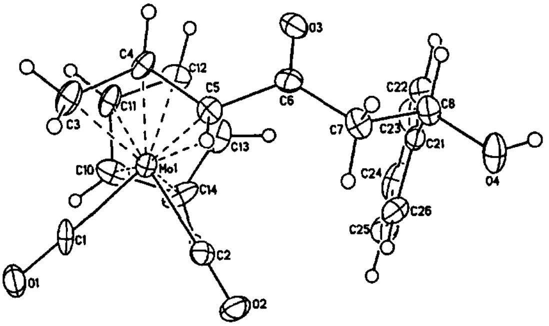
4.The crystals of *2* belong to the monoclinic system, space group P2$_1$/c, a=14.901(7)Å, b=8.611(4)Å, c=13.830(6) Å, β=104.57(3)° . Diffraction data were collected on a Nicolet R3m/V diffractometer using Mo-K$_\alpha$ radiation, final R=0.035 , Rw=0.032. *Final ORTEP drawing is given below.* Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited to the Cambridge Crystallographic Data Center.



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7.Spectroscopic data for 8: IR: ν (NO) 1648 cm^{-1}. ^{1}H NMR(400 MHz, CDCl$_3$) 1.97(complex,2H, CH$_2$), 2.33(dd, 1H, H^1, J=9.9, 1.8 Hz), 2.94(dd, 1H, C*H*(OH), J=6.8Hz, J=2.2 Hz), 2.98 (s, 1H, OH), 4.36(dd, 1H, H^2, J=6.0, 1.8Hz), 4.92(d, 1H, H^4, J=10.0 Hz), 5.04(dd, 1H, C*H*(OH)Ph), 5.81(s,5H,C$_5$H$_5$), 5.91(m, 1H, H^3, J=10.0, 9.9, 6.0 Hz).

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