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DIASTEREOSELECTIVE ALDOL REACTION OF $(\eta^6\text{-X-}C_6H_4COCH_3)Cr(CO)_2L$ COMPLEXES

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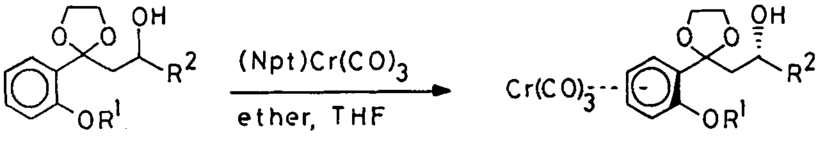
Summary; $(\eta^6\text{-X-}C_6H_4COCH_3)Cr(CO)_2L$ complexes are reacted with dialkylboryl trifluoromethanesulfonate and amine to give diastereoselective aldol condensation products after treatment with aldehydes.

One of the most fundamental carbon-carbon bond forming reactions is the aldol condensation between an enolate and an aldehyde. The various excellent methods have been explored for high stereoselectivity utilizing α-substituted chiral enolates,[1] while the aldol reaction of chiral enolates lacking an α-substituent is still a challenging problem for the achievement of high stereoselection.[2] Recently, transition metal-based aldol reaction[3] has become of interest with respect to the synthetic applications and mechanistic studies. We previously reported[4] that $Cr(CO)_3$ complexation of the compound **1** afforded predominantly one diastereomeric chromium complex **2**, an equivalent of the metal-complexed aldol (eq 1). We now disclose the direct stereoselective aldol condensation of (η^6-arene)chromium complexes, overcoming many disadvantages on the $Cr(CO)_3$ complexation method.

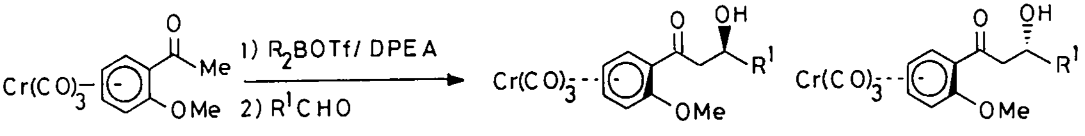


eq 1

1 **2**

After several attempts,[5] the reactions via boron enolates of the chromium complexes were found to afford satisfactory results as follows. The boron enolate generated from the complex **3**, dibutyl trifluoromethanesulfonate and diisopropylethylamine in ether at -78°C gave a mixture of easily separable diastereomers, S*S*-chromium complex **4** (R=Et) and S*R*-complex **5** (R=Et) in a ratio of 90:10 after treatment with propionaldehyde.

The stereochemistry of the major product **4** was determined by the comparison of the corresponding acetate complex with a stereo-defined authentic complex derived from the minor product of $Cr(CO)_3$ complexation reactions. These two type reactions (aldol and complexation reactions) give a different stereoisomer of the chromium complexes as the major product, and are conplementary each other. The use of other dialkylboryl reagents resulted in lower yield (Table I).



3 **4** **5**

Table I

entry	R_2BOTf	R^1CHO	**4** : **5**	yield (%)
1	$(n\text{-Bu})_2BOTf$	EtCHO	90 : 10	80
2	$(c\text{-pentyl})_2BOTf$	EtCHO	91 : 9	45
3	9-BBNOTf	EtCHO	92 : 8	35
4	$(n\text{-Bu})_2BOTf$	C_6H_5CHO	92 : 8	75
5	$(n\text{-Bu})_2BOTf$	Me_2CHO	95 : 5	81

The nature of substituent on the aromatic nucleus and the ligand of the chromium have a significant influence on the stereoselectivity of the aldol reaction. (*o*-Methylacetophenone)$Cr(CO)_2L$ gave low diastereoselection in the aldol reaction (Table II, entries 3,7) and, therefore, the alkoxy substituent at the ortho position is required for the high selectivity. Interestingly, the complexes wth mono phosphinedicarbonyl(*o*-methoxyacetophenone)chromium exhibited a slightly lower selectivity compared with the corresponding tricarbonyl complexes (entries 4,5,8), while 2,4-dimethoxy chromium complexes with phosphine ligand no longer show the diastereoselectivity (entries 6,10).

This aldol reaction of the chromium complexes can be applied to stereoselective synthesis of 1,5-acyclic systems in an optical active form. (S)-Tricarbonyl(*o*-methoxyacetophenone)chromium,[6,7] $[\alpha]_D$ +464°, 99.5%ee, gave the (S,R)-aldol condensation product **9** in 72% yield, along with stereoisomeric (S,S)-complex, $[\alpha]_D$ +262°, in 8% yield by the reaction of the corresponding boron enolate and E-crotonaldehyde. The complex **9** was easily converted into 1,5-syn dimethyl complex[8] **11** through 1,3-anti diacetoxy complex **10** by the stereoselective conversion of the benzylic oxygen to methyl[8,9] and the chirality transfer reaction in the allylic part (Scheme 1).

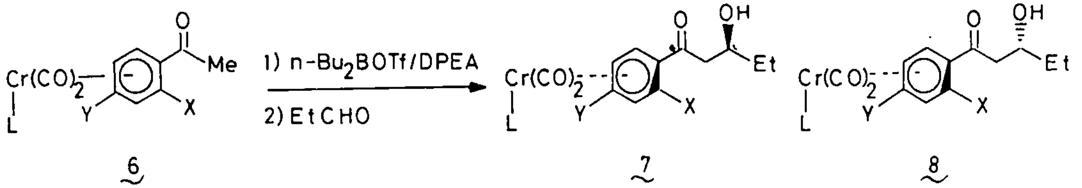
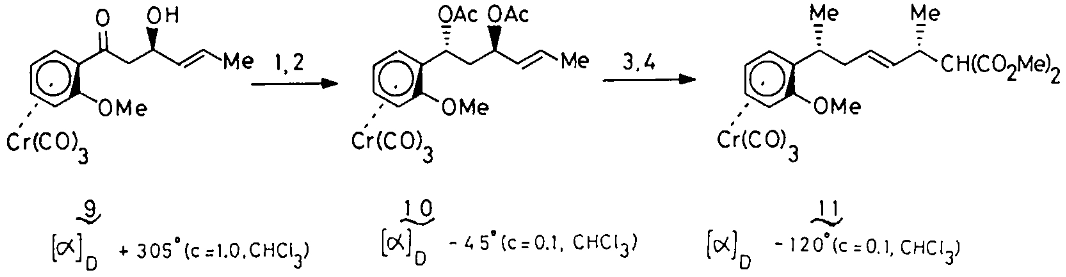


Table II

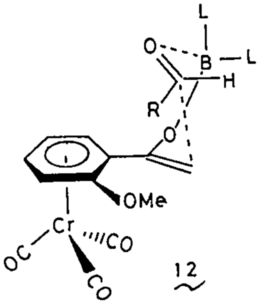
entry	L	X	Y	**7** : **8**	yield (%)
1	CO	OPr^i	H	85 : 15	75
2	CO	OMe	OMe	90 : 10	85
3	CO	Me	H	60 : 40	45
4	Ph$_3$P	OMe	H	88 : 12	50
5	(MeO)$_3$	OMe	H	86 : 14	60
6	Ph$_3$P	OMe	OMe	50 : 50	30
7	Ph$_3$P	Me	H	50 : 50	40
8	(PhO)$_3$P	OMe	H	88 : 12	85
9	(PhO)$_3$P	OPr^i	H	85 : 15	60
10	(PhO)$_3$P	OMe	OMe	50 : 50	80

Scheme 1



(1) $LiAlH_4$/ether (2) Ac_2O/pyr, 84% from **9** (3)$NaCH(CO_2Me)_2/[PdCl(C_3H_5)]_2$/dppe/THF, 99% (4) Me_3Al/CH_2Cl_2, 87%

The following two transition states would be assumed for the aldol condensation of the complex **3**. The anti-boron enolate would attack re-face of aldehyde through a cyclic twist boat transition state[2b] **12**, while the syn-enolate proceeds in si-face attack on the cyclic chair transition state **13**. It is not clear at the present time which conformation would be more preferable, and a further study along this line is underway.



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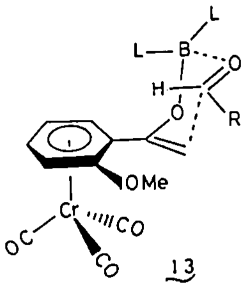

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5 The aldol reaction via lithium or the other metal enolates of (*o*-methoxyacetophenone)$Cr(CO)_2L$ (L=CO, PPh_3, $P(OPh)_3$, $P(OMe)_3$) gave no satisfactory results in both yield and selectivity.

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7 The optical purity was determined by HPLC with Daicel Chiralcel OD.

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