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LETTERS

## Diastereo- and regioselective reactions of $\pi$ -allyl molybdenum complexes with aldehydes

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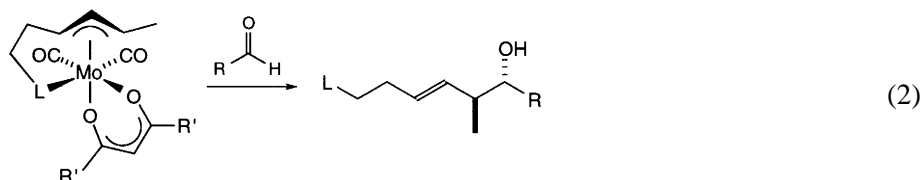
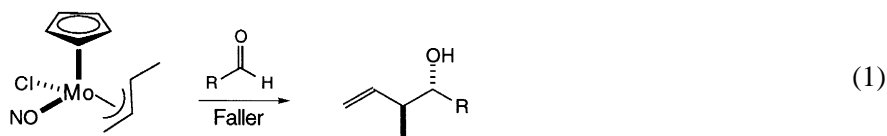
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### Abstract

Remote heteroatom coordination to molybdenum promotes unprecedented selectivity in aldehyde allylation using unsymmetrically substituted allylic metal complexes. © 2000 Elsevier Science Ltd. All rights reserved.

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Allylation of nucleophiles or electrophiles using both main group and transition metal complexes is an important and synthetically useful transformation that is applicable to the stereocontrolled synthesis of acyclic systems.<sup>1,2</sup> For example,  $\eta^3$ -allyl Pd(+2) complexes stand out as highly versatile intermediates for the effective allylation of nucleophiles.<sup>3</sup> On the other hand,  $\eta^1$ -allylstannanes and allylboranes have been found to be particularly useful in the nucleophilic allylation of aldehydes and ketones.<sup>4</sup> Faller has shown that aldehydes undergo condensation with monosubstituted  $\eta^3$ -allylmolybdenum<sup>5</sup> complexes to yield homoallylic alcohols with regio- and diastereocontrol (Eq. (1)).<sup>6–8</sup> As part of our continuing investigation into substrate directable reactions,<sup>9</sup> we investigated the effect of tethered amines and sulfides on the condensation of  $\eta^3$ -allylmolybdenum complexes with carbonyl compounds. We now report a high degree of selectivity in the reaction of aldehydes with both mono- and 1,3-disubstituted  $\eta^3$ -allylmolybdenum complexes (Eq. (2)).



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Molybdenum complexes **3–6** bearing tethered homoallylic amines and sulfides were synthesized by heating a solution of allylic acetates **1** or **2**, Mo(CO)<sub>6</sub> and the sodium salt of diethyl malonate, 2,4-pentanedione or 1,1,1-trifluoro-2,4-pentanedione in THF.<sup>10</sup> The complexes were air stable, prepared in one step compared to Faller's multistep procedure, and could be purified by silica gel chromatography. The structure of **3** was determined crystallographically.<sup>10</sup>

Table 1

Legend for complexes:

1 L=NMe <sub>2</sub>	3 L=NMe <sub>2</sub> , R''=R'=OEt	7 L=NMe <sub>2</sub> , R=Ph
2 L=SMe	4 L=NMe <sub>2</sub> , R', R''=Me, CF <sub>3</sub>	8 L=NMe <sub>2</sub> , R=CH <sub>2</sub> CH <sub>2</sub> Ph
	5 L=SMe, R''=R'=Me	9 L=SMe, R=Ph
	6 L=SMe, R''=R'=OEt	

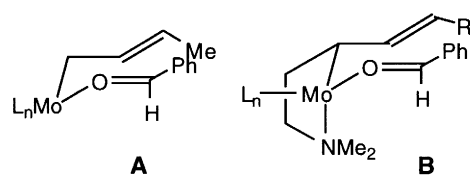
  

Entry	Molybdenum Complex	Aldehyde	Homoallylic alcohol	Yield (%) <sup>a</sup>
1	<b>3</b>	R=Ph	<b>7</b>	84
2	<b>3</b>	R=Ph	<b>7</b>	75 <sup>b</sup>
3	<b>3</b>	R=CH <sub>2</sub> CH <sub>2</sub> Ph	<b>8</b>	73
4	<b>4</b>	R=Ph	<sup>d</sup>	<sup>d</sup>
5	<b>5</b>	R=Ph	<b>9</b>	67 <sup>c</sup>
6	<b>6</b>	R=Ph	<sup>d</sup>	<sup>d</sup>

a) Isolated yield. b) Reaction heated in THF. c) 6:1 mixture of regioisomers  
d) Complex decomposed under reaction conditions.

Treatment of molybdenum complex **3** with benzaldehyde in CH<sub>2</sub>Cl<sub>2</sub> in the presence of MeOH for 48 h at ambient temperature yielded homoallylic alcohol **7** as a single regioisomer (Table 1). No other regioisomeric alcohols could be detected by <sup>1</sup>H NMR spectroscopy (500 MHz). In contrast to prior results<sup>6</sup> (Eq. (1)) where carbon–carbon bond formation occurred only at the more substituted terminus, with these examples, carbon–carbon bond formation occurred exclusively at the unsubstituted terminus. As demonstrated by the results in Table 1, both aliphatic and aromatic aldehydes underwent allylation efficiently and selectively. Heating a solution of complex **3** with benzaldehyde in THF in the presence of MeOH led to a slight decrease in yield, but shortened the reaction time to 24 h (Table 1, entry 2). Changes in the nature of the bidentate ligand had a significant effect on the efficacy of the aldehyde condensation. Substitution of the 2,4-pentanedionate ligand with 1,1,1-trifluoro-2,4-pentanedionate gave complex **4** (1:1 mixture of isomers due to different orientations of the fluoro-substituted pentanedionate ligand) which was completely unreactive toward benzaldehyde even upon heating. Unlike the reactions with amino complex **3**, which were very selective, reaction of sulfide complex **5** with benzaldehyde resulted in the formation of a 6:1 mixture of regioisomers (Table 1, entry 5). The sulfide complex **6** was relatively unstable compared to the corresponding 2,4-pentanedionate derivative **5**, and, while it could be isolated and characterized, it decomposed in situ before significant amounts of aldehyde allylation could be observed (Table 1, entry 6).

The explanation for the diastereoselectivity observed by Faller<sup>6</sup> (Eq. (1)) incorporates a π to σ allyl shift and coordination of the aldehyde to the metal followed by reaction via a chair-like conformation of a six-membered transition state (**A** in Scheme 1). Preferential formation of the less substituted molybdenum–carbon bond provides a rationale for the high regiochemical preference. Using an analogous mechanistic argument for the reactions of **3** and **5**, coordination of the heteroatom to the metal center dictates the formation of a secondary metal–carbon bond with the reaction now being driven to occur at the less substituted allylic terminus (**B** in Scheme 1, R=H).



Scheme 1.

Reaction of the 1,3-unsymmetrically disubstituted  $\pi$ -allyl molybdenum complexes **11** or **12** (prepared from the corresponding amino allylic acetate as described above) with aliphatic or aromatic aldehydes gave rise to the *anti* diastereomer in addition to small amounts of the corresponding regioisomer (Table 2). The examples in Table 2 are noteworthy because of the high levels of regioselective aldehyde allylation observed using unsymmetrically substituted allylic moieties, even when the groups at the allylic termini are similar in size. It is remarkable that complex **11**, which is a 1:1 mixture of isomers, reacts with high regio- and diastereoselectivity. Reaction of complex **12**, bearing a 2,4-pentanedionate chelating ligand rather than a malonate ligand, with benzaldehyde led to the expected homoallylic alcohol **14** in 60% yield, but the reaction required 72 h at ambient temperature. Complex **13** (1:1 mixture of isomers due to different orientations of the fluoro-substituted pentanedionate ligand), bearing the electron deficient 1,1,1-trifluoro-2,4-pentanedionate ligand, failed to react with aldehydes and decomposition of the complex occurred under the reaction conditions. The stereochemical outcome of the reactions in Table 2 can be rationalized as resulting from reaction via a chair-like conformation of a six-membered transition state (Scheme 1, **B** ( $R=CH_3$ )). The relative stereochemistry of alcohol **14** was determined by conversion to ketal **17**<sup>11</sup> (Scheme 2).

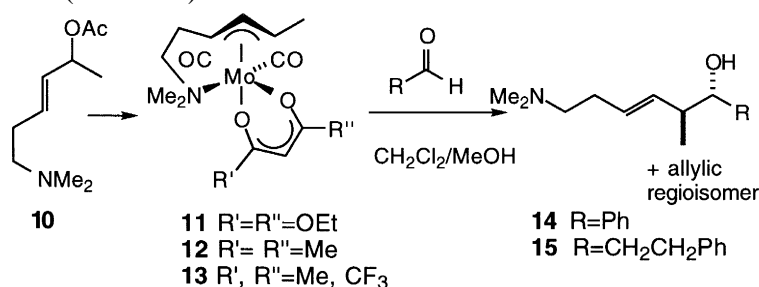
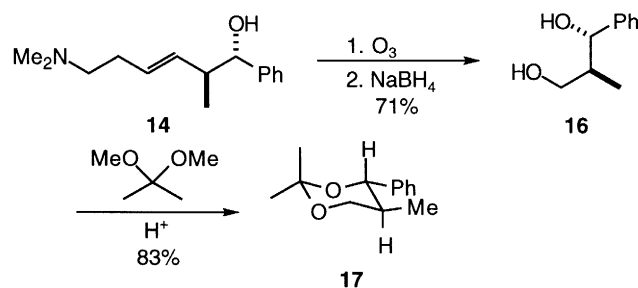


Table 2

Entry	Molybdenum Complex	Aldehyde	Homoallylic alcohol	Isolated yield (%)
1	<b>11</b> <sup>b</sup>	R=Ph	<b>14</b>	77 (9:1) <sup>a</sup>
2	<b>11</b> <sup>b</sup>	R=CH <sub>2</sub> CH <sub>2</sub> Ph	<b>15</b>	76 (10:1) <sup>a</sup>
3	<b>12</b>	R=Ph	<b>14</b>	60 (8:1) <sup>a</sup>
4	<b>13</b>	R=Ph	-- <sup>c</sup>	

a) ratio of allylic regioisomers. The minor regioisomer was a mixture of diastereoisomers. b) Mo complex was a 1:1 mixture of isomers, presumably at the metal center. c) Mo complex decomposed under the reaction conditions.

We have demonstrated that a chelating heteroatom can be used to control the regioselectivity of molybdenum mediated aldehyde allylation thus providing excellent acyclic stereocontrol. The residual amine or sulfide is ideally positioned for further functional group manipulations. Further work in this area is in progress.



Scheme 2.

## Acknowledgements

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