Preparation of homoallylic alcohols by reaction of aldehydes with η^3-allyl- and η^3-crotylmolybdenum complexes

Kevin P. Gable, M. Sundaram Shanmugham, and James D. White

Abstract: η^3-Allyl and η^3-methallyl complexes of molybdenum react with aldehydes to give homoallylic alcohols in preparative yields when water is used as a proton source, but the scope of the reaction is narrowed in the case of the η^3-crotylmolybdenum complex by the formation of both transposed and nontransposed products.

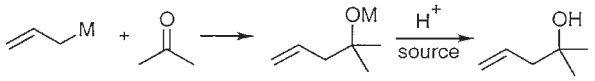
Key words: molybdenum, allylation, chelate model, transposition.

Résumé : Lorsqu'on utilise l'eau comme source de proton, les complexes η^3-allyle et η^3-méthallyle du molybdène réagissent avec les aldéhydes pour conduire aux alcools homoallyliques, avec des rendements préparatifs. Toutefois, dans le cas du complexe η^3-crotylmolybdène, la réaction est limitée par la formation de produits non transposés ainsi que de produits de transposition.

Mots clés : molybdène, allylation, modèle d'un chélate, transposition.

Introduction

The reaction of allylmetal reagents with carbonyl compounds provides a valuable method for the preparation of homoallylic alcohols (eq. [1]). A wide range of metals has been successfully employed in this process even though many allylmetal reagents are unstable and must generally be prepared and used in situ (1). In addition, allylboranes (2) and boronates (3) have found broad utility in applications where a homoallylic alcohol is needed in high enantiomeric excess.

[1] 

In 1989, Faller and co-workers (4) reported that η^3-allyl, η^3-methallyl, and η^3-crotyl complexes of bromo-(cyclopentadienyl)(nitroso)molybdenum react with aldehydes to give homoallylic alcohols. Faller et al. (5) further demonstrated that a chiral η^3-methallylmolybdenum complex could be resolved, and in a NMR experiment showed that its reaction with an aldehyde resulted in high asymmetric induction (6). Although the synthetic potential of these molybdenum compounds as reagents for the preparation of homoallylic alcohols is clear, the scope and limitations of their reactivity remain poorly defined. As part of a program designed to fabricate polyol substructures found in natural products, we were drawn to these π-allylmolybdenum reagents (7) by the fact that they are air and moisture stable substances which react with aldehydes under mild conditions (8).

Received September 27, 1999. Published on the NRC Research Press website on May 19, 2000.

This paper is dedicated to Professor Hanessian.

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Results and discussion

Molybdenum complexes **1**–**3** were prepared from tris(acetonitrile)molybdenum tricarbonyl (**4**) (9) via the dicarbonyl complex **5** using a variant of Faller's protocol (8) in which the bromine ligand was introduced with tetramethylammonium bromide. All three complexes are stable, yellow-orange solids that can be stored for many weeks with no special precautions. The η^3-crotyl complex **3** is a mixture of *syn* and *anti* stereoisomers, and there is evidence that these equilibrate during the reaction with aldehydes.

Since Faller had carried out all reactions of **2** in a mixture of dichloromethane and methanol, we first investigated the effect of varying the solvent on the reaction of **2** with benzaldehyde in the belief that the source of protons could play a pivotal role in this process. The results in Table 1 confirm that this is indeed the case, and that water is the most effective proton source. Optimized conditions for obtaining homoallylic alcohol **6** were realized with 3 equiv of water in dichloromethane; the absence of a proton source or the presence of a more acidic alcohol (CF_3CH_2OH) resulted in a significant proportion of the oxidized byproduct **7**.

The origin of the improved efficacy that the use of water imparts to these allylations bears comment. Faller et al. (5) have noted this effect and have attributed it in part to suppression of hemiacetal formation. However, this cannot be a significant factor. Intermolecular hemiacetal formation from aliphatic aldehydes and methanol is characterized by a small equilibrium constant, and at room temperature this process is

Scheme 1.

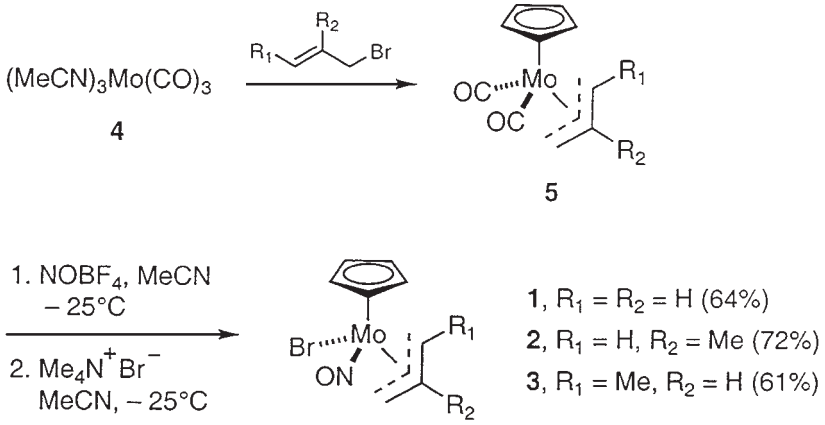
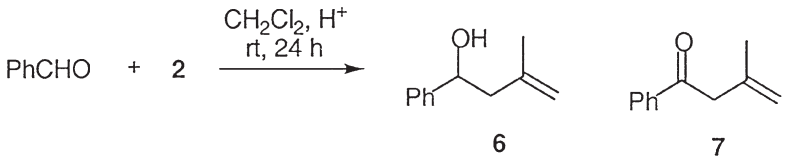


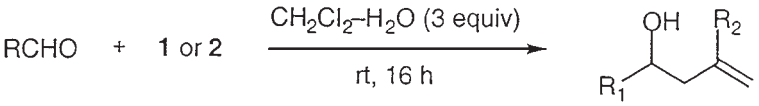
Table 1. Effect of proton source on the reaction of benzaldehyde with **2**.[a]



Solvent	Product(s)	Yield (%)
CH_2Cl_2 + MeOH (3 equiv)	**6**	64
CH_2Cl_2 + MeOH (1:1)	**6**	18
CH_2Cl_2	**6** + **7** (1:1)	52
CH_2Cl_2 + CF_3CH_2OH (3 equiv)	**6** + **7** (1:1)	74
CH_2Cl_2 + H_2O (3 equiv)	**6**	91

[a]Reactions were carried out using a 1.0:1.2 molar ratio of PhCHO:**2**. Increasing the proportion of **2** did not significantly alter yields.

Table 2. Reaction of aldehydes with **1** and **2**.

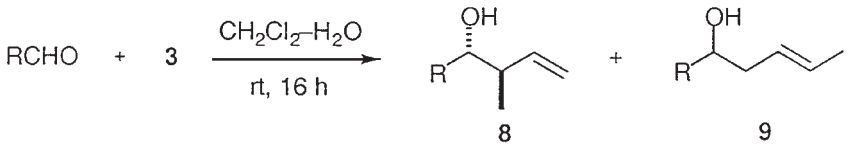


			Product		
Entry	Aldehyde	Reagent	R_1	R_2	Yield (%)
1	*n*-Heptanal	**1**	*n*-C_6H_{13}	H	85
		2	*n*-C_6H_{13}	CH_3	74
2	Cyclohexyl-carboxaldehdye	**1**	C_6H_{11}	H	90
		2	C_6H_{11}	CH_3	74
3	Pivaldehyde	**1**	Me_3C	H	70
			Me_3C	CH_3	76
4	Benzaldehyde	**1**	C_6H_5	H	88
			C_6H_5	CH_3	91
5	2-Heptenal	**1**	*n*-C_6H_{11}	H	89
6	2-Methyl-4-oxazole-carboxaldehyde[a]	**1**	C_4H_4NO	H	90

[a]A.S. Kende, B.E. Blass, and J.R. Henry. Tetrahedron Lett. **36**, 4741 (1995).

rapid compared to the allylation reaction (10). This literature also suggests that the equilibrium for hydration is actually more favored than that for hemiacetal formation. The possibility that pK_a of the proton source is the critical factor is ruled out by the fact that methanol and water have very similar acidities (11). Further, we see that trifluoroethanol leads to marginal improvement over running the reaction without a proton source prior to workup. The isolation of ketone **7**, presumably arising from a β-hydride elimination, suggests that timing of the proton transfer may be linked to binding of the conjugate base to the metal. A weakly Lewis basic species such as trifluoroethanol would not favour the

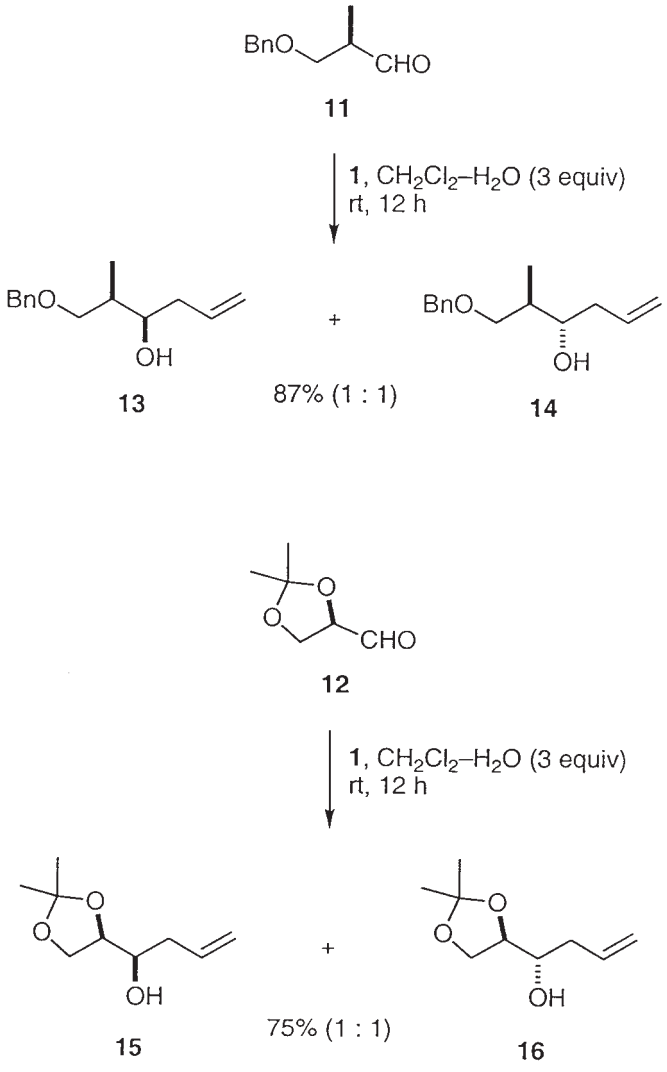
Table 3. Reaction of aldehydes with **3**.



Entry	Aldehyde	Product R	**8**[a]**:9**	Yield (%)
1	*n*-Heptaldehyde	*n*-C_6H_{13}	8:1	54
2	Cyclohexylcarboxaldehyde	C_6H_{11}	1:1	56
3	Pivaldehyde	Me_3C	1:1	64
4	Benzaldehyde	C_6H_5	23:1	87

[a]The *anti:syn* ratio was >98:2.

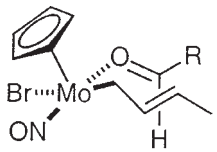
Scheme 2.



alkoxide exchange necessary to free the homoallylic alcohol, despite the enhanced proton availability. Methanol or other alcohols offer an improvement due to inductive donation by the alkyl group. Water, however, can engage in additional π-donation to the moderately oxophilic molybdenum centre, which encourages displacement of the product. Steric interference with other ligands is also minimized by this mechanism.

Application of the optimized conditions described above to the reaction of various aldehydes with 0.2–1 mmol of molybdenum complexes **1** and **2** afforded good to excellent yields of isolated and purified homoallylic alcohols (Table 2). The metal complexes react equally well with hindered (entry 3) and unhindered aldehydes (entry 1); however, they fail to react with ketones. Surprisingly, when the same aldehydes were exposed to molybdenum complex **3**, both transposed (**8**) and nontransposed (**9**) crotylation products were observed, the higher proportion of **9** being obtained with more sterically hindered aldehydes (entries 2 and 3). The configuration of the transposed homoallylic alcohol (**8**) in each case was found to be exclusively *anti* within the limits of detection, consistent with a six-centered, chelate transition state involving η^3-crotylmolybdenum complex **10**. However, the formation of **9** suggests that with **3** either a four-centre transition state or a non-chelate pathway must operate as well.

The question of facial (i.e., Felkin) selectivity in the reaction of molybdenum π-complexes with substrates bearing a



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stereogenic center α to the aldehyde was addressed with (*R*)-3-benzyloxy-2-methylpropionaldehyde (**11**) and glyceraldehyde acetonide (**12**). In both cases, *syn* (**13**, **15**) and *anti* (**14**, **16**) products were formed in equal quantity, indicating complete absence of substrate stereocontrol in these reactions. This is consistent with an observation previously made by Faller et al. (6), and confirms that the overwhelming size of the metal complex dominates the stereochemical outcome with chiral aldehydes.

Conclusions

The reaction of η^3-allyl, η^3-methallyl, and η^3-crotyl complexes of bromo(cyclopentadienyl)(nitroso)molybdenum with aldehydes is shown to be a preparatively useful route to

homoallylic alcohols, supporting observations previously made by Faller and co-workers (4) on the basis of NMR experiments. The reactions are clean, and separation of the alcohol product from molybdenum byproducts presents no problems. The presence of water as a cosolvent is essential for optimum yields, but the role of water in these reactions is unclear. In reactions of η^3-crotyl molybdenum complexes with aldehydes, a complicating factor can be the formation of both transposed and nontransposed products. The latter are prevalent when a sterically hindered aldehyde is employed, indicating that these substrates interact with the bulky molybdenum reagent via a mechanism different from the conventional six-centered chelate model.

Experimental

In a typical procedure, *n*-heptanal (0.096 g, 0.84 mmol) and water (0.045 mL, 2.50 mmol) were added to a stirred solution of **1** (0.315 g, 1.00 mmol) in CH_2Cl_2 (4 mL). The biphasic mixture was stirred at room temperature for 12 h, after which the solvent was evaporated in vacuo. The crude residue was purified by column chromatography on silica gel, using ether–hexane (1:4) as eluent, to give 4-hydroxy-1-decene (0.111 g, 85%) as a colorless oil. The product was identified by comparison of its spectral properties with those described (12).

Acknowledgements

We thank the National Science Foundation (CHE-9619296 and 9711187-CHE) and Parke–Davis Pharmaceutical Research for their generous financial support.

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