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Allylic Substitution Catalyzed by a New Molybdenum Complex

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Abstract: A new molybdenum(II) complex (E), generated in situ from $Mo(CO)_6$ by sequential treatment with $PhCH_2(Et)_3N^+Cl^-$ and CF_3SO_3Ag (3 equiv.), has been found to catalyze the substitution of allylic acetates with MeOH ($4 \rightarrow 5 \leftarrow 6$; $7 \rightarrow 8$; $9 \rightarrow 10$) at rt. The reaction predominantly occurs with an overall retention of configuration ($17 \rightarrow 19$ and $18 \rightarrow 20$).

Allylic substitution is one of the classical reactions of organic chemistry. However, due to a number of competing pathways (S_N2^2 , S_N2 , S_N1 , and elimination), this process is not sufficiently selective in its original form.⁴ In contrast, its transition metal-catalyzed version is characterized by an extraordinary selectivity and predictability. The latter transformation has been shown to proceed via the η^3 -complex 2, which then reacts with a nucleophile (Scheme 1).⁵ Aside from the notorious Pd(0),⁶ several other transition metal complexes have been found to catalyze or mediate this reaction, namely Mo,^{7.8} W,⁹ Fe,¹⁰ Co,¹¹ and Ni.¹² In this preliminary communication, we report on a novel molybdenum complex that can catalyze allylic substitution under very mild conditions.

Scheme 1



Molybdenum hexacarbonyl is a less efficient catalyst for allylic substitution than Pd(0)-complexes. As a result, high temperatures (e.g., refluxing in toluene) and long reaction times (>5h) are usually required.⁷ We reasoned that a more reactive complex might be obtained by modification of the ligands and/or the valency of the metal.

On heating with PhCH₂(Et)₃N⁺Cl⁻ in DME, Mo(CO)₆ was converted into the complex A (Scheme 2),¹³ which was then treated with silver triflate at -30 °C in order to prepare complex **B**. However, in contrast to the behavior of other Ag(I) salts,¹⁴ we observed a spontaneous reduction of Ag(I) to Ag(0), generating a paramagnetic species, for which structure C can be suggested. The latter Mo(I) complex is unstable and disproportionates into Mo(0) and Mo(II) ($C \rightarrow A + D$). Second equivalent of TfOAg effected further oxidation; 3 equivs. in total were required to generate the diamagnetic complex whose structure can be formulated as E.^{15,16}

The reaction of the acetate 4 with MeOH in CH_2Cl_2 in the presence of 10 mol% of E at rt/4h was found to produce ether 5 (12% conversion; Scheme 3).¹⁷⁻¹⁹ The allylic isomer 6 turned out to react faster (91% conversion at rt/4h), affording the same product. Similar catalytic reactions have been

Scheme 2: Bn = PhCH₂; TfO = CF₃SO₃ Mo(CO)₆ $\xrightarrow{BnEt_3N^+Cl^-}$ BnEt₃N⁺[Mo(CO)₅Cl] \xrightarrow{TfOAg} Mo^l(CO)₅Cl + BnEt₃N⁺TfO⁻ + Ag(0) \xrightarrow{TfOAg} \xrightarrow{A} \xrightarrow{C} C BnEt₃N⁺[Mo(CO)₅OTf]⁻ [Mo^{ll}(CO)₅Cl]⁺ OTf \xrightarrow{TfOAg} [Mo^{ll}(CO)₅OTf]⁺ OTf E

accomplished with allylic acetates 7, 9, 17, and 18. In each case only the isomer with a better stabilized double bond (i.e. more substituted or conjugated) has been formed (5, 8, 10, 19, and 20, respective-ly).^{18,20} Notable is the difference in the reaction rates (expressed as conversion) of 4 vs 6 and 7 vs $9.^{21,22}$

Scheme 3: (a), [Mo]-complex E (10 mol%), MeOH, CH₂Cl₂, DME, rt, 4h. Conversion (%) was determined by ¹H NMR spectra of the crude products obtained after 4 h.



In contrast to the readily reacting substrates shown above, other allylic acetates, namely 11 - 16 turned out either to be inert or to react sluggishly (with a stoichiometric amount of E).²³ All this behavior suggests an S_N 1 component in the transition state for ionization.^{24,28}



Stereochemistry of this allylic substitution was elucidated with the aid of epimeric acetates 17 and 18. In both instances, predominant retention of configuration was observed (Scheme 4). Thus, the equatorial acetate 17 furnished mainly the ether 19, whereas the faster reacting axial acetate 18 gave rise to the epimer 20 as the major product.²⁰ These results exclude a common intermediate, such as an uncoordinated allylic cation, and suggest that molybdenum is involved via a facially selective coordination. The overall retention of configuration can, *a priori*, originate either from double inversion or double retention. The latter pathway would, presumably, involve coordination of the reagent to the leaving group^{29,30} so that increasing the Lewis basicity of the carbonyl oxygen should accelerate the reaction.^{25c,29} However, the corresponding carbamates turned out to react considerably more slowly than the acetates 4, 7, and 17, while the overall stereochemistry remained essentially identical to that of the acetates.³¹ These results appear to support the double inversion as the dominant mechanism, analogous to the Pd-catalyzed substitution.⁶

Scheme 4: (a) see Scheme 3



In conclusion: We have developed an efficient molybdenum catalyst capable of promoting allylic substitution of reasonably reactive allylic acetates (4, 6, 7, 9, 17, and 18) with methanol¹⁷ as a typical O-nucleophile³² at rt. Predominant retention of configuration has been observed.

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References and Notes

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- (16) Analogous oxidation of [Mo(CO)₂(bipy)₂]⁺BF₄⁻ with AgBF₄ in MeCN is known to produce [Mo(CO)₂(bipy)₂(MeCN)]²⁺(BF₄⁻)₂. The same product was obtained from Mo(CO)₂(bipy)₂ on treatment with 2 equiv of AgBF₄: Connor, J. A.; James, E. J.; Overton, C.; El Murr, N. J. Chem. Soc., Dalton Trans. 1984, 255.
- (17) The reactions with EtOH and *i*-PrOH are slower.
- (18) Product structures were corroborated by NMR and other spectral techniques and, in several cases, by comparison with authentic samples.
- (19) Typical experiment: To a stirred solution of allylic acetate (0.5 mmol) in CH₂Cl₂ (10 mL) and MeOH (10 mL) was added PhCH₂(Et)₃N⁺[Mo(CO)₅Cl]⁻ (23 mg; 0.05 mmol) at -30 °C followed by a solution of CF₃SO₃Ag (39 mg; 0.15 mmol) in DME (2 mL). The mixture was then allowed to warm to rt and stirred under nitrogen for 4 h. The mixture was then diluted with ether and the solution was washed successively with brine and 5% aq. KHCO₃ and dried with MgSO₄. The solvent was evaporated to give a crude product, which was purified by flash chromatography on silica.
- (20) For 19, see: Henbest, H. B.; Wilson, R. A. L. J. Chem. Soc. 1957, 1958. For 20, see: Shoppee, C. W.; Agashe, B. D.; Summers, G. H. R. J. Chem. Soc. 1957, 3107. The two epimers differ significantly in the coupling pattern of 3β-H and 4-H, which is analogous to that in 17 and 18. The 19:20 ratio was determined by NMR.
- (21) As expected, the catalyst prepared by using 3 equivs. of TfOAg is more reactive than that generated by means of 2 equivs. Thus, while the latter complex (20 mol%) promoted only a 40% conversion of 17, 70% conversion has been observed with the former catalyst (20 mol%) in the same period of time (4h).
- (22) The following conversions have been obtained for stoichiometric reactions (rt/4h): 4 (73%), 6 (100%), 7 (100%), 10 (100%), 17 (93%), 18 (100%).
- (23) In a few instances, stoichiometric reactions exhibited low conversions: 13 (6% + elimination), 14 (15%), 16 (10%). Other acetates (11, 12, and 15) were inert.
- (24) Control experiments showed that the reaction is, indeed, promoted by the molybdenum complex rather than by BnEt₃N⁺TfO⁻ or TfOAg.^{25,26} Moreover, synthesis of the η³-complexes from allyl chloride and R₄N⁺[Mo(CO)₅X]⁻ has been reported earlier.²⁷
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- (32) Although attempts at introducing C- and N-nucleophiles were unsuccessful to date, we believe that this issue may be addressed by further modification of the catalyst³³ and reaction conditions. On the other hand, this method, as it stands, could be used for a facile deprotection of allylic carbonates and carbamates. Work towards this direction is now in progress.
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