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Molybdenum(II)-Catalyzed Allylic Substitution

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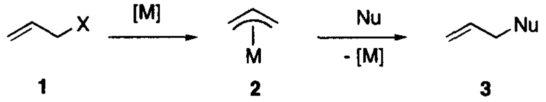
Abstract: The new Mo(II) triflate complex **5** has been found to catalyze the C-C bond forming allylic substitution with silyl enol ethers derived from β-dicarbonyls (e.g., **6** + **12** → **14**) and from simple ketones (e.g., **6** + **13** → **16**) as nucleophiles.

The transition metal-catalyzed allylic substitution, starting with an allylic acetate (**1**, X = OAc), involves the intermediate formation of an η^3-complex **2** (Scheme 1). Subsequent attack of **2** by a nucleophile affords the substitution product **3** with a concomitant release of the metal in its active form.[1,2] Although Pd(0) plays the major role among the catalysts,[2,3] its cost becomes prohibitive for industrial applications[4] in those cases where higher catalyst loading is required. Moreover, use of Pd(0) is essentially confined to the β-dicarbonyl type nucleophiles[2,3,5] and selected organometallics,[2,5] such as organozinc[2,5,6] and organozirconium reagents.[2,5,7]

Scheme 1

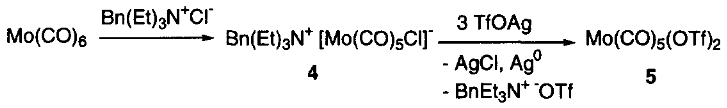


Molybdenum(0) complexes, a cheaper alternative to Pd(0), have also been shown to be effective as catalysts if β-dicarbonyl nucleophiles are employed.[8-10] However, the wider use of Mo(0) is seriously limited by the higher reaction temperature required. Thus, $Mo(CO)_6$ typically requires refluxing in a higher boiling solvent, such as toluene, whereas Pd(0) complexes react in refluxing THF or even at ambient temperature. Moreover, Mo(0) catalysis is further restricted by the narrow range of effective nucleophiles: in fact, to date, only dimethyl malonate and its congeners[8-10] have been successfully applied. Therefore, developing a new catalyst, less expensive and at least as reactive as Pd, effecting reactions with a wider variety of nucleophiles, would represent a considerable improvement of this methodology. In this letter we report on the development of a novel Mo(II) complex that appears to meet these criteria.

Palladium(0) complexes owe their high reactivity to their dissociation in solution, e.g., $(Ph_3P)_4Pd \rightarrow (Ph_3P)_3Pd + Ph_3P$; the resulting 16-electron Pd(0) species is prone to coordinate to an allylic substrate, triggering the reaction.[2] By contrast, $Mo(CO)_6$ is more stable so that a higher reaction temperature for dissociation is required (*vide supra*). We reasoned that appending weakly coordinating ligand(s) to Mo in place of the CO group(s) should improve its readiness to ligand exchange, thereby facilitating the desired reaction.[11] Furthermore, our initial elucidation of the mechanism for the allylic substitution, catalyzed by $Mo(CO)_6$, has suggested coordination of the metal to the Lewis-basic carbonyl oxygen of the leaving acetoxy group prior to the reaction.[10] Hence, increasing the Lewis acidity of the metal should also accelerate the reaction.

Trifluorosulfonate anion is a weakly coordinating ligand that is readily introduced to the organometallic complexes *via* replacement of a coordinated halide on reaction with silver triflate.[12] Since the corresponding chloromolybdate **4** can be readily obtained from $Mo(CO)_6$ on heating with a tetraalkylammonium chloride (Scheme 2),[13,14] we assumed that the required triflate, i.e., $[Mo(CO)_5(OTf)]^-$, would be readily accessible. However, the reaction of **4** with TfOAg turned out to be more complicated. As revealed by cyclic voltammetry and ESR spectroscopy, it involves a redox process, completion of which requires 3 equivs of TfOAg.[15] The resulting Mo(II) complex **5** is reasonably stable in solution and appears to meet the above requirements: (1) it contains a weakly coordinating ligand and (2) it should be more Lewis-acidic than $Mo(CO)_6$ due to the higher oxidation state of the metal.

Scheme 2: Bn = $PhCH_2$; TfO = CF_3SO_3



$$Mo(CO)_6 \xrightarrow{Bn(Et)_3N^+Cl^-} \underset{\mathbf{4}}{Bn(Et)_3N^+\,[Mo(CO)_5Cl]^-} \xrightarrow[\substack{-\,AgCl,\ Ag^0 \\ -\,BnEt_3N^+\,{}^-OTf}]{3\ TfOAg} \underset{\mathbf{5}}{Mo(CO)_5(OTf)_2}$$

In a previous letter,[16] we have shown that the triflate complex **5** can catalyze allylic substitution with *O*-nucleophiles, provided that reactive allylic substrates are employed. Thus, on reaction with methanol at ambient temperature, the allylic acetates **6**, **7**, and the isomeric **11** afforded the corresponding methoxy derivatives **9** and **10**, respectively, whereas **8** proved inert (Scheme 3).[16]

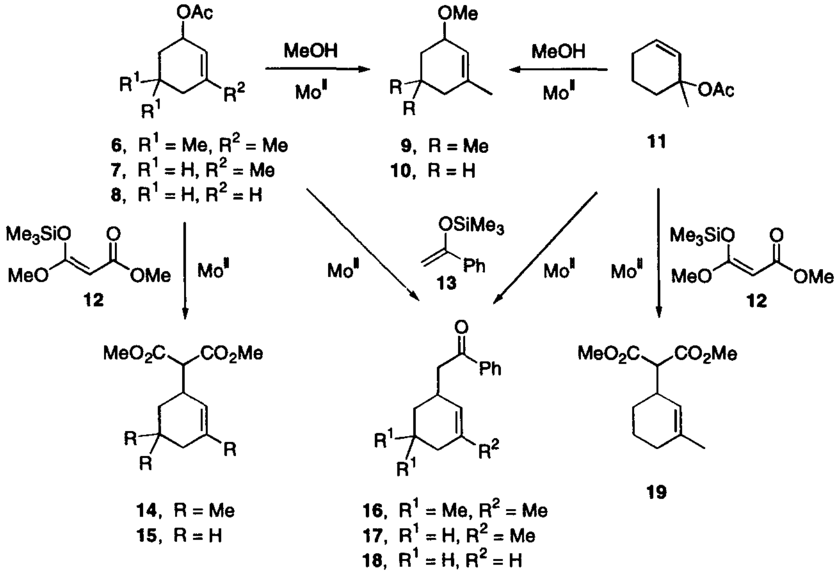
Following the encouraging results obtained with *O*-nucleophiles, we endeavored to develop a C-C bond-forming process. However, initial attempts, employing the usual lithium or sodium salt of dimethyl malonate as the *C*-nucleophile, failed completely under a range of conditions, presumably due to the deactivation of the catalyst through a strong chelation of the metal by the β-dicarbonyl enolate.[17] We reasoned that neutral silyl enol ethers might be less detrimental to the catalyst activity, which proved to be the case. Experimentation with the allylic acetate **6**, silyl enol ether **12**, and the catalyst **5** (5 mol%) met with a modest success, affording the desired compound **14** at ambient temperature in 48% isolated yield (Scheme 3).[18] The less reactive acetate **8** furnished the corresponding product **15** in only 16% yield. Finally, the tertiary acetate **11** proved fairly reactive again, affording the substitution product **19** (55%) at ambient temperature in 1 h. To our knowledge, these reactions represent the first examples of C-C bond formation in synthetic organic chemistry catalyzed by a Mo(II) complex.

In order to probe the scope of this catalytic process, we set out to establish whether or not simple silyl enol ethers could also be utilized as *C*-nucleophiles. If successful, the Mo(II)-catalyst would present a substantial advantage over its Pd(0)-counterparts by accommodating a broader range of nucleophiles.[19] The acetophenone-derived silyl enol ether **13** turned out, in fact, to be even more efficient than its malonate counterpart **12**. Thus, in the presence of the catalyst **5** (5 mol%), the isophorone-derived allylic acetate **6** readily afforded the ketone **16** (65%) on reaction with **13** (rt, 1.5 h),[20] whereas both **7** and **11** furnished the same product **17** (62% and 55%, respectively). On the other hand, **8** reacted sluggishly again, giving the ketone **18** in 14% yield, which further supports the previously suggested[16] substantial involvement of the S_N1 component in the transition state of the reaction.[21]

All reactions proved to be remarkably regioselective (with both nucleophiles) as only one isomer of the product has been detected in each case by high-field NMR.

In conclusion, we have designed a new Mo(II) complex **5**, which catalyzes C-C bond-forming allylic substitution reactions (e.g., **6** + **13** → **16**) at ambient temperature. These findings substantially expand the utility of this catalyst, which was originally confined[16] to the construction of C-O bonds. Further improvement of this Mo(II)-class of catalysts is underway and will be reported in due course.

Scheme 3: $Mo^I = Mo(CO)_5(OTf)_2$ (**5**)



Acknowledgment. We thank EPSRC for grants No. GR/H 92067 and GR/K07140 and EPSRC and AgrEvo UK Ltd for a CASE award to I. B.

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18. The reactions were typically carried out in CH_2Cl_2 at rt with 2 - 5 mol% of the catalyst and a slight excess (1.1 equiv) of the nucleophile. All yields refer to "isolated" yields rather than "GC yields". All new compounds gave satisfactory spectral and analytical data.
19. Attempts at developing the Pd(0)-catalyzed reaction of allylic esters with silyl enol ethers derived from simple ketones, as an extension of the established reactions with stabilized *C*-nucleophiles, have only met with modest success. In the examples reported to date, the more reactive carbonates (rather than acetates) have been employed and some of these reactions seem to work efficiently only as intramolecular processes: (a) Tsuji, J.; Minami, I.; Shimizu, I. *Chemistry Lett.* **1983**, 1325. (b) Tsuji, J.; Minami, I.; Shimizu, I. *Tetrahedron Lett.* **1983**, *24*, 1793. (c) Shimizu, I.; Minami, I.; Tsuji, J. *Tetrahedron Lett.* **1983**, *24*, 1797. (d) Tsuji, J.; Takahashi, K.; Minami, I.; Shimizu, I. *Tetrahedron Lett.* **1984**, *25*, 4783.
20. *Typical experiment:* To a stirred solution of **6** (100 mg; 0.54 mmol) and **13** (115 mg; 0.6 mmol) in CH_2Cl_2 (10 mL) at rt was added $PhCH_2(Et)_3N^+[Mo(CO)_5Cl]^-$ (12 mg, 0.025 mmol) in one portion, followed by a solution of AgOTf (19 mg, 0.075 mmol) in DME (1 mL). The mixture was stirred under nitrogen at rt for 4 h, then diluted with ether (20 mL), and the ethereal solution was washed successively with 5% aq. $NaHCO_3$ and water and dried with $MgSO_4$. The solvent was evaporated under reduced pressure to give a crude product, which was purified by flash chromatography on a silica gel column (15 x 2 cm) with a hexane-ethyl acetate mixture (9:1) to afford pure **16** (85 mg; 65%) as a pale yellow oil: IR ν 1688 (C=O), 1600, 1581, 1450, 1362, 1265 cm^{-1}; ^1H NMR δ (250 MHz, $CDCl_3$) 0.81 and 0.86 (2 x s, 6 H, 5-Me_2), 0.89 (m, 2 H, 6-H_2), 1.42 and 1.73 (2 x m, 2 x 1 H, 4-H_2), 1.55 (br s, 3 H, 3-Me), 2.80 (m, 3 H, CH_2CO and 1-H), 5.16 (s, 1 H, 2-H), 7.36 (t, *J* = 7.2 Hz, 2 H; 3',5'-H), 7.46 (t, *J* = 7.3 Hz, 1 H, 4'-H), 7.87 (d, *J* = 7.0 Hz, 2 H; 2',6'-H); ^{13}C NMR δ (62.9 MHz, $CDCl_3$) 23.9 (q), 25.3 (q), 30.0 (s), 30.4 (d), 31.8 (q), 42.6 (t), 44.1 (t), 45.2 (t), 123.3 (d), 128.1 (d), 128.5 (d), 132.9 (d), 133.7 (s), 137.4 (s), 199.8 (s); MS (EI) *m/z* (rel. intensity) 242 (M^+, 7), 227 (M^+ - Me, 4), 171 (35), 137 (M^+ - PhCO, 1), 122 (M^+ - PhCOMe, 34), 105 (PhCO, 15), 91 (7), 77 (34); HRMS (EI) calcd for $C_{17}H_{22}O$ requires M^+, 242.1670. Found: 242.1670.
21. In this respect, **5** seems to parallel the reactivity of $LiCo(B_9C_2H_{11})_2$, (lithium cobalt-*bis*-dicarbollide) and related Li^+ reagents: (a) Grieco, P. A.; DuBay, W. J.; Todd, L. J. *Tetrahedron Lett.* **1996**, *37*, 8707. (b) Henry, K. J.; Grieco, P. A. *J. Chem. Soc., Chem. Commun.* **1993**, 510.

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