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Allylic Alkylation Catalyzed by Molybdenum Complexes Containing Polydentate Phosphinoalkyl-Silyl Ligands†

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Abstract: The reaction of allyl alcohol derivatives with soft carbon nucleophiles, such as dimethyl sodiomalonate, in the presence of catalytic quantities of silyl-molybdenum hydrido complexes ([MoH_3{Si(R)[$Ph_2PCH_2CH_2P(Ph)C_6H_4$-*o*]$_2$}] or [MoH_3([$Ph_2PCH_2CH_2P(Ph)C_6H_4$-*o*]R_2Si-*P*,*P*,*Si*)]) is probed. The regioselectivity of the reaction and the catalyst activity were found to be highly dependent on the solvents used. With trisubstituted double bond olefins, the products alkylated at the unsubstituted allylic terminus were obtained in 95-99% selectivity. This regioselectivity is complementary to the Ir-catalyzed reactions, in which highly regioselective alkylation at the substituted allylic terminus was achieved. Direct conversion of allylic alcohol was also examined. The reaction of ethylbenzenesulfonylacetate or diethyl malonate proceeds under neutral conditions without addition of bases from outside.

Keywords: high regioselectivity; Tsuji-Trost reaction; trans-influence.

†Dedicated to the memory of Rastko D. Vukicevic, a friend and a fine colleague whose loss has been felt very deeply by so many people.

RUNNING TITLE: ALLYLIC ALKYLATION CATALYZED BY Mo-COMPLEXES

INTRODUCTION

In previous papers, we reported the unexpected formation of the complexes [MoH_3{[$Ph_2PCH_2CH_2P(Ph)C_6H_4$-*o*]$_2$(R)Si-*P,P,P,P,Si*}] (**2**), which were obtained by the thermal reaction of [$MoH_4(dppe)_2$] (**1**, dppe = $Ph_2PCH_2CH_2PPh_2$) with primary silanes $RSiH_3$ (R = Ph, *n*-C_6H_{13}).[1] The resulting complexes possess an unusual quadruply chelated ligand consisting of a P_2SiP_2 framework (Scheme 1). When secondary R_2SiH_2 (R = Ph, C_4H_3S) was

employed in a similar reaction with **2**, a trihydrido complex **3** with a tridentate ligand [MoH_3([$Ph_2PCH_2CH_2P(Ph)C_6H_4$-*o*]R_2Si-*P*,*P*,*Si*)] consisting of a P_2Si framework was isolated.[2]

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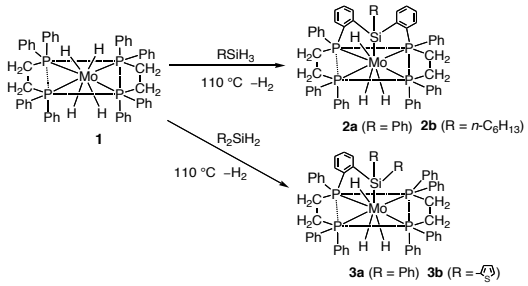
The formation of these silyl-molybdenum complexes is itself very novel, because activation of not only the Si-H bonds but also the ortho C-H bonds of dppe ligands takes place in the same system.



Scheme 1. Reactions of **1** with $RSiH_3$ and R_2SiH_2.

In addition to some interesting reactivities, these silyl-molybdenum complexes have exhibited unique characteristics for catalytic CO_2 fixation,[3] dehydro-polymerization of arylsilanes,[4] and synthesis of polysiloxanes.[5] We think that the catalytic activity of the complexes is due to the strong *trans*-influence of the Si fragment since the parent complex **1** did not catalyse the above processes. The electron-releasing properties and strong *trans*-influence of silyl ligands may alter or enhance the catalytic performance of transition-metal catalysts.[6] Thus, we have an ongoing interest in the application of the complexes as catalysts for organic transformation. In this report, we explored the catalytic activity of complexes **2** and **3** towards the allylic alkylations. The palladium-catalyzed substitution reaction of allylic compounds with various nucleophiles is a well-established method (Tsuji-Trost reaction) and used extensively in organic synthesis.[7] One recent and exciting breakthrough associated with research on the Tsuji-Trost reaction has been the development of a general methods of enantioselectively creating quaternary centers.[8]

EXPERIMENTAL

General procedures

All manipulations were performed under an inert atmosphere of nitrogen or argon using standard Schlenk techniques. The following instrumentation was used for accumulating spectra data: Perkin-Elmer 1600FT spectrometer (infrared), JEOL JNMEX-270, or JEOL JNMGX-500 spectrometers (nuclear magnetic resonance), and JEOL JMS-600 spectrometer (mass). GC

analyses were performed on a Shimadzu GC-14A using 0.33 mm × 50 m glass column packed with CBP1-S50-050.

Materials

Commercially available reagent grade chemicals (Wako Chemical) were used as such without any further purification. Solvents were purified according to standard procedures. Complexes **2** and **3** were prepared by literature procedures.[1, 2] Allylic esters were prepared by the reaction of the corresponding alcohols with acetyl chloride or trifluoroacetic anhydride.

*Allylic alkylation of **4a** (Entry 1)*

A Schelenk flask was charged with complex **2a** (0.050 g, 0.050 mmol), allyl acetate (**4a**, 0.54 ml, 5 mmol), and toluene (10 ml) under argon. In a separate flask, dimethyl malonate (0.69 ml, 6.0 mmol) was added to a slurry of hexane-washed sodium hydride (0.24 g, 6 mmol) in toluene (17.5 ml) under argon. To the resulting suspension of sodium dimethyl malonate was added the former *via* a cannula. After heating at 110 °C for 4h, usual work-up provided dimethyl allylmalonate.

*Allylic alkylation of **4b** (Entry 5)*

A Schelenk flask was charged with complex **2a** (0.050 g, 0.050 mmol), cinnamyl trifluoroacetate (**4b**, 0.30 g, 1.3 mmol), and DMI (10 ml) under argon. In a separate flask, dimethyl malonate (0.30 ml, 2.61 mmol) was added to a slurry of hexane-washed sodium hydride (0.12 g, 3.0 mmol) in DMI (20 ml) under argon. To the resulting suspension of sodium dimethyl malonate was added the former *via* a cannula. Then the mixture was stirred for 48 h at 110 °C. The usual workup and purification by column chromatography on SiO_2 with hexane/ethyl acetate (8/1) gave a linear compound **A** (76%). GLC analysis showed the branched product **B** in 1%. Methyl (*E*)-2-methoxycarbonyl-5-phenyl-4-pentenoate: ^{1}H NMR *d* 2. 81 (td, *J* = 7.25, 1.32 Hz, 2H), 3.54 (t, *J* = 7.25 Hz, 1H), 3.74 (s, 6H), 6.10 (dt, *J* = 15.83, 7.25 Hz, 1H), 6.48 (d, *J* =15.83 Hz, 1H), 7.18-7.35 (m, 5H). MS: 248 (M^+).

*Allylic alkylation of **4c** (Entry 7)*

A Schelenk flask was charged with complex **2a** (0.10 g, 0.10 mmol), geranyl trifluoroacetate (**4c**, 1.18 ml, 5.0 mmol), and toluene (10 ml) under argon. In a separate flask, dimethyl malonate (0.57 ml, 5.0 mmol) was added to a slurry of hexane-washed sodium hydride (0.18 g, 5.0 mmol) in toluene (10 ml) under argon. To the resulting suspension of sodium dimethyl malonate was added the former *via* a cannula. Then the mixture was stirred for 12 h at 110 °C. The usual workup and purification by column chromatography on SiO_2 with hexane/ethyl acetate (10/1) gave a linear compound **A** (39%), which was identical with an authentic sample.[11] GLC analysis

showed the branched product **B** in 1%. By the same procedure, neryl trifluoroacetate was reacted with sodium dimethyl malonate to give a 95:5 mixture of **A** and **B** isomer in 35% yield.

Allylic alkylation of allylic alcohol with ethyl benzenesulfonylacetate (Entry 3)

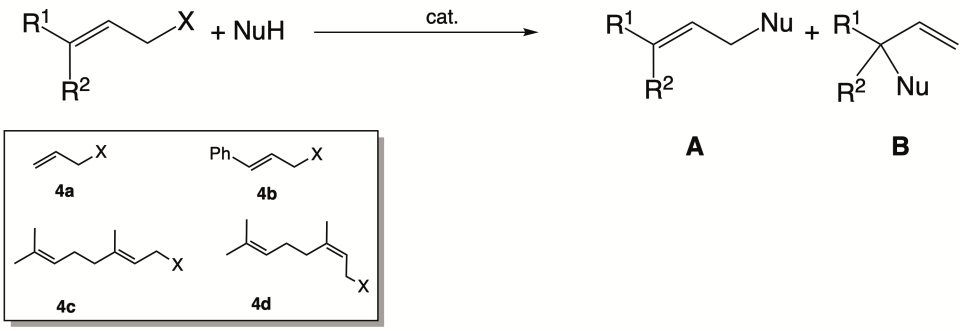
A Schelenk flask was charged with complex **2b** (0.050 g, 0.050 mmol), allylic alcohol (0.34 ml, 5.0 mmol), Tetrabutylammonium Fluoride THF solution (0.25 ml, 0.25 mmol), and toluene (10 ml) under argon. The mixture was stirred for 30 min. To the resulting solution was added ethyl benzenesulfonylacetate (0.0.57 g, 2.5 mmol) and *n*-tetradecane (0.20 ml, 2.0 mmol, internal standard). Then the mixture was stirred for 6 h at 110 °C. The usual workup and purification by column chromatography on SiO_2 with hexane/ethyl acetate (7/1) gave ethyl 2-benzensulfonyl-4-pentenoate (40%): ^{1}H NMR *d* 1.14 (t, *J* = 7.25 Hz, 3H), 2.63~2.84 (m, *2*H), 4.01 (dd, *J* = 10.55, 4.62 Hz, 1H), 4.09 (qur, *J* = 7.25 Hz, 2H), 5.09 (dd, *J* = 10.55, 1.32 Hz, 1H), 5.16 (dd, *J* = 15.50, 1.32 Hz, 1H), 5.68 (ddt, *J* = 15.50, 10.55, 6.59 Hz, 1H), 7.55~7.91 (m, 5H). MS: 269 (M^++1).

Allylic alkylation of allylic alcohol with diethyl malonate (Entry 4)

A Schelenk flask was charged with complex **3a** (0.050 g, 0.046 mmol), allylic alcohol (0.34 ml, 5.0 mmol), Tetrabutylammonium Fluoride THF solution (0.25 ml, 0.25 mmol), and toluene (10 ml) under argon. The mixture was stirred for 30 min. To the resulting solution was added diethyl malonate (0.38 ml, 2.5 mmol) and *n*-tetradecane (0.20 ml, 2.0 mmol, internal standard). Then the mixture was stirred for 12 h at 110 °C. GLC analysis showed allyl diethyl malonate (42%), which was identical with an authentic sample prepared by the conventional palladium process.

RESULTS AND DISCUSSION

We carried out the allylation of dimethyl malonate (Scheme 2). The reaction conditions and the results are summarized in TABLE I.



Scheme 2. Mo-catalyzed allylic alkylation

TABLE I. Scope of the allylic alkylation

Entry (cat.)	Allyl (X)	NuH	**A**:**B**[a]	Yield (%)[j]
1 (**2a**)	**4a** (AcO)	$CH_2(CO_2Me)_2$		94[b]
2 (**1**)	**4a** (AcO)	$CH_2(CO_2Me)_2$		22[a]
3 (**2a**)[d]	**4b** (CF_3CO_2))	$CH_2(CO_2Me)_2$	44:56	12[c]
4 (**2a**)[e,g]	**4b** (CF_3CO_2))	$CH_2(CO_2Me)_2$	98:2	38[c]
5 (**2a**)[f,g]	**4b** (CF_3CO_2))	$CH_2(CO_2Me)_2$	99:1	76[c]
6 (**2a**)[f,ı]	**4b** (CF_3CO_2))	$CH_2(CO_2Me)_2$	99:1	54[c]
7 (**3a**)[d,h]	**4c** (CF_3CO_2))	$CH_2(CO_2Me)_2$	99:1	39[c]
8 (**3a**)[d,h]	**4d** (CF_3CO_2))	$CH_2(CO_2Me)_2$	95:5	35[c]

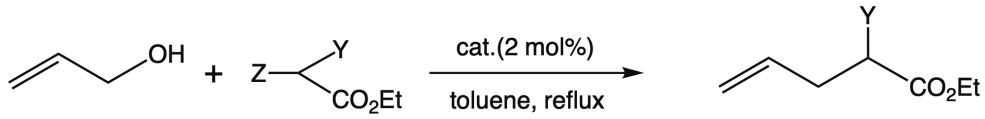
[a] Ratios determined by GLC and ^{1}H NMR; [b]Determined by internal standard method with GLC; [c]Isolated yield; [d]The reaction was carried out in refluxing toluene for 12 h; [e]DMF was the solvent. [f]DMI was the solvent; [g]The reaction was performed with 4 mol% catalyst at 110 °C for 48 h; [h]The reaction was performed with 2 mol% catalyst; [i]The reaction was performed with 4 mol% catalyst at room temperature for 24 h; [j]The products were identified by comparison of their ^{1}H NMR spectra with those reported in the literature for these compounds (see ref. 9 and 11).

The initial reaction employed allyl acetate with dimethyl sodiomalonate in toluene at reflux. The allylation catalyzed by complex **2a** proceeded smoothly (Entry 1). The yield of the reaction was much higher than that obtained for the system with complex **1** (Entry 2), thus the silyl ligand in complex **2** proved to be effective for the transformation. Interest in transition-metal-catalyzed reactions of allyl substrates with nucleophiles stemmed from the issue of regioselectivity. The palladium process tends to occur at the less substituted allylic terminus. However, there are some notable exceptions and the regiocontrol appears somewhat confusing as described below. On the other hand, with molybdenum catalysts, the regioselectivity is often complementary to the Pd-catalyzed reactions. For example, with aryl-substituted allyl systems, molybdenum catalysts favor attack at the more substituted terminus.[9] Accordingly, next experiments focused on the use of cinnamyl, geranyl, and neryl alcohol derivatives as the starting materials (Entries 3~8).

Complex **2a** was found to be ineffective for the conversion of cinnamyl acetate.[10] However, **2a** catalyzed the allylation of the more reactive cinnamyl trifluoroacetate. The regioselectivity of the reaction and the catalyst activity were found to be highly dependent on the solvents used. In toluene, the allylation generated only small amounts of products (12%, Entry 3). The regioselectivity was also considerably lower (44:56). On the other hand, using Dimethylformamide (DMF) facilitated the catalysis (38%, Entry 4). In addition, the nucleophilic substitution takes place regioselectively at unsubstituted side of allylic system

(98:2). This observation is in sharp contrast with that of molybdenum carbonyl complexes system in which the molybdenum catalysts tend to lead to preferential alkylation at the substituted allylic terminus. 1,3-Dimethyl-2-imidazolidinone (DMI) proved to show more advantageous performance, affording the product in high yield (76%, Entry 5) with high regioselectivity (99:1). It is also interesting to note that the allylation in DMI is occurring appreciably at room temperature (Entry 6). Equally good selectivity for attack at the less substituted terminus occurred for both geranyl and neryl trifluoroacetates (Entries 7 and 8). These reactions, however, required using complex **3a** as a catalyst and heating at reflux in toluene. In striking contrast to the result of cinnamyl trifluoroacetate, with DMI, the reactions failed due to an unknown reason. Previously Trost reported that Pd-catalyzed alkylation of geranyl acetate with dimethyl sodiomalonate produced a mixture of regioisomers (**A**:**B** = 90:10). Furthermore, in the case of neryl acetate, the major product of alkylation with dimethyl sodiomalonate arose from attack at the tertiary carbon atom (**A**:**B** = 35:65) and thus the regioselectivity was opposite that of geranyl acetate.[11] These results indicate that the silyl-molybdenum complexes are efficient catalysts for regiospecific alkylation at the unsubstituted allylic terminus.

From the viewpoint of the atom economy, direct conversion of allylic alcohols is far more beneficial. In Pd(0) catalyzed reactions, allylic alcohols are less reactive allylating agents. Several attempts have been reported in this connection. For example, allylation of malonates with allyl alcohols was carried out by using a sp^2-hybridized bidentate phosphine-Pd catalyst.[12] Generally, a poor leaving group hydroxide can be used in the presence of some activators, such as As_2O_3, B_2O_3, and Ti(O-*i*-Pr)$_4$.[13] The hydroxy group is activated by coordination of these Lewis acids. Catalytic conversions of allyl alcohol were also examined (Scheme 3 and Table II).



Scheme 3. Direct conversion of allylic alcohol

TABLE II. Scope of the reactions

Entry (cat.)	Z	Y	Yield (%)[J]
1 (**2a**)	Na	CO_2Et	53
2 (**2a**)	H	SO_2Ph	23
3 (**2b**)[a]	H	SO_2Ph	40
4 (**3b**)[a]	H	CO_2Et	42

[a] TBAF (10 mol%) was used.

The reaction with diethyl sodiomalonate proceeded as with allyl acetate, affording the product in 53% yield (Entry 1). In our case, the allylation occurred without requirement for Lewis acid help. The oxidative addition of allyl alcohol to molybdenum center may be followed by formation of π-allyl molybdenum hydroxide complex, and then the generated hydroxide ion might pick up proton from active methylene compounds. Therefore, we expected that reactions of allyl alcohol proceed under neutral conditions without addition of bases from outside. Substitution reactions under neutral conditions are highly desirable. The test reaction that employed allyl alcohol with diethyl malonate as the pronucleophile failed to produce significant amounts of products. This result mirrors our earlier results in which the reactions of **2a** with dialkyl malonates afforded stable dihydrido (η^1-*O*-enolato) molybdenum complexes.[14] The formation of the enolato complex may anticipate the oxidative addition of allyl alcohol to molybdenum center in the reaction. The first sign of some success came in the use of reactive ethylbenzenesulfonylacetate as the pronucleophile (Entry 2). Particularly, the reaction was enhanced by using complex **2b** along with addition of a catalytic amount of *n*-Bu_4NF (TBAF, Entry 3). In the present case, we may suppose that coordination of F^- at silicon increases the catalytic activity of **2b**. Furthermore, we found that the combination of **3b** and TBAF enables the allylation of diethyl malonate (Entry 4).

CONCLUSION

The silyl-molybdenum complexes were found to be a new catalyst for allylic alkylation. Highly regioselective alkylation at the unsubstituted allylic terminus was achieved. This regioselectivity is complementary to the Ir-catalyzed reactions, in which highly regioselective alkylation at the substituted allylic terminus was achieved.[15] We have also demonstrated that the silyl-molybdenum complexes possess the catalytic activity toward direct conversion of allylic alcohol. To our knowledge, there have so far been no reports of analogous Mo-catalyzed reactions of allylic alcohol under neutral conditions. Taking into account the lower cost of molybdenum compared with palladium, the prospects that it may be more generally useful will be an important direction to pursue.

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