Rhodium complex-catalysed allylic alkylation of allylic acetates

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$[Rh(COD)Cl]_2$–$P(OPh)_3$ (P : Rh = 2–3) is found to be an efficient catalyst for allylic alkylation of allylic acetates with a stabilized carbon nucleophile; alkylation at the more substituted allylic terminus is predominant.

Allylic alkylation is one of the most important carbon–carbon bond-forming reactions catalysed by transition-metal complexes. A wide variety of transition-metal complexes such as palladium,[1] nickel,[2] molybdenum[3] and tungsten[4] have been extensively studied as catalysts or reagents for allylic alkylation. The control of regioselectivity in allylic alkylation is important. Palladium complexes favor alkylation at the less substituted allylic terminus, while molybdenum and tungsten complexes to some extent favor alkylation at the more substituted allylic terminus, which is the most desirable. Much less attention has been paid to rhodium complexes as catalysts for allylic alkylation.[5] In the course of our study on catalysis by rhodium,[6] we found a rhodium complex that is an efficient catalyst for the regioselective allylic alkylation of allylic acetates at the more substituted allylic terminus.

The reaction of (*E*)-2-hexenyl acetate (**1a**) with diethyl sodiomalonate was examined in the presence of a catalytic amount of $[Rh(COD)Cl]_2$ and a phosphorous ligand. The results are summarized in Table 1. Triphenyl phosphite was found to be an efficient ligand. The reaction using three equivalents of triphenyl phosphite to rhodium gave products in 90% yield (entry 3), and compound **2a** was obtained with 74% selectivity. Alkylation at the substituted allylic terminus was predominant. The reaction using two equivalents of triphenyl phosphite to rhodium gave the same product distribution, but a longer reaction time was required for completion (entry 2). Using one equivalent of triphenyl phosphite to rhodium gave a non-selective formation of products in a decreased yield (entry 1). Rhodium phosphine complexes such as $[Rh(COD)Cl]_2$–PPh_3 (P : Rh = 2), $RhCl(PPh_3)_3$, $RhH(PPh_3)_4$ and $RhH(CO)(PPh_3)_3$ were catalytically inactive (entries 4–7) and the starting material was recovered. Addition of triphenyl phosphite to such rhodium phosphine complexes enhanced the catalytic activity considerably. Products were obtained in good yields with the predominant formation of **2a** (entries 8 and 9). Replacement of triphenylphosphine by triphenyl phosphite therefore results in catalytically active rhodium phosphite species.

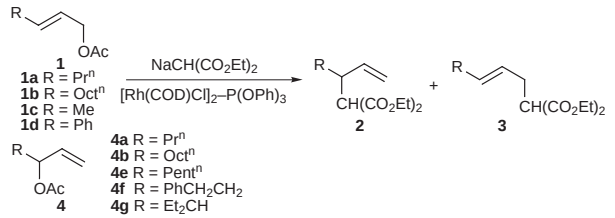
We examined the reaction of a series of allylic acetates with diethyl sodiomalonate in the presence of a catalytic amount of $[Rh(COD)Cl]_2$ and triphenyl phosphite (P : Rh = 3) (Table 2). The regioselectivity was greatly affected by the structure of and the substituent in the allylic acetates. The reaction of the primary allylic acetates (**1a**–**1c**) gave **2** as the major product (Scheme 1): **1b** gave **2b** with 75% selectivity (entry 1); crotyl acetate (**1c**) gave **2c** with 57% selectivity (entry 2). However, with cinnamyl acetate (**1d**), the regioselectivity was opposite to that of **1a**–**1c** (entry 3), and product **3d** was obtained with 75% selectivity. The reactions of the secondary allylic acetates (**4**) were highly regioselective at the substituted allylic terminus to give products **2** with excellent selectivities (entries 4–7). A longer primary alkyl substituent required a prolonged reaction time (entry 5). A secondary alkyl substituent decreased the yield and the selectivity of **2**: **4g** gave **2g** with 65% selectivity (entry 8). The reaction of tertiary allylic acetates (Scheme 2) (**5**) gave moderate yields of product (entries 9 and 10), and a quaternary carbon center can result in these reactions.

Oxidative addition of allylic acetate to the rhodium complex gives a π-allyl rhodium intermediate (Scheme 3). It is well known that carbonium ion character at the substituted allylic terminus is enhanced by triphenyl phosphite as a π-acceptor.[7] Diethyl sodiomalonate is predominantly directed to the substituted allylic terminus. The regioselectivity of the reaction of the 1-alken-3-yl acetates (**4**) is higher than that of (*E*)-2-alkenyl acetate (**1**) (Table 1, entry 3; Table 2, entries 4–7). If the intermediate is a π-allyl rhodium species only, the regioselectivity of both reactions should be same. The difference is explained by allowing for a σ-allyl rhodium intermediate as a minor reaction path; the π-allyl rhodium intermediate equilibrates with a σ-allyl rhodium intermediate.

Table 1 Effect of Rh catalyst on the allylic alkylation of **1a** with $NaCH(CO_2Et)_2$ [a]

Entry	Catalyst	P : Rh	Time/h	Yield/%[b]	Ratio[c] **2a : 3a**	
1[d]	$[Rh(COD)Cl]_2 + P(OPh)_3$	1	16	20	52	48
2[d]	$[Rh(COD)Cl]_2 + P(OPh)_3$	2	16	90	70	30
3[d]	$[Rh(COD)Cl]_2 + P(OPh)_3$	3	1	90	74	26
4[d]	$[Rh(COD)Cl]_2 + PPh_3$	2	24	0	—	
5	$RhCl(PPh_3)_3$	3	24	0	—	
6	$RhH(PPh_3)_4$	4	24	0	—	
7	$RhH(CO)(PPh_3)_3$	3	24	0	—	
8[e]	$RhH(PPh_3)_4 + P(OPh)_3$	7	6	84	70	30
9[e]	$RhH(CO)(PPh_3)_3 + P(OPh)_3$	6	24	70	65	35

[a] A mixture of **1a** (2 mmol), $NaCH(CO_2Et)_2$ (4 mmol), Rh complex (0.08 mmol), ligand and THF (10 ml) was stirred under refluxing THF. [b] Isolated yield based on **1a**. [c] Determined by GLC. [d] $[Rh(COD)Cl]_2$ (0.04 mmol). [e] $P(OPh)_3$ (0.24 mmol).



Scheme 1

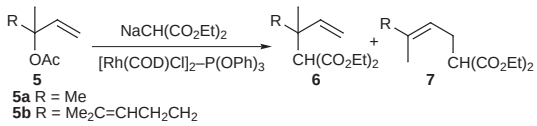
Table 2 Rhodium complex-catalysed allylic alkylation with $NaCH(CO_2Et)_2$ [a]

Entry	Substrate	Time/h	Yield/%[b]	Product	Ratio[c]
1	**1b**	1	94	**2b : 3b**	75 : 25
2	**1c**	1	79	**2c : 3c**	57 : 43
3	**1d**	1	83	**2d : 3d**	25 : 75
4	**4a**	1	86	**2a : 3a**	91 : 9
5	**4b**	7	74	**2b : 3b**	91 : 9
6	**4e**	5	88	**2e : 3e**	92 : 8
7	**4f**	1	87	**2f : 3f**	91 : 9
8	**4g**	22	45	**2g : 3g**	65 : 35
9	**5a**	6	63	**6a : 7a**	100 : 0
10	**5b**	24	57	**6a : 7b**	97 : 3

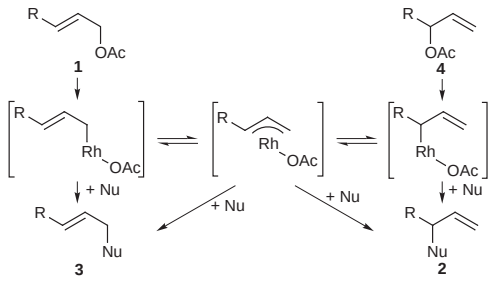
[a] A mixture of allylic acetate (2 mmol), $NaCH(CO_2Et)_2$ (4 mmol), $[Rh(COD)Cl]_2$ (0.04 mmol), $P(OPh)_3$ (0.24 mmol) and THF (10 ml) was stirred under refluxing THF. [b] Isolated yield. [c] Determined by GLC.

The S_N2-like reaction of the σ-allyl rhodium intermediate with diethyl sodiomalonate gives a product which is alkylated at the carbon originally substituted by an acetoxy group. A similar S_N2-like reaction of a σ-allyl rhodium intermediate with a malonate anion has been reported.[5b] Such a reaction of **4** gives the product **2**, whereas that of **1** gives **3**. Thus, allylic alkylation of **4** to **2** is more selective than for **1**.

Further development of the synthetic application and mechanistic studies are underway in our laboratory and will be reported in due course.



Scheme 2



Scheme 3

Experimental

Allylic alkylation of allylic esters

A typical procedure is described for the reaction of **1a** with diethyl sodiomalonate. (*E*)-2-Hexenyl acetate **1a** (284 mg, 2.0 mmol), triphenyl phosphite (74.4 mg, 0.24 mmol), and $[Rh(COD)Cl]_2$ (19.7 mg, 0.04 mmol) were stirred in THF (5.0 ml) under Ar atmosphere. In a separate flask, diethyl malonate (640 mg, 4.0 mmol) was added to a slurry of hexane-washed sodium hydride (96 mg, 4.0 mmol) in THF (5 ml). The resulting clear solution was added to the former mixture by a syringe and the combined mixture was stirred under refluxing THF for 1 h. The progress of the reaction was monitored by GLC. After **1a** was consumed, the reaction mixture was partitioned between diethyl ether and water. The organic layer was separated and the aqueous layer was extracted with diethyl ether. The combined organic layer was concentrated *in vacuo*. The residue was purified by column chromatography (*n*-hexane–ethyl acetate, 98 : 2) to give a mixture of **2a** and **3a** (436 mg; yield 90%).

Ethyl 3-ethenyl-2-ethoxycarbonylhexanoate (2a).[8] ^1H NMR (270 MHz, $CDCl_3$): δ 0.88 (t, $J = 6.9$ Hz, 3H, $CH_3CH_2CH_2$), 1.25 (t, $J = 7.3$ Hz, 3H, CH_3CH_2O), 1.27 (t, $J = 7.3$ Hz, 3H, CH_3CH_2O), 1.33–1.45 (m, 4H, $CH_3CH_2CH_2$), 2.78 (qd, $J = 8.9$, 3.3 Hz, 1H, $CH_2CHCH{=}CH_2$), 3.33 [d, $J = 8.9$ Hz, 1H, $CH(CO_2Et)_2$], 4.15 (q, $J = 7.3$ Hz, 2H, CH_3CH_2O), 4.20 (q, $J = 7.3$ Hz, 2H, CH_3CH_2O), 5.06 (dd, $J = 10.2$, 2.0 Hz, 1H, $CH{=}CH_2$), 5.07 (dd, $J = 17.5$, 2.0 Hz, 1H, $CH{=}CH_2$), 5.65 (dt, $J = 17.5$, 9.9 Hz, 1H, $CH{=}CH_2$); ^{13}C NMR (67.8 MHz, $CDCl_3$); δ 13.7, 14.0 (2C), 20.0, 34.3, 43.8, 56.9, 61.0, 61.1, 117.1, 138.1, 168.1, 168.3.

Ethyl (*E*)-2-ethoxycarbonyl-4-octenoate [(*E*)-3a].[9] ^1H NMR (270 MHz, $CDCl_3$): δ 0.86 (t, $J = 7.3$ Hz, 3H, $CH_3CH_2CH_2$), 1.26 (t, $J = 7.3$ Hz, 6H, CH_3CH_2O), 1.35 (sextet, $J = 7.6$ Hz, 2H, $CH_3CH_2CH_2$), 1.95 (q, $J = 6.9$ Hz, 2H, $CH_3CH_2CH_2$), 2.58 [t, $J = 6.9$ Hz, 2H, $=CHCH_2CH(CO_2Et)_2$], 3.37 [t, $J = 7.6$ Hz, 1H, $CH(CO_2Et)_2$], 4.19 (q, $J = 7.3$ Hz, 4H, CH_3CH_2O), 5.36 (dt, $J = 15.5$, 6.9 Hz, 1H, $CH_2CH{=}$), 5.52 (dt, $J = 15.5$, 6.9 Hz, 1H, $CH_2CH{=}$); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ 13.4, 14.0 (2C), 22.3, 31.8, 34.4, 52.3, 61.2 (2C), 125.4, 133.6, 169.0 (2C).

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