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PALLADIUM-CATALYZED REACTION OF ALLYLIC AMMONIUM BROMIDES WITH NUCLEOPHILES

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Summary

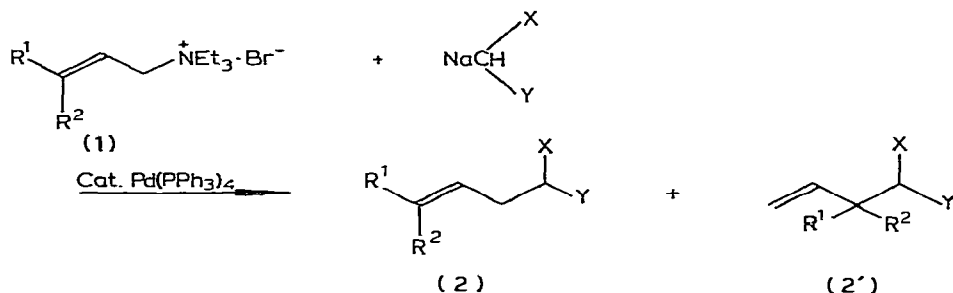
The reactions of allylic triethylammonium bromides and dimethylsulfonium bromide with carbon nucleophiles were catalyzed by tetrakis(triphenylphosphine)palladium to afford olefinic esters and ketones.

Recent years have seen dramatic developments in synthetic applications of transition metal catalyzed or promoted allylic exchange reactions. Such reactions have provided an efficient method for carbon-carbon bond formation. Especially in the palladium-catalyzed allylic alkylation [1], a variety of allylic compounds, such as allylic esters, ethers, alcohols, amines [1b], and sulfones [1c] are employed. Little attention, however, has been paid to the transition metal catalyzed reactions of allylic ammonium or sulfonium salts with nucleophiles other than a Grignard reagent in the presence of copper(I) salt [2], though these groups are known as good leaving groups. Herein, we wish to report the palladium-catalyzed reactions of allylic ammonium and sulfonium salts with carbon nucleophiles.

Results and discussion

Treatment of triethylallylammonium bromide with sodium diethyl malonate in the presence of a catalytic amount of tetrakis(triphenylphosphine)palladium (5 mol%) in THF at room temperature for 24 h to give diethyl allylmalonate (2a) and diethyl diallylmalonate in 62% and 13% yields, respectively. A smaller amount of the palladium catalyst (1 mol%) was also able to catalyze the present reaction. Starting from the carbanion of ethyl phenylsulfonylacetate, the corresponding allylated product 2b was produced. This reaction was also successfully extended to other allylic ammonium bromides as shown in Table 1. Of interest is the fact that the allylic rearranged compound 2f' was obtained as a major product in the case of triethylprenylammonium bromide. The presence

of 1,2-bis(diphenylphosphino)ethane (DIPHOS) in the reaction mixture reduced this selectivity for reasons that are not clear.



Only a trace of the allylated active methylene compound was obtained when cuprous bromide was used instead of tetrakis(triphenylphosphine)palladium. The allylic alkylation did not occur in the absence of the palladium catalyst. A π -allylpalladium complex [1] may be involved as a key intermediate. This is

TABLE 1
REACTION OF ALLYLIC AMMONIUM BROMIDES WITH ACTIVE METHYLENE COMPOUNDS


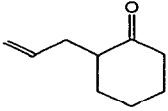

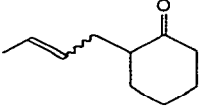
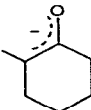
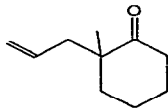
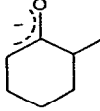
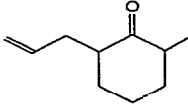
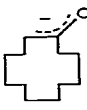
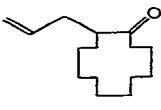
1		NaCHXY		Products 2 Yield (%)	
R ¹	R ²	X	Y		
H	H	CO ₂ Et	CO ₂ Et	CH ₂ =CHCH ₂ CH(CO ₂ Et) ₂ (62) (60) ^a	(2a)
H	H	CO ₂ Et	SO ₂ Ph	CH ₂ =CHCH ₂ CH(CO ₂ Et)(SO ₂ Ph) (60)	(2b)
Ph	H	CO ₂ Et	CO ₂ Et	$ \begin{array}{c} \text{Ph} \\ \\ \text{C}=\text{C}-\text{H} \\ \\ \text{H} \end{array} \text{CH}_2\text{CH}(\text{CO}_2\text{Et})_2 $ (2c)	$ \begin{array}{c} \text{CH}(\text{CO}_2\text{Et})_2 \\ \\ \text{H}_2\text{C}=\text{CHCH} \\ \\ \text{Ph} \end{array} $ (2c')
Me	H	CO ₂ Et	CO ₂ Et	$ \begin{array}{c} \text{Me} \\ \\ \text{C}=\text{C}-\text{H} \\ \\ \text{H} \end{array} \text{CH}_2\text{CH}(\text{CO}_2\text{Et})_2 $ (2d)	$ \begin{array}{c} \text{CH}(\text{CO}_2\text{Et})_2 \\ \\ \text{H}_2\text{C}=\text{CHCH} \\ \\ \text{Me} \end{array} $ (2d')
Me	H	CO ₂ Et	SO ₂ Ph	$ \begin{array}{c} \text{Me} \\ \\ \text{C}=\text{C}-\text{H} \\ \\ \text{H} \end{array} \text{CH}_2\text{CH}(\text{CO}_2\text{Et})(\text{SO}_2\text{Ph}) $ (2e)	$ \begin{array}{c} \text{CH}(\text{CO}_2\text{Et})(\text{SO}_2\text{Ph}) \\ \\ \text{H}_2\text{C}=\text{CHCH} \\ \\ \text{Me} \end{array} $ (2e')
Me	Me	CO ₂ Et	CO ₂ Et	$ \begin{array}{c} (\text{Me})_2\text{C}=\text{CHCH}_2\text{CH}(\text{CO}_2\text{Et})_2 \\ \text{(2f)} \end{array} $ (68) 20/80 (90) ^b 54/46	$ \begin{array}{c} \text{CH}(\text{CO}_2\text{Et})_2 \\ \\ \text{H}_2\text{C}=\text{CHC}(\text{Me})_2\text{CH}(\text{CO}_2\text{Et})_2 \\ \text{(2f')} \end{array} $

^a 1 mol% of tetrakis(triphenylphosphine)palladium was used. ^b 5 mol% of DIPHOS was added.

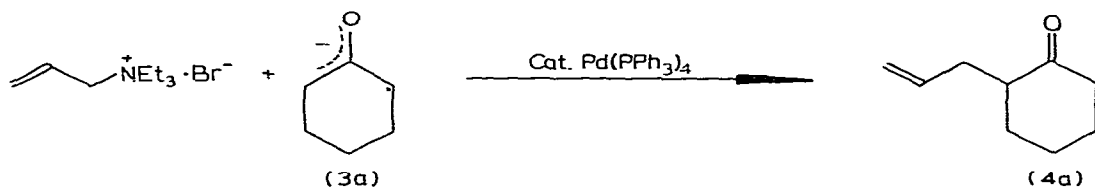
consistent with the report [3] that amine exchange of allylic amines is catalyzed by the palladium(0) catalyst in the presence of acid.

Enolate anions were also allowed to undergo the palladium-catalyzed reaction with allylic ammonium bromides to give olefinic ketones. For example, **3a** reacted with triethylallylammonium bromide in the presence of a catalytic amount of tetrakis(triphenylphosphine)palladium to produce 2-allylcyclohexanone. When the reaction temperature was raised from -78°C , the suspended ammonium salt in THF disappeared below $<0^{\circ}\text{C}$, at which point the allylic exchange reaction was considered to be completed. The formation of O-allylated products was not observed at the present reaction conditions. By regioselective generation of enolate anions from 2-methyl-1-trimethylsilyloxy-1-cyclohexene and 6-methyl-1-trimethylsilyloxy-1-cyclohexene, 2-allyl-2-

TABLE 2
REACTION OF ALLYLIC AMMONIUM BROMIDES WITH ENOLATE ANIONS

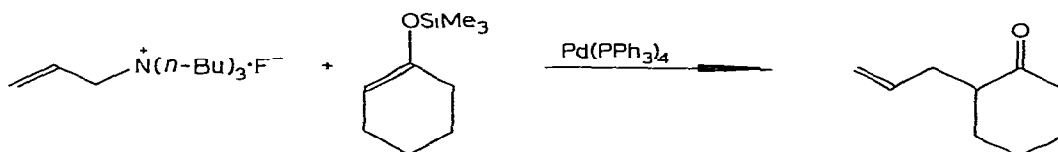
1		Enolate anion	Product 4 yield (%)	
R ¹	R ²			
H	H			(81)
Me	H			(39)
H	H			(80) ^a
H	H			(78) ^b
H	H			(62)

^a The formation of **4d** was not observed. ^b The compound **4c** was formed in $<2\%$ yield.

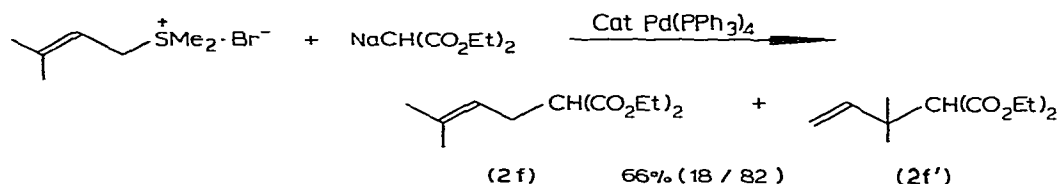


methylcyclohexanone and 2-allyl-6-methylcyclohexanone were produced, respectively. The results are summarized in Table 2.

Enolate anions are well known to be easily generated by the reaction of silyl enol ethers with tetra-*n*-butylammonium fluoride [4]. This prompted us to use allylic ammonium fluorides as sources of an electrophile and fluoride ion. Actually, the reaction of tri-*n*-butylallylammonium fluoride with 1-trimethylsilyloxy-1-cyclohexene was performed in the presence of the palladium(0) catalyst, but 2-allylcyclohexanone was produced in only 10% yield.



Furthermore, allylic sulfonium salts also reacted with sodium diethyl malonate in the presence of a palladium catalyst to give the allylic malonate, as indicated by the following equation. The ratio of the normal product **2f** to the rearranged one **2f'** was almost similar to that obtained in the reaction of



triethylprenylammonium bromide, which shows that the same mechanism may be operative in both reactions.

The results mentioned above reveal that allylic ammonium and sulfonium salts are good substrates for the palladium-catalyzed allylic exchange reaction.

Experimental

Preparation of diethyl allylmalonate from triethylallylammonium bromide

To a mixture of triethylallylammonium bromide (1.33 g, 6 mmol) and tetrakis(triphenylphosphine)palladium (0.35 g, 0.3 mmol) in THF (20 ml), sodium diethyl malonate (6 mmol) in THF (10 ml) was added dropwise at room temperature. The resultant mixture was stirred for 24 h under a nitrogen atmosphere. Water (20 ml) was added to the reaction mixture, which was extracted with ether (2 × 3 ml). The combined ether layers were washed with a saturated aqueous solution of sodium chloride (3 × 30 ml). The organic layer was dried with anhydrous sodium sulfate, filtered and evaporated. The residue

was chromatographed on a silica gel column. Elution with benzene produced diethyl allylmalonate (62%) and diethyl diallylmalonate (13%), which were purified by gas chromatography (conditions: 10% PEG 20M, 140°C). The other allylated compounds shown in Table 1 were prepared by the same procedure. The products, **2** and **2'**, were isolated by gas chromatography, respectively. The products herein were identified by comparison of their IR and NMR spectra with those of authentic samples [1]. For example, **2c**: IR (neat) 1720 and 960 cm^{-1} ; NMR (CDCl_3) δ 1.21 (t, 6H, J 6.8 Hz), 2.80 (2dd, 2H, J 7.9, 7.4, 6.6, and 6.2 Hz), 3.50 (dd, 1H, J 7.9 and 7.4 Hz), 4.17 (q, 4H, J 6.8 Hz), 6.05 (ddd, 1H, J 16.0, 6.6, and 6.2 Hz), 6.49 (d, 1H, J 16.0 Hz); MS, m/e 276 (M^+). **2f**: IR (neat) 1722 and 850 cm^{-1} ; NMR (CDCl_3) δ 1.26 (t, 6H, J 7.0 Hz), 1.62 (s, 1H), 1.66 (d, 1H, J 1.3 Hz), 2.56 (dd, 1H, J 8.6 and 7.9 Hz), 2.58 (dd, 1H, J 7.4 and 7.1 Hz), 3.31 (dd, 1H, J 7.9 and 7.1 Hz), 4.18 (q, 4H, J 7.0 Hz), 5.05 (ddd, 1H, J 8.6, 7.4, and 1.3 Hz); MS, m/e 228 (M^+). **2f'**: IR (neat) 1722, 990, and 915 cm^{-1} ; NMR (CDCl_3) δ 1.25 (t, 6H, J 7.1 Hz), 1.25 (s, 6H), 3.30 (s, 1H), 4.13 (q, 4H, J 7.1 Hz), 4.99 (dd, 1H, J 10.2 and 1.6 Hz), 5.01 (dd, 1H, J 17.6 and 1.2 Hz), 6.04 (dd, 1H, J 17.6 and 10.2 Hz); MS, m/e 228 (M^+).

Preparation of 2-allylcyclohexanone from triethylallylammonium bromide

To a solution of *n*-butyllithium in hexane (3.8 ml, 6 mmol) and THF (15 ml), 1-trimethylsilyloxy-1-cyclohexene (1.02 g, 6 mmol) in THF (5 ml) was added at -78°C . The resulting solution was added dropwise to the mixture of triethylallylammonium bromide (1.33 g, 6 mmol) and tetrakis(triphenylphosphine)-palladium (0.35 g, 0.3 mmol) in THF (10 ml) at -78°C under a nitrogen atmosphere. The resulting mixture was stirred at -78°C for 1 h. The reaction mixture was warmed to room temperature. The suspended ammonium salt disappeared below $<0^\circ\text{C}$. The reaction mixture was left overnight at room temperature. Product was isolated in the same way as above. The residue was chromatographed on a silica gel column. Elution with benzene produced 2-allylcyclohexanone (81%) and diallylcyclohexanone (7%), which were purified by gas chromatography (conditions: 10% PEG 20M, 120°C). The other allylated compounds shown in Table 2 were prepared by the same procedure. In the preparation of **4c**, the formation of **4d** was not detected in an NMR and gas chromatography analyses. These analyses of the allylated products from 6-methyl-1-trimethylsilyloxy-1-cyclohexene showed that **4c** was produced in $<2\%$ yield. The products were identified by comparison of their IR and NMR spectra with those of authentic samples [5]. For example, **4c**: IR (neat) 1705, 1638, 990, and 910 cm^{-1} ; NMR (CDCl_3) δ 1.07 (s, 3H), 1.5–2.7 (m, 10H), 5.00 (dd, 1H, J 16.2 and 2.8 Hz), 5.05 (dd, 1H, J 10.6 and 2.8 Hz), 5.73 (ddd, 1H, J 16.2, 10.6, and 7.5 Hz); MS, m/e 152 (M^+). **4d**: IR (neat) 1710, 1638, 995, and 910 cm^{-1} ; NMR (CDCl_3) δ 1.01 (d, 3H, J 6.7 Hz), 1.2–2.7 (m, 10H), 4.97 (dd, 1H, J 9.4 and 2.5 Hz), 5.00 (ddt, 1H, J 17.8, 2.5, and 1.2 Hz), 5.84 (ddd, 1H, J 17.8, 9.4, and 6.2 Hz); MS, m/e 152.

*Palladium-catalyzed reaction of tri-*n*-butylallylammonium fluoride with 1-trimethylsilyloxy-1-cyclohexene*

To a mixture of tri-*n*-butylallylammonium fluoride (0.55 g, 2 mmol) and tetrakis (triphenylphosphine)palladium (0.23 g, 0.2 mmol) in THF (15 ml),

1-trimethylsilyloxy-1-cyclohexene (0.34 g, 2 mmol) was added dropwise at room temperature. The resulting mixture was stirred for 24 h under a nitrogen atmosphere. Work up was carried out in the same way as mentioned above. Gas chromatography of the extract indicated formation of 2-allylcyclohexanone in 10% yield.

Palladium-catalyzed reaction of dimethylprenylsulfonium bromide with sodium diethyl malonate

To a mixture of dimethylprenylsulfonium bromide (1.10 g, 6 mmol) and tetrakis(triphenylphosphine)palladium (0.35 g, 0.3 mmol) in THF (20 ml), sodium diethyl malonate (6 mmol) in THF (10 ml) was added at room temperature. The resulting mixture was stirred for 24 h under a nitrogen atmosphere. The product was isolated in the same way as above. The residue was chromatographed on a silica gel column. Elution with benzene gave diethyl 3-methyl-2-butenylmalonate (**2f**) and 1,1-dimethyl-2-propenylmalonate (**2f'**) in 66% yield (**2f/2f'** = 18/82), which were purified by gas chromatography.

Acknowledgement

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