Facile Palladium-Catalyzed Decarboxylation Reaction of Allylic β-Keto Esters

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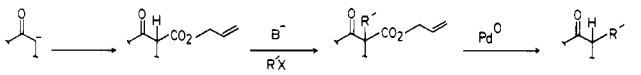
β-Keto esters are important intermediates used for regioselective alkylation of ketones. After their regioselective mono- or dialkylation, mono- or dialkyl ketones are derived by hydrolysis and subsequent decarboxylation. However, usual alkaline hydrolysis of β-keto esters is often complicated by a competing fission reaction to afford esters or acids, particularly when the α-position is disubstituted, and several improved methods for smooth dealkoxycarbonylation have been reported.[1] The ester-cleavage reaction promoted by halides or cyanide ion in aqueous aprotic solvents gives improved yields.[2] More smooth decarboxylation has been carried out with *t*-butyl,[3] 2-tetrahydropyranyl, or benzyl esters of β-keto carboxylic acids,[4] which undergo decarboxylation after acid-catalyzed hydrolysis or hydrogenolysis. We wish to report here allyl β-keto carboxylates as a new entry to β-keto esters which undergo palladium-catalyzed decarboxylation under very mild conditions without using acids or bases.

We have reported that allylic esters can be used for the protection of carboxylic acids.[5] Allylic esters can be converted to free acids easily by palladium-catalyzed reaction with ammonium formate.[6] Then we have found that decarboxylation of β-keto esters can be carried out under very mild conditions by the application of this formate reaction (Scheme I). The deallyloxycarbonylation proceeds smoothly to give ketones in high yields.[7] Some results are shown in Table I.

The reaction can be carried out smoothly with tertiary amine salts (typically triethylamine) of formic acid in THF at room temperature (method A). The reaction conditions are mild and nearly neutral, and hence other functional groups present in the same molecule can be kept intact. For example, methyl ester was not hydrolyzed (run 8). Even more labile tetrahydropyranyl ether remained intact (run 7). Also no retro-Dieckmann product by ring fission of cyclic β-keto esters was obtained (runs 5–11). One serious side reaction expected for the β-keto esters **4** is retro-Michael reaction, but desired deallyloxycarbonylation proceeded selectively by the formate method (run 4). The reaction with ammonium formate did not proceed at room temperature due to poor solubility of ammonium formate in organic solvents but proceeds in boiling dioxane (method B).

Scheme I



Scheme II

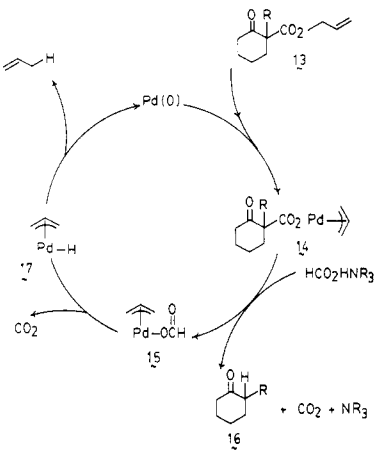
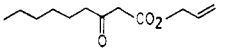
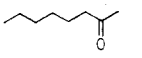
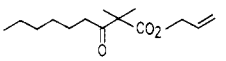
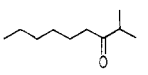
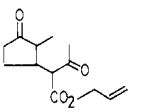
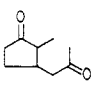
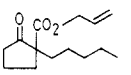
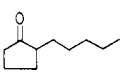
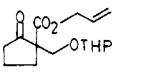
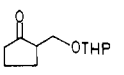
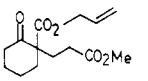
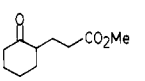
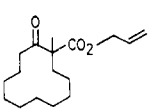
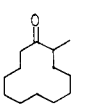


Table I. Palladium-Catalyzed Reaction of Allyl β-Keto Carboxylates with Ammonium Formate

run	ester	method	time, min	product[b]	yield,[c] %
1	 **1**	B	35		(99)
2	 **2**	A	35	 **3**	82 (100)
3	**2**	B	60	**3**	(92)
4	 **4**	A	30		82 (99)
5	 **5**	A	30	 **6**	88 (100)
6	**5**	B	100	**6**	(87)
7	 **7**	A	30	 **8**	77 (95)
8	 **9**	A	30	 **10**	92 (100)
9	**9**	B	70	**10**	(90)
10	 **11**	A	35	 **12**	92 (100)
11	**11**	B	50	**12**	(95)

[a] Method A: ester (1 mmol), $Pd(OAc)_2$ (0.025 mmol), PPh_3 (0.05 mmol), HCO_2HNEt_3 in THF at room temperature (see, Experimental Section). Method B: ester (1 mmol), $Pd(OAc)_2$ (0.025 mmol), PPh_3 (0.05 mmol), ammonium formate (2.0 mmol) in boiling dioxane. [b] All products were identified with authentic samples. [c] Isolated yield: GLC yield in parentheses.

The reaction can be explained by the following mechanism (Scheme II). Oxidative addition of allyl β-keto

(1) House, H. O. "Modern Synthetic Reactions," 2nd ed.; W. A. Benjamin: New York, 1972; pp 492-546.
(2) For review, see: (a) McMurry, J. *Org. React. (N.Y.)* **1976**, *24*, 187–224. (b) Krapcho, A. P. *Synthesis* **1982**, 805–822, 893–914.
(3) Henderson, D.; Richardson, K. A.; Taylor, R. J. K. *Synthesis* **1983**, 996–997.
(4) White, W. L.; Anzeveno, P. B.; Johnson, F. *J. Org. Chem.* **1982**, *47*, 2379–2389.
(5) Tsuji, J.; Yamakawa, T. *Tetrahedron Lett.* **1979**, 613–616.
(6) For recent studies on palladium-catalyzed cleavage reaction of allylic esters, see: (a) Jeffrey, P. D.; McCombie, S. W. *J. Org. Chem.* **1982**, *47*, 587–590. (b) Kunz, H.; Unverzagt, C. *Angew, Chem., Int. Ed. Engl.* **1984**, *23*, 436–437. (c) Kunz, H.; Waldmann, H. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 71–72. (d) Mastalerz, H. *J. Org. Chem.* **1984**, *49*, 4092–4094.
(7) When sodium acetate or morpholine was used as an acceptor nucleophile instead of the formate, α-allyl ketones were obtained as main products by palladium-catalyzed decarboxylation–allylation of allyl β-keto carboxylates.[8]
(8) (a) Shimizu, I.; Yamada, T.; Tsuji, J. *Tetrahedron Lett.* **1980**, *21*, 3199–3202. (b) Tsuda, T.; Chujo, Y.; Nishi, S.; Tawara, K.; Saegusa, T. *J. Am. Chem. Soc.* **1980**, *102*, 6381–6384.

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carboxylate **13** to Pd(0) affords the π-allylpalladium carboxylate complex **14**, which reacts with ammonium formate to give π-allylpalladium formate **15** and ketone **16** after decarboxylation. Decarboxylation of π-allyl palladium formate **15** gives the palladium hydride complex **17**, which undergoes reductive elimination to give propene with regeneration of Pd(0).

Allyl β-keto carboxylates are prepared easily from corresponding ketones by the reaction of diallyl carbonate or allyl chloroformate. Then their alkylation or Michael addition can be carried out easily with weak bases such as K_2CO_3.[9] Finally the removal of the allyl esters is possible by the palladium-catalyzed reaction of formate under mild conditions as reported in this paper.

Experimental Section

General. Boiling points are uncorrected. ^1H NMR spectra were taken at 60 MHz with a Hitachi R-24A spectrometer using CCl_4 as solvent. Chemical Shifts are given in δ units (in ppm) relative to tetramethylsilane as an internal standard. Infrared spectra were recorded on a JASCO IRA-2 spectrophotometer.

Preparation of Allyl β-Keto Carboxylates. Allyl 3-Oxononanoate (1). To a solution of diallyl carbonate (5.0 g, 35.2 mmol) and NaH (50% in mineral oil, 2.8 g, 58.5 mmol) in dry benzene was added 2-octanone (3.0 g, 23.4 mmol), and the mixture was refluxed for 5 h. HCl (3 N) was added to the mixture at 0 °C, and the mixture was extracted with dichloromethane. The extract was washed with brine and dried over $MgSO_4$. After evaporation of the solvent, the residue was distilled under reduced pressure to give 1 (3.97 g, 79%): bp 89–94 °C (3 torr); IR (neat) 3080, 2940, 1740, 1720, 1645, 1630, 995, 935 cm^{-1}; NMR 1.6–2.0 (m, 11 H), 2.45 (t, J = 6 Hz, 3 H), 3.29 (s, 2 H), 4.52 (d, J = 5 Hz, 2 H), 5.0–5.5 (m, 2 H), 5.5–6.3 (m, 1 H). Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 67.99; H, 9.41.

α,α-Disubstituted β-keto esters **2**, **4**, **5**, **9**, and **11** were prepared by the reactions of the β-keto ester **1** with methyl iodide (80%), allyl acetoacetate with 2-methyl-2-cyclopentenone (79%), allyl 2-oxocyclopentanone[10] with pentyl bromide (76%), allyl 2-oxocyclohexanecarboxylate with methyl acrylate (82%), and allyl 2-oxocyclododecanecarboxylate with methyl iodide (82%) using K_2CO_3 as base in boiling acetone according to the literature.[9]

Allyl 3-oxo-2,2-dimethylnonanoate (2): bp 117–120 °C (3 torr); IR (neat) 3080, 2940, 1735, 1715, 1645, 1470, 1380, 1150, 995 cm^{-1}; NMR 0.8–1.0 (t, J = 5 Hz, 3 H), 1.28 (s, 6 H), 1.2–1.7 (m, 8 H), 2.15–2.45 (t, J = 6 Hz), 4.35–4.50 (d, J = 5 Hz, 2 H), 4.95–5.35 (m, 2 H), 5.5–6.1 (m, 1 H). Anal. Calcd for $C_{14}H_{24}O_3$: C, 69.96; H, 10.07. Found: C, 69.73; H, 10.15.

Allyl 2-(2-methyl-3-oxocyclopentyl)-3-oxobutanoate (4): bp 155–158 °C (3 torr); IR (neat) 3080, 2945, 2880, 1735, 1715, 1705, 1645, 1380 cm^{-1}; NMR 0.95–1.23 (d, J = 7 Hz, 3 H), 1.3–2.4 (m, 6 H), 2.2 (s, 3 H), 3.28–3.45 (dd, 1 H, J = 5, 7 Hz), 4.41–4.50 (d, J = 6 Hz, 2 H), 5.0–5.53 (m, 2 H), 5.55–6.0 (m, 1 H). Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.42; H, 7.57.

Allyl 1-pentyl-2-oxocyclopentanecarboxylate (5): bp 137–139 °C (2 torr); IR (neat) 3080, 2925, 2850, 1740, 1715, 1642, 1740, 990 cm^{-1}; NMR 0.8–0.95 (t, J = 3 Hz, 3 H), 1.0–1.5 (m, 8 H), 1.6–2.5 (m, 6 H), 4.3–4.45 (d, J = 5 Hz, 2 H), 4.9–5.35 (m, 2 H), 5.55–6.0 (m, 1 H). Anal. Calcd for $C_{14}H_{22}O_3$: C, 70.55; H, 9.30. Found: C, 70.29; H, 9.45.

Allyl 1-[2-(methoxycarbonyl)ethyl]-2-oxocyclohexanecarboxylate (9): bp 142–143 °C (0.1 torr); IR (neat) 3080, 2940, 2850, 1730, 1705, 1645, 1440, 1380, 990 cm^{-1}; NMR 0.8–2.6 (m, 12 H), 3.55 (s, 3 H), 4.45–4.65 (d, J = 6 Hz, 2 H), 5.05–5.45 (m, 2 H), 5.53–6.0 (m, 1 H). Anal. Calcd for $C_{14}H_{20}O_5$: C, 62.67; H, 7.51. Found: 62.88; H, 7.59.

Allyl 1-methyl-2-oxocyclododecanecarboxylate (11): bp 160 °C (3 torr); IR (neat) 3080, 2925, 1735, 1708, 1645, 1470, 1140, 990 cm^{-1}; NMR 0.9–1.5 (m, 18 H), 1.2 (s, 3 H), 1.7–2.35 (m, 2 H) 4.3–4.5 (d, 2 H, J = 6 Hz) 4.9–5.3 (m, 2 H), 5.4–6.0 (m, 1 H). Anal. Calcd for $C_{17}H_{28}O_3$: C, 72.82; H, 10.06. Found: C, 73.12; H, 10.06.

Allyl 1-[2-(Tetrahydropyranyloxy)methyl]-2-oxocyclopentanecarboxylate (7). A mixture of formaldehyde (37% solution in water, 4.8 mL, 60 mmol), allyl alcohol (8.0 mL, 120 mmol), allyl 2-oxocyclopentanecarboxylate (3.96 g, 20 mmol), and $KHCO_3$ (200 mg, 2 mmol) was vigorously stirred at 0 °C for 15 min and at room temperature for 10 min. Saturated ammonium chloride solution (10 mL) was added to the mixture, and the mixture was extracted with ether. The ethereal solution was washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Distillation of the residue gave allyl 1-(hydroxymethyl)-2-oxocyclopentanecarboxylate (3.5 g, 77%): bp 98 °C (4 torr); IR (neat) 3400–3280, 2940, 1735, 1715, 1645, 1125, 1020 cm^{-1}; NMR 1.9–2.4 (m, 6 H), 3.75 (s, 2 H), 3.9–4.05 (d, J = 4, 1 H), 4.45–4.65 (m, 2 H), 5.0–5.4 (m, 2 H), 5.54–6.2 (m, 1 H).

Allyl 1-(hydroxymethyl)-2-oxocyclopentanecarboxylate (3.5 g, 17.6 mmol) was converted to ether **7** (3.6 g, 72%, after chromatographic purification on SiO_2 with ether–hexane (1:13)) with dihydropyran in the presence of a catalytic amount of p-TsOH in dry CH_2Cl_2 at 0 °C. **7**: IR (neat) 3080, 2925, 1735, 1710, 1645, 1440, 1020 cm^{-1}; NMR 1.4–1.8 (m, 6 H), 2.0–2.5 (m, 6 H), 3.2–4.05 (m, 4 H), 4.4–5.1 (d, J = 4 Hz, 2 H, 1 H), 4.9–5.4 (m, 2 H), 5.5–6.25 (m, 1 H). Anal. Calcd. for $C_{15}H_{22}O_5$: C, 63.81; H, 7.85. Found: C, 63.83; H, 8.07.

General Procedure for Deallyloxycarbonylation of Allyl β-Keto Carboxylates. Palladium-Catalyzed Reaction of Allyl Ester 11 with HCO_2H–Et_3N to the Ketone 12 (Method A). To a stirred solution of palladium acetate (11 mg, 0.05 mmol) and PPh_3 (26 mg, 0.1 mmol) in dry THF (3 mL) was added in one portion a mixture of formic acid (0.18 mL, 4 mmol) and Et_3N (0.83 mL, 5 mmol) in THF (2 mL) at room temperature under argon. The mixture was vigorously stirred and a solution of allyl ester **11** (536 mg, 2 mmol) in dry THF (1 mL) was added, and the resulting mixture was stirred for additional 30 min. The mixture was passed through a short SiO_2 column, followed by ether washing. After the filtrate was concentrated in vacuo, the residue was chromatographed on SiO_2 with hexane–ether (10:1) to afford the ketone **12** (339 mg, 92%).

Registry No. **1**, 97416-33-6; **2**, 83135-37-9; **3**, 5445-31-8; **4**, 97416-34-7; **5**, 83135-35-7; **6**, 4819-67-4; **7**, 97416-35-8; **8**, 97416-36-9; **9**, 83135-28-8; **10**, 10407-33-7; **11**, 83135-36-8; **12**, 16837-94-8; PPh_3, 603-35-0; $CH_3(CH_2)_5COCH_3$, 111-13-7; HCO_2HNEt_3, 585-29-5; diallyl carbonate, 15022-08-9; 2-octanone, 111-13-7; methyl iodide, 74-88-4; allyl acetoacetate, 1118-84-9; 2-methyl-2-cyclopentenone, 1120-73-6; allyl 2-oxocyclopentanecarboxylate, 75265-67-7; pentyl bromide, 110-53-2; allyl 2-oxocyclohexanecarboxylate, 5453-93-0; methyl acrylate, 96-33-3; allyl 2-oxocyclododecanecarboxylate, 97416-37-0; allyl 1-(hydroxymethyl)-2-oxocyclopentanecarboxylate, 97416-38-1; palladium acetate, 3375-31-3; 2-methyl-3-(2-oxopropyl)cyclopentanone, 97416-39-2; ammonium formate, 540-69-2.

(9) Barco, A.; Benetti, S.; Pollini, G. P. *Synthesis* **1973**, 316.
(10) Tsuji, J.; Nisar, M.; Shimizu, I.; Minami, I. *Synthesis* **1984**, 1009.