Palladium(II)-Catalyzed Oxidation of Aldehydes and Ketones. 1. Carbonylation of Ketones with Carbon Monoxide Catalyzed by Palladium(II) Chloride in Methanol

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Unsubstituted or alkyl-substituted cyclic ketones react with $PdCl_2$ in methanol under a CO atmosphere to give mainly acyclic diesters along with some acyclic chloro-substituted monoesters. The monosubstituted cyclic ketones, 2-hydroxy- and 2-methoxycyclohexanone, do not give ring cleavage but rather produce 2-(carbomethoxy)cyclohex-2-en-1-one. ^{13}CO labeling experiments indicate one CO is inserted in forming the diester product so the second ester group must arise from the original ketone group. Two mechanisms are possible for the diester reaction. One involves initial Pd(II)−CO_2CH_3 insertion across the double bond of the enol form of the ketone while the second involves initial addition of Pd(II)−OCH_3 followed by CO insertion into the new Pd(II)−carbon bond formed. Pd(II) elimination and acid-catalyzed ring cleavage produce the second methyl ester group in both routes. The chloro-substituted monoester is formed by initial Pd(II)−Cl insertion across the double bond followed by the acid-catalyzed ring cleavage. The 2-(carbomethoxy)cyclohex-2-en-1-one must result from elimination of water or methanol from the α-ketoester product formed by the initial methoxycarbonylation of the enol form of the ketone. As expected, the acyclic ketone, 2-decanone, formed methyl acetate and a mixture of methyl nonanoate and 1-chlorooctane as products.

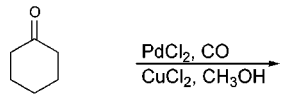
Introduction

The oxidation of carbonyl compounds by metal species is a well-known and widely studied reaction.[1−3] Many of these apparently proceed by oxidation of the enol tautomer. Thus, the oxidation of ketones by the two-electron oxidants, Hg(II), Tl(III), and Mn(VII), were postulated to involve the enol form of the ketone.[4] Some one-electron oxidants such as Mn(III)[5] and tris(1,10-phenanthroline) complexes of Fe(III) and Ru(III),[6] also attack the enol isomer.

The palladium(II)-catalyzed oxidation of olefins is one of the most synthetically useful transition metal catalyzed reactions. One class of such reactions is the carbonylation reaction to give diesters or lactones.[7−9] In comparison, examples of the use of ketones in palladium(II) catalysis as substrates are quite rare. They include telomerizations of butadiene[10] catalyzed by Pd(0) and the dehydration of cyclic ketones.[11−13] An extension of the utilization of ketones as substrates in palladium(II) catalytic chemistry would be a valuable addition to this chemistry. This paper describes the catalytic carbonylation of ketones. Some of these results have been reported in a preliminary communication.[14]

Results

Equation 1illustrates the reaction using cyclohexanone



$$CH_3O_2C(CH_2)_5CO_2CH_3 \;(\mathbf{1}) \;+\; ClCH_2(CH_2)_4CO_2CH_3 \;(\mathbf{2}) \qquad (1)$$

as substrate. The major product is the diester, **1**, with smaller amounts of the chlorinated product, **2**. Table 1 summarizes the results for several ketones.

Carbonylation of α-hydroxy- and α-methoxycyclohexanone, **3**, did not give ring cleavage but rather the

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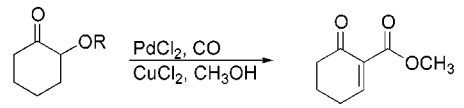
unsaturated β-ketoester, **4**, in eq 2. Carbonylation of the straight chain ketone, 2-decanone, produced methyl acetate, methyl nonanoate, and 1-chlorooctane.

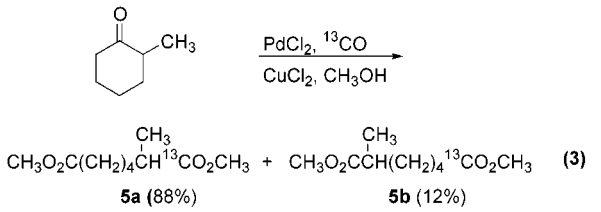


3 **4** (2)

R = H, CH_3

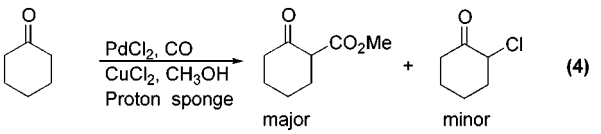
2-Methylcyclohexanone gave products analogous to those obtained from carbonylation of cyclohexanone, and the methyl group allows determination of the position of a ^{13}C label. To test possible mechanisms, 2-methylcyclohexanone was carbonylated in the presence of ^{13}CO in one experiment. Analysis of the two products by ^{1}H and ^{13}C NMR showed that the diester product contains only one labeled carbon, while the chloro compound has no labeled carbon. This result requires that one of the methyl ester groups in the diester product arises from the ketone function.

About 88% of the dimethyl 2-methylpimelate product, **5**, contained the ^{13}C label in the methyl ester group next to the carbon containing the methyl group (**5a** in eq 3). About 12% contained the ^{13}C label in the methyl ester group furthest from the methyl group (**5b** in eq 3).



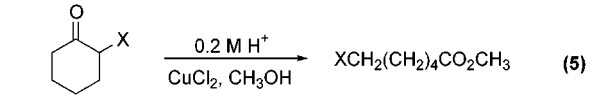
5a (88%) **5b** (12%) (3)

Several control experiments were run to test possible mechanisms. First, the reaction with cyclohexanone was run in the presence of all reactants but $PdCl_2$. No reaction occurred, proving that the reaction was Pd(II)-catalyzed. Second, cyclohexanone was reacted under the usual reaction conditions in the presence of proton sponge to remove any acid present. As shown in eq 4, the major



(4)

product was methyl 2-oxycyclohexanecarboxylate, with traces of 2-chlorocyclohexanone. Thus, the ring cleavage must be acid-catalyzed. Next the methyl 2-oxycyclohexanecarboxylate recovered from the above experiment and a commercial sample of 2-chlorocyclohexanone were reacted with 0.2 M HCl in methanol containing 0.7 M $CuCl_2$. As shown in eq 5, the only products observed in



(5)

X = Cl or CO_2CH_3

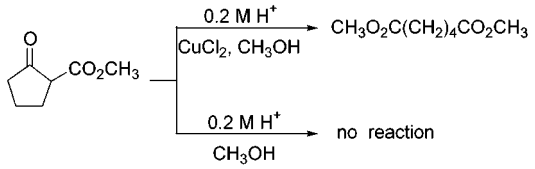
both experiments were the ring cleavage products, methyl 6-chlorohexanoate and dimethyl pimelate, respectively. Finally, the need for both acid and $CuCl_2$ was tested

Table 1. Catalytic Carbonylation of Ketones in Methanol by Palladium(II) Chloride in the Presence of $CuCl_2$[a]

ketone	products (relative yields)	yield, %
cyclopentanone	dimethyl adipate (85%) methyl 5-chloropentanoate (15%)	73
cyclohexanone	dimethyl pimelate (87%) methyl 6-chlorohexanoate (13%)	78
cycloheptanone	dimethyl subarate (90%) methyl 7-chloroheptanoate (10%)	83
2-methylcyclopentanone	dimethyl 2-methyladipate (88%) methyl 5-chlorohexanoate (12%)	78
2-methylcyclohexanone	dimethyl 2-methylpimelate (90%) methyl 6-chloroheptanoate (10%)	78
2-hydroxycyclohexanone	2-(carbomethoxy)cyclohex-2-en-1-one	70
2-methoxycyclohexanone	2-(carbomethoxy)cyclohex-2-en-1-one	53
2-decanone	methyl nonanoate (65%) 1-chlorooctane (35%) methyl acetate (100%)	30

[a] Reaction mixtures contained 0.6 mmol $PdCl_2$, 5 mmol ketone, and 15 mmol $CuCl_2$ in 15 mL of methanol. The CO pressure was approximately 1 atm.

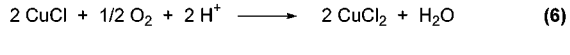
Scheme 1



using commercially available methyl 2-oxocyclopentanecarboxylate. As shown in Scheme 1, ring cleavage occurred only when both HCl and $CuCl_2$ were present but not when only HCl was present.

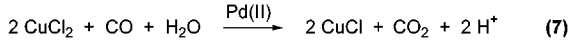
Discussion

The cyclic ketone carbonylation reaction provides a potentially useful route for the preparation of diesters containing one more carbon atom than the original ketone. This results requires that CO is inserted during the course of the reaction, and the ^{13}CO labeling experiments (eq 3) show that one of the ester groups contains a ^{13}CO label. The value of the synthesis could be enhanced by the fact it is a potential air oxidation since the copper(I) chloride is readily reoxidized to copper(II) chloride by oxygen. However, as shown in eq 6, the proton



(6)

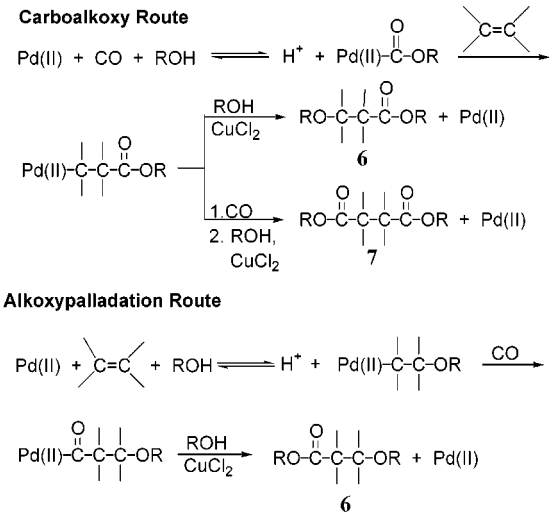
formed during diester formation is removed, and water is formed during the course of the oxidation. If the proton is not initially present, 2-carbomethoxyketone would be the product since, as shown in eq 4, the proton is required for ring cleavage. Of course, if diester is the desired product, extra acid could be added initially. The water formed during the reoxidation will likely react with the CO present in a Pd(II)-catalyzed reaction to form CO_2, resulting in the reduction of more copper(II) chloride (eq 7).



(7)

This side reaction was previously observed for CO reactions using copper(II) chloride as the reoxidant when a dehydrating agent was not present.[7] Thus, the reoxidation step will probably have to be run in a separate reaction in the absence of CO and in the presence of a

Scheme 2



dehydrating agent such as trimethyl orthoformate. Finally, terminally chloride-substituted esters are side products of the reaction. Since CO is not required for this synthesis, these chloride-substituted esters would presumably become the only product in the absence of CO.

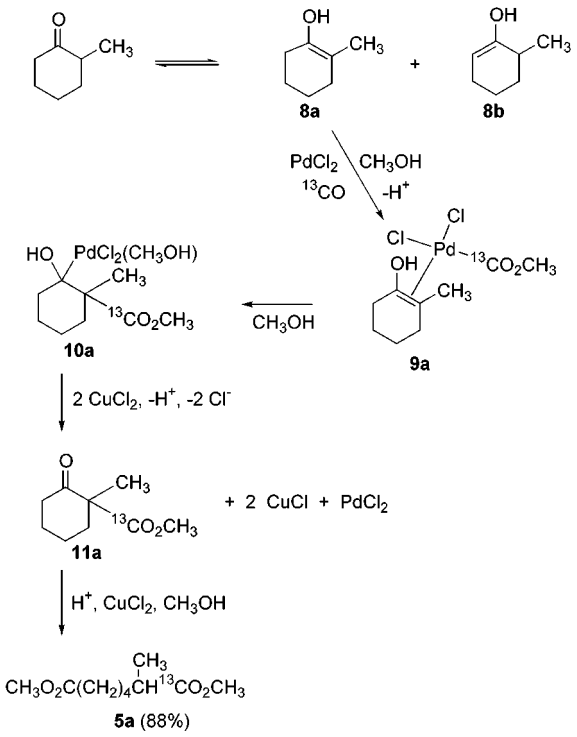
Any mechanism for the carbonylation would be expected to be similar to those previously observed for the carbonylation of simple olefins. Actually, two routes are observed in alcohol solvent: the carboalkoxy and the alkoxypalladation mechanisms. These two pathways are outlined in Scheme 2. There is considerable analogy in palladium(II) catalysis for both routes, and apparently both routes are operative with the predominate one, depending on reaction conditions.[15] Note that the carboalkoxy route explains the presence of succinate esters, **7**, found in addition to the β-alkoxyproprionate ester, **6**, predicted by the alkoxypalladation mechanism.[16]

The carbomethoxy mechanism for 2-methylcyclohexanone that is consistent with all the experimental results is shown in Scheme 3. The initial enolization gives the species **8a** and **8b**. The route for **8a**, which accounts for 88% ofthe labeled products, is illustrated. The route for **8b**, which gives 12% of the labeled products, is entirely analogous. The π-complex, **9a** inserts the carbomethoxy group to give **10a** which decomposes to give **11a**. The final product **5a** arises from ring cleavage of **11a** catalyzed by acid formed during the course of the reaction.

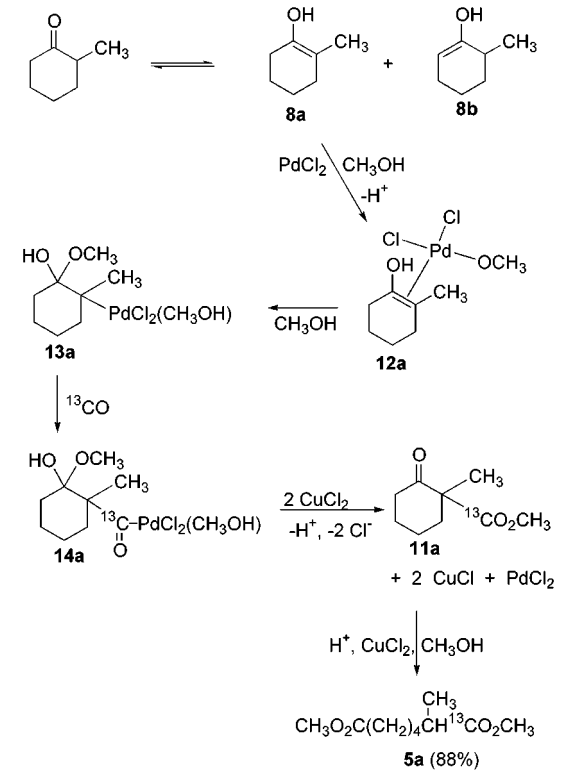
The alkoxypalladation route is outlined in Scheme 4. The initial π-complex, **12a**, undergoes olefin insertion into the Pd−OCH_3 bond to produce **13a** which in turn inserts ^{13}CO into the Pd−carbon bond to form **14a**. Oxidative decomposition of **14a** produces **11a** that undergoes the same ring cleavage as in Scheme 3 to give the final product **5a**. An analogous route with **8b** gives the other isomer **5b** (eq 3).

The route for the chlorine-containing product, shown in Scheme 5, is analogous to the diester route shown in Scheme 3. However chloride, rather than carbomethoxy,

Scheme 3



Scheme 4

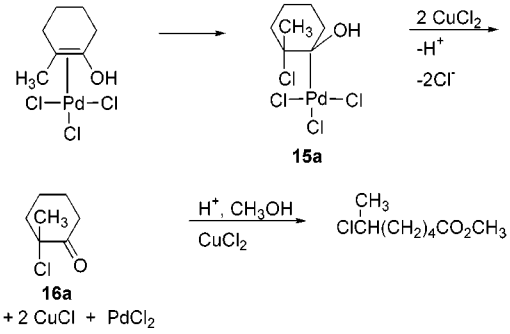


adds to **8a** to give the intermediate **15a** that decomposes in the same fashion as **10a** in Scheme 3 to give **16a** which undergoes ring cleavage to produce methyl 6-chloroheptanoate. The same addition to **8b** would eventually give methyl 6-chloro-2-methylhexanoate. This product was not observed. On the other hand, chloropalladation in the opposite fashion would give an intermediate analogous to **13a** in Scheme 4. This intermediate could insert ^{13}CO and eventually lead to **5a** by the route shown in Scheme 4. It is thus possible that some of the **5a** product is formed

(15) For a discussion of olefin carbonylation, see: Henry, P. M. *Palladium Catalyzed Oxidation of Hydrocarbons*; D. Reidel: Dordrecht, Holland, 1980; pp 193-212.

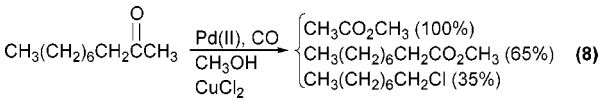
(16) A third mechanism, specific to ketones, involves oxa-π-allylpalladium complexes.[17] These intermediates may very well be operative in some reactions especially when silyl enol ethers, rather than ketones, are the substrates. However, carbonylation only occurs when the silyl ethers cannot undergo β-elimination.[18] Thus this mechanism does not appear applicable to the present system.

Scheme 5



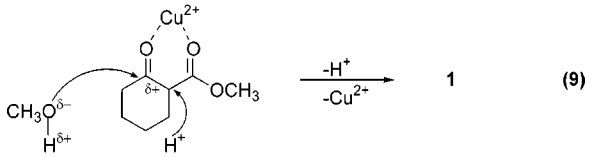
by the chloropalladation route. A similar route with **8b** would produce **5b**. Analogous chloropalladation routes have been observed with simple olefins.[19]

As expected from the results with cyclic olefins, the straight chain ketone, 2-decanone, gives methyl nonanoate, 1-chlorooctane, and methyl acetate (eq 8).



(8)

The control experiments support the proposed mechanisms. In the presence of proton sponge to remove the acid formed, cyclohexanone gives methyl 2-oxycyclohexanecarboxylate (eq 4) rather than the ring-cleaved product, dimethyl pimelate (**1** in eq 1). In the presence of HCl and $CuCl_2$ the methyl 2-oxycyclohexanecarboxylate and 2-chlorocyclohexanone are cleaved to **1** and **2**, respectively (eq 5), demonstrating that the intermediates **11a** and **16a** in Schemes 3, 4, and 5 will cleave under the reaction conditions. The control experiments with methyl 2-oxocyclopentanecarboxylate, shown in Scheme 1, demonstrate that, in fact, *both HCl and $CuCl_2$ are required for the ring cleavage.* As shown in eq 9, the Cu(II) could be

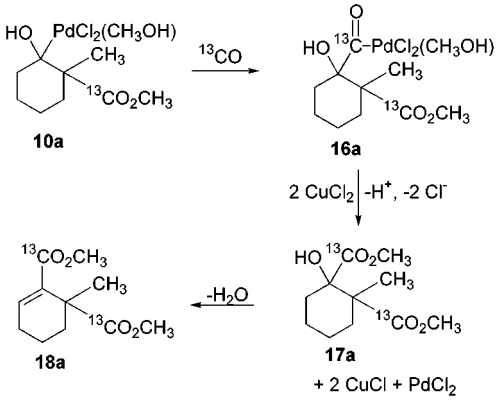


(9)

complexing the carbonyl oxygen, thus making the carbonyl carbon more susceptible to attack by the oxygen of the methanol.

Further studies are required to answer questions concerning some details of the mechanism. One of the major questions concerns the role of the proton on rates of reaction. The effects are complicated and opposing. On one hand both the rates of enolization as well as the reverse reactions shown in Schemes 3 and 4 are acid catalyzed while the value of the equilibrium constant is acid independent. Although the values of these constants have not been determined in methanol, they are known in aqueous solution.[7] Unless the values in methanol are dramatically different from those in water, equilibrium should be established for the entire course of the carbonylation reaction. Thus acid catalysis is not expected for the enolization reaction.

Scheme 6



On the other hand, since complete conversions were not achieved in any of the reactions, inhibition by the acid that is accumulating during the reaction is a likely prospect. The formation of the initial intermediates, **9a** in Scheme 3 and **12a** in Scheme 4, involve the loss of a proton. Thus, acid might be expected to decrease the concentration of these intermediates and decrease the rate of the overall reaction. Experimental evidence supports this acid inhibition for the formation of these species. In the corresponding equilibrium with stable Pt(II) species, acid has been found to inhibit the formation of the carbomethoxy species.[20] The oxidation of simple olefins in methanol, which must involve intermediates similar to **12a**, display acid inhibition.[21] Studies of initial rates of diester formation in the presence and absence of various amounts of added acid will determine the acid dependence of the reaction.

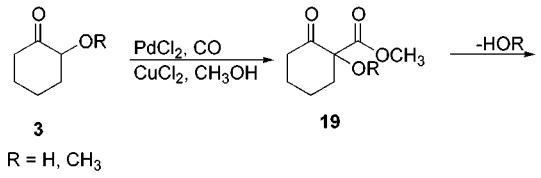
A related question is the effect of acid on the ratio of the chloroester to diester. In the route shown in Scheme 5 acid would not be expected to inhibit the addition of chloride to the enol. Thus, if acid inhibits addition of the carbomethoxy species, the ratio of chloroester to diester should increase during the course of the run. The small amount of chloroester found in the reaction in the presence of proton sponge is consistent with this assumption. This question will be answered by determining the chloroester-to-diester ratios in the rate experiments outlined in the previous paragraph.

The carbomethoxy (Scheme 3), methoxypalladation (Scheme 4), and chloropalladation (Scheme 5) mechanisms illustrate that the intermediates that contain Pd(II) bonded to the carbon containing the hydroxy (**10a** in Scheme 3 and **15a** in Scheme 5) are too unstable to insert another CO before decomposition by Pd(0) elimination. On the other hand, the intermediate containing the Pd(II) bonded to an unsubstituted carbon (**13a** in Scheme 4) is stable enough to insert a CO molecule. There is prior evidence that α-hydroxyl groups greatly increase the ease of removal of Pd(0).[22] An intriguing possibility is that at higher CO pressures CO could be inserted into this Pd(II)−carbon bond before decomposition. For example, as shown in Scheme 6, **10a** in Scheme 3 would give the intermediate **16a** which would decompose to **17a**. Since

(17) Trost, B. M.; Verhoeven, T. R. In *Comprehensive Organometallic Chemistry*; Wilkenson, G.; Stone, F. G. A.; Abel, E. W., Eds.; Pergamon Press: Oxford, 1982; Vol. 8, pp 838−841.
(18) Ito, Y.; Nakatsuka, M.; Kise, N.; Saegusa, T. *Tetrahedron Lett.* **1980**, *21*, 2873−2876.
(19) Tsuji, J.; Morikawa, M.; Kiji, J. *J. Am. Chem. Soc.* **1964**, *86*, 4851−4853.
(20) Byrd, J. E.; Halpern, J. *J. Am. Chem. Soc.* **1971**, *93*, 1634−1636.
(21) Lee, H.-B.; Henry, P. M. *Can. J. Chem.* **1976**, *54*, 1726−1738.
(22) See: Henry, P. M. *Palladium Catalyzed Oxidation of Hydrocarbons*; D. Reidel: Dordrecht, Holland, 1980; pp 76−77.

17a would most likely eliminate water (see following discussion), the final observed product would probably be **18a**.

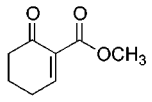
The route for the formation of the unsaturated cyclic ketonic ester, **4**, from α-hydroxy- or α-methoxycyclohexanone in eq 2 is most likely the same as for the other ketones. However, as shown in eq 10, elimination of



3

R = H, CH_3

19



4 (10)

water or methanol happens before ring cleavage can occur. The elimination may be acid-catalyzed so in the presence of proton sponge **19** may be the product.

In summary, this report describes a novel carbonylation of ketones that generally occurs with carbon−carbon bond cleavage to give diesters. A side reaction is the formation of terminally chlorine-substituted acid esters.

Experimental Section

General. ^{1}H and ^{13}C NMR data were recorded on a Varian VXR 400S NMR. All chemical shifts are reported relative to tetramethylsilane as internal standard. GLC analyses were carried out using a GOW-MAC 350 gas chromatography fitted with Carbowax 10 M on 80−100 mesh Chromosorb W-NAW columns.

Materials. All chemicals were purchased from Aldrich Chemical Co., unless otherwise specified, and were used as received. $PdCl_2$ and 2-methylcyclohexanone were purchased from Alfa AEsar and used without further purification. Methanol was distilled over magnesium alkoxide.

General Procedure for the $PdCl_2$-Catalyzed Carbomethoxylation of Ketones. All reactions were conducted in dry glassware under a positive pressure of carbon monoxide of a little over 1 atm. A two-necked round-bottom flask (100 mL) equipped with a magnetic stirring bar, septum, and balloon was charged with $CuCl_2$ (2.0 g, 15.0 mmol), $PdCl_2$ (0.10 g, 0.56 mmol), and methanol (15 mL). The air in the flask was replaced by CO by evacuating on an aspirator and then pressuring with CO through a needle. Then 5 mmol of ketone was injected, and the CO pressure was raised to a little over 1 atm. The reaction mixture was stirred at room temperature for 4 days. After removing the solvent under reduced pressure, the residue was dissolved in CH_2Cl_2, washed with diluted $NaHCO_3$ (20 mL), and dried over $MgSO_4$. CH_2Cl_2 was then removed under reduced pressure, and the residue was purified by either preparative GLC or column chromatography (hexane/AcOEt = 8/2). In every reaction, 15−20% of the starting material was recovered. The percent yields based on ketone were obtained by GLC analysis in the presence of an internal standard.

Carbonylation of Cyclopentanone. Carbonylation of cyclopentanone (0.45 mL, 5.0 mmol) gave dimethyl adipate and methyl 5-chloropentanoate in relative yields of 85% and 15%, respectively, and a chemical yield of 58%. Data for dimethyl adipate: ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.66 (s, 6H), 2.32 (m, 4H), 1.65 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.8, 51.6, 33.7, 24.4. Data for methyl 5-chloropentanoate: ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.68 (s, 3H), 3.56 (t, 2H), 2.36 (t, 2H), 1.80 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.6, 51.6, 44.4, 33.2, 31.8, 22.2.

Carbonylation of Cyclohexanone. Carbonylation of cyclohexanone (0.52 mL, 5.0 mmol) gave dimethyl pimelate, **1**, and methyl 6-chlorohexanoate, **2**, in relative yields of 87% and 13%, respectively, and a chemical yield of 62%. Data for **1**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.66 (s, 6H), 2.32 (m, 4H), 1.65 (m, 4H), 1.38 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.0, 51.5, 33.8, 28.6, 24.6. Data for **2**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.67 (s, 3H), 3.53 (t, J = 6.60 Hz, 2H), 2.33 (t, J = 7.35 Hz, 2H), 1.8 (q, 2H, J = 7.80 Hz, 2H), 1.65 (q, J = 7.80 Hz, 2H), 1.50 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.9, 51.5, 44.8, 33.8, 32.2, 26.4, 24.2.

Carbonylation of Cycloheptanone. Carbonylation of cycloheptanone (0.59 mL, 5.0 mmol) gave dimethyl subarate and 7-chloroheptanoate in relative yield of 90% and 10%, respectively, and a chemical yield of 66%. Data for dimethyl subarate: ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.86 (s, 6H), 2.32 (t, 4H), 1.65 (m, 4H), 1.36 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.1, 51.5, 34.0, 28.8, 25.8. Data for methyl 7-chloroheptanoate: ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.68 (s, 3H), 3.54 (t, 2H), 2.32 (t, 2H), 1.78 (m, 2H), 1.64 (m, 2H), 1.44 (m, 2H), 1.38 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.1, 51.5, 44.9, 33.9, 32.4, 28.4, 26.5, 24.7.

Carbonylation of 2-Methylcyclopentanone. Carbonylation of 2-methylcyclopentanone (0.54 mL, 5.0 mmol) gave dimethyl 2-methyl adipate and methyl 5-chlorohexanoate in relative yields of 88% and 12%, respectively, and a chemical yield of 62%. Data for dimethyl 2-methyl adipate: ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.68 (s, 3H), 3.67 (s, 3H), 2.48 (m, 1H), 2.30 (t, 2H), 1.65 (m, 3H),1.45 (m, 1H), 1.15 (d, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.8, 173.7, 51.4, 51.3, 39.2, 33.6, 33.1, 22.6, 16.9. Data for methyl 5-chlorohexanoate: ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.20 (m, 1H), 3.65 (s, 3H), 2.33 (t, 2H), 1.76 (m, 2H), 1.68 (m, 2H), 1.50 (d, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.8, 50.8, 43.1, 33.7, 30.0, 24.3, 9.6.

Carbonylation of 2-Methylcyclohexanone. Carbonylation of 2-methylcyclohexanone (0.61 mL, 5.0 mmol) gave dimethyl 2-methylpimelate, and methyl 6-chloroheptanoate in relative yields of 90% and 10%, respectively, and in a chemical yield of 64%. Data for dimethyl 2-methylpimelate: ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.68 (s, 3H), 3.67 (s, 3H), 2.48 (m, 1H), 2.30 (t, 2H), 1.65 (m, 6H), 1.15 (d, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.9, 173.8, 51.5, 51.4, 39.3, 33.9, 33.4, 26.8, 24.9, 17.2. Data for methyl 6-chloroheptanoate: ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.14 (m, 1H), 3.64 (s, 3H), 2.32 (t, 2H), 1.72 (m, 2H), 1.65 (m, 2H), 1.50 (d, 3H), 1.43 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.9, 58.5, 51.5, 39.9, 33.9, 26.2, 25.3, 24.1.

Carbonylation of 2-Hydroxycyclohexanone. Carbonylation of 2-hydroxycyclohexanone (0.23 g, 2.0 mmol) gave 2-(carbomethoxy)cyclohex-2-en-1-one, **4**, (0.17 g, 55%) yield. The product was purified by column chromatography (hexane/ethyl acetate = 8/2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.93 (t, J = 4.76 Hz, 1H), 3.60 (s, 3H), 2.52 (t, J = 7 Hz, 2H), 2.43 (q, J = 5.7 Hz, 2H), 1.95 (m,2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.4, 175.0, 151.5, 116.3, 54.7, 38.8, 24.4, 23.0.

Carbonylation of 2-Methoxycyclohexanone. Carbonylation of 2-methoxycyclohexanone (0.26 g, 2.0 mmol) gave 2-(carbomethoxy)cyclohex-2-en-1-one, **4,** (0.11 g, 36%) yield.

Carbonylation of 2-Decanone. Carbonylation of 2-decanone afforded methyl nonanoate, 1-chlorooctane, and methyl acetate in relative yields of 65%, 35%, and 100%, respectively, and a chemical yield of 42%. Data for methyl nonanoate: ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.67 (s, 3H), 2.30 (t, 2H), 1.65 (m, 2H), 1.30 (m, 10H), 0.89 (t, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.4, 51.4, 34.1, 31.8, 29.2, 29.1, 29.0, 24.9, 22.6, 14.1. Data for 1-chlorooctane: ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.54 (t, 2H), 1.78 (m, 2H), 1.45 (m, 2H), 1.30 (m, 8H), 0.89 (t, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ: 45.2, 32.6, 31.7, 29.1, 28.8, 27.0, 22.6, 14.1. Methyl acetate was identified by GLC retention time.

Carbonylation of 2-Methylcyclohexanone in the Presence of ^{13}CO. Carbonylation of 2-methylcyclohexanone (0.52 mL, 5.0 mmol) in the presence of ^{13}CO was carried out as before to give dimethyl 2-methylpimelate (**5**) and methyl 6-chloroheptanoate in relative yield of 85% and 15%, respectively. Analysis by ^{1}H and ^{13}C NMR showed that the product **5** is a mixture of two isomers **5a** and **5b** in relative yield of

88% and 12%, respectively. Data for **5a**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.68 (d, J = 1.6 Hz, 3H), 3.66 (s, 3H), 2.43 (m, 1H), 2.32 (m, 2H), 1.42−1.63 (m, 6H), 1.18 (dd, J = 6.8 and 4.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.9, 173.8 51.6 (d, J = 10.8 Hz), 51.5, 39.5 (d, J = 225.6 Hz), 33.8, 33.1, 26.7, 24.8 (d, J = 11.2 Hz), 17.1. Data for **5b**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.67 (d, J = 1.6 Hz, 3H), 3.65 (s, 3H), 2.40 (m, 1H), 2.30 (m, 2H), 1.42−1.63 (m, 6H), 1.16 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.0, 173.8 51.6, 51.5 (d, J = 10.8 Hz), 39.2 (d, J = 113.6 Hz), 34.2, 33.7, 26.8, 24.7, 17.1.

Control Experiment: "Carbonylation" of Cyclohexanone in the Absence of $PdCl_2$. The reaction was carried out under CO pressure using the balloon method. To a solution of $CuCl_2$ in methanol (12.0 mL) was added cyclohexanone (0.70 g, 5.3 mmol). The resulting green solution was allowed to stir for 24 h. During the stirring period no change in color was observed. The solvent was removed under reduced pressure by a rotary evaporator. The residue was extracted with diethyl ether (3 × 50 mL), dried over $MgSO_4$, and concentrated. ^{1}H and ^{13}C NMR analysis of the residue showed that only starting material was present.

Control Experiment: Ring Cleavage of 2-Chlorocyclohexanone in the Presence of HCl. A 0.25 M HCl solution was prepared in methanol and used in this experiment. To a solution of $CuCl_2$ (1.07 g, 10.8 mmol) in methanol (15.0 mL, contains 0.25 M HCl) was added 2-chlorocyclohexanone (0.70 g, 5.3 mmol). The resulting green mixture was stirred for 24 h. Then methanol was removed under reduced pressure, and the residue was extracted with Et_2O (3 × 50 mL). The combined ether extracts was then washed with aq $NaHCO_3$ and water, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was then chromatographed over silica gel and eluted with 50% hexane and methylene chloride. Two products were isolated. They were identified by ^{1}H and ^{13}C NMR to be the staring material and methyl 6-chlorohexanoate.

Control Experiment: Carbonylation of Cyclohexanone in the Presence of Proton Sponge. To a mixture of $PdCl_2$ (0.196 g, 1.11 mmol), $CuCl_2$ (1.46 g, 10.8 mmol), proton sponge (0.536 g, 2.50 mmol), and 12.0 mL of methanol in a 100 mL round-bottom flask was added cyclohexanone (0.50 g, 5.0 mmol). The light red mixture was allowed to stir for 48 h under CO pressure. A black precipitate was removed by filtration, and the filtrate was concentrated under reduced pressure. The residue was extracted with ether (3 × 50 mL), and the combined extracts were washed with $NaHCO_3$ solution and water, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to produce yellowish-pink-colored residue. The residue was chromatographed on a silica gel column by first eluting with hexane and then with 5% ethyl acetate in hexane. Three products were isolated. Analysis by ^{1}H and ^{13}C NMR showed that the products were cyclohexanone, methyl 2-oxoycyclohexanecarboxylate, and 2-chlorocyclohexanone. Data for methyl 2-oxoycyclohexanecarboxylate: ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.66 (s, 3H), 2.39 (t, J = 7.20, 1H), 2.31 (t, J = 7.40, 2H), 1.64 (m, 4H), 1.46 (m, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.2, 174.0, 51.5, 42.5, 33.8, 28.6, 24.7, 24.5 ppm.

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