Titanocene-Catalyzed Cyclocarbonylation of *o*-Allyl Aryl Ketones to γ-Butyrolactones

Natasha M. Kablaoui,[†] Frederick A. Hicks,[‡] and Stephen L. Buchwald*

Contribution from the Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

Received January 15, 1997[⊗]

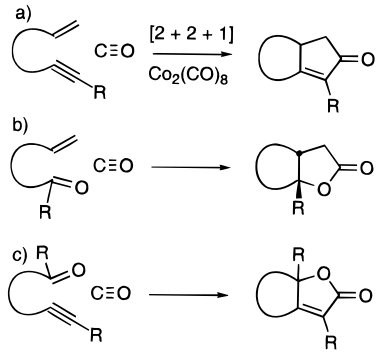
Abstract: A method for the transformation of *o*-allyl aryl ketones to γ-butyrolactones using a catalytic amount of $Cp_2Ti(PMe_3)_2$ or $Cp_2Ti(CO)_2$ is described. This catalytic "hetero Pauson−Khand"-type process proceeds *via* the carbonylation of an oxatitanacycle followed by thermally-induced reductive elimination to form a γ-butyrolactone and to regenerate the catalyst. We have investigated the scope and limitations of this catalytic methodology. Our results are consistent with the view that the key step in this catalytic cycle is formation of a charge transfer complex or involves reversible electron transfer between the catalyst and the substrate.

Introduction and Background

The growing interest in the development of organic reactions mediated and catalyzed by organotransition metals stems from the ability to assemble complex molecules from simple starting materials[1] in a convergent and atom-economical manner.[2] One reaction that exemplifies this concept is the Pauson−Khand reaction, in which an alkyne, an alkene, and carbon monoxide are condensed in a formal [2 + 2 + 1] cycloaddition to form cyclopentenones using $Co_2(CO)_8$ (Scheme 1a).[3] Recently we reported a heteroatom variant of the intramolecular Pauson−Khand reaction mediated by $Cp_2Ti(PMe_3)_2$ in which either the alkyne or the alkene can be replaced by a carbonyl.[4] This new reaction results in the diastereoselective formation of γ-butyrolactones or fused butenolides, respectively (Scheme 1b,c). In that report, we showed that the "hetero Pauson−Khand" reaction is mediated by $Cp_2Ti(PMe_3)_2$ for most enones and enals studied, but acetophenone derivatives can be transformed using a catalytic amount of the titanium complex. We have studied the catalytic cyclocarbonylation of enones in more detail and have found that a variety of olefinic aryl ketones are viable substrates for the catalytic reaction.

Our work on the reductive cyclization of enones using titanocene reagents was inspired by the report of Hewlett and Whitby that $Cp_2Ti(PMe_3)_2$ can react with enones to form bicyclic oxametallacycles **1** (see Scheme 2).[5] Subsequently,

Scheme 1



we[6,7] and Crowe[8] have developed a catalytic reductive cyclization of enones to cyclopentanols which combines oxametallacycle formation with a σ-bond metathesis reaction (Scheme 2). In this process, we postulate that the Ti−O bond of the intermediate oxametallacycle **1** is cleaved *via* a σ-bond metathesis reaction[9] with Ph_2SiH_2 to form a titanocene alkyl hydride, **2**. The hydride then undergoes ligand-induced reductive elimination[10] to regenerate the titanocene catalyst and to form the silylated cyclopentanol, **3**, which can be hydrolyzed to the desired cyclopentanol. We subsequently became interested in processes which utilize the reactivity of the Ti−C bond in the oxatitanacycle **1**. We decided to begin our investigation by studying the formation and decomposition of **1** in the presence of carbon monoxide. We chose CO since insertion to form **4** (Scheme 3) followed by reductive elimination would yield a γ-butyrolactone **5**.

In related all-carbon metallacycles, insertion of CO and isonitriles into the Ti−C bonds is a facile process; there are many examples of enyne cyclocarbonylation using early transition metals.[11−13] Studies conducted by Caulton[14] on the carbonylation (at 1 atm) of the related $Cp_2Zr(Me)X$ system

[†] Fellow of the Organic Chemistry Division of the American Chemical Society, sponsored by Smith-Kline Beecham.

[‡] National Science Foundation Predoctoral Fellow, 1994−1997.

[⊗] Abstract published in *Advance ACS Abstracts,* April 15, 1997.

(1) For lead references, see: (a) Broene, R. D.; Buchwald, S. L. *Science* **1993**, *261*, 1696. (b) Broene, R. D. In *Comprehensive Organometallic Chemistry II*; Hegedus, L. S., Ed.; Pergamon: Oxford, 1995; Vol.12, Chapter 3.7, p 323. (c) Buchwald, S. L.; Broene, R. D. In *Comprehensive Organometallic Chemistry II*; Hegedus, L. S., Ed.; Pergamon: Oxford, 1995; Vol.12, Chapter 7.4, p 771 and references within.

(2) Trost, B. M. *Science* **1991**, *254*, 1471.

(3) Schore, N. E. In *Comprehensive Organometallic Chemistry II*; Hegedus, L. S., Ed.; Pergamon: Kidlington, 1995; Vol. 12, p 703 and references within. For catalytic examples, see: (a) Jeong, N.; Hwang, S. H.; Lee, Y.; Chung, Y. K. *J. Am. Chem. Soc.* **1994**, *116*, 3159. (b) Lee, B. Y.; Chung, Y. K.; Jeong, N.; Lee, Y.; Hwang, S. H. *J. Am. Chem. Soc.* **1994**, *116*, 8793. (c) Pagenkopf, B. L.; Livinghouse, T. J. *J. Am. Chem. Soc.* **1996**, *118*, 2285.

(4) Kablaoui, N. M.; Hicks, F. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 5818.

(5) Hewlett, D. F.; Whitby, R. J. *J. Chem. Soc., Chem. Comm.* **1990**, 1684.

(6) Kablaoui, N. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1995**, *117*, 6785.

(7) Kablaoui, N. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 3182.

(8) Crowe, W. E.; Rachita, M. J. *J. Am. Chem. Soc.* **1995**, *117*, 6787.

(9) Berk, S. C.; Kreutzer, K. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1991**, *113*, 5093.

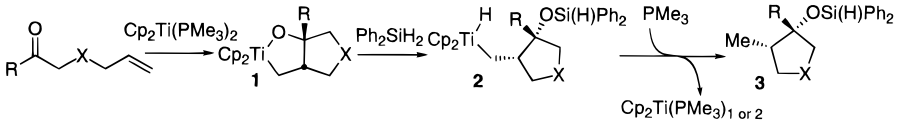
(10) Gell, K. I.; Schwartz, J. *J. Am. Chem. Soc.* **1981**, *103*, 2687.

(11) Grossman, R. B.; Buchwald, S. L. *J. Org. Chem.* **1992**, *57*, 5803.

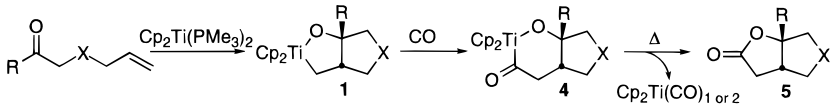
(12) Negishi, E.-i. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Ed.; Pergamon: Oxford, 1991; Vol. 5, pp 1163−1184.

S0002-7863(97)00115-7 CCC: $14.00

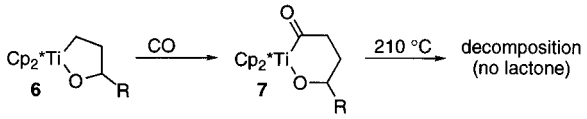
Scheme 2



Scheme 3



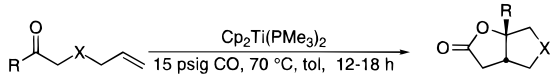
Scheme 4

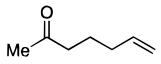
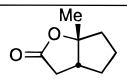
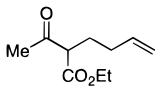
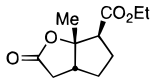
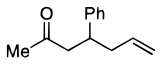
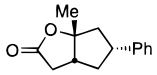
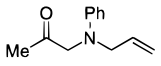
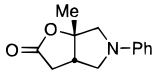
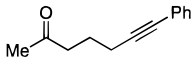
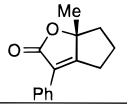


showed that insertion of CO into the Zr−C bond was heavily dependent on the nature of the ligand X. Facility of carbonylation was found to decrease in the series: Me > Cl > OEt, with no carbonylation observed for $Cp_2Zr(Me)OEt$. These results were deemed to reflect the ability of the lone pairs on the alkoxide and chloride to π-donate into the vacant metal orbital, rendering the complex coordinatively saturated (18 e^-) and thus hindering the carbonylation reaction. This study suggested that the carbonylation of early transition metal oxametallacycles would be difficult. Takaya,[15] however, showed that carbonylation did occur in the more electron-rich, and hence less oxophilic, Cp^*_2Ti oxametallacycle systems, **6** (Scheme 4). The CO inserted into the Ti−C bond to form carbonylated metallacycles, **7**, but these metallacycles did not undergo thermally-induced reductive elimination to form γ-butyrolactones; instead they decomposed at elevated temperatures (210 °C).

We[4] and Crowe[16] have found that carbonylation of the titanacycle **1** also occurs, with CO inserting into the Ti−C bond to form carbonylated metallacycle **4** (Scheme 3). We have confirmed the intermediacy of this metallacycle for R = H by X-ray crystallography. In our system, reductive elimination is induced thermally (70 °C) to form γ-butyrolactone **5** and $Cp_2Ti(CO)_2$. Table 1 shows the reaction conditions and several examples of enones cyclocarbonylated using this methodology. A striking feature of the "hetero Pauson−Khand" reaction is that γ-butyrolactones are formed with complete diastereoselectivity. In contrast, both the catalytic reductive cyclization of enones to form cyclopentanols[6−8] and Crowe's similar γ-butyrolactone synthesis,[16] which proceed through the same intermediate metallacycle, **1**, suffer from poor diastereoselectivities in many cases. This discrepancy can be explained by noting that both the catalytic reductive cyclization and Crowe's cyclocarbonylation reaction are run at low temperature (−20 °C and room temperature, respectively); the selectivities observed are therefore realized under conditions of kinetic control.[17] Since the present reaction takes place at 70 °C, complete equilibration to the more thermodynamically stable metallacycle leads to the formation of a single isomer of the γ-butyrolactone.

Table 1. The Stoichiometric Cyclocarbonylation of Enones and an Ynone[4]



Entry	Substrate	Product	Isolated Yield (%)
1			65
2			90
3			92
4			80
5			28

Results and Discussion

The "hetero Pauson−Khand" reaction is the first completely diastereoselective synthesis of γ-butyrolactones from the condensation of an alkene, a carbonyl moiety, and CO. In a single process, two carbon−carbon bonds and two rings are constructed. A drawback to the method is the necessity of using a stoichiometric amount of the metal to carry out the reaction. A catalytic variant of this procedure would be a significant improvement. This not only would decrease the amount of waste produced by reaction but also would make the potential use of expensive chiral catalysts more feasible.

In order to develop a catalytic reaction sequence, the metal coproduct of the initial cyclization, $Cp_2Ti(CO)_2$, must be induced to react again with the starting material. The metal is in the same oxidation state as the original titanocene reagent, $Cp_2Ti(PMe_3)_2$, and the titanocene fragment remains intact. However, due to backbonding, CO forms much stronger bonds with the titanium center than does PMe_3, and therefore $Cp_2Ti(CO)_2$ does not react with most enones to form oxametallacycles, **1**, under thermal conditions. Titanocene dicarbonyl[18] has previously been shown to react with ketenes,[19] acetylenes,[20,21] and CO_2 equiva-

(13) Negishi, E.; Holmes, S. J.; Tour, J. M.; Miller, J. A.; Cedarbaum, F. E.; Swanson, D. R.; Takahashi, T. *J. Am. Chem. Soc.* **1989**, *111*, 3336.

(14) Marsella, J. A.; Moloy, K. G.; Caulton, K. G. *J. Organomet. Chem.* **1980**, *201*, 389.

(15) Mashima, K.; Haraguchi, H.; Oyoshi, A.; Sakai, N.; Takaya, H. *Organometallics* **1991**, *10*, 2731.

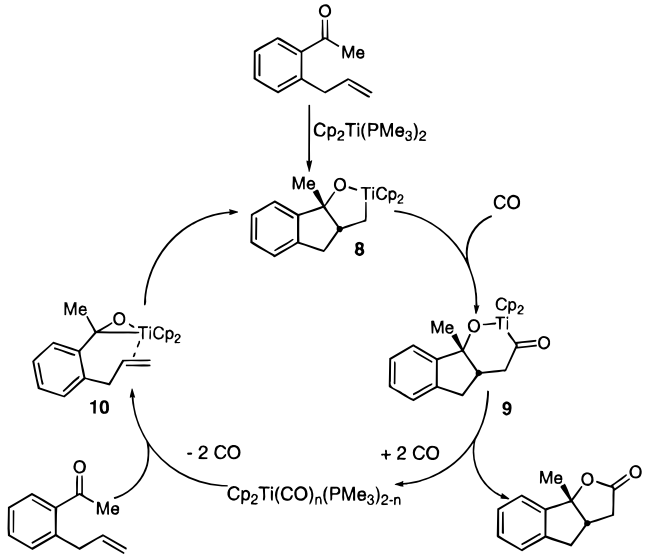
(16) Crowe, W. E.; Vu, A. T. *J. Am. Chem. Soc.* **1996**, *118*, 1557.

(17) The metallacycles in many cases are formed initially as kinetic mixtures of diastereomers which then equilibrate to the thermodynamically favored product. Equilibration is slow at lower temperatures. (See ref 7)

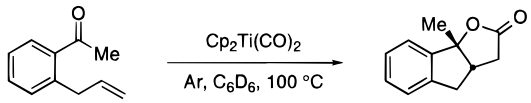
(18) For a review on the reactivity of $Cp_2Ti(CO)_2$, see: Sikora, D. J; Macomber, D. W.; Rausch, M. D. *Adv. Organometallic Chem.* **1986**, *25*, 317.

(19) Fachinetti, G.; Biran, C.; Floriani, C.; Chiesi-Villa, A.; Guastini, C. *J. Am. Chem. Soc.* **1978**, *100*, 1921.

Scheme 5



Scheme 6



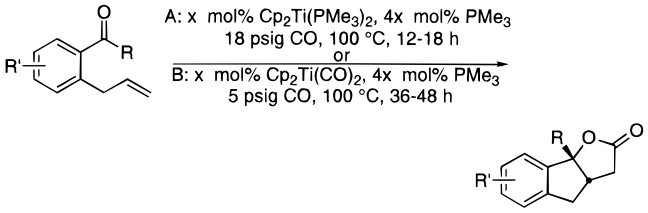
lents.[22] More recently it was reported that $Cp_2Ti(CO)_2$ also reacts with α,β-unsaturated aryl ketones.[23] This encouraged us to try to find a class of enone substrates that would also react with titanocene dicarbonyl, opening the way to the development of a catalytic process.

We have found that conjugated aromatic ketones with a suitably positioned olefin can be converted to γ-butyrolactones using a catalytic amount of the metal complex. In general, the substrates feature a keto moiety and an allyl group situated in an ortho-relationship on an aromatic ring. For example, in our initial communication we reported that *o*-allylacetophenone can be converted to the corresponding lactone in excellent yield using 10 mol % $Cp_2Ti(PMe_3)_2$.[4] The proposed catalytic cycle is shown in Scheme 5. As mentioned above, the key to rendering the cyclocarbonylation catalytic is the ability of *o*-allylacetophenone to react with the $Cp_2Ti(CO)_2$ (or possibly the mixed ligand catalyst $Cp_2Ti(CO)(PMe_3)$, *vide infra*) co-product to form oxametallacycle **8**. In support of the viability of this step in the catalytic cycle, we have found that *o*-allylacetophenone reacts directly with $Cp_2Ti(CO)_2$ to form the γ-butyrolactone upon heating under an atmosphere of argon (Scheme 6).

Table 2 shows the results of the catalytic conversion of *o*-allyl aryl ketones to γ-butyrolactones under the conditions shown in Scheme 7. Catalyst levels range from 5% to 20% depending on the nature of the substrate (*vide infra*). This methodology tolerates various functional groups such as aryl fluorides (entry 3), ethers (entry 5), and esters (entry 6). We have shown that catalytic activity is not limited to *o*-allylacetophenone derivatives, since allylacetonaphthones (entries 7 and 8) and allylbenzophenones (entry 4) are also viable substrates.

Scheme 7 shows the two catalyst systems that have been developed for this transformation. The original system (A) uses

Scheme 7



$Cp_2Ti(PMe_3)_2$ as the catalyst and is run at 18 psig CO for 12−18 h. The addition of excess PMe_3 was found to decrease the amount of catalyst necessary for complete conversion to the product.[24] The second catalyst system (B) uses the commercially available $Cp_2Ti(CO)_2$[25] as the catalyst and is run at only 5 psig CO. In this system, excess PMe_3 is also required.[26] We believe that the excess PMe_3 may be necessary to produce $Cp_2Ti(PMe_3)(CO)$,[27] which may act as a more efficient catalyst than titanocene dicarbonyl, due to the lability of the PMe_3 ligand and/or for electronic reasons. $Cp_2Ti(PMe_3)(CO)$ has been shown to form when $Cp_2Ti(PMe_3)_2$ is heated under CO pressure or when $Cp_2Ti(CO)_2$ is heated in the presence of PMe_3. Trimethylphosphine may also play a role in facilitating the ligand-induced reductive elimination[10] of the organic fragment from intermediate **9**. We are currently investigating the mechanism of this process to enhance our understanding of these observations.

While most of the substrates are cyclocarbonylated efficiently using either catalyst system, substrates that contain structural attributes that make them more difficult to cyclize are transformed more efficiently using $Cp_2Ti(CO)_2$ as a catalyst. We believe that such substrates can participate in destructive side reactions with $Cp_2Ti(PMe_3)_2$ due to the higher reactivity (lability of the PMe_3 ligands) of the complex compared to $Cp_2Ti(CO)_2$; the titanocene is thus destroyed before it can enter into the catalytic cycle.[28] For example, in entry 9, the ketone and the olefin are not held in proximity by a rigid backbone as in the *o*-allyl arylketone cases, so formation of metallacycle **8** is difficult. The substrate in entry 9 is successfully cyclized using $Cp_2Ti(CO)_2$, while $Cp_2Ti(PMe_3)_2$ is an ineffective catalyst.

The use of $Cp_2Ti(CO)_2$ in stoichiometric quantities has allowed us to expand the scope of this hetero Pauson−Khand-type methodology to another problematic enone substrate. Acetophenone derivative **11** does not form any metallacycle upon reaction with $Cp_2Ti(PMe_3)_2$. The cyclization of other 1,7-enones with $Cp_2Ti(PMe_3)_2$ to form six-membered rings has been attempted by us[6,7] and others[5,8] with no success. However, **11** reacts with 0.5 equiv of $Cp_2Ti(CO)_2$ under the conditions shown to form the 6,6,5-tricyclic γ-butyrolactone, **12** (Scheme 8). While this substrate is not transformed to the lactone catalytically, it is the first example of the cyclization of an enone to form a six-membered ring using a titanocene reagent.

Catalytic Activity. We believe that olefinic aryl ketone derivatives can be converted to γ-butyrolactones catalytically because of their ability to displace the CO ligands on Cp_2Ti-

(20) Fachinetti, G.; Floriani, C.; Marchetti, F.; Mellini, M. *J. Chem. Soc., Dalton Trans.* **1978**, 1398.

(21) He, X.; Hartwig, J. F. *J. Am. Chem. Soc.* **1996**, *118*, 1696.

(22) Pasquali, M.; Floriani, C.; Chiesi-Villa, A.; Guastini, C. *J. Am. Chem. Soc.* **1979**, *101*, 4740.

(23) Schobert, R.; Maaref, F.; Durr, S. *Synlet* **1995**, 83.

(24) For *o*-allylacetophenone, 7.5 mol % $Cp_2Ti(PMe_3)_2$, at 18 psig CO, 24 h: with PMe_3: 100% conversion, without PMe_3: 65% conversion.

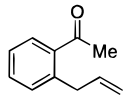
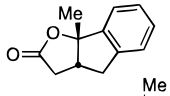
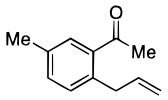
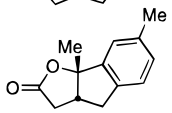
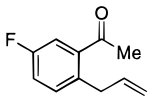
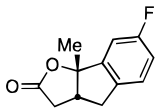
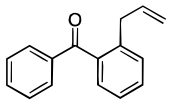
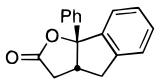
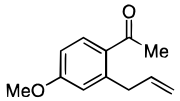
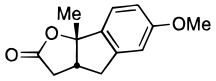
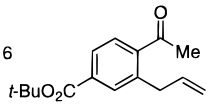
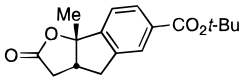
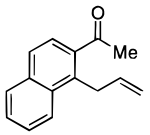
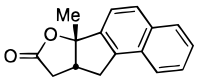
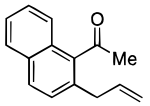
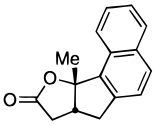
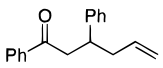
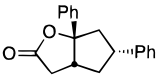
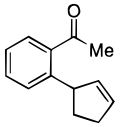
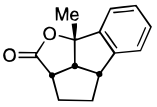
(25) Titanocene dicarbonyl is available from Strem or is easily prepared: Sikora, D. J.; Moriarty, K. J.; Rausch, M. D. In *Inorganic Synthesis*; Angelici, R. J., Ed.; John Wiley and Sons, Inc.: New York, 1990; Vol. 28, p 248.

(26) For *o*-allylacetophenone, 5 mol % $Cp_2Ti(CO)_2$, at 5 psig CO, 24 h: with PMe_3: 85% conversion, without PMe_3: 50% conversion.

(27) Edwards, B. H.; Rogers, R. D.; Sikora, D. J.; Atwood, J. L.; Rausch, M. D. *J. Am. Chem. Soc.* **1983**, *105*, 416.

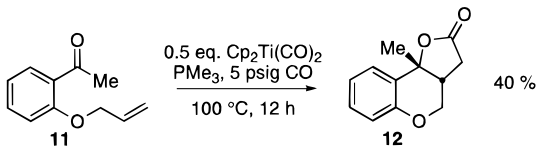
(28) For example, under some conditions, ketones have been found to react with the cyclopentadienyl rings of $Cp_2Ti(PMe_3)_2$ to form fulvenes with concommitant destruction of the titanocene framework: Gleiter, R.; Wittwer, W. *Chem. Ber.* **1994**, *127*, 1797.

Table 2. Results of the Catalytic "Hetero Pauson−Khand" Reaction

Entry	Substrate	Product	% cat. (cat. system)[a]	% PMe_3	Yield (%)[b]
1			7.5 (A) 7.5 (B)	30 30	91 96
2			10 (A) 7.5 (B)	— 30	89 84
3			10 (A)	40	80
4			5 (A)	20	97
5			20 (A)	50	74
6			7.5 (A)	30	93
7			10 (A)	40	87
8			7.5 (A) 7.5 (B)	30 30	92 94
9[c]			20 (B)	100	81
10			10 (A) 5 (B)	40 20	82 84

[a] System A: $Cp_2Ti(PMe_3)_2$, 18 psig CO, PMe_3, toluene, 12−18 h. System B: $Cp_2Ti(CO)_2$, 5 psig CO, PMe_3, toluene, 36−48 h. [b] Yields (an average of 2 or more runs) refer to isolated compound of >95% purity as assessed by 1H NMR, GC, and elemental analysis. [c] Isolated as a 14:1 mixture of isomers.

Scheme 8



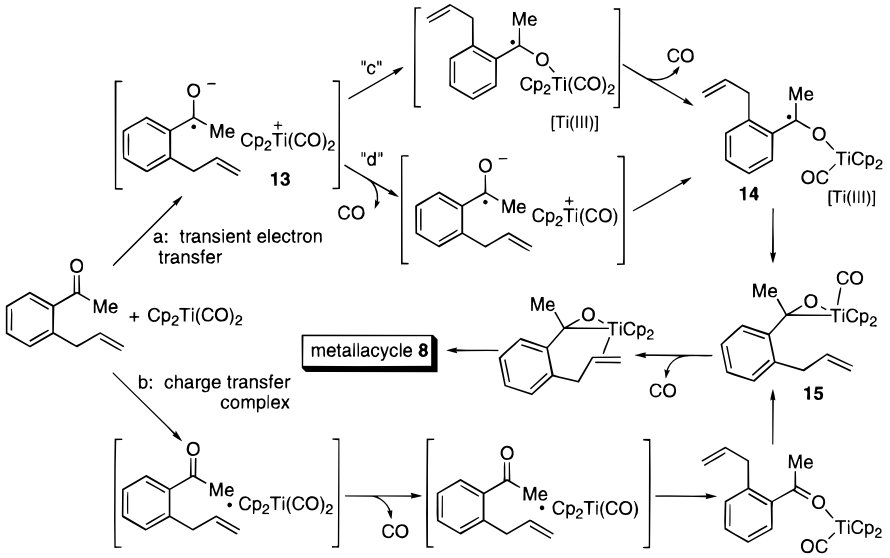
$(CO)_2$ to form a metallacycle either by transient electron transfer (Scheme 9, pathway "a") or by forming a charge transfer complex (Scheme 9, pathway "b").[29] Both of these possible pathways rely on acetophenone acting as an electron acceptor[30] for the titanium center; the shift in electron density away from the titanium reduces the backbonding interactions with the carbonyl ligands, labilizing them towards dissociative substitution by the enone substrate.[31] In pathway "a", a formal electron transfer is proposed, resulting in the ketyl radical of the acetophenone and a titanium cation as the tight ion pair, **13**. The formation of the Ti(III) alkoxide complex, **14**, can either proceed *via* a pentacoordinate Ti−alkoxide complex followed by loss of CO (pathway "c") or by dissociation of the CO followed by alkoxide formation (pathway "d"). Collapse of the diradical **14** leads to the Ti(IV)−ketone complex, **15**. The alkene replaces the remaining carbonyl ligand and then cyclization leads to metallacycle **8**. In pathway "b", a charge transfer complex is formed in which no formal change in oxidation state

(29) (a) Eberson, L. *Electron Transfer Reactions in Organic Chemistry*; Springer Verlag: New York; 1987. (b) Eberson, L. *New J. Chem.* **1992**, *16*, 151. (c) Kochi, J. K. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1227. (d) Ashby, E. C. *Acc. Chem. Res.* **1988**, *21*, 414.

(30) For some examples of aromatic ketones acting as electron acceptors in charge transfer reactions, see: (a) Ashby, E. C.; Goel, A. B.; Argyropoulos, J. N. *Tetrahedron Lett.* **1982**, *23*, 2273. (b) Ashby, E. C.; Argyropoulos, J. N. *J. Org. Chem.* **1986**, *51*, 472. (c) Fukuzumi, S.; Okamoto, T. *J. Am. Chem. Soc.* **1994**, *116*, 1994. (d) Abe, M.; Oku, A. *J. Org. Chem.* **1995**, *60*, 3065.

(31) For a review on electron transfer induced substitution reactions on metal carbonyl complexes, see: Albers, M. O.; Coville, N. J. *Coord. Chem. Rev.* **1984**, *53*, 227.

Scheme 9



occurs, but a shifting of electron density within the complex[32] away from the titanium center causes the labilization of the first carbonyl ligand and the subsequent formation of metallacycle **8**.

While our mechanistic hypothesis has not yet been rigorously tested, the proposed mechanism is consistent with the results shown in Table 2. An electron donating group para to the carbonyl on the acetophenone moiety would be expected to diminish the electron-accepting ability of the substrate; indeed, *p*-methoxy-*o*-allylacetophenone (Table 2, entry 5) can only be transformed to a low yield of the lactone using 20 mol % catalyst. Conversely, an electron withdrawing group para to the carbonyl on the acetophenone moiety would be expected to facilitate electron transfer; *p*-*tert*-butylcarboxyl-*o*-allylacetophenone (Table 2, entry 6) is converted to the lactone with 7.5 mol % catalyst in excellent yield. Based on the reduction potential of benzophenone,[33] it would be expected to be a better electron acceptor than acetophenone; indeed, it was found that *o*-allylbenzophenone (entry 4) can be converted to the corresponding lactone using 5 mol % catalyst in 97% isolated yield.

In the related intramolecular McMurry-type reactions[34] of oxo amides to indoles using low valent titanium catalysts,[35,36] Fürstner has provided evidence for an aryl titanaoxacyclopropane species similar to **15** as an intermediate in the process.[36] In accord with our preliminary results, they have found that there is a correlation between the electronic properties of the aryl ketone and the rate of the reaction; diaryl ketones react significantly faster than arylalkyl ketones. We have noticed similar trends in our work and are currently carrying out kinetic studies to quantify our results.

Conclusion

In summary, we have developed the first catalytic method for the formation of γ-butyrolactones from enones containing an arylketone moiety using $Cp_2Ti(PMe_3)_2$ or $Cp_2Ti(CO)_2$. We are currently working to extend the scope of this catalytic reaction to include nonaryl ketone-containing substrates through the use of electron transfer catalysts. In addition, more detailed mechanistic and kinetic studies are underway.

Experimental Section

General Considerations. All manipulations involving air-sensitive materials were conducted in a Vacuum Atmospheres glovebox under an atmosphere of argon or using standard Schlenk techniques under argon. THF was distilled under argon from sodium/benzophenone ketyl before use. Toluene was distilled under argon from molten sodium, and CH_2Cl_2 was distilled under nitrogen from CaH_2. Pyridine was distilled under argon from CaH_2. Bis(trimethylphosphine)titanocene, $Cp_2Ti(PMe_3)_2$, was prepared from titanocene dichloride (obtained from Boulder Scientific, Boulder, CO) by the procedure of Binger et. al.[37] and was stored in a glovebox under argon. Titanocene dicarbonyl is commercially available from Strem Chemicals and is also readily synthesized from titanocene dichloride.[38] *o*-Allylacetophenone was prepared by a Stille coupling of allyltributyltin and *o*-bromoacetophenone.[39] *o*-Iodoacetophenone was synthesized by a modified Sandmeyer procedure.[40] 2-Bromo-4-*tert*-butylcarboxylacetophenone was synthesized according to the procedure described by Wakselman.[41] The enone 1,3-diphenyl-5-hexen-1-one was synthesized by allylation of *trans*-chalcone with allyltrimethylsilane and $TiCl_4$.[42] 2-Iodobenzophenone is commercially available from Trans World Chemicals. All other reagents were available from commercial sources and were used without further purification, unless otherwise noted.

Flash chromatography was performed on E. M. Science Kieselgel 60 (230−400 mesh) unless otherwise noted. Yields refer to isolated yields of compounds of greater than 95% purity as estimated by capillary GC and ^{1}H NMR analysis, and, in the cases of unknown compounds, elemental analysis. Yields indicated in this section refer to a single experiment, while those reported in the tables are an average of two or more runs, so the numbers may differ slightly. All compounds were characterized by ^{1}H NMR, ^{13}C NMR, and IR spectroscopies. Previously unreported compounds were also characterized by elemental analysis (E & R Analytical Laboratory, Inc.). Nuclear magnetic

(32) (a) Kaim, W. *Acc. Chem. Res.* **1985**, *18*, 160. (b) Kochi, J. K. *Organometallic Mechanisms and Catalysis*; Academic Press: New York, 1978.

(33) Asano, T.; Ohkata, K.; Hanafusa, T. *Chem. Lett.* **1974**, *10*, 1149.

(34) Fürstner, A.; Bogdanovic, B. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2442.

(35) Fürstner, A.; Jumbam, D. N. *Tetrahedron* **1992**, *48*, 5991.

(36) Fürstner, A.; Hupperts, A.; Ptock, A.; Janssen, E. *J. Org. Chem.* **1994**, *59*, 5215.

(37) Binger, P.; Müller, P.; Benn, R.; Rufinska, A.; Gabor, B.; Krüger, C.; Betz, P. *Chem. Ber.* **1989**, *122*, 1035−1042.

(38) Sikora, D. J.; Moriarty, K. J.; Rausch, M. C. In *Inorganic Synthesis*; Angelici, R. J., Ed.; John Wiley and Sons, Inc.: New York, 1990; Vol. 28, p 248.

(39) Yasuo, F.; Suzuki, Y.; Tanaka, Y.; Tominaga, T.; Takeda, H.; Sekine, H.; Morito, N.; Miyaoca, Y. *Heterocycles* **1977**, *6*, 1604.

(40) Heaney, H.; Millar, I. T. *Organic Synthesis*; Wiley & Sons: New York, 1990; Vol. V, p 1120.

(41) Joyeau, R.; Yadav, L. D. S.; Wakselman, M. *J. Chem. Soc., Perkin Trans. I* **1987**, 1899.

(42) Sakurai, H.; Hosomi, A.; Hayashi, J. *Organic Synthesis*; Wiley & Sons: New York, 1990; Vol. VII, pp 443.

resonance (NMR) spectra were recorded on a Varian XL-300, a Varian XL-500, or a Varian Unity 300. Splitting patterns are designated as follows: s, singlet; d, doublet; dd, doublet of doublets; t, triplet; q, quartet; qd, quartet of doublets; m, multiplet. All ^{1}H NMR spectra are reported in δ units, parts per million (ppm) downfield from tetramethylsilane. All ^{13}C NMR spectra are reported in ppm relative to deuterochloroform. Infrared (IR) spectra were recorded on a Perkin-Elmer 1600 Series Fourier transform spectrometer. Gas chromatography (GC) analysis were performed on a Hewlett-Packard 5890 gas chromatograph with a 3392A integrator and FID detector using a 25 m capillary column with cross-linked SE-30 as a stationary phase.

Preparation of the Enone Starting Materials: General Procedure for the Conversion of 2′-Hydroxyacetophenones into 2′-Allylacetophenones. In a dry Schlenk flask, the 2′-hydroxyacetophenone and pyridine (20−30 mL) were combined under argon and cooled to 0 °C. Triflic anhydride was added slowly, and the reaction mixture was allowed to slowly warm to room temperature overnight. The mixture was diluted with diethyl ether (50 mL) and washed with 1 N aqueous HCl solution (2 × 50 mL) followed by brine (50 mL). The organic layer was dried over $MgSO_4$, and the solvent was removed *in vacuo*. The crude product was purified by flash chromatography and immediately used in the next step. Using an adaptation of Farina's procedure,[43] the triflate, 1.1 equiv allyltributyltin, 0.02 equiv Pd_2dba_3, 0.16 equiv P(2-furyl)$_3$, 3 equiv LiCl (anhydrous), and THF were combined in a dry Schlenk flask fitted with a reflux condenser and heated to 85 °C for 18 h. The crude reaction mixture was diluted with diethyl ether (50 mL), shaken vigorously with saturated aqueous KF solution (25 mL) for 5 min, then washed with brine, and dried over $MgSO_4$. Purification by flash chromatography yielded the desired allylacetophenone.

2′-Allyl-5′-methylacetophenone (Table 2, Entry 2). Using the general procedure, 2′-hydroxy-5′-methylacetophenone (2.3 g, 15 mmol) and triflic anhydride (2.8 mL, 17 mmol) were converted to the desired product. Purification by flash chromatography (hexane:diethyl ether = 3: 2) afforded 2.5 g (57% yield) of a clear oil. The triflate (2.45 g, 8.7 mmol) was reacted with allyltributyltin (3.23 mL, 10.4 mmol), Pd_2dba_3 (0.16 g, 0.2 mmol), P(2-furyl)$_3$ (0.32 g, 1.4 mmol), LiCl (1.1 g, 26 mmol), and THF (20 mL). The crude product was purified by flash chromatography (hexane:diethyl ether = 9:1) to afford 1.2 g (79% yield) of a clear oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.44 (s, 1 H); 7.23 (m, 1 H); 7.16 (d, J = 7.9 Hz, 1 H); 5.96 (m, 1 H); 4.99 (m, 2 H); 3.60 (d, J = 6.4 Hz, 2 H); 2.56 (s, 3 H); 2.37 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 202.3, 138.2, 137.8, 136.7, 135.8, 132.3, 131.3, 129.7, 115.5, 37.7, 29.9, 21.1. IR (neat): 2977, 2921, 1686, 1355, 1267, 1205, 1182, 914, 829 cm^{-1}. Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.62; H, 8.01.

2′-Allyl-5′-fluoroacetophenone (Table 2, Entry 3). Using the general procedure, 2′-hydroxy-5′-fluoroacetophenone (3.1 g, 20 mmol) and triflic anhydride (4.1 mL, 24 mmol) were converted to the desired product. Kugelrohr distillation followed by recrystallization from CH_2Cl_2 and hexane afforded 3.9 g (68% yield) of white crystalline material. The triflate (2.8 g, 9.8 mmol) was reacted with allyltributyltin (3.42 mL, 11 mmol), Pd_2dba_3 (0.179 g, 0.2 mmol), P(2-furyl)$_3$ (0.36 g, 1.5 mmol), LiCl (1.2 g, 28 mmol), and THF (10 mL). The crude product was purified by flash chromatography (hexane:diethyl ether = 19: 1) to afford 0.87 g (50% yield) of a clear oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.31 (dd, J = 9.1 Hz, J = 2.7 Hz, 1 H); 7.27 (m, 1 H); 7.12 (td, J = 8.2 Hz, J = 2.7 Hz, 1 H); 5.95 (m, 1 H); 4.99 (m, 2 H); 3.60 (d, J = 6.4 Hz, 2 H); 2.55 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 201.0, 161.0 (J_F = 245 Hz), 139.6 (J_F = 5.5 Hz), 137.4, 135.4 (J_F = 3.1 Hz), 133.0 (J_F = 7.3 Hz), 118.5 (J_F = 21 Hz), 116.1, 115.8 (J_F = 22 Hz), 37.3, 30.0. IR (neat): 3079, 1694, 1488, 1357, 1262, 1191, 911, 871 cm^{-1}. Anal. Calcd for $C_{11}H_{11}FO$: C, 74.14; H, 6.22. Found: C, 74.18; H, 6.25.

2-Allylbenzophenone (Table 2, Entry 4).[39,44] In a dry resealable Schlenk flask, 2-iodobenzophenone (1.0 mL, 5.4 mmol), allyltributyltin (1.85 mL, 5.9 mmol), palladium tetrakis(triphenylphosphine) (63 mg, 0.054 mmol), and benzene (1 mL) were combined. The reaction mixture was heated to 100 °C for 24 h and then cooled to room temperature. The solvent was removed *in vacuo*, and the residue was dissolved in diethyl ether (10 mL), washed with 10% aqueous KF solution (10 mL), and then dried over $MgSO_4$. The solvent was removed *in vacuo*, and the crude product was purified by flash chromatography (hexane:diethyl ether = 46:1) to afford 0.9 g (75% yield) of a clear oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.80 (d, J = 7.3 Hz, 2 H); 7.59 (t, J = 7.2 Hz, 1 H); 7.45 (m, 3 H); 7.30 (m, 3 H); 5.88 (m, 1 H); 4.96 (m, 2 H); 3.45 (d, J = 6.5 Hz, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 198.1, 139.2, 139.1, 138.8, 138.0, 137.1, 133.4, 130.6, 130.4, 128.9, 128.6, 125.9, 116.4, 37.7. IR (neat): 3062, 1666, 1597, 1448, 1315, 1269, 925, 703, 638 cm^{-1}.

2′-Allyl-4′-methoxyacetophenone (Table 2, Entry 5). Using the general procedure, 2′-hydroxy-4′-methoxyacetophenone (2.5 g, 15 mmol) and triflic anhydride (2.8 mL, 17 mmol) were converted to the desired product. Flash chromatography (hexane:diethyl ether = 3:2) afforded 2.1 g (47% yield) of a colorless oil. The triflate (1.5 g, 5.0 mmol) was reacted with allyltributyltin (1.87 mL, 6.0 mmol), Pd_2dba_3 (0.092 g, 0.1 mmol), P(2-furyl)$_3$ (0.19 g, 0.8 mmol), LiCl (0.64 g, 15 mmol), and THF (10 mL). The crude product was purified by flash chromatography (hexane:diethyl ether = 4:1) to afford 0.6 g (63% yield) of a clear oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.73 (d, J = 8.2 Hz, 1 H); 6.77 (m, 2 H); 5.98 (m, 1 H); 5.02 (m, 2 H); 3.85 (s, 3 H); 3.72 (d, J = 6.5 Hz, 2 H); 2.54 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 199.7, 162.2, 143.7, 137.5, 132.6, 130.0, 116.9, 115.8, 110.9, 55.4, 38.8, 29.3. IR (neat): 2974, 1675, 1602, 1567, 1354, 1250, 1134, 1031 cm^{-1}. Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42 Found: C, 75.67; H, 7.32.

2′-Allyl-4′-*tert*-butylcarboxylacetophenone (Table 2, Entry 6). Using Stille coupling conditions,[39] 2′-bromo-4′-*tert*-butylcarboxylacetophenone[41] (1.6 g, 5.4 mmol), allyltributyltin (1.83 mL, 6 mmol), and tetrakis(triphenylphosphine)palladium (0.31 g, 0.3 mmol) were combined in a dry sealable Schlenk flask with benzene (3 mL). The reaction was heated to 100 °C for 12 h, and then the solvent was removed *in vacuo*. The crude reaction mixture was diluted with diethyl ether (25 mL), washed with H_2O (25 mL) and 10% aqueous KF solution, and dried over $MgSO_4$. The crude product was purified by flash chromatography (hexane:diethyl ether = 9:1) to afford 0.91 g (65% yield) of a clear oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.88 (m, 2 H); 7.62 (d, J = 8.4 Hz, 1 H); 5.97 (m, 1 H); 5.04 (m, 2 H); 3.65 (d, J = 6.4 Hz, 2 H); 2.57 (s, 3 H); 1.60 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 202.2, 165.0, 141.9, 139.4, 137.0, 134.3, 132.1, 128.4, 127.3, 116.4, 81.7, 37.8, 30.2, 28.3. IR (neat): 2978, 1717, 1702, 1394, 1368, 1356, 1301, 1254, 1166, 1117, 771 cm^{-1}. Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 73.86; H, 7.57.

1′-Allyl-2′-acetylnaphthalene (Table 2, Entry 7). Using the general procedure, 1′-hydroxy-2′-acetylnaphthalene (2.8 g, 15 mmol) and triflic anhydride (2.8 mL, 16.5 mmol) were converted to the desired product. Flash chromatography (hexane:diethyl ether = 3:1) followed by Kugelrohr distillation afforded 1.3 g (27% yield) of a colorless oil. The triflate (1.27 g, 4 mmol) was reacted with allyltributyltin (1.49 mL, 4.8 mmol), Pd_2dba_3 (45 m g, 0.05 mmol), P(2-furyl)$_3$ (0.096 g, 0.4 mmol), LiCl (0.51 g, 12 mmol), and THF (5 mL). The crude product was purified by flash chromatography (hexane:diethyl ether = 19:1) to afford 0.48 g (57% yield) of a clear oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.16 (m, 1 H); 7.85 (m, 1 H); 7.80 (d, J = 8.5 Hz, 1 H); 7.53 (m, 3 H); 6.09 (m, 1 H); 5.04 (dd, J = 1.8 Hz, J = 24.8 Hz, 1 H); 5.00 (dd, J = 1.6 Hz, J = 31.6 Hz, 1 H); 4.02 (dt, J = 5.9 Hz, J = 1.6 Hz, 2 H); 2.65 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 204.1, 137.3, 137.2, 135.0, 134.6, 132.5, 128.7, 127.2, 127.1, 126.9, 125.8, 124.2, 116.1, 33.0, 31.1. IR (neat): 3005, 1692, 1468, 1352, 1269, 1235, 814 cm^{-1}. Anal. Calcd for $C_{15}H_{14}O$: C, 85.68; H, 6.71. Found: C, 85.80; H, 6.54.

2′-Allyl-1′-acetylnaphthalene (Table 2, Entry 8). Using the general procedure, 2′-hydroxy-1′-acetylnaphthalene (2.8 g, 15 mmol) and triflic anhydride (2.8 mL, 16.5 mmol) were converted to the desired product. Flash chromatography (hexane:diethyl ether = 3:1) followed by Kugelrohr distillation afforded 3.8 g (80% yield) of a yellow solid. The triflate (1.27 g, 4 mmol) was reacted with allyltributyltin (1.49 mL, 4.8 mmol), Pd_2dba_3 (45 m g, 0.05 mmol), P(2-furyl)$_3$ (0.096 g, 0.4 mmol), LiCl (0.51 g, 12 mmol), and THF (5 mL). The crude product was purified by flash chromatography (hexane:diethyl ether = 19:1) to afford 0.5 g (59% yield) of a clear oil. ^{1}H NMR (300 MHz,

(43) Farina, V.; Krishnan, B. *J. Am. Chem. Soc.* **1991**, *113*, 9585.
(44) Rosenfeldt, F.; Erker, G. *Tetrahedron Lett.* **1980**, *21*, 1637.

$CDCl_3$): δ 7.82 (m, 2 H); 7.60 (m, 1 H); 7.49 (m, 2 H); 7.35 (d, J = 8.5 Hz, 1 H); 5.98 (m, 1 H); 5.08 (m, 2 H); 3.47 (dt, J = 6.4 Hz, J = 1.6 Hz, 2 H); 2.64 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 208.0, 139.0, 136.6, 132.1, 131.9, 129.1, 129.0, 128.4, 127.8, 127.0, 125.9, 124.2, 116.7, 37.6, 33.5. IR (neat): 3056, 1698, 1508, 1417, 1351, 1244, 1203, 918, 819, 756 cm^{-1}. Anal. Calcd for $C_{15}H_{14}O$: C, 85.68; H, 6.71. Found: C, 85.58; H, 6.53.

2′-(3-cyclopentene)acetophenone (Table 2, Entry 10). Using the procedure of Larock,[45] 2-iodoacetophenone (3.05 g, 12.3 mmol), cyclopentene (5.4 mL, 61 mmol), palladium acetate (0.139 g, 0.62 mmol), triphenylphosphine (0.162 g, 0.62 mmol), (nBu)$_4$NCl (anhydrous, 3.32 g, 12.3 mmol), KOAc (3.63 g, 37 mmol), and DMF (30 mL) were combined in a dry Schlenk flask fitted with a reflux condenser and heated to 100 °C for 17 h. The reaction mixture was diluted with water and extracted with diethyl ether (3 × 20 mL). The combined organic layers were washed with brine (30 mL) and dried over $MgSO_4$. The solvent was removed *in vacuo*, and the crude material was purified by flash chromatography (hexane:diethyl ether = 19:1) to afford 0.58 g (25% yield) of a colorless oil, which was a 9:1 mixture of the desired product to the isomeric 2′-(4-cyclopentene)acetophenone. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.56 (d, J = 7.7 Hz, 1 H); 7.39 (m, 1 H); 7.31 (d, J = 6.8 Hz, 1 H); 7.26 (m, 1 H); 5.97 (m, 1 H); 5.81 (m, 1 H); 4.39 (m, 1 H); 2.60 (s, 3 H); 2.56 (m, 2 H); 2.45 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 203.2, 146.0, 134.3, 132.7, 131.6, 130.0, 128.4, 128.3, 125.9, 47.7, 34.4, 32.6, 30.6. IR (neat): 2849, 1686, 1443, 1356, 1264, 1241, 760, 741, 600 cm^{-1}. Anal. Calcd for $C_{13}H_{14}O$: C, 83.83; H, 7.58. Found: C, 84.01; H, 7.72.

***O*-Allyl-2′-hydroxyacetophenone.**[46] In a dry Schlenk flask under argon, sodium carbonate (2.12 g, 20 mmol), THF (20 mL), DMF (20 mL), and then 2′-hydroxyacetophenone (2.41 mL, 20 mmol) were combined. Allyl bromide (2.60 mL, 30 mmol) was added, and the reaction mixture was heated to reflux for 20 h. After cooling to room temperature, the reaction mixture was diluted with diethyl ether (50 mL) and water (50 mL) and then extracted with diethyl ether (2 × 30 mL). The combined organic layers were then washed with saturated $CuSO_4$ solution (3 × 20 mL), 1 N aqueous NaOH solution (2 × 30 mL), and brine and dried over $MgSO_4$, and the solvent was then removed *in vacuo*. The crude material was purified by flash chromatography (hexane:diethyl ether = 6:1) to afford 1.4 g (40% yield) of a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.74 (dd, J = 1.2 Hz, J = 7.6 Hz, 1 H); 7.44 (t, J = 6.6 Hz, 1 H); 6.97 (m, 2 H); 6.10 (m, 1 H); 5.39 (m, 2 H); 4.65 (d, J = 5.3 Hz, 2 H); 2.65 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 200.1, 158.1, 133.7, 132.8, 130.6, 128.8, 120.9, 118.4, 112.9, 69.6, 32.2. IR (neat): 1674, 1597, 1483, 1450, 1424, 1358, 1294, 1238, 758 cm^{-1}.

General Procedure for the Conversion of Enones to γ-Butyrolactones. Catalyst System A. In an argon-filled glovebox, a dry sealable Schlenk flask was charged with the enone, $Cp_2Ti(PMe_3)_2$, PMe_3, and toluene (2 mL). [Note: the enone was run through a plug of activated alumina in the glovebox and stored under argon. On particularly humid days, the alumina had to be dried under vacuum at 180 °C overnight prior to use to effectively dry the substrate.] The flask was removed from the glovebox, attached to a Schlenk line under Ar, evacuated, and backfilled with 18 psig CO. **Caution:** Appropriate precautions should be taken when performing reactions under elevated CO pressure. The reaction was heated to 100 °C for 12−18 h. After cooling the reaction mixture to room temperature, the CO was cautiously released in the hood. The crude reaction mixture was filtered through a plug of silica gel with the aid of diethyl ether and purified by flash chromatography.

Catalyst System B. In an argon-filled glovebox, a dry sealable Schlenk flask was charged with the enone, $Cp_2Ti(CO)_2$, PMe_3, and toluene (2 mL). [Note: the enone was run through a plug of activated alumina in the glovebox and stored under argon. On particularly humid days, the alumina had to be dried under vacuum at 180 °C overnight prior to use to effectively dry the substrate.] The flask was removed from the glovebox, attached to a Schlenk line under Ar, evacuated, and backfilled with 5 psig CO. **Caution:** Appropriate precautions should be taken when performing reactions under elevated CO pressure. The reaction was heated to 100 °C for 36−48 h. After cooling the reaction mixture to room temperature, the CO was cautiously released in the hood. The crude reaction mixture was filtered through a plug of silica gel with the aid of diethyl ether and purified by flash chromatography.

***cis*-2,3,4,6a-Tetrahydro-6a-methyl-2*H*-indanyl[*b*]furan-2-one (Table 2, Entry 1).** Using catalyst system A, $Cp_2Ti(PMe_3)_2$ (12 mg, 7.5 mol %) and PMe_3 (16 μL, 30 mol %) were used to convert *o*-allylacetophenone (80 mg, 0.50 mmol) to the desired product. Purification by flash chromatography (hexane:diethyl ether = 1:1) yielded 86 mg (91% yield) of a clear colorless oil. Using catalyst system B, $Cp_2Ti(CO)_2$ (9 mg, 7.5 mol %) and PMe_3 (16 μL, 30 mol %) were used to convert *o*-allylacetophenone (80 mg, 0.50 mmol) to 90 mg (96% yield) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.42 (m, 1 H); 7.28 (m, 3 H); 3.31 (dd, J = 7.1 Hz, J = 16.5 Hz, 1 H); 2.95 (m, 2 H); 2.83 (dd, J = 2.0 Hz, J = 16.45 Hz, 1 H); 2.40 (m, 1 H); 1.74 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.1, 142.5, 141.1, 129.6, 127.6, 125.3, 124.2, 95.4, 44.2, 36.9, 36.6, 25.0. IR (neat): 2929, 1766, 1442, 1379, 1206, 1066, 954, 768 cm^{-1}. Anal. Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.36; H, 6.54.

***cis*-2,3,4,6a-Tetrahydro-6a-methyl-4′-methyl-2*H*-indanyl[*b*]furan-2-one (Table 2, Entry 2).** Using catalyst system A, $Cp_2Ti(PMe_3)_2$ (16 mg, 10 mol %) was used to convert 2′-allyl-5′-methylacetophenone (87 mg, 0.50 mmol) to the desired product. Purification by flash chromatography (hexane: ethyl ether = 1:1) yielded 90 mg (89% yield) of a white solid. Using catalyst system B, $Cp_2Ti(CO)_2$ (9 mg, 7.5 mol %) and PMe_3 (16 μL, 30 mol %) were used to convert 2′-allyl-5′-methylacetophenone (87 mg, 0.50 mmol) to 87 mg (87% yield) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.23 (s, 1 H); 7.13 (m, 2 H); 3.25 (dd, J = 7 Hz, J = 16.5 Hz; 1 H); 2.95 (m, 2 H); 2.77 (dd, J = 2.4 Hz, J = 16.5 Hz, 1 H); 2.38 (m, 1 H); 2.36 (s, 3 H), 1.72 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.3, 133.7, 129.1, 128.6, 121.7, 116.2, 115.8, 86.5, 35.6, 27.8, 27.6, 16.1, 12.4. IR (KBr): 2918, 2847, 1751, 1493, 1310, 1242, 1208, 1147, 1069, 936, 858, 810. Mp = 82−84 °C. Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.20; H, 7.18.

***cis*-2,3,4,6a-Tetrahydro-6a-methyl-4′-Fluoro-2*H*-indanyl[*b*]furan-2-one (Table 2, Entry 3).** $Cp_2Ti(PMe_3)_2$ (16 mg, 10 mol %) and PMe_3 (20 μL, 40 mol %) were used to convert 5-fluoro-*o*-allylacetophenone (89 mg, 0.5 mmol) to the desired product. Purification by flash chromatography (hexane:diethyl ether = 1:1) afforded 82 mg (80% yield) of a clear oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.19 (m, 1 H); 7.08 (m, 3 H); 3.27 (dd, J = 6.8 Hz, J = 15.6 Hz, 1 H); 2.95 (m, 2 H); 2.79 (d, J = 16.5 Hz, 1 H); 2.41 (m, 1 H); 1.72 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.0, 162.8 (J_F = 244 Hz), 144.7 (J_F = 8 Hz), 136.5, 126.8 (J_F = 8 Hz), 117.2 (J_F = 23 Hz), 111.2 (J_F = 22 Hz), 95.0, 45.0, 36.7, 36.4, 25.1. IR (neat): 2972, 1769, 1599, 1487, 1307, 1257, 1202, 1187, 925, 817 cm^{-1}. Anal. Calcd for $C_{12}H_{11}FO_2$: C, 69.89; H, 5.38. Found: C, 69.73; H, 5.25.

***cis*-2,3,4,6a-Tetrahydro-6a-phenyl-2*H*-indanyl[*b*]furan-2-one (Table 2, Entry 4).** $Cp_2Ti(PMe_3)_2$ (9 mg, 5 mol %) and PMe_3 (11 μL, 20 mol %) were used to convert *o*-allylbenzophenone (116 mg, 0.52 mmol) to the desired product. Purification by flash chromatography (hexane: diethyl ether = 1:1) afforded 110 mg (97% yield) of a clear oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.30 (m, 8 H); 7.17 (d, J = 7.7 Hz, 1 H); 3.47 (dd, J = 8.1 Hz, J = 16.5 Hz, 1 H); 3.25 (m, 1 H); 2.95 (m, 2 H); 2.51 (dd, J = 5.2 Hz, J = 18.1 Hz, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.3, 142.8, 142.7, 143.3, 130.0, 128.7 (2), 128.1, 126.3, 125.3, 125.2, 98.5, 47.5, 37.7, 36.6. IR (neat): 3028, 1769, 1448, 1231, 1189, 1146, 1001, 976, 754, 700 cm^{-1}. Anal. Calcd for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64. Found: C, 81.73; H, 5.80.

***cis*-2,3,4,6a-Tetrahydro-6a-methyl-3′-methoxy-2*H*-indanyl[*b*]furan-2-one (Table 2, Entry 5).** Using catalyst system A, $Cp_2Ti(PMe_3)_2$ (33 mg, 20 mol %) and PMe_3 (33 μL, 60 mol %) were used to convert 4′-methoxy-6′-allylacetophenone (95 mg, 0.50 mmol) to the desired product. Purification by flash chromatography (hexane: ethyl ether = 1:1) yielded 80 mg (74% yield) of a white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.31 (d, J = 8.4 Hz, 1 H); 6.83 (dd, J = 8.5 Hz, J = 2.4 Hz, 1 H); 6.74 (d, J = 2.3 Hz, 1 H); 3.80 (s, 3 H); 3.27 (dd, J = 7.5 Hz, J = 16.6 Hz, 1 H); 2.95 (m, 2 H); 2.78 (dd, J = 3.3 Hz, J = 16.5 Hz, 1 H); 2.43 (m, 1 H); 1.71 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.0, 161.6, 143.4, 135.2, 125.3, 114.4, 110.2, 95.2, 55.7,

(45) Larock, R. C.; Gong, W. H.; Baker, B. E. *Tetrahedron Lett.* **1989**, *30*, 2603.

(46) Woulfe, S. R.; Miller, M. J. *J. Org. Chem.* **1986**, *51*, 3133.

44.9, 37.4, 36.9, 25.3. IR (KBr): 1750, 1503, 1305, 1243, 1138, 1064, 913, 837 Mp = 73−75 °C. Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.63; H, 6.63.

***cis*-2,3,4,6a-Tetrahydro-6a-methyl-3′-*tert*-butylcarboxylate-2*H*-indanyl[*b*]furan-2-one (Table 2, Entry 6).** Using catalyst system A, $Cp_2Ti(PMe_3)_2$ (10 mg, 7.5 mol %) and PMe_3 (12 μL, 30 mol %) were used to convert 4′-*tert*-butylcarboxylate-6′-allylacetophenone (130 mg, 0.50 mmol) to the desired product. Purification by flash chromatography (hexane: ethyl ether = 1:1) yielded 136 mg (93% yield) of a white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.93 (d, *J* = 8.0 Hz, 1 H); 7.87 (s, 1 H); 7.45 (d, *J* = 8.0 Hz, 1 H); 3.33 (dd, *J* = 7.5 Hz, *J* = 16.5 Hz, 1 H); 2.97 (m, 2 H); 2.87 (d, *J* = 16.8 Hz, 1 H); 2.39 (m, 1 H); 1.73 (s, 3 H); 1.59 (s, 9 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 175.5, 165.5, 147.0, 141.3, 134.1, 129.4, 126.8, 124.3, 94.7, 81.5, 44.8, 36.9, 36.7, 28.4, 25.2. IR (KBr): 2971, 1758, 1708, 1458, 1417, 1335, 1298, 1169, 1095, 955, 772 cm^{-1}. Mp = 95−97 °C. Anal. Calcd for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 71.02; H, 7.21.

***cis*-2,3,4,6a-Tetrahydro-6a-methyl-1′,2′-benzo-2*H*-indanyl[*b*]furan-2-one (Table 2, Entry 7).** Using catalyst system A, $Cp_2Ti(PMe_3)_2$ (16 mg, 10 mol %) and PMe_3 (20 μL, 40 mol %) were used to convert 1′-allyl-2′-acetyl-napthalene (100 mg, 0.48 mmol) to the desired product. Purification by flash chromatography (hexane:ethyl ether = 1:1) yielded 97 mg (87% yield) of a pale yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.91 (m, 1 H); 7.82 (m, 2 H); 7.54 (m, 3 H); 3.62 (dd, *J* = 7.5 Hz, *J* = 17.0 Hz, 1 H); 3.19 (m, 2 H); 3.10 (m, 1 H); 2.50 (dd, *J* = 4.9 Hz, *J* = 17.1 Hz, 1 H); 1.82 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.3, 139.6, 137.6, 134.,3, 130.3, 128.9, 128.8, 126.8, 126.7, 124.6, 121.5, 96.5, 44.1, 37.3, 35.8, 25.4. IR (KBr): 2968, 1760, 1296, 1229, 1141, 1065, 916, 811, 756 cm^{-1} Mp = 131 - 134 °C. Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.89; H, 6.13.

***cis*-2,3,4,6a-Tetrahydro-6a-methyl-3′,4′-benzo-2*H*-indanyl[*b*]furan-2-one (Table 2, Entry 8).** Using catalyst system A, $Cp_2Ti(PMe_3)_2$ (12 mg, 7.5 mol %) and PMe_3 (15 μL, 30 mol %) were used to convert 1′-acetyl-2′-allyl-napthalene (100 mg, 0.48 mmol) to the desired product. Purification by flash chromatography (hexane:ethyl ether = 1:1) yielded 103 mg (92% yield) of a white solid. Using catalyst system B, $Cp_2Ti(CO)_2$ (6 mg, 7.5 mol %) and PMe_3 (11 μL, 30 mol %) were used to convert 1′-acetyl-2′-allylnaphthalene (75 mg, 0.36 mmol) to 78 mg (93% yield) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.26 (d, *J* = 8.4 Hz, 1 H); 7.85 (dd, *J* = 8.0 Hz, *J* = 17.0 Hz, 2 H); 7.52 (m, 2 H); 7.34 (d, *J* = 8.4 Hz, 1 H); 3.39 (dd, *J* = 6.7 Hz, *J* = 16.5 Hz, 1 H); 3.01 (m, 3 H); 2.37 (dd, *J* = 7.5 Hz, *J* = 16.3 Hz, 1 H); 1.94 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.4, 137.8, 137.2, 133.8, 130.8, 129.6, 128.9, 127.1, 125.9, 124.3, 123.5, 97.1, 45.7, 37.1, 36.5, 25.6. IR (KBr): 1766, 1412, 1250, 1211, 1093, 955, 938, 812, 752 cm^{-1}. Mp = 103−106 °C. Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.78; H, 6.04.

***cis*-Hexahydro-6a-phenyl-5-*endo*-phenyl-2H-cyclopenta[*b*]furan-2-one (Table 2, Entry 9).** Using catalyst system B, $Cp_2Ti(CO)_2$ (23 mg, 20 mol %) and PMe_3 (51 μL, 1 equiv) were used to convert 1,3-diphenyl-5-hexen-2-one (0.125 g, 0.5 mmol) to the desired product. Purification by flash chromatography (hexane:diethyl ether = 9:1) yielded 120 mg (86% yield) of a 14:1 mixture of diastereomers of a white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.35 (m, 10 H); 3.53 (m, 1 H); 2.97 (m, 1 H); 2.4−2.8 (m, 5 H); 1.83 (q, *J* = 12.4 Hz, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.4, 143.9, 142.2, 128.7, 128.7, 127.7, 126.9, 126.8, 123.9, 96.2, 49.6, 48.5, 46.0, 41.3, 34.1. IR (KBr): 3026, 2966, 1775, 1600, 1452, 1179, 970, 699 cm^{-1}. Mp = 89−91 °C. Anal. Calcd for $C_{19}H_{18}O_2$: C, 81.99; H, 6.52. Found: C, 81.80; H, 6.39.

Table 2, Entry 10. Using catalyst system A, $Cp_2Ti(PMe_3)_2$ (8 mg, 10 mol %) and PMe_3 (10 μL, 40 mol %) were used to convert 2′-(3-cyclopentene) acetophenone (47 mg, 0.25 mmol) to the desired product. The starting enone was contaminated with approximately 9% of the isomeric 2′-(4-cyclopentene) acetophenone, which was carried through the reaction and recovered unchanged. Purification by flash chromatography (hexane:diethyl ether = 3:2) yielded 44 mg (82% yield) of a colorless oil. Using catalyst system B, $Cp_2Ti(CO)_2$ (6 mg, 5 mol %) and PMe_3 (10 μL, 20 mol %) were used to convert 2′-(3-cyclopentene)-acetophenone (93 mg, 0.5 mmol) to 88 mg (82% yield) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.35 (m, 3 H); 7.22 (d, *J* = 6.5 Hz, 1 H); 3.81 (dd, *J* = 7.4 Hz, *J* = 13.1 Hz, 1 H); 3.37 (t, *J* = 9.7 Hz, 1 H); 3.25 (m, 1 H); 2.13 (m, 2 H); 1.89 (m, 1 H); 1.78 (s, 3 H); 1.74 (m, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 179.5, 145.9, 143.5, 130.2, 128.0, 124.8, 124.3, 93.5, 56.1, 50.0, 47.1, 35.0, 32.1, 26.4. IR (neat): 2965, 1758, 1223, 1145, 1129, 1064, 761 cm^{-1}. Anal. Calcd for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59. Found: C, 78.51; H, 6.62.

Compound 12. Using general procedure B, $Cp_2Ti(CO)_2$ (59 mg, 0.25 mmol) and PMe_3 (52 μL, 1 equiv) were used to convert *o*-allyl-2′-hydroxyacetophenone (88 mg, 0.5 mmol) to the desired product. Purification by flash chromatography (hexane:diethyl ether = 3:2) yielded 44 mg (43% yield) of the a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45 (dd, *J* = 1.6 Hz, *J* = 7.8 Hz, 1 H); 7.22 (td, *J* = 1.6 Hz, *J* = 6.7 Hz, 1 H); 7.02 (dd, *J* = 1.1 Hz, *J* = 8.0 Hz, 1 H); 6.87 (dd, *J* = 1.1 Hz, *J* = 8.3 Hz, 1 H); 4.19 (m, 1 H); 4.10 (dd, *J* = 10.4 Hz, *J* = 2.6 Hz, 1 H); 2.71 (m, 3 H); 1.82 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 175.1, 153.4, 130.2, 129.0, 124.0, 122.5, 117.4, 81.2, 64.3, 41.3, 31.1, 28.5. IR (neat): 2977, 1770, 1488, 1306, 1230, 1129, 944, 762 cm^{-1}. Anal. Calcd for $C_{12}H_{12}O_3$: C, 70.58; H, 5.92. Found: C, 70.49; H, 5.99.

Acknowledgment. We thank the National Institutes of Health (GM 34917) for their generous support of this work. N.M.K. is a National Cancer Institute Predoctoral Trainee supported by NIH Cancer Training Grant CI T32CAO9112. Additional support from Pfizer and from the Dow Chemical Company is also gratefully acknowledged. We thank Boulder Scientific for a gift of Cp_2TiCl_2. N.M.K. thanks the American Chemical Society Organic Division, Smith-Kline Beecham, and Boehringer Ingelheim Inc. for additional support in the form of predoctoral fellowships. F.A.H. thanks the National Science Foundation for a predoctoral fellowship. We acknowledge the helpful comments of a referee who suggested an alternate explanation for the role of trimethylphosphine in this reaction.

JA970115B