Scope of the Intramolecular Titanocene-Catalyzed Pauson−Khand Type Reaction[1]

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

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

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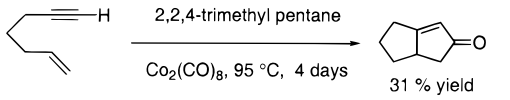
Abstract: A Pauson−Khand type conversion of enynes to bicyclic cyclopentenones employing the commercially available precatalyst titanocene dicarbonyl is described. This methodology shows excellent functional group tolerance for a group 4 metallocene-catalyzed process. The scope and limitations of this cyclization with respect to 1,6-, 1,7- and 1,8-enynes with a variety of terminal alkyne substituents, chiral enynes, and enynes containing substituted olefins are described in detail. A mechanism involving carbonylation of an intermediate titanacyclopentene has been proposed.

Introduction

In the field of organic chemistry, the search for new and more efficient methods of carbon−carbon bond formation for application in the total synthesis of complex molecules continues to be a major theme. Recently, an important area of investigation toward this end has involved transition metal-mediated and -catalyzed cycloaddition reactions. This work has allowed for the combination of unsaturated functional groups in ways which are either difficult or impossible without the action of a transition metal complex. Examples of this approach include the intramolecular Diels−Alder[2] and Alder−Ene[3] cyclization of unactivated substrates, the homo-Diels−Alder reaction,[4] [2 + 2 + 2] alkyne cyclotrimerization,[5] intramolecular triene−ene cyclization,[6] [5 + 2] cyclopropyl enyne and diene[7] and [4 + 4] 1,3-diene cycloadditions.[8] The possibility also exists for asymmetric induction with the use of chiral ligands, and a number of excellent reviews on the progress in this field have been published recently.[9] The proof of the utility of these methods lies in their elegant applications to total synthesis.[10]

The most thoroughly investigated and utilized transition metal-mediated cycloaddition reaction is the Pauson−Khand reaction.[11] First reported in 1973,[12] the overall transformation involves the formal [2 + 2 + 1] cycloaddition of an alkyne, an alkene, and CO to produce a cyclopentenone (Scheme 1).[13] The first intramolecular version was reported by Schore in 1981 (eq 1).[14] This work demonstrated the synthetic potential inherent



(1)

in an intramolecular Pauson−Khand cyclization, which allows for the formation of two rings and three new carbon−carbon bonds. Subsequently, a large body of work has been reported which has culminated in the utilization of the intramolecular cyclization in a number of efforts in total synthesis.[15] Initial application to synthesis was hampered by the low to moderate yields of cyclopentenone and harsh reaction conditions which were required. A number of improvements on the early protocols have been reported,[16] but the one which has been most widely adopted is the use of amine-oxide promoters, which allows for

[†] Current Address: Department of Chemistry, University of North Carolina at Chapel Hill, CB 3290, Chapel Hill, NC 27599.

[‡] Current address: Department of Chemistry and Chemical Biology, Harvard University, 12 Oxford St., Cambridge, MA 02138.

(1) This paper has been adapted, in part, from the following thesis: Hicks, F. A., Ph.D. Dissertation, Massachusetts Institute of Technology, 1999.

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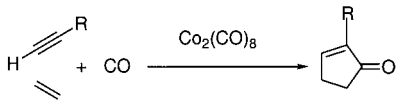
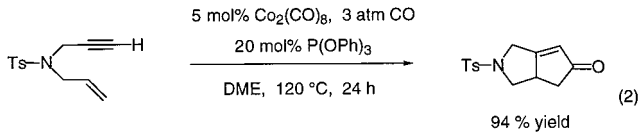
Scheme 1



the formation of cyclopentenones in good to excellent yield under extremely mild conditions (0 °C to rt).[17−19]

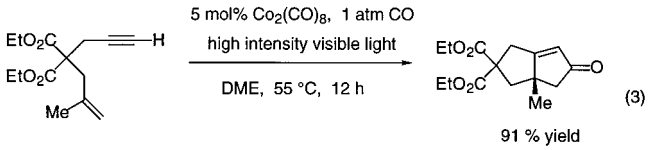
One of the limitations of these Pauson−Khand type reactions in comparison to many of the other cycloaddition reactions mentioned above is the requirement for a stoichiometric amount of a metal complex. Few examples of Pauson−Khand cyclizations employing substoichiometric amounts of Co,[20] including a single intermolecular example employing only 0.22 mol % $Co_2(CO)_8$,[21] appeared prior to the past five years. During this period a number of truly catalytic intramolecular Pauson−Khand cyclizations have been developed.[22]

A major impediment to a Co-catalyzed process has been the formation of inactive cluster complexes such as $Co_4(CO)_{12}$. In an attempt to prevent the formation of such species, Jeong and co-workers found that the addition of the coligand $P(OPh)_3$ allowed for the cyclocarbonylation of a variety of enynes with 3−10 mol % $Co_2(CO)_8$ under 3 atm CO (eq 2).[23] It should be



noted that with stoichiometric Pauson−Khand reactions, the presence of a phosphine or phosphite ligand on the dicobalt complex has been reported to lead to a dramatic rate decrease.[1,24]

Another interesting version of the intramolecular Pauson−Khand cyclization has been developed by Livinghouse.[25] He exploited the known propensity of $Co_2(CO)_8$ to lose a CO ligand upon irradiation to generate a catalytically active species under extremely mild conditions (1 atm CO, 50 °C) (eq 3). Upon



further investigation, it was found that this reaction could be carried out thermally if the reaction temperature was maintained in a narrow range (at 60 °C).[26] Additionally, the use of air-stable alkyne−Co complexes as precatalysts was reported.[27]

Chung and Jeong reported that (indenyl)Co(cod) was a precatalyst for the cyclization of two 1,6-enynes (DME, 100 °C, 15 atm CO, 40 h).[28] The presence of the indenyl ligand appeared crucial as the corresponding complexes $CpCo(CO)_2$ and CpCo(cod) were completely inactive under the same reaction conditions. Chung later found that low valent cobalt complexes generated in situ from $Co(acac)_2$ and $NaBH_4$ could serve as catalysts for the conversion of several 1,6-enynes to enones (CH_2Cl_2, 100 °C, 30−40 atm CO, 48 h).[29] It was proposed that the $NaBH_4$ served not only to reduce the cobalt but also to stabilize the reactive intermediates and prevent the formation of unreactive clusters and complexes. However, in a more recent report by Chung, $Co_4(CO)_{12}$, one of the purportedly inactive complexes, could in fact be used as a precatalyst for the Pauson−Khand reaction in both an inter- and intramolecular fashion under moderately high CO pressures (CH_2Cl_2, 150 °C, 10 atm CO, 24 h).[30] Another cobalt cluster, methylidynetricobalt nonacarbonyl, has also proven to be an effective catalyst (toluene, 120 °C, 7 atm CO).[31] Jeong has developed a catalytic Pauson−Khand reaction which can be carried out in supercritical CO_2.[32]

Although the Pauson−Khand reaction refers only to Co-mediated processes, a variety of other transition metals are also capable of effecting stoichiometric Pauson−Khand type enyne cyclizations. These reactions offer the possibility of developing catalytic processes which may exhibit complementary reactivity when compared to the cobalt-based procedures. In addition to $Co_2(CO)_8$, other transition metal carbonyl complexes, such as $Fe(CO)_4$(acetone),[33] $W(CO)_5$(THF),[34] $Cr(CO)_5F$,[35] $Cp_2Mo_2(CO)_4$,[36] and $Mo(CO)_6$[37] react stoichiometrically with enynes

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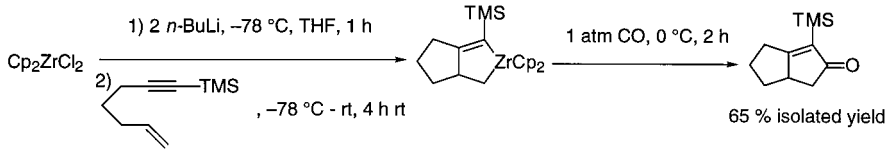
Scheme 2



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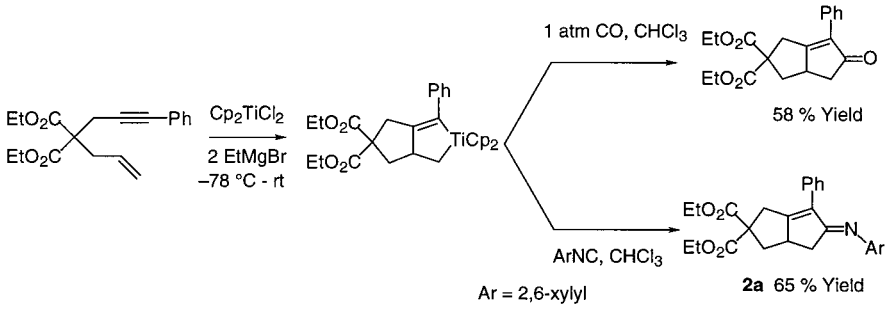

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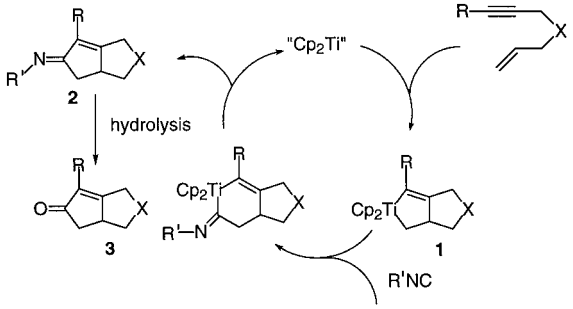
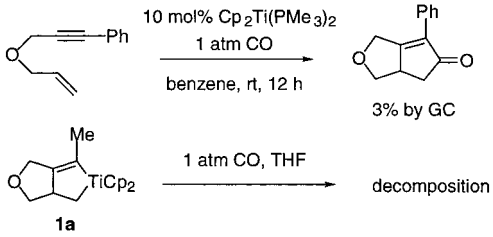


Scheme 5



in a similar fashion. In a different approach, Negishi has shown that bicyclic zirconacyclopentenes can be formed from "Cp_2Zr" and an enyne. The resultant metallacycles can be transformed under an atmosphere of CO into cyclopentenones (Scheme 2).[38,39]

During the development of a complementary enyne cyclocarbonylation procedure involving "Cp_2Ti" (from Cp_2TiCl_2 and 2 equiv EtMgBr), which displayed greater tolerance for oxgenated functional groups in comparison to "Cp_2Zr", it was noted that the treatment of the titanacyclopentene intermediates with isonitriles, which are isoelectronic with CO, produced the analogous iminocyclopentenes (**2a**) and isonitrile complexes of titanocene (Scheme 3).[40] A related iminocyclopentene synthesis promoted by Ni complexes had previously been reported by Tamao.[41]

The observation of the Cp_2Ti(II) isonitrile complexes led to the formulation of the catalytic cycle shown in Scheme 4. While the use of isonitriles such as *t*-BuNC led to rapid catalyst deactivation, the use of trialkylsilylcyanides (R′ = Et_3Si,(*tert*-butyl)$(Me)_2Si$),[42] which exist in tautomeric equilibria with minor amounts of the isocyanides (∼99:1 for trialkylsilyl cyanides), allowed for the effective catalytic formation of the iminocyclopentenes.[43,44] Although the silylimines **2** obtained from this reaction proved too unstable to isolate, they could be hydrolyzed to the corresponding cyclopentenones **3**; however, the troublesome imine hydrolysis provided disappointing yields (43−80%). After this work, a Ni-catalyzed variant of this process was developed by adapting Tamao's stoichiometric reaction[41] to the use of silylcyanides.[45] This methodology represented an improvement over the titanium-catalyzed reaction in terms of substrate scope, with enynes containing 1,2-disubstituted olefins, aliphatic ketones, and nitriles proving to be compatible with the reaction conditions employed.

Attempts were also made to effect a direct titanocene-catalyzed enyne cyclocarbonylation employing CO rather than R′NC; however, the conditions initially investigated failed to produce significant quantities of cyclopentenone (Scheme 5). This finding was in accord with the earlier studies on the stoichiometric carbonylation of titanacyclopentenes.[40] Exposure of a THF solution of titanacyclopentene **1a** to an atmosphere of CO led only to decomposition of the titanacycle without the production of the desired cyclopentenone (Scheme 5). Only when the reaction was carried out in $CHCl_3$ were reasonable yields of cyclopentenone obtained; under these conditions the titanocene moiety is oxidized to Cp_2TiCl_2, which apparently prevents a destructive interaction between a low valent titanium intermediate and the nascent enone. The use of $CHCl_3$, however, removes the Ti from the oxidation state necessary for catalysis.

Following our work on stoichiometric titanium-mediated enyne cyclocarbonylations,[40] a related cyclocarbonylation of enones was investigated.[46] It was found that titanacycles derived from $Cp_2Ti(PMe_3)_2$ and a variety of enones and an ynone could be carbonylated to yield γ-butyrolactones and a butenolide in a

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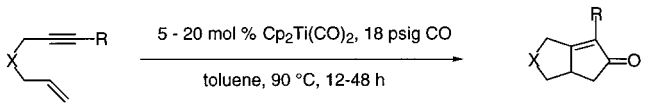
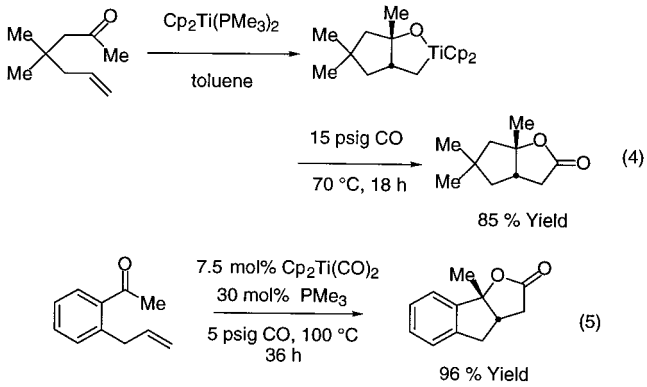
Scheme 6



stoichiometric fashion (eq 4). Upon further investigation, it was shown that a certain class of enones, *o*-allyl aryl ketones, could be catalytically converted to γ-butyrolactones using either $Cp_2Ti(PMe_3)_2$ or $Cp_2Ti(CO)_2$ as precatalysts (eq 5).[47]



These findings prompted a reinvestigation of the titanocene-catalyzed Pauson−Khand type reaction utilizing $Cp_2Ti(CO)_2$ as a precatalyst. It was discovered that under conditions which were similar to those used for the *o*-allyl aryl ketone cyclocarbonylations, a diverse collection of enynes could be catalytically converted to the corresponding enones (Scheme 6).[48] In this paper, we disclose a thorough study of this reaction which allows the more accurate assessment of the scope of this process.

After our initial publication on this work, complexes of two other transition metals have been shown to serve as precatalysts for this transformation. Murai and Mitsudo, separately, reported similar enyne cyclocarbonylations catalyzed by $Ru_3(CO)_{12}$.[49,50] Quite recently, $[RhCl(CO)_2]_2$[51] and $[RhCl(CO)(dppp)]_2$[52] have also been shown to be effective catalysts for this transformation (Scheme 7). A comparison of the synthetic scope of the different intramolecular Pauson−Khand type cyclizations which have been reported will also be discussed.

Results and Discussion

Optimization of Reaction Conditions. The standard reaction conditions for the titanocene-catalyzed enyne cyclocarbonylation are shown in Scheme 6. They involved combining the commercially available titanocene dicarbonyl with toluene and an enyne in a resealable Schlenk flask, evacuating and refilling the Schlenk flask with CO, and heating the Schlenk flask for the prescribed time. In addition to toluene, THF was found to serve as an effective solvent for the cyclization process (substrate from Table 1, entry 2). With this substrate, using 2.5 mol % titanocene dicarbonyl, reactions conducted in DME, 1,4-dioxane, and toluene led to similar levels of conversion to the enone product (~40% (GC)). Hexane (~38% conversion (GC)) and Et_2O (~30% conversion (GC)) were found to be poor solvents for this reaction when 5 mol % $Cp_2Ti(CO)_2$ was employed. Procedures employing DMF and pyridine gave essentially no enone product. The reaction temperature is important for timely conversion of the enyne to cyclopentenone; the cyclization of the substrate from Table 1, entry 2 is complete within 12 h at 90 °C with 5 mol % $Cp_2Ti(CO)_2$. At 75 °C, only 60% conversion (GC) was observed in 12 h, and the use of 10 mol % catalyst at 45 °C led to only 85% conversion (GC) to the enone in the same amount of time. More dilute reaction conditions (2.1 mM vs 8.3 mM in $Cp_2Ti(CO)_2$) could be employed to effect complete conversion of the same substrate with only 2.5 mol % catalyst in toluene. Attempts to perform catalytic cyclizations with CO pressures higher than 18 psig (e.g., 60 psig and 80 psig) led to no improvement in conversion to product (substrate from Table 1, entry 2). However, there is an interesting dichotomy between substrates which require 18 psig CO to reach complete conversion and those which can also be cyclized at 5 psig CO (vide infra). Finally, because the importance of an added ligand had been demonstrated in the titanocene-catalyzed cyclocarbonylation of *o*-allyl aryl ketones[47] and in Jeong's[23] catalytic Pauson−Khand reaction, the effects of added PMe_3 were investigated. A number of enynes were surveyed (Table 1, entries 1, 4, 5 and 8, and Table 3, entries 1 and 3), and the difference in the conversion to product realized for cyclizations with and without PMe_3 (up to 4 equiv) was not greater than 10%.

Two closely related general protocols have been utilized for this reaction. In protocol A, the catalyst and toluene were added to a Schlenk flask in a glovebox, and the enyne was subsequently added afterward on a Schlenk line under Ar. In protocol B, all three components were added to the Schlenk flask in the glovebox (See Experimental Section). The two protocols work equally well for freshly prepared enynes. However, prolonged storage of some enyne substrates outside the glovebox led to partial decomposition or the acquisition of adventitious moisture, and a concomitant decrease in conversion to cyclopentenone was observed. Generally, if the substrates were passed through a pipet filled with neutral alumina in the glovebox just prior to use, conversion to the enone was restored to the maximum level. However, to circumvent the need for this periodic repurification, many enynes were stored in the glovebox and utilized with protocol B.

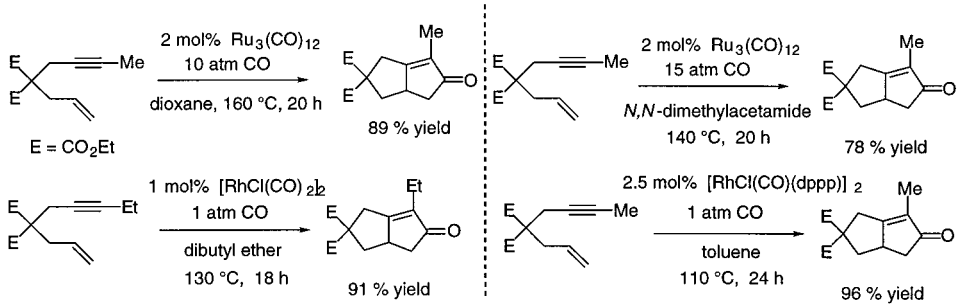
Proposed Mechanism. The mechanism which we tentatively propose for the titanocene-catalyzed Pauson−Khand type reaction is shown in Scheme 8. Initial CO dissociation from $Cp_2Ti(CO)_2$ yields titanocene monocarbonyl **4**, which reacts with the alkyne portion of the enyne to provide η^2-alkyne carbonyl complex **5**.[53] Loss of another equivalent of CO leads to **6** which provides titanacyclopentene **1** upon insertion of the olefin into the Ti−C bond of the titanacyclopropene. Subsequent CO coordination gives **7** which upon migratory insertion of the bound CO into the Ti−C sp^3 bond yields acyl complex **8**.[54] Reductive elimination from **8** releases the cyclopentenone and regenerates the reactive $Cp_2Ti(II)$ fragment, probably containing

(46) Kablaoui, N. M.; Hicks, F. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 5818.
(47) Kablaoui, N. M.; Hicks, F. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1997**, *119*, 4424.
(48) Hicks, F. A.; Kablaoui, N. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 9450.
(49) Morimoto, T.; Chatani, N.; Fukumoto, Y.; Murai, S. *J. Org. Chem.* **1997**, *62*, 3762.
(50) Kondo, T.; Suzuki, N.; Okada, T.; Mitsudo, T.-a. *J. Am. Chem. Soc.* **1997**, *119*, 6187.
(51) Koga, Y.; Kobayashi, T.; Narasaka, K. *Chem. Lett.* **1998**, 249.
(52) Jeong, N.; Lee, S.; Sung, B. K. *Organometallics* **1998**, *17*, 3642.

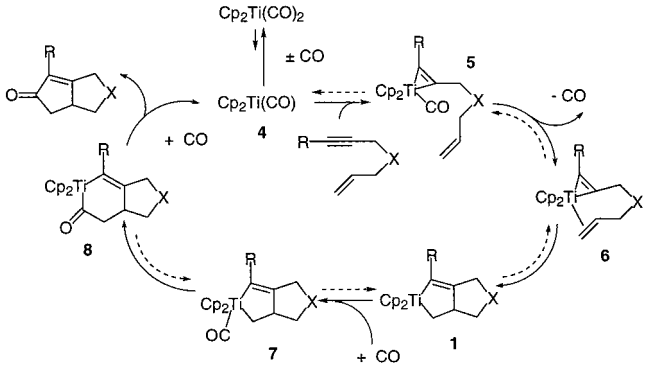
(53) For the formation of an η^2-alkyne carbonyl complex from $Cp_2Ti(CO)_2$, see: Fachinetti, G.; Floriani, C. *J. Chem. Soc., Chem. Commun.* **1974**, 66.

(54) The insertion of RNC and CO has been demonstrated to occur regiospecifically into the M−C sp^3 bond of related group 4 metallacycles. (a) Càmpora, J.; Buchwald, S. L.; Guitérrez-Puebla, E.; Monge, A. *Organometallics* **1995**, *14*, 2039. (b) Erker, G.; Kropp, K. *J. Organomet. Chem.* **1980**, *194*, 45. (c) Grossman, R. B. Ph.D. Dissertation, Massachusetts Institute of Technology, 1992.

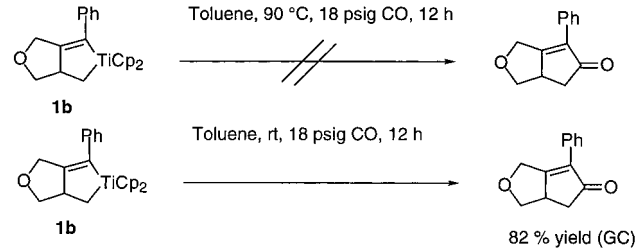
Scheme 7



Scheme 8



Scheme 9



a CO or another ligand. This mechanism is analogous to the one previously proposed for the iminocyclopentene synthesis and the enone cyclocarbonylation.[43,44,47]

Although delineation of the details of this process awaits a thorough kinetic and mechanistic study, one step deserves further comment at this time. On the basis of our initial work on the stoichiometric carbonylation of titanacyclopentenes (Scheme 5), the intermediacy of titanacyclopentenes in this catalytic process was called into question.[40] Attempts to effect stoichiometric carbonylations of titanacyclopentenes **1b** failed to produce cyclopentenone at 90 °C; however, a stoichiometric reaction conducted at room temperature demonstrated the chemical competence of **1b** as an intermediate by providing a reasonable yield of the corresponding cyclopentenone (Scheme 9). The use of **1b**, generated in situ from $Cp_2Ti(PMe_3)_2$ and the corresponding enyne, as a precatalyst also resulted in reduced levels of conversion to cyclopentenone in comparison to the use of $Cp_2Ti(CO)_2$ (Scheme 10). In combination with the dependence of enyne conversion upon catalyst concentration (vide supra), these results speak to the need to restrict the concentration of **1** under the catalytic reaction conditions (e.g., 90 °C). One explanation for this restriction would be a bimolecular catalyst decomposition pathway involving **1**.

Synthetic Scope. Inspection of entry 2 in Table 1 reveals several advantages of this cyclocarbonylation methodology in comparison to our previously reported titanocene-catalyzed route to cyclopentenones via the intermediate iminocyclopentenes.[43,44] The yields for the direct cyclocarbonylation are consistently higher than those previously obtained for the indirect route as the yield-limiting imine hydrolysis has been circumvented. Additionally, the quantity of catalyst required for the cyclocarbonylation is typically less than that for the iminocyclopentene synthesis. These differences are noted in the tables for substrates which have been studied with both catalyst systems.

Scheme 10

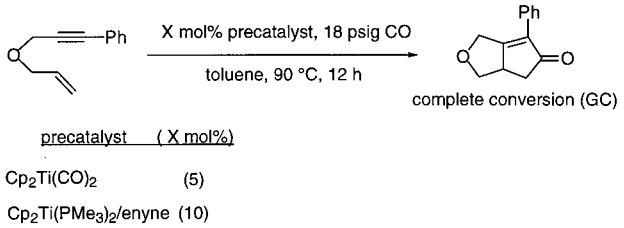


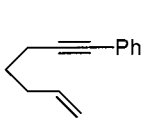
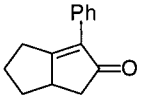
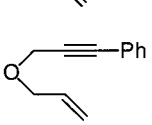
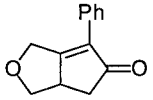
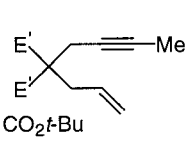
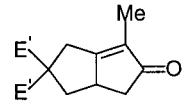
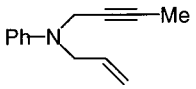
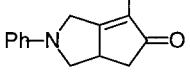
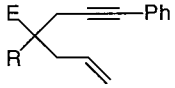
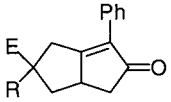
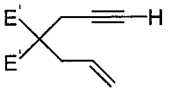
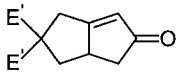
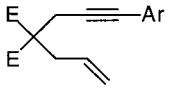
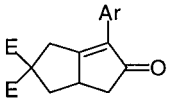
Table 1 summarizes our findings indicating the functional group tolerance of the titanocene-catalyzed Pauson−Khand type reaction. In general, one of the major drawbacks of early transition metal-catalyzed and -mediated processes as compared to those catalyzed by late transition metal complexes is the poor levels of functional group tolerance which are seen. As with the previously reported titanium-catalyzed iminocyclopentene synthesis, enynes containing aliphatic ethers, amines, both *tert*-butyl and ethyl esters (entries 2−5), and both TIPS- and Bn-protected alcohols (Table 3, entries 1 and 2) are readily cyclized to the corresponding enones. Unlike the iminocyclopentene system, the cyclocarbonylation reaction has also been shown to tolerate substrates containing aliphatic nitriles and ketones (entries 6 and 7). This difference can be attributed to differences in the precatalysts employed: $Cp_2Ti(PMe_3)_2$ versus $Cp_2Ti(CO)_2$. In stoichiometric reactions, treatment of $Cp_2Ti(PMe_3)_2$ with either of the enynes mentioned above (entries 6 and 7) leads to rapid decomposition of the titanocene complex as indicated by the disappearance of signals for the cyclopentadienyl peaks in the ^{1}H NMR. It has been demonstrated that both nitriles[55] and ketones[56] are capable of replacing a PMe_3 ligand from $Cp_2Ti(PMe_3)_2$. It is probably this lability of the PMe_3 ligand which leads to decomposition of the titanocene moiety. However, $Cp_2Ti(CO)_2$ is fairly unreactive toward CO substitution by nitriles and aliphatic ketones,[47] relative to alkynes,[53] preventing or slowing decomposition of the catalyst.

Another advantage of the titanocene-catalyzed enyne cyclocarbonylation over related group 4 cyclizations is its ability to accommodate an enyne containing a terminal alkyne (entry 8). The formation of group 4 metallacyclopentenes from terminal

(55) Doxsee, K. M.; Garner, L. C.; Juliette, J. J. J.; Mouser, J. K. M.; Weakley, T. J. R.; Hope, H. *Tetrahedron* **1995**, *51*, 4321.

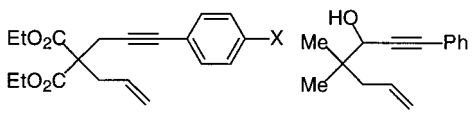
(56) (a) Gleiter, R.; Wittwer, W. *Chem. Ber.* **1994**, *127*, 1797. (b) Reference 47.

Table 1. Examples Which Demonstrate the Functional Group Tolerance of the Titanocene-Catalyzed Pauson-Khand Type Reaction

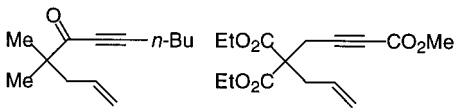
Entry	Substrate	Product	Mol% $Cp_2Ti(CO)_2$	Yield (%)	R_3SiCN Yield (%)
1			5	87	80
2			5	92	66
3	 $E' = CO_2t\text{-Bu}$		5	89	70
4			10	88	
5 - 7	 $E = CO_2Et$		5 R = E, 5	95	
			6 R = CN, 7.5	75 (1:1)	
			7 R = C(O)Me, 7.5	93 (1:1)	
8			20	85	
9 - 15			9 Ar = *p*-MeC_6H_4, 5	86	
			10 Ar = *p*-$MeOC_6H_4$, 5	91	
			11 Ar = *p*-ClC_6H_4, 5	87	
			12 Ar = *p*BrC_6H_4, 5	91	
			13 Ar = *p*EC_6H_4, 5	86	
			14 Ar = *p*CNC_6H_4, 7.5	72	
			15 Ar = *p*$CF_3C_6H_4$, 5	91	

alkyne-containing enynes has been a limitation in processes involving group 4 metallocenes.[38,39] While several approaches have been developed recently for the stoichiometric cyclization of terminal enynes by group 4 metal complexes,[57] there have been no reports to date of catalytic reactions. The cyclocarbonylation process allows us to effect the catalytic cyclization of terminal enynes, although the amount of catalyst required for complete conversion to the corresponding enone is quite high.

We have also extensively explored reactions of substrates containing functionalized aromatic groups using this methodology. As can be seen from Table 1, ethers (entry 10), halides (entries 11 and 12), esters (entry 13), nitriles (entry 14), and a trifluoromethyl group (entry 15) could be accommodated. Reactions of substrates containing a nitro (**9**) or methyl ketone (**10**) group on the aromatic ring produced no cyclopentenone. Other functional groups which have proven incompatible with this methodology include unprotected alcohols (**11**) as well as α,β-propargylic ketones (**12**) and esters (**13**).



X = NO_2 **9**, C(O)Me **10** **11**

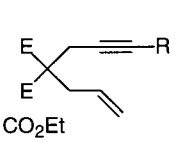
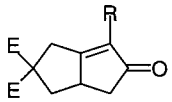
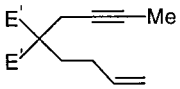
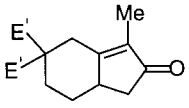
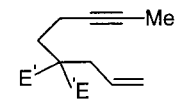
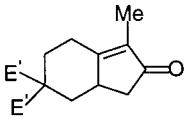
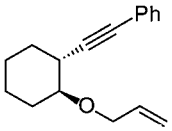
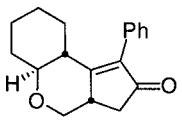


12 **13**

One limitation of the iminocyclopentene synthesis involved the inability to convert enynes possessing sterically hindered

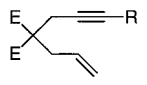
(57) (a) Urabe, H.; Hata, T.; Sato, F. *Tetrahedron Lett.* **1995**, *36*, 4261. (b) Miura, K.; Funatsu, M.; Saito, H.; Ito, H.; Hosomi, A. *Tetrahedron Lett.* **1996**, *37*, 9059. (c) Barluenga, J.; Sanz, R.; Fañanás, F. J. *J. Chem. Soc., Chem. Commun.* **1995**, 1009. (d) Barluenga, J.; Sanz, R.; Fañanás, F. J. *Chem.—Eur. J.* **1997**, *3*, 1324.

Table 2. Effects of the Size of the Alkyne Substituent (R) and the Length of the Carbon Tether Connecting the Alkene and Alkyne

Entry	Substrate	Product	Mol% $Cp_2Ti(CO)_2$	psig CO	Yield (%)	R_3SiCN Yield (%)
	 E = CO_2Et					
1	R = Me		5	18	91	71
2	R = *n*-Pr		5	18	92	
3	R = *i*-Pr		15	18	86	
			10	5	85	
4	R = *c*-Pentyl		15	18	83	
			10	5	83	
5			10	18[b]	88	71
6	 E' = $CO_2(t\text{-Bu})$		10	5[a]	85	
7			5	18	90 (1 isomer)	67

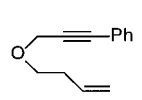
[a] Reaction produces similar yields at 18 psig CO. [b] Reaction conducted only once.

terminal alkyne substituents to product. This was attributed to the small size of the titanocene fragment.[44] An investigation of the reaction of substrates which contain a variety of alkyne substituents (Table 2) revealed that the catalytic cyclocarbonylation reaction also suffered from the same limitations. While enynes for which R = Me and *n*-Pr (Table 2, entries 1 and 2) were easily converted to the corresponding enones, the cyclization, while high yielding, proved more difficult with branched groups such as R = *i*-Pr and cyclopentyl (Table 2, entries 3 and 4). In instances where R = TMS (**14**) or *t*-Bu (**15**), no formation of cyclopentenone was observed.

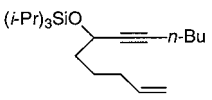


R = TMS **14**, *t*-Bu **15**

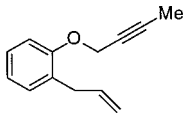
The vast majority of successful Pauson−Khand type reactions reported to date employ 1,6-enynes as substrates.[11] To explore the ability of this catalyst system to cyclize homologous substrates, a study involving the cyclization of 1,7- and 1,8-enynes was undertaken. It was found that cyclization was facile with conformationally biased 1,7-enynes (the Thorpe−Ingold Effect)[58] containing diesters (Table 2, entries 5 and 6) or in a substrate where the two groups were positioned on contiguous carbons of a ring system (entry 7). However, neither the simple 1,7-enyne **16** nor the monosubstituted derivative **17** could be converted to product. All attempts to cyclize 1,8-enynes, **18** and **19**, also failed to produce any observable enone.



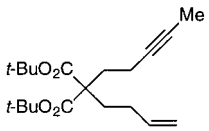
16



17



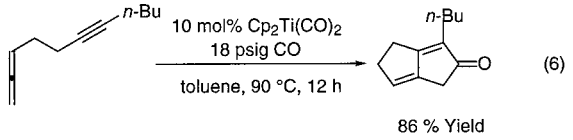
18



19

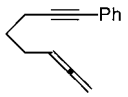
A number of reports have appeared recently describing the cyclization of allenynes promoted by complexes of Mo, Co, and Zr to provide either α-methylenecyclopentenones or conjugated dieneones, depending on the metal complex and substrate employed (Scheme 11).[59] When a 1,5-allenyne was subjected to our standard reaction conditions, clean and regioselective formation of the corresponding dieneone was observed (eq 6). Attempts to cyclize the simple 1,6-allenyne **20**

(58) (a) DeTar, D. F.; Luthra, N. P. *J. Am. Chem. Soc.* **1980**, *102*, 4505. (b) Eliel, E. L. *Stereochemistry of Carbon Compounds*; McGraw-Hill: New York, 1962; p 168.



(6)

were met with poor levels of conversion, although the product which was obtained was exclusively the α-methylenecyclopentenone.



20

We also studied the cyclization of chiral 1,6-enynes, which revealed some intriguing differences between the titanocene-catalyzed iminocyclopentene synthesis and the cyclocarbonylation process. For the cyclocarbonylation reactions, some general selectivity patterns were observed with respect to the location of the chiral center on the enyne. Substrates substituted in the allylic position (Table 3, 1 and 2) were cyclized with only moderate levels of stereoinduction, while those substituted in the propargylic position (Table 3, 3 − 5) were converted to enone with high levels of diastereoselectivity.

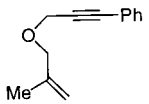
When the dr of the enones obtained from the cyclocarbonylation reaction are compared to those obtained from hydrolysis of the corresponding iminocyclopentenes, some differences are apparent. While general trends are observed for the cyclocarbonylation reaction with respect to selectivity versus the position of enyne substitution, the cyclopentenones which are obtained from the iminocyclopentene synthesis from propargyl- (entry 3 (1.6:1) vs entry 4 (5:1)) and allyl-substituted (entry 1(12:1) vs entry 2 (1.2:1)) enynes are produced with variable levels of diastereoselectivity. Analyzing the dr of the enones resulting from hydrolysis of the intermediate silylimines, however, is not the most accurate way to assess the diastereoselectivity of the cyclization reaction since equilibration of different diastereomers or selective decomposition of one isomer may occur. This is especially relevant considering the problematic nature of the silylimine hydrolysis. When the dr's of the iminocyclopentenes are analyzed and compared to those seen for cyclopentenones formed by the cyclocarbonylation, some differences in the selectivity of the two methodologies are still noted.

Despite these disparities, the same major isomer was observed for both methodologies in each case. The formation of the major isomer which is observed for enynes substituted in either the propagylic or the allylic positions (only the propargylic case has been pictured) has previously been rationalized as arising from unfavorable 1,3-diaxial interactions in one of the two lowest-energy intermediates (**21a** and **b**) whose formation precedes cyclization (Scheme 12).[44] Though caution should be used when attributing the selectivity of metallacycle formation to ground-state interactions, similar steric considerations are also expected to differentiate the energies of the diastereomeric transition states en route to metallacycles **22a** and **b**. Since these same interactions are expected to be present in all subsequent intermediates and transition states in the mechanism, the same general trends are to be predicted, regardless of which step determines the diastereoselectivity of enone formation.[61]

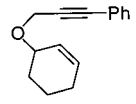
Examination of the elementary steps of the mechanism outlined in Scheme 12 reveals a number of potential origins for the quantitative differences between the diastereomeric ratios seen in titanacyclopentenes, iminocyclopentenes and cyclopentenones. In stoichiometric reactions, the formation of chiral group 4 metallacyclopentenes such as **22** has been demonstrated to be reversible; equilibration can proceed through binding of the two diastereotopic olefin faces and subsequent reinsertion into the titanacyclopropene moiety.[62] The dr's shown for the titanacyclopentenes in Table 3 represent the thermodynamic ratio obtained after heating the titanacycles for 12 h at 105 °C; however, these values are essentially unchanged from the initial ones observed at room temperature.[63] The fact that the product dr's sometimes vary substantially from these metallacycle dr's indicates that the thermodynamic stability of the diastereomeric titanacycles does not determine the dr of the enone products in all cases.

One reason the final product dr's do not reflect the thermodynamic titanacycle dr's could involve kinetic trapping of the metallacycles via a migratory insertion process involving carbon monoxide or isonitrile. Given that isonitriles tend to react more rapidly (as compared to carbon monoxide) and in an irreversible fashion with respect to migratory insertion,[64] it is possible that the ratio of products arising from the silylimine reaction more closely reflects a kinetic ratio of intermediate metallacyclopentenes than does the ratio of cyclopentenones derived from the cyclocarbonylation process. In contrast, CO migratory insertions have been demonstrated to be reversible in group 4 metallocene chemistry.[64] The reversibility allows for an equilibrium to be established between diastereomeric acyl intermediates **23a** and **b** (Scheme 12) which would not be possible or would be less likely in the iminoacyl case. Finally, a kinetic partitioning at the point of CO or isonitrile insertion cannot be ruled out as a possible origin for the dissimilar dr's arising from the two protocols.

The use of enyne substrates containing substituted olefins was also investigated in the titanocene-catalyzed Pauson−Khand type reaction. The cyclization of a 1,1-disubstituted olefin-containing enyne (Table 4, entry 1) proved to be quite facile; however, the presence of the diester substituents was important to the success of this cyclization as a related substrate containing an ether linkage in lieu of a diester, (**24**), could not be completely converted to the corresponding enone even using 20 mol % $Cp_2Ti(CO)_2$. Analogously, enynes possessing cyclic 1,2-disubstituted olefins (Table 4, entries 2 and 3) are cyclized diastereoselectively to the corresponding tricyclic enones. As in the iminocyclopentene synthesis, the ether-containing enyne **25** was not a viable substrate.



24



25

Attempts to cyclize enynes which have acyclic 1,2-disubstituted olefins revealed some interesting nuances. When an enyne

(59) (a) Kent, J. L.; Wan, H.; Brummond, K. M. *Tetrahedron Lett.* **1995**, *36*, 2407. (b) Ahmar, M.; Locatelli, C.; Colombier, D.; Cazes, B. *Tetrahedron Lett.* **1997**, *38*, 5281. (c) Brummond, K. M.; Wan, H. *Tetrahedron Lett.* **1998**, *39*, 931. (d) Brummond, K. M.; Wan, H.; Kent, J. L. *J. Org. Chem.* **1998**, *63*, 6535.

(60) See ref. 44 for a detailed discussion.

(61) For related discussions on the diastereoselective formation of group 4 metallacyclopentenes in a stoichiometric fashion, see: (a) RajanBabu, T. V.; Nugent, W. A.; Taber, D. F.; Fagan, P. J. *J. Am. Chem. Soc.* **1988**, *110*, 7128. (b) Pagenkopf, B. L.; Lund, E. C.; Livinghouse, T. *Tetrahedron* **1995**, *51*, 4421.

(62) (a) Agnel, G.; Owczarczyk, Z.; Negishi, E.-i. *Tetrahedron Lett.* **1992**, *33*, 1543. (b) Reference 39.

(63) In the case of the titanacycle for entry 4, heating caused complete decomposition. The dr in the table therefore represents the value obtained at room temperature.

(64) Durfee, L. D.; Rothwell, I. P. *Chem. Rev.* **1988**, *88*, 1059.

Scheme 11

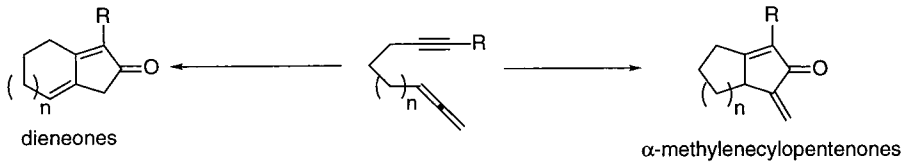
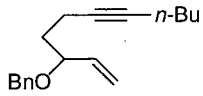
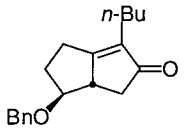
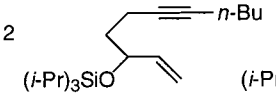
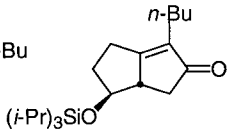
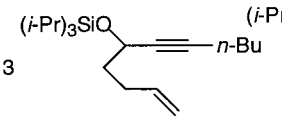
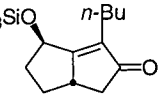
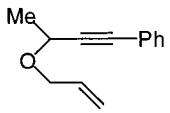
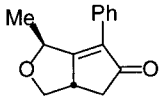
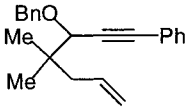
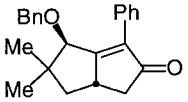
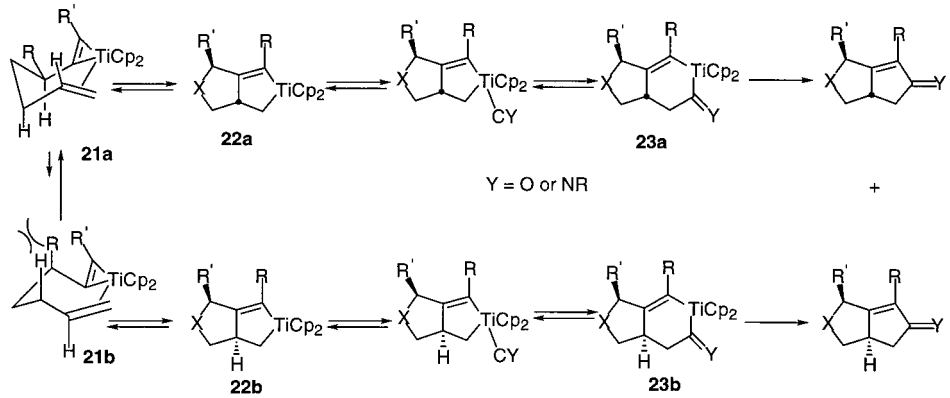


Table 3. Diastereoselective Cyclization of Chiral Enynes

Entry	Substrate	Product	Mol% $Cp_2Ti(CO)_2$	Yield (%) (d.r.)	R_3SiCN Enone Yield (%) (d.r.)	R_3SiCN Silylimine (d.r.)	Titanacycle (d.r.)
1			7.5	92 (3.5:1)	45 (12:1)	(7:1 - 9:1)	(4:1)
2			5	86 (2.3:1)	63 (1.2:1)	(~2:1)	(2.5:1)
3			10	92 (8:1)	54 (1.6:1)	(4:1)	(1.2:1)
4			5	94 (10:1)	71 (5:1)	~1 isomer	(10:1)
5			5	94 1 isomer	---	---	---

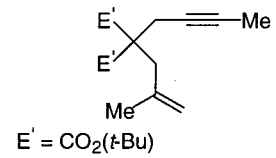
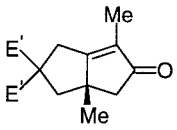
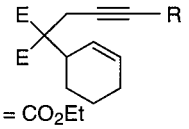
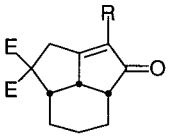
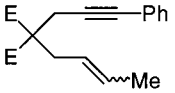
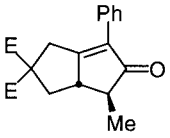
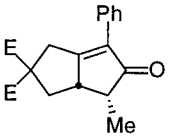
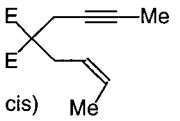
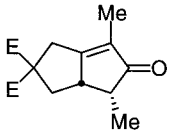
Scheme 12



composed of a 3:1 mixture of trans:cis isomers (Table 4, entry 4) was subjected to the standard reaction conditions, the corresponding enone was obtained in only moderate yield with a trans:cis ratio which was slightly higher than in the starting enyne. Interestingly, a 12% yield of **27** was also produced by a cycloisomerization pathway. A plausible mechanism for the formation of **27** involving sequential β-hydride elimination and reductive elimination from metallacycle **26** is shown in Scheme 13.[65] When pure *trans*- and *cis*-enynes (Table 4, entries 5−7)

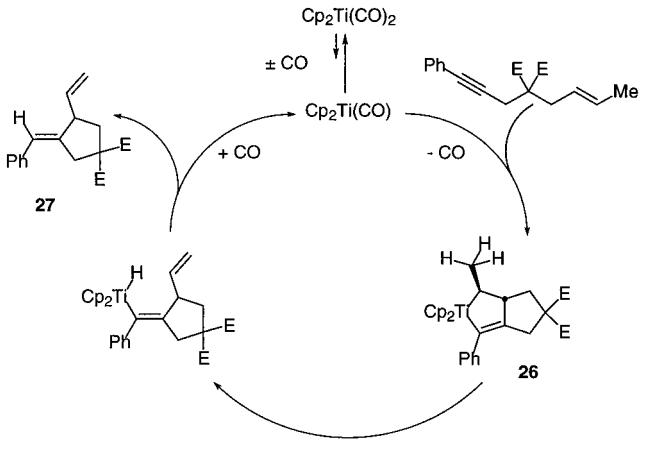
(65) It has been found that good yields of the cycloisomerization product can be obtained in the absence of CO: Sturla, S. J.; Kablaoui, N. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 1976.

Table 4. Cyclization of Enynes Containing Disubstituted Olefins

Entry	Substrate	Product	Mol% $Cp_2Ti(CO)_2$	Yield (%)	trans:cis	psig CO
1,1-disubstituted						
1	 E' = CO_2(*t*-Bu)		5	94	-------	18[a]
cyclic cis 1,2-disubstituted						
2			R=Ph, 10	91		5[b]
3	E = CO_2Et		R=Me, 10	86		5[b]
acyclic 1,2-disubstituted						
4	 (3:1 trans)		20	67	4:1	5
5	(24:1 trans)		20	57	4.2:1	5[d]
6	(24:1 cis)		20	79	1:1.9	5
7	 (24:1 cis)		20	58	1:2	5[c]

[a] Only attempted at 18 psig CO. [b] Only attempted at 5 psig CO. [c] Can also be performed at 18 psig CO. [d] Reaction conducted only once.

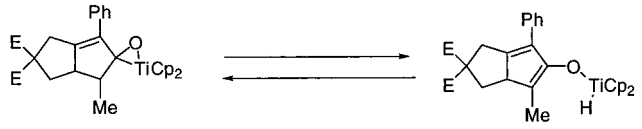
Scheme 13



were separately subjected to the cyclization reaction, mixtures of *trans*- and *cis*-enones were produced in all cases. Interestingly, the cycloisomerization product **27** was obtained only from the reaction of the *trans*-enyne (entry 5); none was observed for either of the *cis*-olefin-containing enynes.

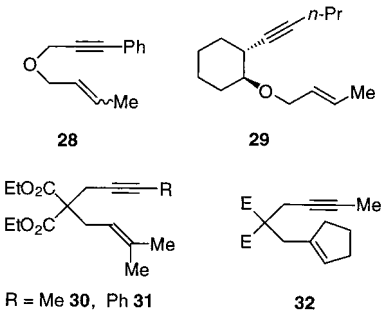
Several plausible mechanisms for the epimerization of the enone products can be proposed. The isomerization must occur after metallacyclization and at a point where enyne cannot be reformed. Otherwise cycloisomerization products would be observed from the conversion of *cis*- to *trans*-enynes. One mechanism for isomerization involves a reversible β-hydride elimination from an η^2-ketone complex (Scheme 14). This type of process has been invoked for related enones produced from zirconacyclopentenes.[38,66] Alternatively, the enone could be formed stereoselectively and then isomerized afterward, perhaps with the titanocene fragment serving the role of a Lewis acid catalyst.

Scheme 14



As with enynes containing cyclic 1,2-disubstituted olefins, attempts to cyclize substrate **28**, which lacks the geminal diester substitution, met with failure. In a similar fashion, **29**, a 1,7-enyne possessing an acyclic 1,2-disubstituted olefin was not a suitable substrate for the catalytic cyclization. All attempts to cyclize trisubstituted olefin-containing enynes (**30**−**32**) were also unsuccessful.

(66) Kemp, M. I.; Whitby, R. J.; Coote, S. J. *Synthesis* **1998**, 552.



Effects of CO Pressure on Conversion. A final aspect of the Ti-catalyzed Pauson−Khand type cyclization which warrants discussion is the variable pressure dependence on CO noted in the Tables. For a simple 1,6-enyne (Table 1, entry 2), 18 psig CO is required for high levels of enyne conversion to cyclopentenone. On the other hand, enynes which possess features which make them more difficult to cyclize, such as bulky alkyne substituents (Table 2, entries 3 and 4), a longer tethering chain as in 1,7-enynes (Table 2, entry 6), and olefin substitution (Table 4, entry 7), can be cyclized at both 5 and 18 psig CO. One explanation for this disparity can be found in the relative rates of titanacyclopentene formation (**1**, Scheme 8) for the different substrates. The simple enyne would be expected to form **1** most readily; under lower CO pressures the build up of **1** could lead to premature catalyst decomposition (see earlier discussion on catalyst concentration effects). Thus, higher CO pressures are required to inhibit metallacycle formation and promote catalyst stability. In the case of enynes which are more difficult to cyclize, there is no need for elevated CO pressure to limit the concentration of **1** in solution.

Comparison of Catalytic Pauson−Khand Type Reactions. It is useful at this point to compare the synthetic utility of the published catalytic Pauson−Khand type methodologies. There are two general classes which show similar reactivity profiles—those methods which employ complexes of Co and those involving complexes of other transition metals: Ti, Ru,[49,50] and Rh.[51,52] For the most thoroughly investigated Co-based procedures, Jeong's $P(OPh)_3$ system,[23] Livinghouse's photochemical[25] and thermal protocols,[27] and Sugihara's methylidynetricobalt cluster catalyst,[31] the cyclization of simple 1,6-enynes containing terminal alkynes (**33**) appears to work well. However, it is hard to assess the generality of these approaches with regard to the effect of alkyne substitution since substrates with substituted alkynes have not been thoroughly studied. With the Co cluster catalyst, a series of analogous enynes with different substituents (**34**−**36**) could be converted to the corresponding enones in similar yields with the same level of catalyst loading. Though the scope of functional group compatibility has not been explored in depth, the ability to cyclize an enyne containing an unprotected alcohol (**37**) seems to indicate the cobalt systems are, as expected, more tolerant of polar functional groups than is the Ti methodology. This is also consistent with what has previously been observed in stoichiometric Pauson−Khand reactions.[11] Additionally, though 1,7-enynes (**38** and **39**) and 1,6-enynes containing 1,1- and 1,2-disubstituted olefins (**40**−**45**) (see Figure 1) have been cyclized effectively with these cobalt systems, all examples of these classes of substrates reported to date contain terminal alkynes.

The opposite trend in efficiency vs level of alkyne substitution is seen for the reactions employing other transition metal catalysts. The cyclization of enynes containing terminal alkynes is problematic for all of these systems; however, as with the $Cp_2Ti(CO)_2$ catalyst, enynes with a wide range of alkyne substituents have been efficiently transformed to product with the $Ru_3(CO)_{12}$ and Rh catalysts (**46**−**48**). Additionally, the Ru catalysts are better able to accommodate alkyne substituents such as a TMS group (**46**) than is the Ti catalyst. For the Rh systems, either significant amounts of desilylated enone were obtained or poor levels of conversion were observed for reactions of TMS-substituted enynes. As with the titanium system, the ruthenium-based catalyst can cyclize 1,6-enynes containing 1,1- and 1,2-disubstituted olefins (**51** and **53**) (Figure 2); the one reported attempt to cyclize a 1,7-enyne with a Ru catalyst was unsuccessful. While $[RhCl(CO)_2]_2$ was demonstrated to be a successful precatalyst for the cyclization of a 1,1-disubstituted olefin-containing enyne (**52**), no mention was made of attempts to use substrates with 1,2-disubstituted olefins or 1,7-enynes with either of the Rh precatalysts. As with the Co systems, the levels of functional group compatibility have not been explored in detail with the Ru and Rh catalysts, but a tolerance for protected alcohols and aliphatic ketones coupled with the inability to cyclize an enyne with an ester conjugated to the alkyne seems to mirror what has been observed for the Ti system. The Ru catalyst has also been shown to tolerate the presence of nitrogen-containing heterocycles (**49** and **50**), a class of functional groups unexplored in the Ti chemistry.

Conclusion

The development of the first early transition metal-catalyzed Pauson−Khand type enyne cyclocarbonylation utilizing commercially available titanocene dicarbonyl has been described. The functional group tolerance for this process is excellent for an early transition metal-mediated reaction, with the compatibility of nitriles, methyl ketones, and terminal alkynes being of particular note. There are still limitations with respect to unprotected alcohols, aryl methyl ketones, nitro groups, and propargylic ketones and esters. The titanocene catalyst has proven capable of cyclizing a variety of both 1,6- and 1,7-enynes and 1,1- and 1,2-disubstituted olefin-containing enynes. With acyclic 1,2-disubstituted olefin containing enynes, a cycloisomerization process was detected as a competing reaction and the use of geometrically pure *cis*- or *trans*-olefins led to the formation of mixtures of epimeric enone products. A mechanism for the cyclocarbonylation involving reductive enyne cyclization to provide a bicyclic titanacyclopentene which undergoes CO insertion and subsequent reductive elimination to provide the observed enone has been proposed. The synthetic scope of the Ti catalyst system appears to be complementary to Co-based protocols with respect to alkyne substitution and similar to the Ru- and Rh-based catalysts.

Experimental Procedures

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. $Cp_2Ti(CO)_2$ was purchased from Strem Chemicals, and it was further purified by dissolution in hexane and filtration through Celite in a glovebox under argon followed by concentration in vacuo. CO was scientific grade (minimum purity 99.997%) from MG Industries. **Note: It is important to take appropriate safety precautions when dealing with CO, particularly at elevated pressures; all reactions should be conducted in an efficient fume hood behind a blast shield.** Unless otherwise stated, enynes were prepared as previously reported.[44,45,67] Enyne syntheses described herein are unoptimized. All

(67) Hicks, F. A.; Berk, S. C.; Buchwald, S. L. *J. Org. Chem.* **1996**, *61*, 2713.

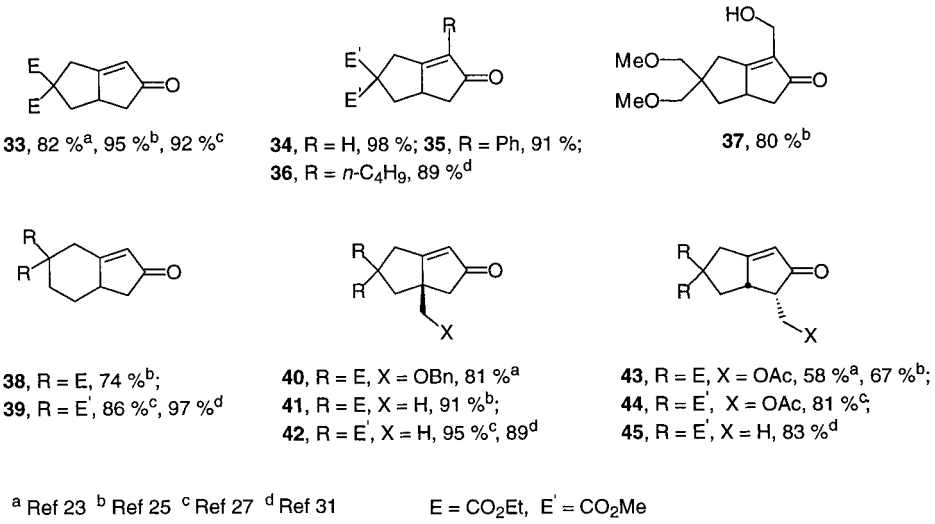


Figure 1. Cobalt-based catalytic Pauson−Khand reactions.

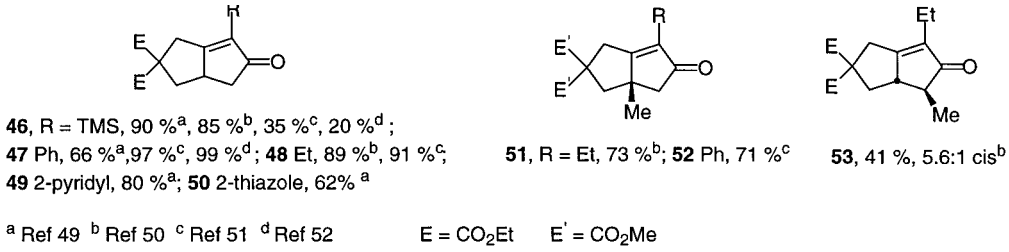


Figure 2. Ruthenium- and rhodium-based catalytic Pauson−Khand reactions.

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). 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 case of unknown compounds, elemental analysis or in one instance (eq 6) HRMS. **In general, yields indicated in this section refer to a single experiment, while those reported in the tables are an average of two or more runs, and thus the numbers may differ slightly**. Nuclear magnetic 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; bs, broad singlet; d, doublet; dd, doublet of doublets; t, triplet; at, apparent triplet; q, quartet; aquintet, apparent quintet; 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 deuteriochloroform. Infrared (IR) spectra were recorded on a Perkin-Elmer 1600 series Fourier transform spectrometer. Gas chromatography (GC) analyses were performed on a Hewlet-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. Elemental analyses were performed by E + R Analytical Laboratory, Inc. and Micro-Analysis, Inc.

***N*-Allyl-*N*-(2-butynyl)-*N*-phenylamine (Table 1, Entry 4).** 2-Butyn-1-ol (10.0 mL, 133.3 mmol), NEt_3 (20.0 mL, 143.4 mmol) and THF (150 mL) were added to a dry Schlenk flask under Ar. The flask was cooled in an ice bath and mesyl chloride (10.6 mL, 133.3 mmol) was added slowly inducing the formation of a thick, white precipitate. The ice bath was removed after the addition, and the reaction was allowed to warm to room temperature. After 1.5 h, the crude reaction mixture was filtered through a pad of Celite with THF and concentrated. In a separate dry Schlenk flask under Ar, *N*-allyl aniline (17.2 mL, 126.4 mmol) and THF (200 mL) were cooled to −78 °C. A solution of *n*-BuLi in hexanes (2.5 M, 50.6 mL, 126.4 mmol) was added slowly, and the reaction was allowed to stir for 1 h at −78 °C. Slow addition of the crude mesylate to this solution was followed by warming to room temperature. After 24 h at room temperature, the reaction mixture was quenched with H_2O (100 mL) and extracted with ether (2 × 100 mL). The combined organic layers were washed with 1 N HCl (2 × 50 mL) and saturated brine and dried over $MgSO_4$. Purification by vacuum distillation provided 15.7 g (67%) of a colorless liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (m, 2 H); 6.87 (d, J = 8.1 Hz, 2 H); 6.79 (t, J = 7.5 Hz, 1 H); 5.92 (m, 1 H); 5.24 (m, 1 H); 3.99 (m, 4 H); 1.82 (t, J = 2.1 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.7, 134.4, 129.3, 129.2, 117.7, 116.5, 113.9, 79.5, 75.2, 53.8, 39.1. IR (neat, cm^{-1}) 3061, 2918, 1599, 1504, 1346, 1229, 1174, 990, 922, 748, 691. Anal. Calcd for $C_{13}H_{15}N$: C, 84.27; H, 8.17. Found: C, 84.31; H, 8.16.

Ethyl 4-Cyano-1-phenyl-6-hepten-1-yne-4-carboxylate (Table 1, Entry 6). In a dry Schlenk flask under Ar, K_2CO_3 (3.5 g, 25 mmol), acetone (250 mL), allyl bromide (1.7 mL, 20 mmol), and 3-phenyl-2-propynyl ethyl malononitrile (3.8 g, 16.7 mmol), obtained from the corresponding propargyl bromide and the sodium salt of ethyl malononitrile, were combined. The reaction mixture was stirred at room temperature for 12 h and then at reflux for 3 h. After the reaction mixture was cooled to room temperature, solids were removed by vacuum filtration and washed with acetone. The acetone solution was concentrated in vacuo and was purified via vacuum distillation to provide 3.9 g (92%) of a light yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (m, 2 H); 7.25 (m, 3 H); 5.79 (m, 1 H); 5.25 (m, 2 H); 4.26 (q, J = 7.2 Hz, 2 H); 3.00 (d, J = 16.8 Hz, 1 H); 2.93 (d, J = 16.8 Hz, 1 H); 2.72 (d, J = 7.2 Hz, 2 H); 1.28 (t, J = 7.2 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.4, 131.9, 130.2, 128.6, 128.4, 122.6, 121.6, 118.1, 85.2, 82.2, 63.2, 48.8, 40.1, 27.4, 14.2. IR (neat, cm^{-1}) 2983, 2247, 1743, 1491, 1442, 1221, 1144, 1096, 931, 856, 758, 692. Anal. Calcd for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41. Found: C, 76.19; H, 6.33.

Ethyl 4-Acetyl-1-phenyl-6-hepten-1-yne-4-carboxylate (Table 1, Entry 7). In a dry Schlenk flask under Ar, KO*t*-Bu (2.5 g, 22 mmol), 18-crown-6 (trace), and benzene (70 mL) were combined and stirred. Allyl ketomalonate (3.4 g, 20 mmol), obtained from allyl bromide and the sodium salt of ketomalonate, was added followed by 1-chloro-3-phenyl-2-propyne. The reaction mixture was heated to reflux for 6 h. After the reaction mixture was cooled to room temperature, it was partitioned between H_2O (50 mL) and ether (100 mL). The organic layer was washed with 50 mL each of 1 N HCl, H_2O, 1 N NaOH, and H_2O and dried over Na_2SO_4. The crude reaction mixture was concentrated in vacuo and was purified via vacuum distillation to provide 3.2

g (56%) of a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 (m, 2 H); 7.26 (m, 3 H); 5.59 (m, 1 H); 5.16 (m, 2 H); 4.22 (q, J = 7.2 Hz, 2 H); 2.96 (s, 2 H); 2.88 (dd, J = 7.2, 14.4 Hz, 1 H); 2.78 (dd, J = 7.2, 14.4 Hz, 1 H); 2.20 (s, 3 H); 1.26 (t, J = 7.2 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.0, 170.7, 132.0, 131.8, 128.4, 128.2, 123.3, 120.0, 84.6, 83.9, 63.2, 62.0, 36.2, 26.8, 22.8, 14.3. IR (neat, cm^{-1}) 2980, 1717, 1442, 1357, 1280, 1206, 1070, 1018, 924, 856, 758, 692. Anal. Calcd for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 76.15; H, 7.26.

Di-*tert*-butyl 6-Hepten-1-yne-4,4-dicarboxylate (Table 1, Entry 8). Diisopropylamine (1.4 mL, 10 mmol) and THF (25 mL) were added to a dry Schlenk flask under Ar. A solution of *n*-BuLi (1.6 M in hexanes, 6.25 mL, 10 mmol) was added slowly, and the reaction mixture was allowed to stir 30 min at room temperature. Allyl di-*tert*-butyl malonate (2.56 g, 10 mmol) was added, and the flask was equipped with a reflux condenser under Ar and heated to reflux. After 16 h, the reaction mixture was cooled to −78 °C, and propargyl bromide (1.1 mL, 80 wt % in toluene, 10 mmol) was slowly added. The reaction mixture was allowed to warm to room temperature and quenched with saturated aqueous NH_4Cl (50 mL). Extraction with ether (3 × 50 mL), washing with saturated brine, and drying over $MgSO_4$ provided the crude product. Purification via flash column chromatography (hexane:ether 95:5) provided 2.5 g (85%) of a white solid, mp 62−64 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.58 (m, 1 H); 5.14 (m, 2 H); 2.73 (m, 4 H); 1.97 (t, J = 2.7 Hz, 1 H); 1.42 (s, 18 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.2, 132.3, 119.7, 81.9, 79.5, 71.3, 57.4, 36.4, 28.0, 21.6. IR (KBr, cm^{-1}) 2981, 2933, 1724, 1371, 1305, 1251, 1229, 1143, 1072, 932, 844. Anal. Calcd for $C_{17}H_{26}O_4$: C, 69.36; H, 8.90. Found: C, 69.47; H, 8.81.

Diethyl 1-(*p*-Methylphenyl)-6-hepten-1-yne-4,4-dicarboxylate (Table 1, Entry 9). The enyne was prepared from diethyl-6-hepten-1-yne-4,4-dicarboxylate[68] (1.05 g, 4.4 mmol) and 4-iodotoluene (959 mg, 4.4 mmol) via the procedure of Grissom.[69] The crude reaction mixture was purified via flash column chromatography (hexane:ether 9:1) to provide 1.01 g (70%) of a clear liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 (d, J = 8.1 Hz, 2 H); 7.09 (d, J = 8.1 Hz, 2 H); 5.72 (m, 1 H); 5.20 (m, 2 H); 4.24 (q, J = 7.2 Hz, 4 H); 3.03 (s, 2 H); 2.89 (d, J = 6 Hz, 2 H); 2.34 (s, 3 H); 1.28 (t, J = 7.2 Hz, 6 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.6, 137.6, 131.7, 131.2, 128.6, 119.9, 83.3, 61.2, 56.8, 36.3, 23.2, 21.1, 13.8. IR (neat, cm^{-1}) 2981, 1735, 1510, 1444, 1367, 1288, 1213, 1143, 1067, 924, 857, 817. Anal. Calcd for $C_{20}H_{24}O_4$: C, 73.15; H, 7.37. Found: C, 73.28; H, 7.53.

Diethyl 1-(*p*-Methoxyphenyl)-6-hepten-1-yne-4,4-dicarboxylate (Table 1, Entry 10). Prepared as in Table 1, entry 9, with diethyl-6-hepten-1-yne-4,4-dicarboxylate (1.05 g, 4.4 mmol) and 4-iodoanisole (1.03 g, 4.4 mmol). The crude reaction mixture was purified via flash column chromatography (hexane:ether 85:15) to provide 1.16 g (77%) of a clear liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (d, J = 8.7 Hz, 2 H); 6.80 (d, J = 8.7 Hz, 2 H); 5.69 (m, 1 H); 5.17 (m, 2 H); 4.22 (q, J = 7.2 Hz, 4 H); 3.80 (s, 3 H); 2.99 (s, 2 H); 2.86 (d, J = 7.2 Hz, 2 H); 1.26 (t, J = 7.2 Hz, 6 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.1, 159.5, 133.2, 132.2, 119.8, 115.6, 114.0, 83.4, 82.9, 61.7, 57.2, 55.4, 36.8, 23.7, 14.3. IR (neat, cm^{-1}) 2981, 2838, 1732, 1607, 1510, 1465, 1443, 1290, 1033, 833. Anal. Calcd for $C_{20}H_{24}O_5$: C, 69.75; H, 7.02. Found: C, 69.75; H, 6.90.

Diethyl 1-(*p*-Chlorophenyl)-6-hepten-1-yne-4,4-dicarboxylate (Table 1, Entry 11). Prepared as in Table 1, entry 9, with diethyl-6-hepten-1-yne-4,4-dicarboxylate (1.05 g, 4.4 mmol) and 4-chloro-1-iodobenzene (1.05 g, 4.4 mmol). The crude reaction mixture was purified via flash column chromatography (hexane:ether, 9:1) to provide 844 mg (55%) of a clear liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.18 (d, J = 8.7 Hz, 2 H); 7.12 (d, J = 8.7 Hz, 2 H); 5.57 (m, 1 H); 5.07 (m, 2 H); 4.11 (q, J = 7.2 Hz, 4 H); 2.90 (s, 2 H); 2.75 (d, J = 7.5 Hz, 2 H); 1.14 (t, J = 7.2 Hz, 6 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.7, 133.9, 132.9, 131.9, 128.5, 121.8, 119.8, 85.6, 82.4, 61.6, 57.0, 36.7, 23.5, 14.1. IR (neat, cm^{-1}) 2961, 1735, 1490, 1289, 1215, 1191, 1090, 1015, 925, 857, 829. Anal. Calcd for $C_{19}H_{21}ClO_4$: C, 65.42; H, 6.07. Found: C, 65.58; H, 5.90.

Diethyl 1-(*p*-Bromophenyl)-6-hepten-1-yne-4,4-dicarboxylate (Table 1, Entry 12). Prepared as in Table 1, entry 9, with diethyl-6-hepten-1-yne-4,4-dicarboxylate (1.19 g, 5.0 mmol) and 4-bromo-1-iodobenzene (1.41 g, 5.0 mmol). The crude reaction mixture was purified via flash column chromatography (hexane:ether, 95:5) to provide 1.44 g (73%) of a clear liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 (d, J = 8.4 Hz, 2 H); 7.14 (d, J = 8.4 Hz, 2 H); 5.59 (m, 1 H); 5.09 (m, 2 H); 4.14 (q, J = 7.2 Hz, 4 H); 2.92 (s, 2 H); 2.77 (d, J = 7.2 Hz, 2 H); 1.18 (t, J = 7.2 Hz, 6 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9, 133.2, 132.0, 131.6, 122.4, 122.3, 120.0, 85.9, 82.5, 61.8, 57.1, 36.8, 23.7, 14.3. IR (neat, cm^{-1}) 2981, 2936, 1734, 1486, 1289, 1215, 1190, 1071, 1012, 925, 857, 825. Anal. Calcd for $C_{19}H_{21}BrO_4$: C, 58.03; H, 5.38. Found: C, 57.90; H, 5.59.

Diethyl 1-(Ethyl-4′-benzoate)-6-hepten-1-yne-4,4-dicarboxylate (Table 1, entry 13). Prepared as in Table 1, entry 9, with diethyl-6-hepten-1-yne-4,4-dicarboxylate (1.19 g, 5.0 mmol) and ethyl 4-iodobenzoate (1.38 g, 5.0 mmol). The crude reaction mixture was purified via flash column chromatography (hexane:ether, 85:15) to provide 1.58 g (82%) of a clear liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (d, J = 8.4 Hz, 2 H); 7.42 (d, J = 8.4 Hz, 2 H); 5.67 (m, 1 H); 5.19 (m, 2 H); 4.37 (q, J = 7.2 Hz, 2 H); 4.23 (q, J = 7.2 Hz, 4 H); 3.04 (s, 2 H); 2.87 (d, J = 7.5 Hz, 2 H); 1.39 (t, J = 7.2 Hz, 3 H); 1.27 (t, J = 7.2 Hz, 6 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9, 166.2, 131.7, 129.8, 128.0, 120.0, 87.9, 83.1, 61.9, 61.2, 57.1, 36.8, 23.8, 14.5, 14.3. IR (neat, cm^{-1}) 2982, 2937, 1736, 1606, 1367, 1273, 1214, 1106, 1021, 925, 858, 770, 697. Anal. Calcd for $C_{22}H_{26}O_6$: C, 68.38; H, 6.78. Found: C, 68.66; H, 7.08.

Diethyl 1-(*p*-Cyanophenyl)-6-hepten-1-yne-4,4-dicarboxylate (Table 1, Entry 14). Prepared as in Table 1, entry 9, with diethyl-6-hepten-1-yne-4,4-dicarboxylate (1.19 g, 5.0 mmol) and 4-iodobenzonitrile (1.15 g, 5.0 mmol). The crude reaction mixture was purified via flash column chromatography (hexane:ether, 9:1) to provide 1.04 g (61%) of a clear liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (d, J = 8.4 Hz, 2 H); 7.45 (d, J = 8.4 Hz, 2 H); 5.66 (m, 1 H); 5.18 (m, 2 H); 4.23 (q, J = 7.2 Hz, 4 H); 3.04 (s, 2 H); 2.84 (d, J = 7.8 Hz, 2 H); 1.27 (t, J = 7.2 Hz, 6 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.8, 132.3, 132.1, 131.8, 128.3, 120.1, 118.6, 111.5, 89.7, 61.9, 57.0, 36.8, 23.7, 14.3. IR (neat, cm^{-1}) 3079, 2982, 2228, 1732, 1642, 1605, 1502, 1444, 1367, 1290, 1215, 1096, 926, 842. Anal. Calcd for $C_{20}H_{21}NO_4$: C, 70.78; H, 6.24. Found: C, 70.96; H, 6.18.

Diethyl 1-(*p*-Trifluoromethylphenyl)-6-hepten-1-yne-4,4-dicarboxylate (Table 1, Entry 15). Prepared as in Table 1, entry 9, with diethyl-6-hepten-1-yne-4,4-dicarboxylate (2.38 g, 10.0 mmol) and 4-trifluoromethyl-1-iodobenzene (1.47 mL, 10.0 mmol). The crude reaction mixture was purified via flash column chromatography (hexane:ether, 95:5) to provide 2.60 g (68%) of a clear liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (d, J = 8.4 Hz, 2 H); 7.42 (d, J = 8.4 Hz, 2 H); 5.63 (m, 1 H); 5.14 (m, 2 H); 4.18 (q, J = 7.2 Hz, 4 H); 2.99 (s, 2 H); 2.82 (d, J = 7.2 Hz, 2 H); 1.22 (t, J = 7.2 Hz, 6 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9, 132.1, 131.9, 130.1, 129.7, 127.2, 125.9, 125.4, 125.3, 122.3, 120.1, 87.5, 82.5, 61.9, 57.1, 36.9, 23.7, 14.3. IR (neat, cm^{-1}) 3080, 2983, 2224, 1736, 1616, 1324, 1216, 1127, 1018, 925, 843. Anal. Calcd for $C_{20}H_{21}F_3O_4$: C, 62.82; H, 5.54. Found: C, 62.96; H, 5.47.

Di-*tert*-butyl 8-nonen-2-yne-6,6-dicarboxylate (Table 2, Entry 6). Sodium hydride (480 mg, 20 mmol) was added to a dry Schlenk flask in the glovebox. The Schlenk flask was removed from the glovebox and attached to a Schlenk line under Ar. THF (50 mL) and di-*tert*-butyl malonate (4.47 mL, 20 mmol) were added to the flask, and the reaction mixture was allowed to stir at room temperature. In a separate dry Schlenk flask under Ar, THF (50 mL), NEt_3 (3.07 mL, 22 mmol) and 3-pentyn-1-ol (1.84 mL, 20 mmol) were cooled in an ice bath. Dropwise addition of mesyl chloride (1.55 mL, 20 mmol) to this solution resulted in the formation of a thick, white precipitate. The ice bath was removed, and the reaction mixture was allowed to warm to room temperature. After 1 h at room temperature, the crude mesylate solution was cannula-filtered into the malonate anion solution. After the addition was complete, the reaction mixture was allowed to stir at room temperature for 15 h. Then a reflux condenser was attached under

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Ar, and the reaction was heated to reflux for another 22 h. After cooling to room temperature, the reaction mixture was quenched with saturated NH_4Cl (50 mL) and extracted with ether (3 × 50 mL). The combined organic layers were washed with saturated brine and dried over $MgSO_4$. Purification via vacuum distillation provided 3.16 g (56%) of the desired monoalkylated malonate product. The malonate deprotonation procedure was repeated with NaH (144 mg, 6 mmol) in THF (10 mL) and the new malonate derivative (1.58 g, 5.6 mmol) in THF (10 mL). Allyl bromide was added to this mixture, and the reaction was allowed to stir 14 h at room temperature. The workup procedure described above was also employed for this reaction. Purification via flash column chromatography (hexane:ether, 95:5) provided 1.55 g (86%) of a white solid, mp 36−38 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.66 (m, 1 H); 5.09 (m, 2 H); 2.54 (d, J = 7.5 Hz, 2 H); 2.01 (m, 4 H); 1.73 (s, 3 H) 1.42 (s, 18 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2, 132.7, 119.0, 81.6, 78.5, 76.0, 57.8, 36.9, 31.8, 28.1, 14.1, 3.7. IR (KBR, cm^{-1}) 2976, 2919, 1724, 1458, 1368, 1305, 1248, 1221, 1139, 1084, 987, 931, 844. Anal. Calcd for $C_{19}H_{30}O_4$: C, 70.76; H, 9.38. Found: C, 70.59; H, 9.30.

3-(Benzyloxy)-4,4-dimethyl-1-phenyl-6-hepten-1-yne (Table 3, Entry 5). In a dry Schlenk flask under Ar, phenylacetylene (10 mL, 91.2 mmol) and THF (200 mL) were combined, and the flask was cooled with an ice bath. A solution of *n*-BuLi (2.5 M in hexanes, 44 mL, 109.4 mmol) was added, and after 10 min the ice bath was removed. After the addition of 2,2-dimethyl-4-penten-1-al[70] (10.2 g, 91.2 mmol), the reaction mixture was allowed to stir at room temperature for 21 h and at 60 °C for 8 h. After cooling to room temperature, the reaction mixture was quenched with saturated aqueous NH_4Cl (150 mL) and partitioned between ether (300 mL) and H_2O (2 × 100 mL). The combined aqueous phase was extracted with ether (2 × 100 mL), and the combined organic layers were dried over $MgSO_4$. The crude product was concentrated in vacuo and purified twice by vacuum distillation to provide 12.4 g (63%) of 4,4-dimethyl-1-phenyl-6-hepten-1-yn-3-ol. NaH (900 mg, 36 mmol) was added to a dry Schlenk flask in the glovebox. The Schlenk flask was removed from the glovebox and attached to a Schlenk line under Ar. THF (100 mL) was added, and the Schlenk flask was cooled with an ice bath. 4,4-Dimethyl-1-phenyl-6-hepten-1-yn-3-ol (6.42 g, 30 mmol) and benzyl bromide (4.3 mL, 36 mmol) were added to the Schlenk flask, and the reaction mixture was stirred at room temperature for 19 h. The Schlenk flask was recooled with an ice bath, and the reaction mixture was quenched with saturated aqueous NH_4Cl (100 mL). After addition of ether (200 mL), the organic phase was washed with 50 mL each of 1 N NaOH, H_2O, 1 N HCl, and H_2O. The organic phase was dried over $MgSO_4$, and the crude product was concentrated in vacuo and was purified via vacuum distillation to provide 6.6 g (72%) of a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48−7.25 (m, 10 H); 5.81 (m, 1 H); 5.04 (m, 2 H); 4.90 (d, J = 12 Hz, 1 H); 4.53 (d, J = 12 Hz, 1 H); 3.99 (s, 1 H); 2.23 (m, 2 H); 1.06 (s, 3 H); 1.03 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.6, 135.2, 131.9, 128.4, 128.3, 128.0, 127.6, 123.2, 117.6, 87.2, 77.0, 61.2, 43.3, 38.9, 23.5, 23.2. IR (neat, cm^{-1}) 2965, 2870, 1704, 1639, 1598, 1489, 1453, 1384, 1324, 1270, 1069, 915, 756, 692. Anal. Calcd for $C_{22}H_{24}O$: C, 87.08; H, 7.65. Found: C, 86.72; H, 7.52.

9,10-Undecadien-5-yne (eq 6). This compound was obtained by a modification of the procedure of Crabbé.[71] To a dry Schlenk flask under Ar were added sequentially THF (50 mL), 1,5-decadiyne (2.01 mL, 15 mmol), CuI (2.90 g, 7.5 mmol), diisopropylamine (4.22 mL, 30 mmol), and paraformaldehyde (680 mg, 37.5 mmol). A reflux condenser was attached under Ar, and the reaction mixture was heated to reflux for 14 h. After cooling to room temperature, the reaction mixture was quenched with 1 N HCl (2 × 100 mL) and 1 N NaOH (2 × 100 mL), washed with saturated brine, and dried over $MgSO_4$. Excess solvent was removed by distillation at atmospheric pressure, with subsequent vacuum distillation of the product and in vacuo removal of trace solvent to provide 534 mg (24%) of the desired allenyne as a clear oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.12 (aquintet, J = 6.6 Hz, 1 H); 4.58 (m, 2 H); 2.17−2.04 (m, 6 H); 1.38−1.32 (m, 4 H); 0.79 (m, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.7, 89.1, 81.1, 79.5, 75.4, 31.4, 28.4, 22.1, 19.0, 18.6, 13.9. IR (neat, cm^{-1}) 2957, 2930, 2861, 1957, 1435, 844. Anal. Calcd for $C_{11}H_{16}$: C, 89.11; H, 10.89. Found: C, 88.80; H, 10.86.

Di-*tert*-butyl 7-methyl-7-octen-2-yne-5,5-dicarboxylate (Table 4, Entry 1). Diisopropylamine (2.1 mL, 15 mmol) and THF (15 mL) were added to a dry two-neck flask under Ar. The flask was cooled in an ice bath, and a solution of *n*-BuLi (2.5 M in hexanes, 6 mL, 15 mmol) was added. This solution was transferred via cannula under Ar into another flask containing (2-butynyl) di-*tert*-butyl malonate (3 g, 11.2 mmol) in THF (25 mL) at −78 °C. After addition was complete, the reaction mixture was allowed to stir for 15 min at −78 °C, followed by addition of 1-bromo-2-methylpropene (1.57 mL, 15.6 mmol). The reaction mixture was allowed to warm to room temperature and was maintained at room temperature for 19 h. The reaction mixture was quenched with saturated aqueous NH_4Cl and partitioned between ether (50 mL) and H_2O (50 mL). The organic layer was washed with saturated aqueous $CuSO_4$ (2 × 50 mL) and saturated brine (2 × 50 mL). Subsequent drying over $MgSO_4$ and concentration in vacuo provided the crude product. Purification via vacuum distillation followed by flash column chromatography (hexane:ether, 97:3) provided 2.17 g (60%) of the pure product as a clear liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.82 (s, 1 H); 4.79 (s, 1 H); 2.63 (m, 4 H); 1.69 (t, J = 2.6 Hz, 3 H); 1.66 (s, 3 H); 1.40 (s, 18 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9, 141.0, 115.7, 81.6, 78.7, 57.6, 39.4, 28.0, 23.8, 23.1. IR (neat, cm^{-1}) 2977, 2932, 1729, 1644, 1458, 1368, 1246, 1219, 1167, 1141, 1071, 898, 849. Anal. Calcd for $C_{19}H_{30}O_4$: C, 70.77; H, 9.38. Found: C, 70.65; H, 9.15.

Diethyl 4-(3-Cyclohexenyl)-1-phenylbut-1-yne-4,4-dicarboxylate (Table 4, Entry 2). The malonate deprotonation procedure described for Table 2, entry 6, was employed with NaH (185 mg, 7.7 mmol) and (3-cyclohexenyl) diethyl malonate (1.68 g, 7 mmol) in THF (30 mL). Crude 3-phenyl-2-propyn-1-mesylate, prepared as described for Table 1, entry 4 with 3-phenyl-2-propyn-1-ol (1.06 g, 8 mmol), NEt_3 (1.25 mL, 9 mmol) and mesyl chloride (619 μL, 8 mmol) in THF (30 mL), was cannula-filtered into the solution, and the reaction mixture was allowed to stir for 15 h at room temperature. The workup procedure described above for Table 2, entry 6, was also employed for this reaction. Purification via flash column chromatography (hexane:ether, 95:5) provided 1.78 g (72%) of a clear liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (m, 2 H); 7.26 (m, 3 H); 5.75 (m, 2 H); 4.20 (m, 4 H); 3.19 (m, 1 H); 3.08 (d, J = 17.1 Hz, 1 H); 2.99 (d, J = 17.1 Hz, 1 H); 1.88 (m, 4 H), 1.55 (m, 1 H); 1.40 (m, 1 H); 1.24 (m, 6 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2, 170.1, 131.8, 129.1, 128.4, 128.1, 128.0, 123.7, 85.5, 83.4, 61.5, 60.7, 39.1, 25.1, 24.5, 23.4, 22.6, 14.3. IR (neat, cm^{-1}) 2980, 2935, 1731, 1491, 1443, 1269, 1221, 1190, 1095, 1073, 1050, 757, 692. Anal. Calcd for $C_{22}H_{26}O_4$: C, 74.55; H, 7.39. Found: C, 74.68; H, 7.58.

Diethyl 5-(3-Cyclohexenyl)-pent-2-yne-5,5-dicarboxylate (Table 4, Entry 3). The malonate deprotonation procedure described for Table 2, entry 6, was employed using NaH (528 mg, 22 mmol) and diethyl malonate (3.04 mL, 20 mmol) in THF (50 mL). 3-Bromocyclohexene was added to the solution, and the reaction mixture was allowed to stir 18 h at room temperature. The reaction mixture was quenched with saturated NH_4Cl (50 mL) and extracted with ether (3 × 50 mL). The combined organic layers were washed with saturated brine and dried over $MgSO_4$. Purification via vacuum distillation provided 3.5 g (73%) of the desired monoalkylated malonate. The deprotonation procedure was repeated on the new malonate derivative (1.68 g, 7 mmol) with NaH (185 mg, 7.7 mmol) in THF (40 mL). 1-Bromo-2-butyne (700 μL, 8 mmol) was added to the solution, and the reaction mixture was allowed to stir 15 h at room temperature. The workup procedure described above for Table 2, entry 6, was also employed for this reaction. Purification via vacuum distillation provided 1.43 g (70%) of the desired enyne as a clear liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.72 (m, 2 H); 4.17 (m, 4 H); 3.08 (m, 1 H); 2.76 (m, 2 H); 1.85 (m, 4 H); 1.72 (t, J = 2.7 Hz, 3 H); 1.55 (m, 1 H); 1.32 (m, 1 H); 1.21 (m, 6 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.4, 170.2, 128.7, 128.3, 78.7, 74.2, 61.4, 61.3, 60.5, 38.7, 25.1, 24.4, 23.1, 22.6, 14.3, 14.2. IR (neat cm^{-1}) 2980, 2935, 1730, 1445, 1367, 1220, 1190, 1096, 1051, 861,

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724. Anal. Calcd for $C_{17}H_{24}O_4$: C, 69.84; H, 8.27. Found: C, 69.51; H, 8.28.

Diethyl 1-Phenyl-6-octen-1-yne-4,4-dicarboxylate (Table 4, Entry 4). Sodium hydride (540 mg, 22.5 mmol) was added to a dry Schlenk flask in the glovebox. The Schlenk flask was removed from the glovebox and attached to a Schlenk line under Ar. THF (150 mL) was added, and the reaction mixture was cooled in an ice bath. 3-Phenyl-2-propynyl diethyl malonate (5.5 g, 20 mmol), obtained from diethyl malonate anion and 1-bromo-3-phenyl-2-propyne, was added to the flask, and the reaction mixture was allowed to stir at 0 °C for 10 min. 1-Bromo-2-butene was added, and the temperature was maintained between 0 °C and room temperature for 12 h. The reaction mixture was cooled to 0 °C, quenched with saturated aqueous NH_4Cl (40 mL), and partitioned between H_2O (20 mL) and ether (100 mL). The organic layer was separated and washed with 30 mL each of 0.5 N aqueous HCl, saturated aqueous $NaHCO_3$, H_2O, and saturated brine and dried over $MgSO_4$. The crude product was concentrated in vacuo and was purified via vacuum distillation to provide 5.5 g (84%) of a clear oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38−7.24 (m, 5 H); 5.62 (m, 1 H); 5.29 (m, 2 H); 4.20 (m, 4 H); 3.00 (s, 2 H); 2.90 (d, J = 6.0 Hz, 1 H min); 2.79 (d, J = 7.4 Hz, 2 H maj); 1.67 (m, 3 H); 1.26 (m, 6 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2, 131.8, 130.6, 129.0, 128.3, 124.3, 123.5, 123.4, 84.8, 83.5, 61.7, 57.4, 57.3, 35.6, 29.7, 23.6, 18.2, 14.3, 13.2. IR (neat, cm^{-1}) 2982, 2936, 1732, 1598, 1491, 1443, 1366, 1279, 1205, 1050, 969, 858, 758, 692. Anal. Calcd for $C_{20}H_{24}O_4$: C, 73.13; H, 7.37. Found: C, 73.30; H, 7.30.

Diethyl *trans*-1-Phenyl-6-octen-1-yne-4,4-dicarboxylate (Table 4, Entry 5). In a flame-dried Schlenk flask, *trans*-2-butene-1-ol (1.28 mL, 15 mmol), NEt_3 (2.30 mL, 16.5 mmol), and THF (30 mL) were combined and cooled to 0 °C. Slow addition of mesyl chloride (1.16 mL, 15 mmol) resulted in the formation of a thick, white precipitate. To a separate flame-dried Schlenk flask in the glovebox, NaH (0.26 g, 10.8 mmol) was added. The Schlenk flask was removed from the glovebox and placed on a vacuum line under Ar. THF (50 mL) was added, and the solution was cooled to 0 °C. (3-Phenyl-2-propynyl) diethyl malonate (2.74 g, 10 mmol), obtained from diethyl malonate anion and 3-phenyl-2-propyn-1-mesylate, was added slowly to the NaH suspension, and the reaction mixture was allowed to warm to room temperature after the addition was complete. After 1 h at room temperature, the reaction mixture was cooled again to 0 °C, and the crude mesylate solution prepared earlier was cannula-filtered into the malonate anion solution. After the additon was complete, the reaction was allowed to warm to room temperature and to stir 12 h at room temperature. Workup was performed as stated above for Table 2, entry 6. Purification via flash column chromatography (hexane:ether, 9:1) provided 2.45 g (75%) of a clear liquid: ^{1}H NMR matched that of the major isomer for Table 4, entry 4, with ~4% of the cis isomer also present in the sample. Anal. Calcd for $C_{20}H_{24}O_4$: C, 73.13; H, 7.37. Found: C, 73.30; H, 7.30.

Diethyl *cis*-1-Phenyl-6-octen-1-yne-4,4-dicarboxylate (Table 4, Entry 6). The procedure employed was analogous to that for Table 4, entry 5, with the use of *cis*-2-butene-1-ol (1.23 mL, 14.4 mmol), NEt_3 (2.20 mL, 15.8 mmol), THF (30 mL), and mesyl chloride (1.10 mL, 14.2 mmol) for the first part and (3-phenyl-2-propynyl) diethyl malonate (2.61 g, 9.5 mmol) and NaH (0.25 g, 10.4 mmol) for the second part. Purification via flash column chromatography (hexane:ether, 9:1) provided the desired enyne as a clear liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.2−7.4 (m, 5 H); 5.67 (m, 1 H); 5.24 (m, 1 H); 4.20 (m, 4 H); 3.00 (s, 2 H); 2.90 (d, J = 8.0 Hz, 2 H); 1.69 (d, J = 6.7 Hz, 3 H); 1.27 (t, J = 7.12 Hz, 6 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.3, 131.8, 129.1, 128.4, 128.1, 123.5, 85.0, 83.5, 61.8, 57.4, 29.7, 14.3, 13.3. IR (neat, cm^{-1}) 2981, 2936, 1735, 1598, 1490, 1442, 1366, 1289, 1206, 1095, 1068, 858, 757, 692. Anal. Calcd for $C_{20}H_{24}O_4$: C, 73.13; H, 7.37. Found: C, 72.74; H, 7.12.

Diethyl *cis*-7-Nonen-2-yne-5,5-dicarboxylate (Table 4, Entry 7). The procedure employed was analogous to that described above with the use of *cis*-2-butene-1-ol (1.15 mL, 13.4 mmol), NEt_3 (2.07 mL, 14.8 mmol), THF (30 mL), and mesyl chloride (1.04 mL, 13.4 mmol) for the first part and (2-butynyl) diethyl malonate (1.8 g, 9 mmol) and NaH (0.24 g, 10 mmol) for the second part. Purification via flash column chromatography (hexane:ether, 95:5) provided 1.56 g (64%) of a clear liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.62 (m, 1 H); 5.21 (m, 1 H); 4.20 (m, 4 H); 2.81 (d, J = 7.8 Hz, 2 H); 2.73 (d, J = 2.4 Hz, 2 H); 1.75 (t, J = 2.4 Hz, 3 H); 1.66, (dd, J = 6.4, 1.0 Hz, 3 H); 1.25 (t, J = 7.3 Hz, 6 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.3, 128.6, 123.4, 78.6, 73.8, 61.5, 57.1, 29.4, 22.8, 14.1, 13.0, 3.5. IR (neat) 2982, 2922, 1736, 1445, 1336, 1289, 1207, 1096, 1068, 1045, 860, 701. Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.65; H, 8.33. Found: C, 67.90; H, 8.37.

General Procedure A for the Conversion of Enynes to Cyclopentenones. In an argon-filled glovebox, a dry resealable Schlenk flask was charged with $Cp_2Ti(CO)_2$ (0.025 mmol) and toluene (2−3 mL). The flask was removed from the glovebox and attached to a Schlenk line under Ar. The enyne (0.50 mmol) was added, and the Schlenk flask was evacuated and backfilled with 18 psig CO. **Caution:** Appropriate precautions should be taken when performing reactions using carbon monoxide, particularly under elevated pressure. The reaction mixture was heated to 90 °C for 12−48 h. After the reaction mixture was cooled to room temperature, the CO was cautiously released in the hood. The crude reaction mixture was filtered through a pad of silica gel with additional ether (100 mL) and concentrated in vacuo.

General Procedure B for the Conversion of Enynes to Cyclopentenones. In an argon-filled glovebox, a dry resealable Schlenk flask was charged with $Cp_2Ti(CO)_2$ (0.025 mmol), toluene (2−3 mL), and enyne (0.50 mmol). The flask was removed from the glovebox, attached to a Schlenk line, evacuated, and backfilled with 18 psig CO. **Caution:** Appropriate precautions should be taken when performing reactions under elevated pressure. The reaction protocol was conducted in an analogous fashion to procedure A after this point.

2-Phenylbicyclo[3.3.0]oct-1-en-3-one (Table 1, Entry 1). General procedure A was used to convert 1-phenyl-6-hepten-1-yne[44] (86 mg, 0.50 mmol) to the desired product in 15 h. Purification by flash chromatography (hexane:ether, 7:3) afforded 88 mg (89% yield) of a clear oil. The ^{1}H NMR spectrum matched the published spectrum.[44]

2-Phenyl-7-oxabicyclo[3.3.0]oct-1-en-3-one (Table 1, Entry 2). General procedure A was used to convert 3-(allyloxy)-1-phenyl-1-propyne[44] (85 μL, 0.50 mmol) to the desired product in 12 h. Purification by flash chromatography (hexane:ether, 3:7) afforded 89 mg (89% yield) of a clear oil. The ^{1}H NMR spectrum matched the published spectrum.[44]

Di-*tert*-butyl 2-Methyl-3-oxobicycl[3.3.0]oct-1-ene-7,7-dicarboxylate (Table 1, Entry 3). General procedure A was used to convert di-*tert*-butyl 7-octen-2-yne-4,4-dicarboxylate[44] (154 mg, 0.50 mmol) to the desired product in 14 h. Purification by flash chromatography (hexane:ether, 4:1) afforded 147 mg (88% yield) of a clear oil. The ^{1}H NMR spectrum matched the published spectrum.[44]

2-Methyl-7-phenyl-7-azabicyclo[3.3.1]oct-1-en-3-one (Table 1, Entry 4). General procedure A was used to convert *N*-(3-phenyl-2-butynyl)-*N*-allylaniline (93 mg, 0.50 mmol) to the desired product in 12 h. Purification by flash chromatography (hexane:ether, 3:7) afforded 98 mg (92% yield) of a light orange solid, mp 112−114 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (m, 2 H); 6.75 (t, J = 7.2 Hz, 1 H); 6.63 (d, J = 7.2 Hz, 2 H); 4.32 (d, J = 15.6 Hz, 1 H); 3.95 (m, 2 H); 3.31 (bs, 1 H); 2.74 (m, 2 H); 2.25 (d, J = 18 Hz, 1 H); 1.79 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.0, 165.3, 138.5, 124.0, 120.5, 108.2, 103.1, 43.4, 39.0, 33.0, 31.0. IR (KBR, cm^{-1}) 2827, 1716, 1684, 1601, 1507, 1368, 1304, 1149, 1052, 753, 692. Anal. Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09. Found: C, 78.69; H, 7.17.

Diethyl 2-Phenyl-3-oxobicyclo[3.3.0]oct-1-ene-7,7-dicarboxylate (Table 1, Entry 5). General procedure A was used to convert diethyl 1-phenyl-6-hepten-1-yne-4,4-dicarboxylate[45] (157 mg, 0.50 mmol) to the desired product in 12 h. Purification by flash chromatography (hexane:ether, 2:1) afforded 162 mg (95% yield) of a white solid, mp 78−80 °C. The ^{1}H NMR spectrum matched the published spectrum.[45]

Ethyl 7-Cyano-2-phenyl-3-oxobicyclo[3.3.0]oct-1-ene-7-carboxylate (Table 1, Entry 6). General procedure A with 0.0375 mmol $Cp_2Ti(CO)_2$ was used to convert ethyl 4-cyano-1-phenyl-6-hepten-1-yn-4-carboxylate (118 mg, 0.50 mmol) to the desired product in 12 h. Purification by flash chromatography (hexane:ether, 3:2) afforded 100 mg (76% yield) of a 1:1 mixture of diastereomers as a white solid. The ^{1}H NMR spectrum matched the published spectrum.[45]

Ethyl 7-Acetyl-2-phenyl-3-oxobicyclo[3.3.0]oct-1-ene-7-carboxylate (Table 1, Entry 7). General procedure A with 0.0375 mmol $Cp_2Ti(CO)_2$ was used to convert ethyl-4-acetyl-1-phenyl-6-hepten-1-yne-4-carboxylate (126 mg, 0.50 mmol) to the desired product in 12 h. Purification by flash chromatography (hexane:ether, 1:1) afforded 131 mg (93% yield) of a 1:1 mixture of diastereomers as a yellow oil. The ^{1}H NMR spectrum matched the published spectrum.[45]

Di-*tert*-butyl 3-Oxobicyclo[3.3.0]oct-1-ene-7,7-dicarboxylate (Table 1, Entry 8). General procedure A was used to convert di-*tert*-butyl 6-hepten-1-yne-4,4-dicarboxylate (73 mg, 0.25 mmol) to the desired product in 12 h. Purification by flash chromatography (hexane:ether, 1:1) afforded 73 mg (90% yield) of a white solid, mp 115−117 °C: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.91 (s, 1 H); 3.25 (d, J = 18.8 Hz, 1 H); 3.15 (d, J = 18.8 Hz, 1 H); 3.17 (m, 1 H); 2.69 (dd, J = 12.7 Hz, J = 7.6 Hz, 1 H); 2.62 (dd, J = 17.8 Hz, J = 6.4 Hz, 1 H); 2.12 (dd, J = 17.8 Hz, J = 3.4 Hz, 1 H); 1.65 (t, J = 12.7 Hz, 1 H); 1.49 (s, 9 H); 1.46 (s, 9 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.0, 186.5, 170.9, 170.1, 125.6, 82.2, 82.1, 62.3, 45.2, 42.4, 38.9, 35.1, 28.0 (2). IR (KBr, cm^{-1}) 2980, 1719, 1701, 1676, 1289, 1167, 1140. Anal. Calcd for $C_{18}H_{26}O_5$: C, 67.06; H, 8.13. Found: C, 66.85; H, 8.13.

Diethyl 2-(*p*-Methylphenyl)-3-oxobicyclo[3.3.0]oct-1-ene-7,7-dicarboxylate (Table 1, Entry 9). General procedure B was used to convert diethyl 1-(*p*-methylphenyl)-6-hepten-1-yne-4,4-dicarboxylate (172 mg, 0.50 mmol) to the desired product in 18 h. Purification by flash chromatography (hexane:ether, 3:2) afforded 169 mg (91% yield) of a white solid, mp 99−101 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 (d, J = 8.8 Hz, 2 H); 6.94 (d, J = 8.8 Hz, 2 H); 4.28 (q, J = 7.2 Hz, 2 H); 4.17 (qd, J = 3, 7.2 Hz, 2 H); 3.83 (s, 3 H); 3.63 (d, J = 19.2 Hz, 1 H); 3.26 (d, J = 19.5 Hz, 1 H); 3.11 (m, 1 H); 2.81 (m, 2 H); 2.29 (dd, J = 3.3, 17.7 Hz, 1 H); 1.75 (at, J = 12.6 Hz, 3 H); 1.31 (t, J = 7.2 Hz, 3 H); 1.23 (t, J = 7.2 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.5, 177.2, 171.7, 170.8, 159.5, 134.9, 129.8, 123.6, 113.9, 62.2, 62.0, 61.4, 55.3, 42.8, 42.7, 38.8, 36.0, 14.1, 14.0. IR (KBr, cm^{-1}) 2982, 1728, 1704, 1606, 1571, 1271, 1182, 1120, 1061, 1030, 835. Anal. Calcd for $C_{21}H_{24}O_6$: C, 67.73; H, 6.50. Found: C, 67.59; H, 6.31.

Diethyl 2-(*p*-Methoxyphenyl)-3-oxobicyclo[3.3.0]oct-1-ene-7,7-dicarboxylate (Table 1, Entry 10). General procedure B was used to convert diethyl 1-(*p*-methoxyphenyl)-6-hepten-1-yne-4,4-dicarboxylate (164 mg, 0.50 mmol) to the desired product in 14 h. Purification by flash chromatography (hexane:ether, 3:2) afforded 161 mg (90% yield) of a white solid, mp 96−98 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 (d, J = 7.8 Hz, 2 H); 7.21 (d, J = 7.8 Hz, 2 H); 4.27 (q, J = 7.2 Hz, 2 H); 4.16 (m, 2 H); 3.64 (d, J = 19.2 Hz, 1 H); 3.27 (d, J = 19.2 Hz, 1 H); 3.11 (m, 1 H); 2.80 (m, 2 H); 2.36 (s, 3 H); 2.29 (dd, J = 3, 18 Hz, 1 H); 1.76 (at, J = 12.6 Hz, 1 H); 1.31 (t, J = 7.2 Hz, 3 H); 1.22 (t, J = 7.2 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.3, 178.2, 171.7, 170.8, 138.1, 135.4, 129.2, 128.4, 128.2, 62.2, 62.0, 61.4, 42.9, 42.7, 38.8, 36.0, 21.4, 14.2, 14.1. IR (KBr cm^{-1}) 2982, 1730, 1698, 1514, 1270, 1187, 1066, 927, 891, 857, 821. Anal. Calcd for $C_{21}H_{24}O_5$: C, 70.77; H, 7.03. Found: C, 70.74; H, 6.79.

Diethyl 2-(*p*-Chlorophenyl)-3-oxobicyclo[3.3.0]oct-1-ene-7,7-dicarboxylate (Table 1, Entry 11). General procedure B was used to convert diethyl 1-(*p*-chlorophenyl)-6-hepten-1-yne-4,4-dicarboxylate (174 mg, 0.50 mmol) to the desired product in 14 h. Purification by flash chromatography (hexane:ether, 2:1) afforded 174 mg (92% yield) of a white solid, mp 83−85 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (d, J = 8.4 Hz, 2 H); 7.37 (d, J = 8.4 Hz, 2 H); 4.28 (q, J = 7.2 Hz, 2 H); 4.18 (m, 2 H); 3.63 (d, J = 19.2 Hz, 1 H); 3.27 (d, J = 19.2 Hz, 1 H); 3.13 (m, 1 H); 2.74 (m, 2 H); 2.30 (dd, J = 3.3, 18 Hz, 1 H); 1.76 (at, J = 12.6 Hz, 1 H); 1.31 (t, J = 7.2 Hz, 3 H); 1.23 (t, J = 7.2 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.9, 179.5, 171.6, 170.7, 134.4, 134.1, 129.8, 129.5, 128.7, 62.4, 62.1, 61.4, 43.1, 42.6, 38.7, 36.0, 14.2, 14.1. IR (KBr, cm^{-1}) 2982, 1729, 1696, 1492, 1271, 1179, 1092, 1066, 927, 890, 824. Anal. Calcd for $C_{20}H_{21}ClO_5$: C, 63.75; H, 6.21. Found: C, 63.47; H, 5.91.

Diethyl 2-(*p*-Bromophenyl)-3-oxobicyclo[3.3.0]oct-1-ene-7,7-dicarboxylate (Table 1, Entry 12). General procedure B was used to convert diethyl 1-(*p*-bromophenyl)-6-hepten-1-yne-4,4-dicarboxylate (197 mg, 0.50 mmol) to the desired product in 18 h. Purification byflash chromatography (hexane:ether, 7:3) afforded 190 mg (90% yield) of a white solid, mp 94−95 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (d, J = 8.6 Hz, 2 H); 7.45 (d, J = 8.5 Hz, 2 H); 4.28 (q, J = 7.2 Hz, 2 H); 4.18 (m, 2 H); 3.62 (d, J = 18.9 Hz, 1 H); 3.25 (d, J = 19.4 Hz, 1 H); 3.13 (m, 1 H); 2.84 (m, 2 H); 2.30 (dd, J = 3.3, 18.0 Hz, 1 H); 1.76 (at, J = 12.7 Hz, 1 H); 1.31 (t, J = 7.2 Hz, 3 H); 1.24 (t, J = 7.2 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.7, 179.6, 171.5, 134.4, 131.7, 130.1, 130.0, 122.4, 62.3, 62.1, 61.4, 43.1, 42.6, 38.7, 36.0, 14.2, 14.1. IR (KBr, cm^{-1}) 2984, 1722, 1707, 1487, 1276, 1155, 1061, 1008, 821, 604. Anal. Calcd for $C_{20}H_{21}BrO_5$: C, 57.02; H, 5.02. Found: C, 57.00; H, 5.53.

Diethyl 2-(Ethyl-4′-benzoate)-3-oxobicyclo[3.3.0]oct-1-ene-7,7-dicarboxylate (Table 1, Entry 13). General procedure B was used to convert diethyl 1-(ethyl-4′-benzoate)-6-hepten-1-yne-4,4-dicarboxylate (193 mg, 0.50 mmol) to the desired product in 15 h. Purification by flash chromatography (hexane:ether, 7:3) afforded 183 mg (88% yield) of a white solid, mp 87−88 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (d, J = 8.4 Hz, 2 H); 7.62 (d, J = 8.4 Hz, 2 H); 4.34 (q, J = 7.2 Hz, 2 H); 4.25 (q, J = 7.2 Hz, 2 H); 4.14 (m, 2 H); 3.63 (d, J = 19.5 Hz, 1 H); 3.26 (d, J = 19.5 Hz, 1 H); 3.14 (m, 1 H); 2.80 (m, 2 H); 2.29 (dd, J = 33, 18 Hz, 1 H); 1.74 (at, J = 12.6 Hz, 1 H); 1.36 (t, J = 7.2 Hz, 3 H); 1.28 (t, J = 7.2 Hz, 3 H); 1.19 (t, J = 7.2 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.6, 181.0, 171.5, 170.6, 166.3, 135.3, 134.6, 129.9, 129.6, 128.3, 62.3, 62.1, 61.3, 61.0, 43.2, 42.7, 38.6, 36.1, 14.4, 14.1, 14.0. IR (neat, cm^{-1}) 2982, 2937, 1714, 1650, 1608, 1448, 1367, 1272, 1181, 1103, 928, 858, 774, 705. Anal. Calcd for $C_{23}H_{26}O_6$: C, 66.65; H, 6.32. Found: C, 66.44; H, 6.49.

Diethyl 2-(*p*-Cyanophenyl)-3-oxobicyclo[3.3.0]oct-1-ene-7,7-dicarboxylate (Table 1, Entry 14). General procedure B was used to convert diethyl 1-(*p*-cyanophenyl)-6-hepten-1-yne-4,4-dicarboxylate (113 mg, 0.33 mmol) to the desired product in 16 h. Purification by flash chromatography (hexane:ether, 1:1) afforded 86 mg (70% yield) of a yellow liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (m, 4 H); 4.30 (q, J = 7.2 Hz, 2 H); 4.19 (q, J = 7.2 Hz, 2 H); 3.67 (d, J = 19.5 Hz, 1 H); 3.30 (d, J = 19.5 Hz, 1 H); 3.20 (m, 1 H); 2.87 (m, 2 H); 2.34 (dd, J = 3.3, 18 Hz, 1 H); 1.78 (at, J = 12.6 Hz, 1 H); 1.32 (t, J = 7.2 Hz, 3 H); 1.24 (t, J = 7.2 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.2, 182.0, 171.3, 170.6, 135.6, 133.9, 132.2, 128.9, 118.8, 111.7, 62.4, 62.2, 61.3, 43.4, 42.6, 38.6, 36.1, 14.1, 14.0. IR (neat, cm^{-1}) 2984, 2937, 2227, 1722, 1702, 1656, 1274, 1254, 1181, 1158, 1061, 926, 857. Anal. Calcd for $C_{21}H_{21}NO_5$: C, 68.65; H, 5.76. Found: C, 68.41; H, 5.79.

Diethyl 2-(*p*-Trifluoromethylphenyl)-3-oxobicyclo[3.3.0]oct-1-ene-7,7-dicarboxylate (Table 1, Entry 15). General procedure B was used to convert diethyl 1-(*p*-trifluoromethylphenyl)-6-hepten-1-yne-4,4-dicarboxylate (191 mg, 0.50 mmol) to the desired product in 14 h. Purification by flash chromatography (hexane:ether, 4:1) afforded 191 mg (93% yield) of a clear liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (d, J = 8.4 Hz, 2 H); 7.65 (d, J = 8.4 Hz, 2 H); 4.29 (q, J = 7.2 Hz, 2 H); 4.18 (m, 2 H); 3.68 (d, J = 19.5 Hz, 1 H); 3.30 (d, J = 19.5 Hz, 1 H); 3.19 (m, 1 H); 2.86 (m, 2 H); 2.33 (dd, J = 3.3, 18 Hz, 1 H); 1.79 (at, J = 12.7, 1 H); 1.32 (t, J = 7.2 Hz, 3 H); 1.23 (t, J = 7.2 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.5, 181.1, 171.5, 170.7, 134.6, 134.4, 130.2, 129.8, 128.8, 126.0, 125.4, 125.3. IR (neat, cm^{-1}) 2983, 2939, 1732, 1651, 1616, 1411, 1324, 1273, 1120, 1066, 1017, 928, 839, 686. Anal. Calcd for $C_{21}H_{21}F_3O_5$: C, 61.46; H, 5.16. Found: C, 61.77; H, 5.16.

Diethyl 2-Methyl-3-oxobicyclo[3.3.0]oct-1-ene-7,7-dicarboxylate (Table 2, Entry 1). General procedure A was used to convert diethyl 7-octen-2-yne-4,4-dicarboxylate[44] (126 mg, 0.50 mmol) to the desired product in 15 h. Purification by flash chromatography (hexane:ether, 3:2) afforded 129 mg (92% yield) of a clear liquid. The ^{1}H NMR spectrum matched the published spectrum.[44]

Diethyl 2-Propyl-3-oxobicyclo[3.3.0]oct-1-ene-7,7-dicarboxylate (Table 2, Entry 2). General procedure A was used to convert diethyl 9-decen-4-yne-7,7-dicarboxylate[45] (140 mg, 0.50 mmol) to the desired product in 13 h. Purification by flash chromatography (hexane:ether, 2:1) afforded 138 mg (90% yield) of a clear liquid. The ^{1}H NMR spectrum matched the published spectrum.[45]

Diethyl 2-Isopropyl-3-oxobicyclo[3.3.0]oct-1-ene-7,7-dicarboxylate (Table 2, Entry 3). General procedure B was used except at 5 psig CO to convert diethyl 2-methyl-8-nonen-3-yn-6,6-dicarboxylate[45]

(140 mg, 0.25 mmol) to the desired product in 48 h. Purification by flash chromatography (hexane:ether, 2:1) afforded 65 mg (85% yield) of a clear liquid. The ^{1}H NMR spectrum matched the published spectrum.[45]

Diethyl 2-Cyclopentyl-3-oxobicyclo[3.3.0]oct-1-ene-7,7-dicarboxylate (Table 2, Entry 4). General procedure B was used except at 5 psig CO to convert diethyl 1-cyclopentyl-6-hepten-1-yne-4,4-dicarboxylate[45] (77 mg, 0.25 mmol) to the desired product in 48 h. Purification by flash chromatography (hexane:ether, 2:1) afforded 66 mg (81% yield) of a clear liquid. The ^{1}H NMR spectrum matched the published spectrum.[45]

Di-*tert*-butyl 2-Methyl-3-oxobicyclo[3.4.0]non-1-en-8,8-dicarboxylate (Table 2, Entry 5). General procedure A was used to convert di-*tert*-butyl 8-nonen-2-yne-4,4-dicarboxylate[44] (81 mg, 0.25 mmol) to the desired product in 14 h. Purification by flash chromatography (hexane:ether, 7:3) afforded 77 mg (88% yield) of a clear liquid. The ^{1}H NMR spectrum matched the published spectrum.[44]

Di-*tert*-butyl 2-Methyl-3-oxobicyclo[3.4.0]non-1-en-7,7-dicarboxylate (Table 2, Entry 6). General procedure B was used except at 5 psig CO to convert di-*tert*-butyl 8-nonen-2-yne-3,3-dicarboxylate (80 mg, 0.25 mmol) to the desired product in 16 h. Purification by flash chromatography (hexane:ether, 7:3) afforded 75 mg (86% yield) of a white solid, mp 60−62 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.76 (m, 2 H); 2.55 (m, 3 H); 2.37 (m, 1 H); 1.92 (d, J = 18.9 Hz, 1 H); 1.65 (m, 4 H); 1.47 (s, 9 H); 1.41 (s, 9 H); 1.33 (d, J = 12.9 Hz, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.5, 173.1, 170.6, 169.9, 133.8, 81.9, 81.7, 56.0, 41.2, 38.8, 36.3, 31.1, 28.0, 27.9, 24.9, 7.8. IR (neat, cm^{-1}) 2980, 2934, 1725, 1706, 1660, 1455, 1370, 1297, 1254, 1166, 1073, 1027, 845. Anal. Calcd for $C_{20}H_{30}O_5$: C, 68.55; H, 8.63. Found: C, 68.60; H, 9.00.

(Table 2, Entry 7). General procedure A was used to convert *trans*-1-(allyloxy)-2-(phenylethynl)cyclohexane (120 mg, 0.50 mmol)[67] to the desired product in 24 h. Purification by flash chromatography (hexane:ether, 1:4) afforded 125 mg (93% yield) of an off-white solid, mp 116−118 °C. Lit. mp 118−120 °C. The ^{1}H NMR spectrum matched the published spectrum.[67]

2-Butyl-6-(benzyloxy)bicyclo[3.3.0]oct-1-en-3-one (Table 3, Entry 1). General procedure A with 0.0375 mmol $Cp_2Ti(CO)_2$ was used to convert 3-(benzyloxy)-1-undecen-6-yne[44] (128 mg, 0.50 mmol) to the desired product in 12 h. Purification by flash chromatography (hexane:ether, 4:1) afforded 130 mg (92% yield) of a 3.5:1 mixture of diastereomers as a pale yellow oil. The ^{1}H NMR spectrum matched the published spectrum. Identification of the major isomer was based upon comparison to the published spectrum.[44]

2-Butyl-6-(triisopropylsilyloxy)bicyclo[3.3.0]oct-1-en-3-one (Table 3, Entry 2). General procedure B was used to convert 3-((triisopropylsilyl)oxy)-1-undecen-6-yne[67] (163 mg, 0.50 mmol) to the desired product in 14 h. Purification by flash chromatography (hexane:ether, 95:5) afforded a combined 154 mg (88% yield) of a 2.3:1 mixture of diastereomers as a clear oil. The isomers were separated and characterized. Major isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.82 (m, 1 H); 2.88 (m, 1 H); 2.74−2.62 (m, 2 H); 2.48 (m, 1 H); 2.31−2.15 (m, 3 H); 2.10−1.99 (m, 2 H); 1.43−1.37 (m, 2 H); 1.28 (m, 2 H); 1.06 (s, 21 H); 0.89 (t, J = 7.3 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.2, 179.3, 138.2, 77.8, 52.1, 41.0, 35.8, 30.3, 24.4, 23.5, 22.9, 18.2, 14.1, 12.4. IR (neat, cm^{-1}) 2942, 2866, 1710, 1665, 1464, 1376, 1263, 1132, 1068, 996, 882, 833, 682. Anal. Calcd for $C_{21}H_{38}O_2Si$: C, 71.94; H, 10.92. Found: C, 72.23; H, 10.77. Minor isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.40 (at, J = 3.5 Hz, 1 H); 2.82 (m, 1 H); 2.60−2.38 (m, 4 H); 2.21−2.09 (m, 4 H); 1.41 (m, 2 H); 1.27 (m, 2 H); 1.01 (m, 2 H); 0.87 (m, 21 H); 0.87 (t, J = 7.2 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.8, 181.7, 137.2, 71.4, 51.0, 36.8, 36.7, 30.2, 23.8, 23.6, 22.8, 18.2 (2), 14.1, 12.5. IR (neat, cm^{-1}) 2942, 2866, 1707, 1667, 1464, 1366, 1247, 1170, 1134, 1086, 1053, 882, 678. Assignment of the major isomer was based upon analogy to a related allylic amide derived from the same enyne.[67]

2-Butyl-8-((triisopropylsilyl)oxy)bicyclo[3.3.0]oct-1-en-3-one (Table 3, Entry 3). General procedure A with 0.05 mmol $Cp_2Ti(CO)_2$ was used to convert 5-((triisopropylsilyl)oxy)-1-undecen-6-yne[44] (162 mg,0.50 mmol) to the desired product in 16.5 h. Purification by flash chromatography (hexane:ether, 95:5) afforded 167 mg (95% yield) of an 8:1 mixture of diastereomers as a pale yellow oil. The ^{1}H NMR spectrum matched the published spectrum. Identification of the major isomer was based upon comparison to the published spectrum.[44]

2-Phenyl-8-methyl-7-oxabicyclo[3.3.0]oct-1-en-3-one (Table 3, Entry 4). General procedure B was used to convert 3-(allyloxy)-1-phenyl-1-butyne[44] (93 mg, 0.50 mmol) to the desired product in 24 h. Purification by flash chromatography (hexane:ether, 7:3) afforded 102 mg (95% yield) of a 10:1 mixture of diastereomers as a clear liquid. The ^{1}H NMR spectrum matched the published spectrum. Identification of the major isomer was based upon comparison to the published spectrum.[44]

8-(Benzyloxy)-7,7-dimethyl-2-phenylbicyclo[3.3.0]oct-1-en-3-one (Table 3, Entry 5). General procedure B was used to convert 3-(benzyloxy)-4,4-dimethyl-1-phenyl-hepten-1-yne (152 mg, 0.50 mmol) to the desired product in 15 h. Purification by flash chromatography (hexane:ether, 85:15) afforded 156 mg (94% yield) of a single diastereomer as a pale yellow solid. Attempts to establish the relative configuration by nOe studies were unsuccessful. The assignment is based upon a comparison of the shift of the allylic proton in the NMR spectrum with a series of related enones obtained from other Pauson−Khand type cyclizations.[15b,33b] Mp 107−109 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47−7.22 (m, 10 H); 4.55 (d, J = 11.4 Hz, 1 H); 4.47 (d, J = 11.4 Hz, 1 H); 4.12 (s, 1 H); 3.35 (m, 1 H); 2.86 (dd, J = 6.6, 18 Hz, 1 H); 2.19 (dd, J = 6.6, 18 Hz, 1 H); 2.11 (dd, J = 9.9, 12.6 Hz, 1 H); 1.25 (s, 3 H); 1.14 (dd, J = 8.1, 12.6 Hz, 1 H); 0.97 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.0, 180.5, 138.7, 138.1, 131.4, 128.8, 128.4, 127.9, 127.8, 83.4, 72.3, 45.0, 44.7, 44.1, 39.9, 30.1, 23.8. IR (KBr, cm^{-1}) 2953, 2860, 1706, 1498, 1444, 1381, 1302, 1105, 1031, 927, 736, 694. Anal. Calcd for $C_{23}H_{23}O_2$: C, 83.10; H, 7.28. Found: C, 83.01; H, 7.18.

2-Butylbicyclo[3.3.0]oct-1,5-dien-3-one (eq 6). General procedure A was used with 0.05 mmol $Cp_2Ti(CO)_2$ to convert 9,10-undecadien-5-yne (74 mg, 0.50 mmol) to the desired product in 12 h. Purification by flash chromatography (hexane:ether, 7:3) afforded 102 mg (83% yield) of a clear oil. The product decomposes upon prolonged storage at room temperature. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.95 (s, 1 H); 2.80 (m, 6 H); 2.24 (t, J = 7.5 Hz, 2 H); 1.45 (m, 2 H); 1.29 (m, 2 H); 0.88 (t, J = 7.5 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.0, 172.5, 135.2, 125.1, 119.6, 26.9, 26.7, 20.9, 16.1, 14.8, 13.8, 5.0. IR (neat) 2926, 2857, 1696, 1447, 1307, 1209, 1052, 899. Exact mass calcd for $C_{12}H_{16}O$ $[M]^+$: 176.1201. Found: 176.1201.

Di-*tert*-butyl 2,5-Dimethylbicyclo[3.3.0]oct-1-ene-7,7-dicarboxylate (Table 4, Entry 1). General procedure A with 0.0125 mmol $Cp_2Ti(CO)_2$ was used to convert di-*tert*-butyl 6-methyl-7-octen-2-yn-5,5-dicarboxylate (81 mg, 0.25 mmol) to the desired product in 12 h. Purification by flash chromatography (hexane:ether, 4:1) afforded 83 mg (95% yield) of a white solid, mp 79−81 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.26 (d, J = 17.7 Hz, 1 H); 3.02 (d, J = 17.7 Hz, 1 H); 2.45 (d, J = 13.8 Hz, 1 H); 2.37 (d, J = 17.4 Hz, 1 H); 2.29 (d, J = 17.4 Hz, 1 H); 1.67 (s, 3 H); 1.47 (s, 9 H); 1.41 (s, 9 H); 1.09 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.5, 172.7, 161.9, 161.7, 122.3, 73.0, 72.8, 52.7, 42.2, 38.5, 35.6, 23.9, 18.8, 17.7. IR (neat, cm^{-1}) 2976, 2931, 1725, 1677, 1456, 1369, 1280, 1143, 1063, 918, 845, 734. Anal. Calcd for $C_{20}H_{30}O_5$: C, 68.55; H, 8.63. Found: C, 68.54; H, 8.55.

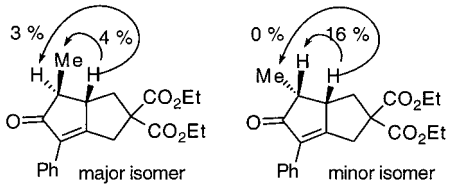
(Table 4, Entry 2). General procedure A with 5 psig CO was used to convert diethyl 1-phenyl-4-(2-cyclohexenyl)-but-1-yn-4,4-dicarboxylate (88 mg, 0.25 mmol) to the desired product in 12 h. Purification by flash chromatography (hexane:ether, 7:3) afforded 96 mg (91% yield) of a white solid, mp 141−143 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 (d, J = 7.2 Hz, 2 H); 7.36 (t, J = 7.2 Hz, 2 H); 7.29 (t, J = 7.2 Hz, 1 H); 4.22 (m, 4 H); 3.75 (dd, J = 1.8 Hz, 21.3 Hz, 1 H); 3.75 (m, 2 H); 2.95 (m, 1 H); 2.85 (m, 1 H); 2.08 (m, 1 H); 1.64 (m, 1 H); 1.45 (m, 1 H); 1.25 (m, 7 H); 1.05 (m, 1 H); 0.66 (m, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.7, 166.8, 162.6, 160.1, 123.6, 122.7, 119.6, 119.1, 119.0, 57.0, 53.1, 52.9, 38.6, 37.8, 32.4, 26.3, 16.2, 14.3, 13.9, 5.3, 5.2. IR (KBr, cm^{-1}) 2948, 1734, 1697, 1446, 1239, 1184, 1145, 1062, 1036, 749, 693. Anal. Calcd for $C_{23}H_{26}O_5$: C, 72.23; H, 6.85. Found: C, 72.37; H, 7.10.

(Table 4, Entry 3). General procedure A with 5 psig CO was used to convert diethyl 4-(2-cyclohexenyl)-pent-2-yn-4,4-dicarboxlate (73

mg, 0.25 mmol) to the desired product in 36 h. Purification by flash chromatography (hexane:ether, 3:2) afforded 71 mg (88% yield) of a white solid, mp 52−54 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.17 (m, 4 H); 3.49 (d, J = 20 Hz, 1 H); 3.20 (bs, 1 H); 2.97 (d, J = 20 Hz, 1 H); 2.88 (m, 1 H); 2.67 (m, 1 H); 1.96 (m, 1 H); 1.66 (s, 3 H); 1.57 (m, 1 H); 1.38 (m, 1 H); 1.18 (m, 7 H); 0.89 (m, 1 H); 0.60 (m,1 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.3, 166.3, 162.7, 160.3, 121.4, 56.8, 52.9, 52.8, 38.2, 36.5, 32.9, 24.1, 16.4, 14.1, 14.0, 5.2, 5.1. IR (neat) 2938, 2858, 1732, 1668, 1447, 1366, 1254, 1151, 1039, 963, 857, 701. Anal. Calcd for $C_{18}H_{24}O_5$: C, 67.47; H, 7.55. Found: C, 67.29; H, 7.67.

(Table 4, Entry 4). General procedure A with 5 psig CO and 0.10 mmol $Cp_2Ti(CO)_2$ was used to convert diethyl 1-phenyl-6-octen-1-yn-4,4-dicarboxylate (164 mg, 0.50 mmol) to the desired product as a 4:1 mixture of isomers in 12 h. Purification by flash chromatography (hexane:ethyl ether, 3:1) afforded 120 mg (67% yield) of a colorless oil. In one case, the two isomers were separated for characterization. Major isomer (*trans*) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 (d, J = 7.0 Hz, 2 H); 7.41 (t, J = 7.2 Hz, 2 H); 7.32 (t, J = 7.3 Hz, 1 H); 4.29 (q, J = 6.5 Hz, 2 H); 4.18 (m, 2 H); 3.64 (d, J = 19.6 Hz, 1 H); 3.29 (d, J = 20.0 Hz, 1 H); 2.87 (dd, J = 7.5 Hz, J = 12.1 Hz, 1 H); 2.76 (m, 1 H); 2.30 (qd, J = 7.2 Hz, J = 3.6 Hz, 1 H); 1.81 (t, J = 12.1 Hz, 1 H); 1.32 (t, J = 7.5 Hz, 3 H); 1.30 (d, J = 7.5 Hz, 3 H); 1.23 (t, J = 7.2 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.0, 176.2, 171.8, 170.9, 134.8, 131.4, 128.5 (2), 128.3, 62.3, 62.1, 61.7, 51.9, 50.0, 38.4, 36.1, 14.2, 14.1, 14.0. Minor isomer (*cis*) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 (d, J = 7.0, 2 H); 7.41 (t, J = 7.5 Hz, 2 H); 7.32 (d, J = 7.5 Hz, 1 H); 4.28 (q, J = 7.2 Hz, 2 H); 4.18 (q, J = 7.2 Hz, 2 H); 3.68 (d, J = 19.6 Hz, 1 H); 3.27 (d, J = 19.7 Hz, 1 H); 3.22 (m, 1 H); 2.68 (m, 1 H); 2.58 (dd, J = 7.7 Hz, J = 12.4 Hz, 1 H); 1.31 (t, J = 7.0 Hz, 3 H); 1.24 (t, J = 7.2 Hz, 3 H); 1.16 (d, J = 7.7 Hz, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.8, 178.1, 171.8, 171.0, 133.5, 131.3, 128.6, 128.4, 128.3, 62.4, 62.3, 60.9, 47.3, 44.0, 36.2, 33.7, 14.3, 14.2, 13.7. IR (neat, cm^{-1}) 2981, 1732, 1650, 1446, 1367, 1269, 1230, 1179, 1065, 697. Anal. Calcd for $C_{21}H_{24}O_5$ (mixture of isomers): C, 70.77; H, 6.79. Found: C, 70.77; H, 6.70. A nOe study was undertaken in C_6D_6 to determine the relative configurations of the isomers observed. For the isomer with the C-4 methyl cis to the ring junction hydrogen (major isomer), irradiation of the C-5 H at δ 2.51 gave a 4% enhancement at the C-4 methyl and a 3% enhancement at the C-4 H. For the isomer with the C-4 methyl trans to the ring junction hydrogen (minor isomer), irradiation of the C-5 H at δ 2.51 gave no enhancement at the C-4 methyl and a 16% enhancement at the C-4 H. Based on these observations, the configurations of the two isomers were assigned as shown.

(Table 4, Entry 5). General procedure B with 5 psig CO was used to convert diethyl *trans*-1-phenyl-6-octen-1-yn-4,4-dicarboxylate (82 mg, 0.25 mmol) to the desired product as a 4.2:1 mixture of isomers in 48 h. Purification by flash chromatography (hexane:ethyl ether, 3:1) afforded 50 mg (57% yield) of a colorless oil. The ^{1}H NMR spectrum confirmed the same major isomer as for entry 4.



(Table 4, Entry 6). General procedure B with 5 psig CO was used to convert diethyl *cis*-1-phenyl-6-octen-1-yn-4,4-dicarboxylate (82 mg, 0.25 mmol) to the desired product as a 1:1.6 mixture of isomers in 48 h. Purification by flash chromatography (hexane:ethyl ether, 3:1) afforded 73 mg (82% yield) of a colorless oil. The ^{1}H NMR spectrum revealed the major isomer to be the opposite of that for entry 4.

(Table 4, Entry 7). General procedure A with 5 psig CO was used to convert *cis*-diethyl 7-nonen-2-yn-4,4-dicarboxylate (67 mg, 0.25 mmol) to the desired product as a 2:1 mixture of isomers in 48 h. Purification by flash chromatography (hexane:ethyl ether, 9:1) afforded 44 mg (60% yield) of a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) mixture δ 4.23 (m, 2 H's each); 3.20 (m, 3 H major, 2 H minor); 2.81 (dd, J = 7.4 Hz, J = 12.9 Hz, 1 H minor); 2.60 (m, 2 H major, 1 H minor); 2.08 (m, 1 H minor); 1.80 (t, J = 13.6 Hz, 1 H major); 1.70 (m, 1 H minor); 1.71 (s, 3 H each); 1.27 (m, 6 H major, 9 H minor); 1.04 (d, J = 6.9 Hz, 3 H major). ^{13}C NMR (75 MHz, $CDCl_3$) mixture δ 213.0, 176.8, 175.5, 171.8, 171.3, 132.2, 131.0, 62.2, 62.1, 61.2, 60.6, 51.8, 48.6, 47.1, 42.9, 38.8, 34.3, 34.1, 14.2, 14.1, 13.5, 8.7. IR (neat, cm^{-1}) 3027, 1777, 1685, 1494, 1448, 1275, 1232, 1193, 977, 915, 755, 700. Anal. Calcd for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53. Found: C, 65.03; H, 7.56. The major isomer was assigned by comparison of spectroscopic data to the products from Table 2, entry 4.

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