The Design and Mechanism of Palladium Catalysts for Synthesis of Methylene Lactones by Cyclocarbonylation of Acetylenic Alcohols

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Abstract: The Pd(II)-catalyzed cyclocarbonylation of acetylenic alcohols to methylene lactones proceeds through carboalkoxypalladium intermediates, followed by intramolecular cis addition to the triple bond. Such intermediates have been independently synthesized, isolated, and found to undergo appropriate interconversions. A $PdI_2/Bu_3P/CH_3CN$ catalyst system gives rates first order in CO pressure, with the rate-determining step evidently being the uptake of CO by Pd. The use of an $SnCl_2$ cocatalyst ($PdCl_2/2Ph_3P/SnCl_2/CH_3CN$) labilizes the coordination sphere of the palladium, dissociating Cl^- and forming a cation which is a much faster cyclocarbonylation catalyst. The rate is now independent of CO pressure and first order in Pd and in substrate. The rate-determining step is coordination of the substrate, followed by rapid uptake of CO and completion of the cyclocarbonylation reaction. As the carboalkoxy intermediates also react intermolecularly with terminal acetylenes, yields in the catalytic cyclocarbonylation reaction improve substantially when it is run at concentrations below 0.3 M.

Introduction

As we considered the possibility of the catalytic synthesis of methylene lactones by cyclocarbonylation of appropriate acetylenic alcohols, it seemed likely that an appropriate catalyst system could be constructed from a $PdCl_2$/thiourea system which had been reported to catalyze the formation of various methyl maleates, fumarates, muconates, and gluconates from acetylene, air carbon monoxide, and methanol.[2] The system was attractive because, depite the lack of any knowledge of its mechanism of action, it seemed possible that it catalyzed the carboalkoxylation of triple bonds without involving a metal hydride—an involvement we deemed undesirable because of the potential of metal hydrides for catalyzing side reactions such as acetylene trimerization and double-bond migration. The success of this approach[3] has prompted both empirical optimization of the catalyst system[4] and the present investigation of its mechanism of action, which has then allowed further systematic improvements.[5]

The carboalkoxylation of acetylenes

$$HC{\equiv}CH + ROH + CO \rightarrow H_2C{=}CHCO_2R \quad (1)$$

is remarkable in that, on paper, it can be carried out in two fundamentally different ways, each of which is a sequence of steps well precedented in the literature of homogeneous catalysis. The first way, Scheme I, begins with nucleophilic attack by an alcohol on a coordinated carbonyl group, followed by acetylene insertion and protic cleavage.

The second way, Scheme II, begins with a metal hydride and its addition to an acetylene, followed by carbonylation and alcoholysis, regenerating the hydride. Although one can write a wide variety of more detailed mechanisms for this reaction, the fundamental distinction remains: Does $Pd\text{-}CO_2R$ (Scheme I) or Pd-H (Scheme II) add to the triple bond?

Both schemes have, in some form, been suggested as mechanisms for carboalkoxylation reactions, particularly with olefinic substrates (which have received far more investigation than acetylenes). Fenton has suggested a Scheme I type $Pd\text{-}CO_2H$ intermediate in the hydrocarboxylation of olefins,[6] and Heck has suggested a $Pd\text{-}CO_2R$ intermediate in the dicarboalkoxylation of olefins (and acetylenes as well).[7] Stille and co-workers have called a $Pd\text{-}CO_2CH_3$ complex "the most probable intermediate" in the catalytic formation of dimethylsuccinic diesters from 2-butene, carbon monoxide, and methanol,[8a] and they have explained product distributions and relative reaction rates for the carbonylation of a wide variety of olefins in methanol as the result of cis carbomethoxypalladation.[8b] On the other hand, a hydride mechanism (as in Scheme II) is still generally written[9,10] for the formation of acrylic acid derivatives from acetylene, nickel carbonyl, acid, and water or an alcohol (frequently called a Reppe reaction). A hydride mechanism has recently been suggested by Knifton for the carbomethoxylation of acetylenes with bimetallic Sn-Pd and Sn-Pt catalysts,[11] and was given earlier for analogous reactions with olefinic substrates.[12] A hydride mechanism for carbonylation of acetylenes with palladium catalysts has also been endorsed[13] by Tsuji, who did much of the pioneering work in this area.

Although in 1975 Consiglio and Pino[14] could still emphasize that both Schemes I and II were viable explanations for their observation of cis stereochemistry in palladium-catalyzed carboalkoxylation of olefins, the case for Scheme I is now very strong for most reactions involving olefinic substrates. For acetylenic substrates, however, the question has remained open. There has been no report of the reaction of an isolable, well-characterized carboalkoxy palladium complex with an acetylene. We now present such a report as part of our investigation of the mechanism of catalytic methylene lactone synthesis.

Scheme I

$$M\text{—}CO + ROH \rightarrow MCO_2R + H^+ \quad (2)$$

$$MCO_2R + HC{\equiv}CH \rightarrow MCH{=}CHCO_2R \quad (3)$$

$$MCH{=}CHCO_2R + H^+ \rightarrow H_2C{=}CHCO_2R + M \quad (4)$$

Scheme II

$$M\text{—}H + HC{\equiv}CH \longrightarrow MCH{=}CH_2 \quad (5)$$

$$MCH{=}CH_2 + CO \longrightarrow M\overset{O}{\overset{\|}{C}}CH{=}CH_2 \quad (6)$$

$$M\overset{O}{\overset{\|}{C}}CH{=}CH_2 + ROH \longrightarrow H_2C{=}CHCO_2R + M\text{—}H \quad (7)$$

Results and Discussion

Our initial mechanistic investigations were carried out with the $PdI_2/Bu_3P/CH_3CN$ (system I) modification of our basic

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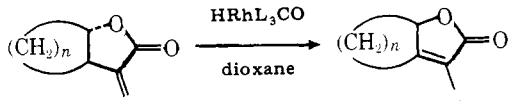
Pd(II) catalyst system. It gives synthetic results comparable to those achieved by the original $PdCl_2$/thiourea system,[4] but has the mechanistic advantage of remaining homogeneous for many half-lives.

As the isomerization of double bonds is a well-known property of metal hydrides, we first considered whether the position of the double bond in our methylene lactone products was the result of kinetic or thermodynamic control. The former seemed likely in view of some results in the natural product literature. An attempt to hydrogenate the exo double bond in the sesquiterpene lactone damsin had led to the isolation of some of the butenolide, the internal double bond isomer.[15] However, the precise extent of the equilibrium distribution of the double-bond position was not established, and in any case we required such knowedge for the α-methylene lactones, such as **1**, produced by our catalytic reactions.

Treatment of **1a** and **1b** with a metal hydride known to be an excellent double-bond isomerization catalyst, $HRh(PPh_3)_3CO$,[16,17] produced **2a** and **2b** as principal prod-



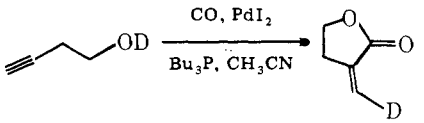
(8)

1a, $n = 4$
b, $n = 5$

2a, $n = 4$
b, $n = 5$

ucts. **1a** and **1b** disappeared completely in 2 days at 25 °C. The double-bond isomerization equilibrium thus overwhelmingly favors the endocyclic double bond in **2**, so reactions forming **1** must proceed with kinetic control of the position of the double bond. This result argues against a Scheme II mechanism, although not compellingly (the acetylene of the substrate might compete so effectively against the product double bond for the catalytic hydride that product isomerization would not occur). It is worth noting that no butenolide product, such as **2**, has ever been observed even as a byproduct in any of our catalytic reactions.

We next explored the question of the origin of the exo methylene protons. The hydroxyl proton of 3-butyn-1-ol was deuterium labeled and the catalytic synthesis of the lactone performed with this substrate. The deuterium was incorporated exclusively in the exo methylene, entirely cis to the carbonyl of the lactone.



(9)

This conclusion rests on the assumption that the downfield proton (δ 6.2) of α-methylene-γ-butyrolactone is cis to the lactone carbonyl. This assumption is supported by our observation that the downfield proton shifts 2.62 times as much as the upfield proton upon addition of $Eu(fod)_3$ to a solution of α-methylene-γ-butyrolactone in $CDCl_3$.

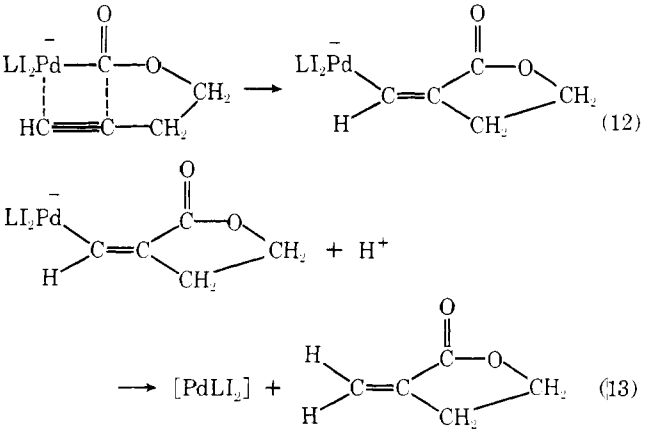
The above results can both be explained by a Scheme I mechanism, illustrated for 3-butyn-1-ol, where L = Bu_3P. Although osmometric molecular weight measurements show that $[PdLI_2]_2$ is predominantly dimeric in CH_3CN,[18] reaction 13 produces $[PdLI_2]$ and it is probable that the complex remains monomeric during the catalytic sequence. The proton generated in reaction 11 may remain attached to the organopalladium anion to some extent before its use in reaction 13.

There is ample justification, by precedent and analogy, for all of reactions 10–13. It is well-known that coordinated carbonyls, particularly those where π back-bonding is small and ν_{CO} is comparatively high, are subject to attack by nucleophiles.[19,20] For platinum carbonyl cations reactions like (11) have been extensively studied, and are reversible.[21,22] (We have chosen not to write reaction 11 as reversible, although there is no evidence either way.) A carbonyl bound to a neutral

proposed mechanism for system I

$$[PdLI_2] + CO \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} LPdI_2(CO) \quad (10)$$

$$LPdI_2(CO) + HOCH_2CH_2C{\equiv}CH \xrightarrow{k_2} LPdI_2CO_2CH_2CH_2C{\equiv}CH + H^+ \quad (11)$$



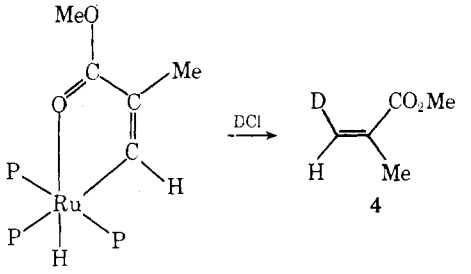
(12)

(13)

platinum(II) is approximately as susceptible to nucleophilic attack as is a coordinated olefin.[23]

Reaction 12 represents intramolecular acetylene insertion, or cis addition to the triple bond. The closest analogy, as it also involves insertion into a Pd-(sp^2)C bond, is the insertion of acetylenes into palladium vinyl bonds—known to proceed with cis stereochemistry.[24] Although arguments have recently been made to the contrary, suggesting that at least with M-H bonds acetylene insertion can occur trans,[25] the prevailing opinion[26,27] is that such reactions, when concerted and nonradical, involve cis addition. (In an extension of their analysis of olefin insertion reactions, Thorn and Hoffmann[28] make it clear that they regard cis stereochemistry as the rule in acetylene insertion reactions.)

Reaction 13 is merely the protic cleavage of a vinyl-palladium bond, a process of which there are many examples.[29] If it proceeds with retention of stereochemistry at vinyl carbon, it explains the results of the deuterium-labeling experiment above, reaction 9. This stereochemical result was, until recently, a presumption rather than a conclusion: the cis addition of metal hydrides to olefins was frequently established by determining the stereochemistry of the olefin resulting after acid cleavage of the vinyl complex, and *assuming* retention of stereochemistry during that step.[30] However, there are now two pieces of direct evidence. Yamomoto, Ibers, and co-workers have taken a vinyl ruthenium complex **3**, the structure of which had been established crystallographically, and treated it with DCl (reaction 14).[31] The fact that methyl *cis*-β-deuter-

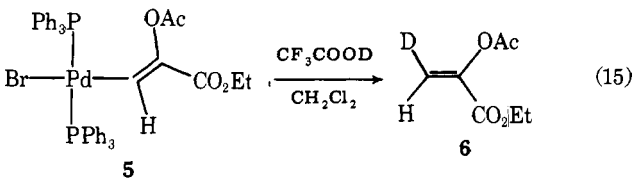


(14)

3 **4**

iomethacrylate (**4**) is obtained unequivocally establishes retention of stereochemistry.

Bosnich and co-workers have recently demonstrated that this conclusion is also valid for palladium (reaction 15). The



(15)

5 **6**

structure of **5** is known from X-ray crystallography, and the location of the deuterium in **6** has been determined by ^1H NMR analysis of a Diels–Alder adduct with cyclopentadiene.[32]

The mechanism (reactions 10–13) offers a straightforward explanation of the observed kinetic control of the double-bond location as the methylene lactone carbon skeleton is assembled. If the addition in reaction 12 is cis, it can only proceed in the direction indicated, for the opposite direction of addition would form an impossibly strained six-membered ring containing a trans double bond.

Neutral model compounds for the proposed catalytic intermediates can be prepared and shown to react as suggested. Appropriate trans carboalkoxypalladium complexes can be prepared by adaptation of a reaction first reported by Fitton[33] and later generalized by Otsuka,[34] the addition of chloroformates to Pd(0) complexes (reaction 17). The chloroformates

$HOCH_2CH_2C{\equiv}CR + COCl_2$

7a, R = CH_3
b, R = H
c, R = $SiMe_3$

$\xrightarrow[\text{ether}]{25\ ^\circ C}$ $ClCO_2CH_2CH_2C{\equiv}CR$ (16)

8a, R = CH_3
b, R = H
c, R = $SiMe_3$

$Pd(Ph_3P)_4 + ClCO_2CH_2CH_2C{\equiv}CR$

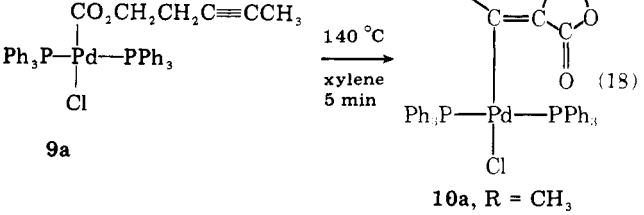
8a, R = CH_3
c, R = $SiMe_3$

$\xrightarrow[\text{toluene}]{80\ ^\circ C}$ $Ph_3P{-}Pd(CO_2CH_2CH_2C{\equiv}CR){-}PPh_3$ (Cl) (17)

9a, R = CH_3
c, R = $SiMe_3$

are easily made by treatment of the appropriate acetylenic alcohol with phosgene (reaction 16). Attempted oxidative addition of the unprotected acetylenic chloroformate **8b** to PdL_4 results in competitive reaction at the terminal triple bond and a complex reaction mixture.

The carboalkoxy derivative **9a** is the first carboalkoxypalladium complex to contain a triple bond also. The fact that the triple bond is internal and the presence of two bulky triphenylphosphine ligands should make the insertion much slower than in the catalytic system, and under aprotic conditions the vinylic insertion product should be stable. We can thus, at higher temperature, obtain reaction 18, in which both the

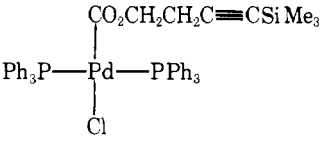


(18)

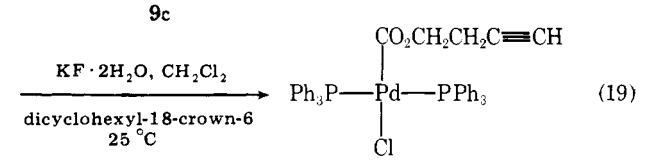
9a **10a**, R = CH_3

starting material and the product are analogous to those in reaction 12 in our proposed mechanism, but with a methyl substituent on the acetylene.

Performing an analogous model reaction with the terminal acetylene **9b**, R = H, is more difficult. As direct preparation of **9b** is not possible, one must attempt the removal of the trimethylsilyl group from the protected terminal acetylene **9c**. A number of standard methods fail, apparently because they attack the carboalkoxypalladium moiety ($AgNO_3/KCN$[35] and KF in DMF[36]). Because of the low affinity of F^- for Pd(II), it seemed likely that some variation of the fluoride ion method would work, and the use of a crown ether seemed indicated. The reaction is surprisingly sensitive to choice of solvent and crown ether, but $KF{\cdot}2H_2O$, CH_2Cl_2, and dicyclohexyl-18-crown-6 produce the desired result (reaction 19). Although **9b**



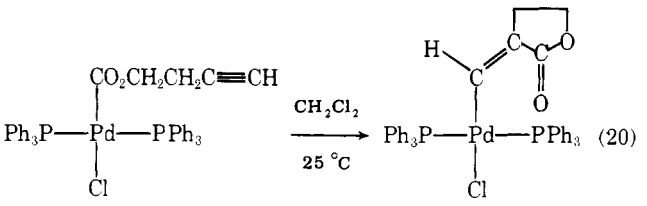
9c



(19)

9b

is spectroscopically observable (characteristic IR band at 3300 cm^{-1}), it disappears at roughly the same rate it is formed (within a few hours at room temperature) to give the insertion product **10b**, R = H (reaction 20). This reaction is now directly

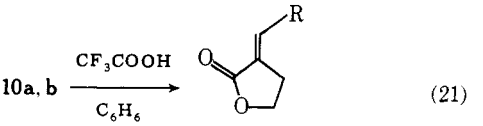


(20)

9b **10b**

parallel to reaction 12 in our proposed mechanism. (The use of anhydrous KF gives **10b** in good yield without observable intermediates; under these circumstances removal of Me_3Si probably gives an acetylide anion which undergoes insertion before protonation.)

Upon addition of acid, both **10a** and **10b** are cleaved, yielding free α-ethylidene and α-methylene lactones (reaction 21).



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11a, R = CH_3
b, R = H

The cleavage reaction is much faster for **10b**, R = H, than it is for **10a**, R = CH_3. Combining this result with the ones above (reactions 18 and 20), it appears that both acetylene insertion and cleavage of the resulting vinyl complex are faster for terminal acetylenes than for internal ones. It is therefore not surprising that the catalytic reaction is ineffective in the formation of α-alkylidene lactones from carbon monoxide and internal acetylenic alcohols.[4]

Kinetics. Catalyst System I. The progress of a typical reaction catalyzed by system I (PdI_2, Bu_3P, CH_3CN), monitored by GLC with 3-butyn-1-ol (**7b**) as substrate and naphthalene as internal standard, is shown in Figure 1. The rate of formation of α-methylene-γ-butyrolactone (**11b**) (plotted as turnovers—moles of product per mol of catalyst) is initially constant and the reaction mixture is homogeneous. Eventually,

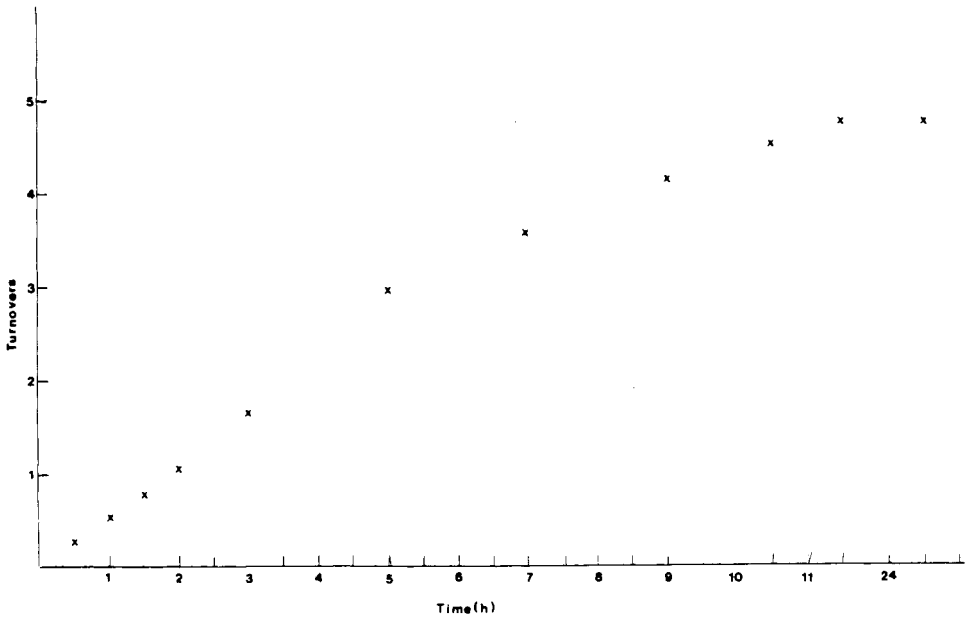


Figure 1. Progress of a tpyical 3-butyn-1-ol cyclocarbonylation reaction with $PdI_2/PBu_3/CH_3CN$ catalyst (system I).

palladium metal begins to precipitate out and the reaction rate decreases (stopping completely, in the case shown in Figure 1, after 10 h). Rate data have been taken from the slope of plots like Figure 1 during the initial homogeneous, constant-rate phase and are given in Table I.

The rates at 60 °C as a function of CO pressure are shown in Figure 2. The reaction is approximately first order in carbon monoxide pressure. At 60 °C, assuming the concentration of CO to be 0.067 M under a pressure of 7.8 atm,[37,38] the rate constant k_{obsd} in eq 22 is 1.4×10^{-2} L/mol·s.

$$\text{rate} = k_{obsd}[Pd][CO] \tag{22}$$

Comparable data for rate as a function of substrate concentration, shown in Figure 3, make it clear that above 1.0 M the rate is independent of substrate concentration. (Below 1.0 M the rate appears to decrease, but the concentration of product during the initial homogeneous period is so low that accurate rate measurement is not possible.) Together these data are consistent with the rate law given in eq 23, where k_1 is the rate constant for CO coordination to Pd(II) in reaction 10, k_{-1} is the rate of loss of CO in the reverse of reaction 10, and k_2 is the rate of acetylenic alcohol reaction with the Pd(II) carbonyl (reaction 11), [P] is the concentration of the α-methylene-γ-butyrolactone product **11b**, and [S] is the concentration of the starting material **7b**. Under normal reaction conditions, i.e., with [S] above 1.0 M, $k_2[S]$ is apparently much larger than k_{-1}, and the rate law reduces to eq 22, with $k_{obsd} = k_1$. The rate-determining step is thus the coordination of CO to Pd(II) in eq 10.

$$\frac{d[P]}{dt} = \frac{k_2 k_1 [Pd][CO][S]}{k_{-1} + k_2[S]} \tag{23}$$

The same should be true for any substrate as long as $k_2[S]$ remains much greater than k_{-1} and all subsequent steps are fast. The fact that rates are much slower in a few cases, such as the attempted conversion of 4-pentyn-1-ol (**12**) to α-methylene-δ-valerolactone (**13**),[4] shows that these conclusions do not always hold; the longer carbon chain in 4-pentyn-1-ol, for example, doubtless retards the rate of the insertion step, reaction 12.

Design of Catalyst System II. The kinetic results above demonstrate that the rate of reaction 10 is the maximum rate at which catalysis by system I can proceed. This is unfortunate, as it means that the palladium is not used efficiently: only that small fraction which has been carbonylated is available for reaction with substrate. A system which more readily coordinates carbon monoxide will thus be a much better catalyst.

Table I. Rate of Cyclocarbonylation of **7b** by Catalyst System I[a]

entry	P_{CO}, atm	[**7b**], M	rate[b]
1	1.7	1.7	0.25
2	2.4	1.7	0.58
3	3.0	1.7	0.86
4	3.7	1.7	0.98
5	4.4	1.7	1.3
6	6.8	1.7	2.1
7	7.8	1.7	3.2
8	4.4	3.2	1.2
9	4.4	0.98	1.1
10	4.4	0.16	0.55

[a] All reactions were performed at 60 °C in acetonitrile. $[PdI_2] = [PBu_3] = 0.027$ M. [b] Moles of product, **11b**, formed per mol of palladium per h.

This was one of several considerations prompting investigation of $SnCl_2$ as a possible cocatalyst. Such systems, with both palladium and platinum, have a long history of effectiveness as catalysts for many reactions,[11,12,39-41] and Bailar in particular[40] has suggested reasons for the unique effectiveness of $SnCl_2$ as a cocatalyst. It gives rise to the trichlorostannyl ligand, which is a strong π acceptor and a weak σ donor, and has a high trans effect.[42] One would thus expect the chloride ligand in a complex such as *trans*-$Pd(Ph_3P)_2Cl(SnCl_3)$ to be labile with regard to displacement by donor solvents or carbon monoxide.

Furthermore, the trichlorostannyl ligand is known to promote five coordination in complexes such as $Pt(H)(SnCl_3)(CO)(PPh_3)_2$[41] and $Pt(SnCl_3)_5^{3-}$.[42] (Its high trans effect may well be due to its ability to stabilize the five-coordinate intermediate involved in associative substitution reactions.) This should facilitate the insertion of acetylene in steps such as reaction 12 above—where a five-coordinate intermediate may well be involved. There is good evidence for ethylene insertion via a five-coordinate intermediate in the $SnCl_2$-catalyzed formation of $Pt(C_2H_5)ClL_2$ from C_2H_4 and $PtHClL_2$.[43,44]

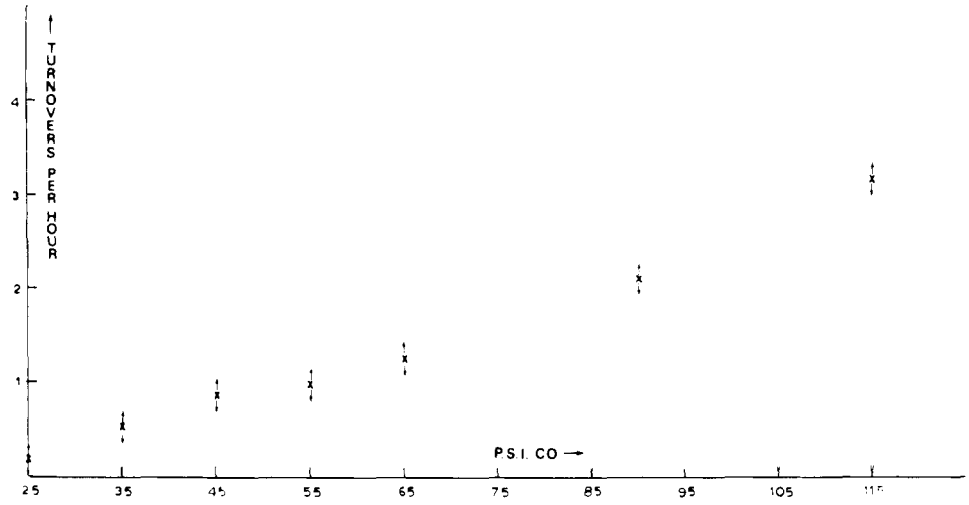


Figure 2. Dependence of the initial rate of 3-butyn-1-ol cyclocarbonylation upon CO pressure (system I—$PdI_2/PBu_3/CH_3CN$).

Finally, but importantly, bimetallic $SnCl_2/PdL_2Cl_2$ systems have been reported by Knifton to be effective catalysts for the carboalkoxylation of olefins[12] and acetylenes.[11] This precedent, however, becomes less auspicious on detailed examination, for a Scheme II mechanism, involving a palladium hydride, is proposed,[11,12] which seems likely to be incompatible with the desired exo double bond position in a methylene lactone.

A solution (catalyst system II) of $PdCl_2$, $2Ph_3P$, and anhydrous $SnCl_2$ in dry acetonitrile in fact proves to be an excellent catalyst for cyclocarbonylation of acetylenic alcohols to α-methylene lactones—far superior in both rate (upon comparison of the data in Table I and entry 7 in Table V, it is seen to be over 100 times faster) and yield to system I.[4] We have therefore examined the mechanism of action of system II, in order to determine whether it still follows a Scheme I route and, if so, how that route differs from that established (reactions 10–13) for catalyst I.

Nature of Catalyst System II. The active species in this system is *not* the same as that in the bimetallic Pt–Sn and Pd–Sn systems used by Knifton.[11,12] The latter involved alcohols, usually methanol, either as solvent or in large excess and generally employed $SnCl_2 \cdot 2H_2O$ (although the substitution of anhydrous $SnCl_2$ was said to make no difference).[11,12] With system II the use of anhydrous $SnCl_2$ and dry acetonitrile is essential; the presence of water, as in the form of $SnCl_2 \cdot 2H_2O$, causes loss of all catalytic activity for the cyclocarbonylation of 3-butyn-1-ol (runs 1 and 2, Table II).

Furthermore, α-methylene lactones are not stable under the conditions of the Knifton system. When $PdCl_2$, excess $SnCl_2 \cdot 2H_2O$, and excess CH_3OH in methyl isobutyl ketone are stirred under 7.8 atm of CO at 70 °C for 3 h (typical Knifton carboalkoxylation conditions[12]), the resulting red solution isomerizes the α-methylene lactone **1a** to the corresponding butenolide **2a** (reaction 24). This result is consistent

$$PdCl_2 + 2Ph_3P \xrightarrow[\text{excess } SnCl_2 \cdot 2H_2O]{\text{7.8 atm CO, 70°C, 3 h}} \underset{\text{CH}_3\text{OH, methyl isobutyl ketone}}{\overset{\mathbf{1a} \rightarrow \mathbf{2a}}{}} \quad (24)$$

with the presence of the $Pd(H)(SnCl_3)(Ph_3P)_2$ which Knifton has suggested is the catalytically active species in a Scheme II mechanism.[11,12]

Finally, the Knifton system is most efficient at a Sn/Pd ratio of 5, with significant rate decreases both above and below this point.[12] Our catalyst II system is independent of the Sn/Pd ratio (compare runs 3 and 4, Table II). All of these results demonstrate that the active species are different in these two superficially similar Sn/Pd catalyst systems.

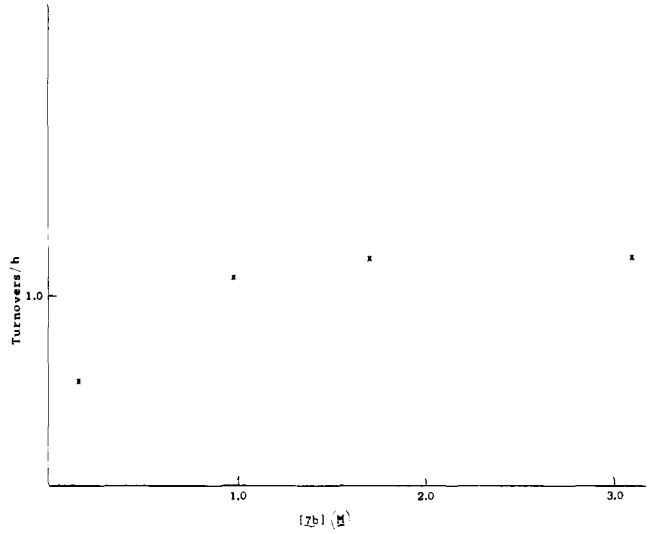


Figure 3. Dependence of the initial rate of 3-butyl-1-ol cyclocarbonylation upon substrate concentration (system I—$PdI_2/PBu_3/CH_3CN$).

What, then, *is* the active species in the system II cyclocarbonylation catalyst? We shall look at each ingredient in succession and determine what species are present in solution. First, the addition of 2 equiv of triphenylphosphine to $PdCl_2$ in acetonitrile produces *trans*-$Pd(Ph_3P)_2Cl_2$ (**14**). The stereochemistry of $Pd(PPh_3)_2Cl_2$ can be unequivocally assigned as trans in the solid state from IR evidence.[45] Although many phosphine complexes PdL_2X_2 are now known to be substantially cis in solution in polar solvents,[46] the pattern of the aromatic ring protons in the NMR in CD_3CN solution is consistent with that reported by Nelson and co-workers[47] to be characteristic of a trans configuration.[48,49] That complex can be precipitated by addition of diethyl ether and identified by elemental analysis and by comparison of its $\nu_{Pd\text{-}Cl}$ (357 cm^{-1}) with the literature values.[45]

When 1 equiv of $SnCl_2$ is added to a CH_3CN solution of $PdCl_2$ and $2Ph_3P$ and stirred for a few hours, addition of diethyl ether precipitates $(Pd(PPh_3)_2(SnCl_3)Cl$ (**15**). The IR spectrum contains bands at 335, 320, and 310 cm^{-1}, two of which are those characteristic of a coordinated trichlorostannyl ligand[50] and one of which is $\nu_{Pd\text{-}Cl}$. Trans stereochemistry for **15** is suggested by its dark yellow color[46] and confirmed by its behavior in solution (see below).

Table II. Cyclocarbonylation of **7b** with Various Ligands and Cocatalysts[a]

entry	Pd halide, M	ligand, M	cocatalyst, M	T, °C	**7b**, M	yield,[b] %
1	$PdCl_2$, 0.05	PBu_3, 0.05	$SnCl_2 \cdot 2H_2O$, 0.05	60	1.8	0
2	$PdCl_2$, 0.05	PBu_3, 0.05	$SnCl_2$, 0.05	60	5.3	36 (3.6)
3	$PdCl_2$, 0.07	PBu_3, 0.14	$SnCl_2$, 0.07	70	2.4	31 (10)
4	$PdCl_2$, 0.07	PBu_3, 0.14	$SnCl_2$, 0.35	70	2.4	31 (10)
5	$PdCl_2$, 0.07	PPh_3, 0.07	$SnCl_2$, 0.07	75	1.0	50 (8.4)
6	$PdCl_2$, 0.07	PPh_3, 0.14	$SnCl_2$, 0.07	75	1.0	100 (16)
7	$PdCl_2$, 0.07	PPh_3, 0.07	$SnCl_2$, 0.14	75	1.0	50 (8.8)

[a] Reaction conditions: P_{CO} = 7.8 atm, 17 h. [b] GLC analysis of product **11b**; figure in parentheses is turnovers per palladium.

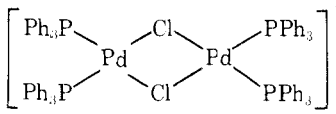
Table III. Conductances of Catalyst Mixtures and Separate Components

entry	solute (10^{-4} M)[a]	T, °C	$10^5 \Lambda$, mho	Λ_e, mho·cm²/mol
1	$2PPh_3$, $PdCl_2$, $SnCl_2$ (4.67)	60	11.6	124
2	$2PPh_3$, $PdCl_2$, $SnCl_2$ (4.67), CO[b]	60	11.6	124
3	$(PPh_3)_2PdCl_2$ (6.07)	60	2.66	21.8
4	$(PPh_3)_2PdCl_2$ (6.07), CO[b]	60	2.94	24.1
5	$(PPh_3)_2Pd(Cl)(SnCl_3)$ (1.92)	60	4.95	129
6	$SnCl_2$ (160)	60	26.2	8.19
7	$(n\text{-}Bu_4N)Br$ (3.75)	22	11.9	159
8	$(n\text{-}Bu_4N)Br$ (3.75)	60	15.5	207

[a] In acetonitrile. [b] Carbon monoxide saturated solution under 2 atm of carbon monoxide.

Conductivity measurements (Table III) make it clear that **15** is not intact in acetonitrile solution. The conductivity of a solution of $SnCl_2$ is negligible (entry 6) and that of a solution of **14** (entry 3) is small, but when both are present (entry 1) the conductivity rises to 124 mho·cm²/mol (at 60 °C), at the bottom end of the range characteristic of 1:1 electrolytes in CH_3CN.[51] The most straightforward explanation is the solvolysis of Cl^- by CH_3CN, giving the cation **16**, $[Pd(PPh_3)_2(SnCl_3)(CH_3CN)]^+Cl^-$. It, **15**, and all planar complexes in the catalytic cycle probably possess trans stereochemistry about Pd, reflecting the trans effect of the $SnCl_3$ ligand. (A single peak, at δ 45 ppm, is observed in the ^{31}P NMR spectrum of **16**.) The addition of $SnCl_2$, then, has labilized the coordination sphere of palladium as expected, but by solvolysis of Cl^- even in the absence of CO.

That solvolysis of chloride ion accounts for the conductivity can be confirmed by independent synthesis of the cation **16** (reaction 25) from the known[52,53] dimeric dication **17**. As



17

$$\xrightarrow{CH_3CN} 2\textit{trans}\text{-}[Pd(PPh_3)_2(SnCl_3)(CH_3CN)]^+ + 2BF_4^- \quad (25)$$

16

shown in Table IV, entries 1 and 2, the catalytic activity of both systems is the same and the same active palladium complex must therefore be present. As entries 3 and 4 (Table IV) show, the same catalytically active species is also generated by reactions 26 and 27, confirming that the presence or absence of chloride ion makes no difference to the catalytic activity of the system and that the active species, **16**, does not coordinate it.

$$\mathbf{17} + 2Bu_4N^+SnCl_3^- \xrightarrow{CH_3CN} 2\,\mathbf{16} + 2BF_4^- + 2Bu_4N^+ + 2Cl^- \quad (26)$$

Table IV. Comparison of Cyclocarbonylation Rates for **16** Independently Generated from Various Cocatalysts[a]

entry	Pd complex	cocatalyst	turnover rate[b]
1	**15**	none	1.5
2	**17**	$SnCl_2$	1.2
3	**17**	$[(CH_3)_4N]^+SnCl_3^-$	1.2
4	**17**	$SnCl_2$ followed by $[(CH_3)_4N]^+Cl^-$	1.2

[a] All runs performed with [**7b**] = 0.30 M; [Pd] = 0.0027 M; P_{CO} = 5.1 atm; T = 75 °C; acetonitrile solvent; Pd:Sn = 1.1. [b] Moles of **11b** formed per mol of Pd per min.

$$\mathbf{17} + 2SnCl_2 \xrightarrow{CH_3CN} \xrightarrow{Bu_4N^+Cl^-} 2\,\mathbf{16} + 2BF_4^- + 2Bu_4N^+ + 2Cl^- \quad (27)$$

Extensive investigation of the IR and UV spectra of **16** also shows no evidence for significant binding of either terminal acetylenes (such as 1-heptyne) or alcohols (such as 1-butanol) even when large excesses are added; there is similarly no evidence for significant binding by **16** of the substrate acetylenic alcohol **7b**, i.e., the binding constant in reaction 28 must be unfavorable:

$$\mathbf{16} + S \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} L_2Pd(SnCl_3)S \quad (28)$$

Furthermore, examination of the IR spectrum of **16** in CH_3CN under reaction conditions (75 °C and 0.01 M concentration of Pd) with 50 and 100 psi of CO showed no evidence for ν_{CO} from 2190 to 1900 cm^{-1},[54] indicating that the equilibrium in (29) is far to the left.

$$\mathbf{16} + CO \underset{k_{-4}}{\overset{k_4}{\rightleftharpoons}} L_2Pd(SnCl_3)CO \quad (29)$$

The conductivity (Table III, entries 1 and 2) also shows no significant effect from the presence of CO. These results are not surprising: the trichlorostannyl ligand labilizes the coordination site trans to it, but there is no reason it should increase the equilibrium binding of anything, particularly the π-acceptor carbonyl ligand.

Kinetic studies have clarified the mechanism of action of system II. Rate data were once again taken from the initial linear portion of plots of turnovers per unit time. As is evident from a typical plot with 3-butyn-1-ol (**7b**) as substrate, Figure 4, system II, in contrast to system I, loses its activity very slowly, and is still active after several days. Product formation usually ceases only after the catalyst has run out of substrate, and reactions can be restarted by adding fresh substrate.

Rate data are given in Table V as a function of CO pressure (entries 1–5) and initial substrate concentration (entries 12–16), and plotted in Figures 5 (CO pressure) and 6 (substrate concentration). It is apparent from Figure 5 that the rate

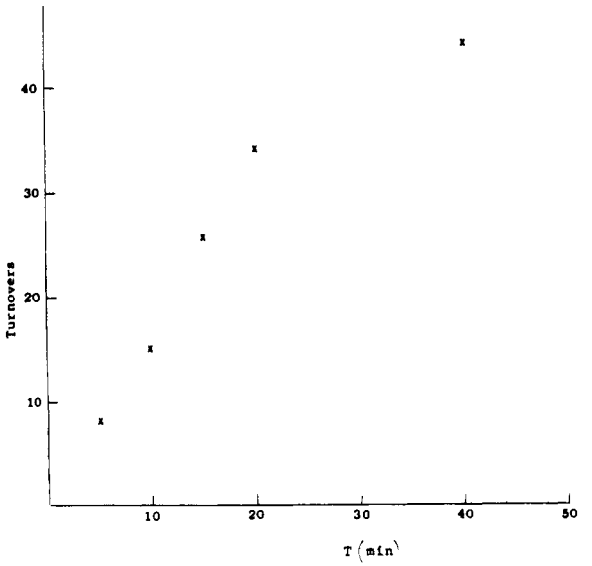


Figure 4. Progress of a typical 3-butyn-1-ol cyclocarbonylation reaction with $PdCl_2/2PPh_3/SnCl_2/CH_3CN$ catalyst (system II).

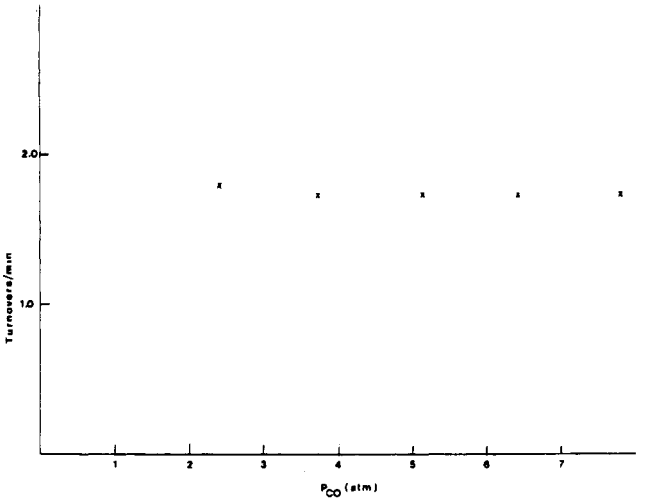


Figure 5. Dependence of the initial rate of 3-butyn-1-ol cyclocarbonylation upon CO pressure (system II—$PdCl_2/2PPh_3/SnCl_2/CH_3CN$).

Table V. Rates of Cyclocarbonylation of **7b** and **12** by System II at Various P_{CO} and Substrate Concentrations[a]

entry	P_{CO}, atm	temp, °C	substrates, M	rate[b]
1	2.4	75	**7b**, 0.30	1.8
2	3.7	75	**7b**, 0.30	1.7
3	5.1	75	**7b**, 0.30	1.7
4	6.4	75	**7b**, 0.30	1.7
5	7.8	75	**7b**, 0.30	1.7
6	5.1	75	**12**, 0.28	0.60
7	6.4	75	**12**, 0.28	0.54
8	7.8	75	**12**, 0.28	0.60
9	7.8	75	**12**, 0.23	0.34
10	7.8	75	**12**, 0.48	1.4
11[c]	5.1	75	**7b**, 0.3	1.8
12	5.1	65	**7b**, 0.056	0.24
13	5.1	65	**7b**, 0.085	0.44
14	5.1	65	**7b**, 0.192	0.78
15	5.1	65	**7b**, 0.288	0.96
16	5.1	65	**7b**, 0.451	1.48

[a] Reaction conditions: 0.004 M $PdCl_2$, 0.004 M $SnCl_2$, 0.008 M PPh_3, acetonitrile solvent. [b] Moles of product formed per mol of Pd per min, by GLC. [c] [Pd] = 0.008 M.

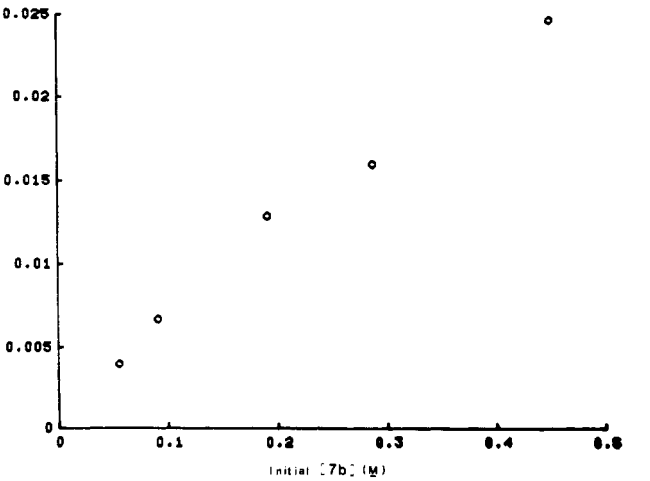


Figure 6. Dependence of the initial rate of 3-butyn-1-ol cyclocarbonylation upon substrate concentration (system II—$PdCl_2/2PPh_3/SnCl_2/CH_3CN$).

is now *independent* of CO pressure from 20 to 100 psi. This result contrasts with the CO dependence of system I. The rate is first order (Figure 6) in **7b**, and also dependent upon the nature of the substrate (compare entries 3–5 and 6–8 in Table V), again in contrast to system I. The assumption that the reaction is first order in palladium is confirmed by the fact that the rate, in turnover per unit time, is independent of the concentration of Pd (compare entries 3 and 11, Table V). The rate law for system II is thus

$$\text{rate} = k_{obsd}[\text{Pd}][\text{substrate}] \qquad (30)$$

where $k_{obsd} = 2.3 \times 10^1$ L/mol·s.

As turnovers with system II are high, the presence or absence of product from 1 equiv of substrate is not noticeable under catalytic conditions. It is thus necessary to dispose of the possibility that the active catalyst is generated by the reaction of **16** with an initial 1 equiv of substrate. Reaction of **16** in CH_3CN with 2 equiv of **7b** at 75 °C in the absence of CO for 2 h—a period during which scores of turnovers would have occurred if CO had been present—gave only unreacted **7b** and **16**. The catalytically active species is thus **16** and not some other species (such as a hydride) formed by initial reaction of it with substrate. (A slow reaction of **16** and substrate to form an active species is ruled out by the observation—see Figure 4—that the initial turnover rate never increases.)

As the *equilibrium constants* for binding both substrate S and CO to **16** are insignificant, and the rate of the catalytic reaction is first order in S and independent of CO pressure, the rate-determining step

$$\mathbf{16} + \text{S} \xrightarrow{k_3} \text{L}_2\text{Pd}(\text{SnCl}_3)(\text{S})^+ \ (\mathbf{18}) \qquad (31)$$

must be the forward step, rate constant k_3, from the unfavorable substrate binding equilibrium, eq 28. CO must be introduced in a subsequent fast step. Recalling the ability of the $SnCl_3$ ligand to stabilize five coordination, we write the carbonyl adduct **19** from reaction 32 as five coordinate.[44,55] Subsequent steps are analogous to those established (reactions 11–13) for system I, and must also be faster than reaction 31. Both systems I and II thus proceed by Scheme I mechanisms.

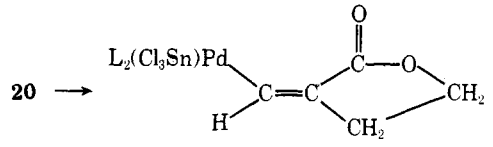
System II is faster than system I because the trichlorostannyl ligand makes the palladium coordination shell more labile. It

$$18 + CO \xrightarrow[\text{fast}]{k_2} L_2Pd(SnCl_3)(S)(CO)^+ \quad (32)$$

19

$$19 \longrightarrow L_2Pd(SnCl_3)(COCH_2CH_2C{\equiv}CH) + H^+ \quad (33)$$

20



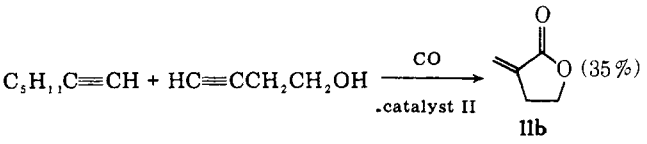
21

$$21 + H^+ \longrightarrow 11b + 16 \quad (35)$$

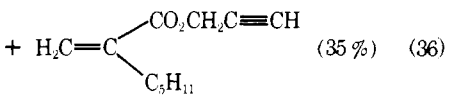
induces the solvolysis of chloride ion, although the resulting cation can coordinate CO only after prior coordination of substrate has increased the electron density on palladium. The rate with system II is thus dependent on substrate concentration and independent of CO pressure, precisely the opposite situation to that found with system I.

None of the evidence above indicates which end of the substrate coordinates in reaction 31. The need for increased electron density in order to bind CO suggests that it is the alcohol end, and kinetic studies[56] of the intermolecular carboalkoxylation of terminal acetylenes (see below) support this suggestion. Reaction 32 thus leaves the substrate alcohol and the coordinated carbonyl in the same coordination shell in **19** and facilitates nucleophilic attack (reaction 33).

Trapping of Carboalkoxy Intermediates by Intermolecular Reaction with Acetylenes. Although the rate of the acetylene insertion reaction 34 is fast compared to that of the rate-determining step (reaction 31), the fact that we were able to observe acetylene insertion directly in the model systems (reactions 18 and 20) suggests that the process is slow enough to permit competition by an external terminal acetylene. As a trap we have used 1-heptyne. When a 1:1 mixture of it and 3-butyn-1-ol (**7b**) is added to a system II reaction 0.10 M in Pd, the unsaturated ester **22** is formed in 35% yield based on **7b** (reaction 36). No other stereoisomers of **22** are found.



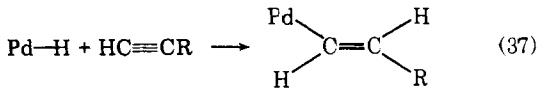
11b



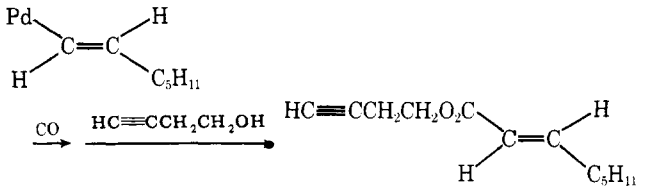
22

The formation of **22** is logically explained by insertion of the triple bond of 1-heptyne into the Pd-C bond of the $PdCO_2CH_2CH_2C{\equiv}CH$ intermediate, **20,** in competition with insertion of the intramolecular triple bond, followed by protic cleavage. (It should be noted that the external 1-heptyne is competitive because it is present in large excess compared to Pd, and therefore to $PdCO_2CH_2CH_2C{\equiv}CH$.) The observation of **22** is therefore consistent with a Scheme I mechanism.

Recalling, however, that Scheme II mechanisms can also produce such unsaturated esters, it is important to note the stereochemistry about the double bond in **22.** In systems for which Scheme II mechanisms have been proposed (e.g., the Knifton system for the carboalkoxylation of alkynes, where $HPd(SnCl_3)(PPh_3)_2$ has been proposed as the active species[11]), Pd-H addition is assumed to occur preferentially in the direction shown in reaction 37, and the preference must be enhanced for steric reasons when bulky phosphine ligands are present. This results in the attachment of the palladium to the terminal carbon.



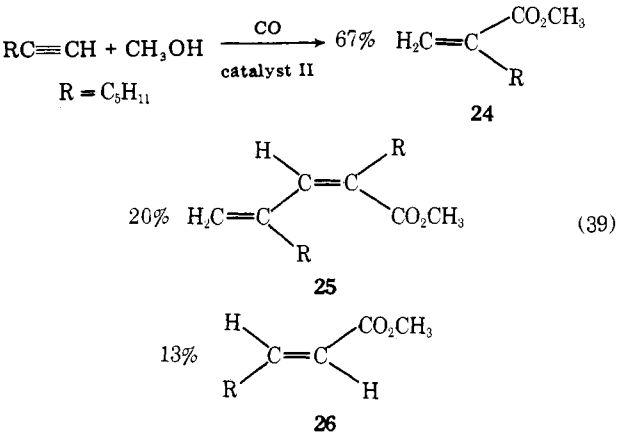
Any Scheme II mechanism in which the hydride displays the same regioselectivity[57-61] will thus produce, in preference to **22,** its isomer **23** with trans stereochemistry (reaction 38).



23

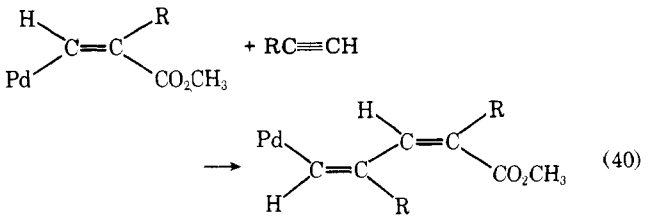
The fact that no **23** was detected argues strongly for a Scheme I mechanism, and also indicates that the regioselectivity of our $Pd-CO_2R$ species is analogous to that shown for Pd-H in reaction 37.

The selectivity of the carboalkoxypalladium species formed in our catalyst II system has been further examined by the use of methanol as substrate alcohol. Carbomethoxylation of an external acetylene is now the only possible reaction. With 1-heptyne (reaction 39), the products **24** and **25** resulting from



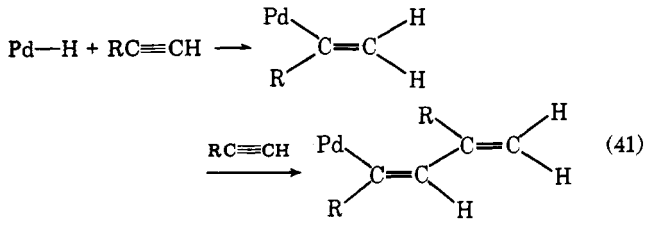
addition of palladium to the terminal carbon predominate, although some methyl 2-octenoate (**26**) is found as a minor product.

The doubly unsaturated ester **25** arises from insertion of a second 1-heptyne (reaction 40) into a Pd-vinyl bond of the



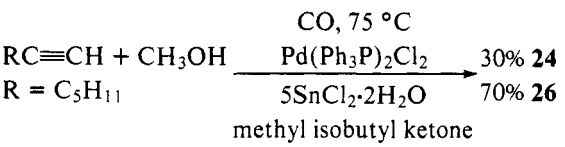
principal initial insertion product. This second insertion is analogous to those occurring in Pd-catalyzed acetylene trimerization,[24] with the palladium once again preferring the terminal carbon. A Scheme II mechanism, while it can account for the formation of **25,** can do so only by two consecutive uncharacteristic insertions, in each of which the palladium becomes attached to the substituted, more hindered, internal carbon (reaction 41).

We have also performed this reaction with the catalyst described by Knifton[11] (reaction 42). The regioselectivity is



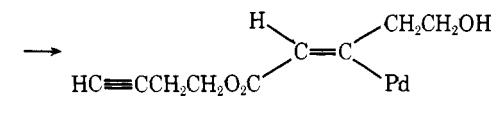
(41)

comparable to that reported[11] and opposite to that seen with our catalyst system II. These results confirm our conclusion that the active species in the Knifton system differs from that in system II, and are compatible with Knifton's suggestion of a Scheme II mechanism with $HPd(SnCl_3)(PPh_3)_2$ as the active catalyst in his system.[11]



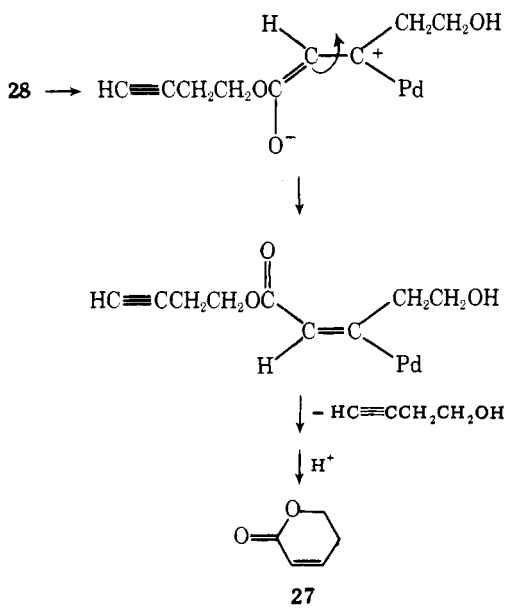
(42)

A Minor Puzzle Concerning a Minor Product. All reactions with 3-butyn-1-ol (**7b**) as substrate yield trace amounts of 5,6-dihydro-2-pyrone (**27**). Although the yield of **27** is at most 1% of that of α-methylene-γ-butyrolactone, it does not result from any impurities in the 3-butyn-1-ol. Neither reactions 32–35 nor any other Scheme I or Scheme II mechanism provide any obvious explanation. Some sort of trans addition, or cis–trans isomerization, is required. A possibility is the isomerization and transesterification process shown as reaction 44, $Pd—CO_2CH_2CH_2C{\equiv}CH + HC{\equiv}CCH_2CH_2OH$



(43)

28



(44)

after initial addition of the carboalkoxypalladium in the less favored direction to another substrate triple bond (reaction 43). Numerous authors,[62] most recently Canziani, Garlaschelli, and Malatesta,[62a] have proposed isomerizations similar to reaction 44. The above, admittedly speculative, mechanism is supported by the fact that larger amounts of **27** are found at high substrate concentrations.

Synthetic Implications of the Mechanism of Action of Catalyst II. The fact that we have been able to trap carboalkoxypalladium intermediates with 2.0 M 1-heptyne (reaction 36) suggests that the terminal acetylene of a second substrate molecule may also be able to compete with intramolecular insertion (reaction 34), forming species such as **28** and high polymers. Lower substrate concentrations should thus improve the yield of our catalytic cyclocarbonylation reactions with system II.

Table VI. Effect of Substrate Concentration on Yield with Catalyst System II[a]

entry	$[L_2Pd(Cl)SnCl_3]$, M	[**7b**], M	time, h	yield,[b] %
1[c]	0.003	0.056	3	91 (17)
2	0.004	0.30	3	97 (56)
3	0.004	0.56	3	80 (113)
4[d]	0.07	1.5	13	70 (16)
5	0.07	5.1	7	38 (40)

[a] Reaction conditions: P_{CO} = 7.8 atm, acetonitrile solvent, L = PPh_3. [b] By GLC. Figure in parentheses is number of turnovers per palladium. [c] P_{CO} = 5.1 atm. [d] L = PBu_3.

As Table VI shows, this approach proves successful with 3-butyn-1-ol. (It is unlikely that such considerations are as important in fused-ring cases as they are with substrates such as 3-butyn-1-ol, where the triple bond is unhindered and very effective as an external acetylene.) The advantages gained with dilution (decrease in polymer formation and increase in yield of methylene lactone) must, however, be balanced against the disadvantage of a decrease in rate (recall that reaction 31 is rate determining). As entries 2 and 3 in Table VI suggest, 0.3 M seems to be the highest concentration at which the yield remains virtually quantitative. Use of catalyst II with substrate at this concentration has proven effective for the cyclocarbonylation of many substrates in good yields, most notably 4-pentyn-1-ol, with which previous catalyst systems had given very poor results.[4]

Conclusions

With both system I and system II the cyclocarbonylation of ethynyl alcohols to methylene lactones proceeds through a carboalkoxypalladium intermediate, as in Scheme I, and not through a hydride as in Scheme II. Such carboalkoxy intermediates may be prepared by the addition of appropriate chloroformates to PdL_4, and they undergo intramolecular insertions of the triple bond as suggested. Under catalytic conditions the carboalkoxy intermediates may be trapped by terminal acetylene, with the stereochemistry of the products showing that the palladium becomes preferentially attached to the terminal carbon. As additional molecules of substrate are also terminal acetylenes capable of trapping the carboalkoxy intermediate, yields are greatly improved when the catalytic cyclocarbonylation reaction is run at concentrations below 0.3 M.

System I (PdI_2, Bu_3P, CH_3CN) has a low affinity for CO, and the rate under most conditions is thus first order in CO pressure and independent of substrate concentration. The trichlorostannyl ligand in system II ($PdCl_2$, $2Ph_3P$, $SnCl_2$, CH_3CN) labilizes the coordination sphere of the palladium, increasing the turnover rate, yield, and lifetime of the catalyst. The rate is independent of CO pressure and first order in substrate, the rate-determining step now being coordination of the substrate alcohol to the solvolyzed active catalyst, $[PdL_2(SnCl_3)(CH_3CN)]^+$. This permits the rapid uptake of CO and completion of the cyclocarbonylation reaction.

Experimental Section

Air-sensitive compounds were synthesized and handled under a nitrogen atmosphere using standard bench top techniques utilizing

airless glassware.[63] Nitrogen was purified by passage through a BASF oxygen scavenger and Linde 3A molecular sieves. Toluene, diethyl ether, hexane, and pentane were dried over Linde 3A molecular sieves (activated by heating to 250 °C under vacuum) and deoxygenated by bubbling dry nitrogen through them. Acetonitrile was dried over calcium hydride for 3 days, then distilled from phosphorus pentoxide under nitrogen and stored under nitrogen. Acetone was distilled from K_2CO_3 under nitrogen and then stored under a nitrogen atmosphere.

Tetrakis(triphenylphosphine)palladium(0),[64] $[(PPh_3)_2PdCl]_2^{2+}(BF_4^-)_2$,[53] and tetrabutylammonium trichlorostannate[65] were prepared by known procedures. Organic substrates, ligands, and metal salts were commercial products used without further purification.

Infrared spectra were obtained on a Perkin-Elmer 283 spectrophotometer. ^1H NMR spectra were obtained on a Varian A-60 spectrometer or a Varian XL-100 spectrometer. ^{31}P spectra were obtained on the Varian XL-100. Reactions were monitored, and analyzed by GLC on a Perkin-Elmer 3920 gas chromatograph with a thermal conductivity detector. Analytical GLC was done on an 8 ft × 1/4 in. aluminum column packed with 5% DEGS on Chromosorb PNAW, 60/80 mesh (column A), or on a 8 ft × 1/4 in. aluminum column packed with 5% CW20M on Chromosorb PNAW, 60/80 mesh (column B). Preparative GLC was done on an 8 ft × 3/8 in. aluminum column packed with the same stationary phase and support as column A (column C).

Cyclocarbonylation and Carbomethoxylation Apparatus. Reactions requiring a carbon monoxide atmosphere were carried out in the following apparatus. A brass cross-tee fitted with a stainless steel adapter was connected to a 6-oz Fischer-Porter pressure vessel, sealed by a Viton A O-ring. The cross-tee was also fitted with a ball valve in the arm directly above the pressure vessel (allowing addition of liquids and withdrawal of aliquots by syringe), with a needle valve connected to a carbon monoxide source and with a brass tee fitted with a pressure gauge and pressure release safety valve. Sequential use of the needle valve and the ball valve allowed flushing of the apparatus with carbon monoxide.

Isolation of the Butenolide 2a. The methylene lactone **1a**[3,4] (276 mg) was treated with 276 mg of $RhH(CO)(PPh_3)_3$[16,17] in 5 mL of dioxane for 5 days at room temperature under N_2, and then with 200 mg of $RhH(CO)(PPh_3)_3$ in 10 mL of dioxane for 60 h at 60 °C. Addition of diethyl ether produced a yellow precipitate. The filtrate was poured through 5 g of neutral alumina to ensure complete removal of catalyst and analyzed by GLC (column A, 160 °C). No **1a** remained, but there were two peaks of longer retention time. The peak of longest retention time was collected by preparative GLC (column C) and further purified by preparative TLC (silica gel, 80:20 benzene/EtOAc) to give an authentic sample of the known[66] butenolide **2a.**

Isomerization of 1a. A solution of 152 mg of **1a** and 92 mg of $Rh(CO)(H)(PPh_3)_3$ in 5 mL of dioxane was stirred at 25 °C for 48 h. GLC analysis of the products indicated the complete disappearance of **1a** and the production of the butenolide **2a**[66] which was identified by coinjection on two columns (columns A and B) with a characterized sample isolated as stated above.

Isomerization of 1b. In a manner similar to that for **1a,** 85 mg of **1b**[4] was stirred with 46 mg of $Rh(H)(CO)(PPh_3)_3$ in 5 mL of dioxane for 16 h. GLC analysis (column A) of the products indicated the complete disappearance of **1b** and the appearance of two product peaks. Preparative GLC (column C) resulted in the isolation of the known **2b** which was characterized by comparison with its reported spectra.[66]

α-Methylene-γ-butyrolactone-d_1 (11b-d_1). Four 50-mL flasks were fitted with serum caps and flushed with N_2, and each was then charged with 2 mL of D_2O. A 5% Et_2O solution of 3-butyn-1-ol (**7b**) was added by syringe to the first flask, which then was shaken vigorously. The flask was placed in a salt/ice bath, the water layer frozen, then the ethereal layer syringed off and transferred to the next flask. The final ethereal solution was placed over K_2CO_3 (anhydrous) under a N_2 atmosphere and distilled to yield 4 mL of **7b-d_1** which was >90% deuterated (by integration of the NMR).

To a solution of 0.67 mmol of palladium dichloride and 0.6 mmol of tri-*n*-butylphosphine in 20 mL of acetonitrile at 55 °C was added 29.2 mmol of 3-butyn-1-ol-d_1 (>90% deuterated by NMR). The resulting solution was stirred under 4.4 atm of carbon monoxide for 17 h. After that time the reaction solution was reduced in volume and passed through a 5 × 1 in. neutral alumina (grade I) column (250 mL of diethyl ether). The diethyl ether was removed in vacuo, resulting in 0.53 g of a yellow oil. Preparative GLC (column C, 160 °C) of that oil afforded 0.48 g of **11b-d_1** (17%). Integration of the ^1H NMR of the product indicated that it was 69% deuterated in the downfield proton of the exo methylene. Addition of 50 mg of $Eu(fod)_3$ to the NMR sample shifted the downfield resonance 2.62 times as much as the resonance of the undeuterated position, indicating that the deuterium had been incorporated in the exo methylene in the position cis to the carbonyl.

4-Trimethylsilyl-3-butyn-1-ol (7c). A 500-mL three-neck flask was equipped with a pressure-equalizing addition funnel and placed under a nitrogen atmosphere, then charged with 150 mL of 1.6 M *n*-butyllithium in hexane (240 mmol). To that solution was added dropwise at 0 °C 9 mL (119 mmol) of **7b** with vigorous stirring, the resulting solution being stirred for 9 h at room temperature. After that time, 240 mmol of trimethylsilyl chloride (0.5 M in pentane) was added to the solution over a period of 15 min; then the solution was stirred under a nitrogen atmosphere for 24 h. The flask was fitted with an air-powered stirrer and chilled to 0 °C, 120 mmol (100 mL, 0.12 M) of hydrochloric acid was added dropwise with stirring, and the resulting two-phase system was stirred vigorously at room temperature for 24 h to effect cleavage of the trimethylsilyl ether. The organic layer was then decanted. The water layer was saturated with ammonium chloride and extracted thoroughly (10 × 50 mL) with diethyl ether. The combined organic layers were dried over K_2CO_3. Volatiles were removed on a rotary evaporator to give a yellow oil that was distilled at reduced pressure affording 14.1 g of the known[68] **7c** (99 mmol, 83%): bp 65–67 °C (4 mm); ^1H NMR ($CDCl_3$) δ 0.13 (s, 9 H, $Si(CH_3)_3$), 1.94 (s, 1 H, OH), 2.52 (t, J = 6 Hz, 2 H, $\equiv CCH_2$), 3.80 (t, J = 6 Hz, 2 H, $-CH_2O$); IR (KBr) 3380 (br), 2182 (s), 1030, 840 cm^{-1}. Anal. ($C_7H_{14}OSi$) C, H.

3-Pentyn-1-yl Chloroformate (8a). Diethyl ether (100 mL) was placed in a three-neck 250-mL flask fitted with a pressure-equalizing dropping funnel equipped with a serum cap, a gas inlet tube (long enough so that it bubbled below the surface of the ether), and a drying tube loaded with Drierite. The outlet of the drying tube was connected by Tygon tubing to a backup trap and two bubblers connected in series and filled with saturated potassium hydroxide solution. The inlet tube was connected through a glass tee to a nitrogen source and to a phosgene source. The system was first purged with nitrogen, then, with nitrogen flowing, chilled to 0 °C by an ice bath. The nitrogen flow was stopped and phosgene introduced to the system at a flow rate sufficient to maintain slow bubbling in the second bubbler. Phosgene flow was maintained until the diethyl ether was saturated with it. (This was determined by observing the bubbling of the gas from the tip of the inlet tube.) Upon saturation of the solution the tip of the gas inlet tube was raised above the solution, the phosgene flow shut off, and the nitrogen flow resumed. Then 2.79 g (33.2 mmol) of **7a** was introduced to the dropping funnel by syringe through the serum cap and added dropwise to the solution with stirring. The solution was allowed to warm to room temperature and stirred under nitrogen overnight. The gas inlet tube was then lowered below the surface of the solution and the solution purged of phosgene by bubbling nitrogen for 4 h. The diethyl ether was then removed on the rotary evaporator and the resulting yellow liquid distilled at reduced pressure to afford 4.94 g (30.2 mmol, 91%) of **8a:** bp 95–97 °C (45 mmHg); ^1H NMR ($CDCl_3$) δ 1.80 (t, J = 3 Hz, $\equiv CCH_3$), 2.58 (m, 2 H, $-CH_2C\equiv$), 4.36 (t, J = 7 Hz, $-CH_2CO$); IR 2180, 1779, 1250, 1150 cm^{-1}. Anal. ($C_6H_7ClO_2$), C, H.

4-Trimethylsilyl-3-butyn-1-yl Chloroformate (8c). In a manner directly analogus to the procedure for **8a,** substituting **7c** for **7a,** 2.63 g (18.4 mmol) of **7c** afforded 3.34 g (16.3 mmol, 88%) of **8c:** bp 43–45 °C (0.02 mmHg); ^1H NMR ($CDCl_3$) δ 0.16 (s, 9 H, $\equiv CSi(CH_3)_3$), 2.80 (t, J = 7 Hz, 2 H, $\equiv CCH_2-$), 4.42 (t, J = 7 Hz, 2 H, $-CH_2O$); IR (neat) 2180, 1779, 1250, 1150 cm^{-1}. Anal. ($C_8H_{13}ClO_2Si$) C, H.

Bis(triphenylphosphine)(carbopent-3-yn-1-oxy)palladium(II) Chloride (9a). In a manner similar to that used by Otsuka to make other carboalkoxypalladium compounds,[34] 3-pentyn-1-yl chloroformate (**8a,** 2.9 mmol) was added to a solution of $Pd(Ph_3)_4$ in 20 mL of toluene at 80 °C under a nitrogen atmosphere and stirred for 4 h. The volume of the solution was reduced in vacuo and the product precipitated by the addition of 75 mL of hexane. The precipitate was filtered under nitrogen, recrystallized from toluene/hexane, washed with hexane, and dried for 12 h in vacuo yielding 0.61 g of **9a** (0.79 mmol, 88%) as pale yellow crystals: ^1H NMR ($CDCl_3$) δ 1.42 (t, J = 3 Hz, 3 H), 1.73 (m, 2 H), 3.07 (t, J = 7 Hz, 2 H); IR (CH_2Cl_2) 1660, 1096 cm^{-1}. Anal. ($C_{42}H_{37}ClO_2P_2$), C, H, Cl, P.

Bis(triphenylphosphine)[carbo(4-trimethylsilyl)-3-butyn-1-oxy]-palladium(II) Chloride (9c). Following exactly the procedure given for **9a**, 1.40 mmol of **8c** was reacted with 1.11 mmol of $Pd(PPh_3)_4$ in 25 mL of toluene at 80 °C for 4 h. The product was precipitated, recrystallized, and dried in vacuo to yield 0.91 g of **9c** (0.97 mmol, 88%) as pale yellow crystals: ^1H NMR ($CDCl_3$) δ 0.06 (s, 9 H, $SiMe_3$), 1.72 (t, J = 6 Hz, 2 H), 2.75 (t, J = 6 Hz, 2 H); IR (KBr) 2180, 1665 cm^{-1}. Anal. ($PdC_{44}H_{43}ClO_2P_2Si$) C, H, Cl.

In the far IR ν_{Pd-Cl} occurs at 332 cm^{-1}, a value which agrees well with those reported by Otsuka and co-workers for complexes $PdL_2(CO_2R)Cl$, made by the same method, to which they assign trans stereochemistry about Pd.[34] Furthermore, the pattern in the aromatic region of the ^1H NMR spectrum of **9a** and **9c** agrees with that said by Nelson and co-workers[47] to be characteristic of trans phenylphosphines on Pd. Complexes **9a** and **9c** are thus trans.

Vinyl Palladium Complex 10a. A solution of 0.97 mmol of **9a** in 0.80 mL of xylene was refluxed for 30 min, then filtered, all under a nitrogen atmosphere. To the filtrate was added 200 mL of hexane, yielding a precipitate that upon recrystallization from methylene chloride/hexane afforded 0.59 mmol (60%) of **10a:** ^1H NMR (C_6D_6) δ 1.48 (m, 2 H), 1.82 (m, 3 H), 3.39 (t, 2 H); IR (KBr) 1725, 1610 cm^{-1}; (CsI) 290 cm^{-1}. Anal. ($PdC_{42}H_{37}ClP_2O_2$) H, Cl; C: calcd, 64.9; found, 64.02.

Vinyl Palladium Complex 10b. To a solution of 0.53 mmol of **9c** and 0.346 g of dicyclohexyl-18-crown-6 in 10 mL of methylene chloride was added 1.8 g of KF (anhydrous) and the solution was then stirred for 6 h at room temperature. After that time the excess KF was removed by filtration and the filtrate passed through a 4 × ½ in. silica gel column (acetonitrile, 200 mL). The solvent was removed from the eluent in vacuo and the resulting solid was recrystallized twice from CH_2Cl_2/hexane and dried for 24 h in vacuo, affording 0.31 mmol (58%) of **6b** as white crystals: ^1H NMR (C_6D_6) δ 1.45 (m, 2 H), 3.20 (t, 2 H), 7.32 (tt, 1 H); IR (KBr) 1734, 1599 cm^{-1}, (CsI) 292 cm^{-1}. Anal. ($PdC_{41}H_{35}ClO_2P_2$), H, Cl; C: calcd, 64.5; found, 63.91.

The triplet of triplets at δ 7.32 corresponding to the vinyl proton has J = 7.0 and 2.0 Hz, the latter presumably due to splitting by the allylic protons. Thus $^3J_{P-H}$ = 7 Hz, for two equivalent phosphorus nuclei. On this basis, and on the evidence of the aromatic region of the ^1H NMR spectrum of **10a** and **10b**,[47] the stereochemistry about Pd is trans in both **10a** and **10b.**

IR examination of aliquots from the above reaction showed only **9c** and **10b.** However, when $KF{\cdot}2H_2O$ was used instead of KF in the cleavage reaction, IR examination of aliquots showed the formation and disappearance (in a few hours at room temperature) of the intermediate **9b,** identified by its characteristic acetylenic ν_{C-H} at 3300 cm^{-1}.

α-[(*E*)-Ethylidene]-γ-butyrolactone (11a) from 10a. A solution of 0.13 mmol of **10a,** 45 mg of tetramethylammonium chloride, and 2 mL of CF_3CO_2H in 20 mL of benzene was refluxed for 48 h. The solvent was then removed in vacuo and the products were redissolved in a minimum of methylene chloride along with 13.5 mg of naphthalene. GLC analysis (column A, 160 °C), with subsequent preparative GLC (column C, 160 °C) of the sole organic product detectable by GC, and characterization of that product by ^1H NMR and IR indicated a 45% (0.06 mmol) yield of the known[69] **11a.**

α-Methylene-γ-butyrolactone (11b) from 10b. A solution of 134 mg of **10b** in 2 mL of methylene chloride and 2 mL of CF_3CO_2H was stirred for 30 min at room temperature. Solvent was removed in vacuo and the residue redissolved in methylene chloride after addition of 4.0 mg of naphthalene. GLC analysis (column A, 160 °C) indicated a yield of 32% **11b** from **10b.**

Kinetics. Catalyst System I. In a typical run the apparatus described above was first charged with 0.18 mmol of palladium diiodide, 0.18 mmol of tri-*n*-butylphosphine, and 1.105 mmol of naphthalene (as an internal GLC standard). The apparatus was then flushed twice with carbon monoxide, 5.8 mL of CH_3CN added by syringe through the ball valve, the apparatus flushed with carbon monoxide again, and the solution stirred under 3.7 atm of carbon monoxide at 60 °C until completely homogeneous (ca. 1 h). To that deep red solution was then added 11.1 mmol of 3-butyn-1-ol by syringe. Starting from that time aliquots (30–50 μL) were withdrawn by syringe every 0.5 h for 3 h and analyzed by GLC (column A, 160 °C). After the removal of each aliquot the apparatus was flushed with carbon monoxide and repressurized to 3.7 atm. After 3 h, aliquots were taken each 1 h for the next 5 h. Final aliquots were taken at t = 12 h and t = 29 h. The analysis of the data consisted of converting the number of millimoles of **11b** detected by GLC into turnovers of substrate per palladium and plotting that number vs. reaction time, yielding a graph such as Figure 1.

Chloro(trichlorostannyl)bis(triphenylphosphine)palladium(II) (15). A mixture of 0.6 mmol of palladium dichloride, 0.6 mmol of anhydrous stannous chloride, and 1.2 mmol of triphenylphosphine in 100 mL of acetonitrile was stirred for 12 h at 75 °C under a nitrogen atmosphere. Removal of 75 mL of solvent in vacuo followed by addition of 250 mL of diethyl ether resulted in the precipitation of a yellow, crystalline solid. Recrystallization from CH_2Cl_2/hexane afforded 490 mg (92%) of bright yellow crystals of **15:** IR (CsI) 1475, 1430, 1090, 335, 320, 310 (sh) cm^{-1}. Anal. ($PdC_{36}H_{30}Cl_4P_2Sn$) C, H, Cl.

Kinetics of System II. These studies were carried out using the same apparatus and basic method as for system I. In a typical experiment, 0.059 mmol of anhydrous stannous chloride, 0.62 mmol of naphthalene, and 0.118 mmol of triphenylphosphine were stirred under 6.4 atm of carbon monoxide in 15.6 mL of acetonitrile at 75 °C until the solution was homogeneous. To this solution was added by syringe 4.8 mmol of 3-butyn-1-ol. Using that point as t = 0, aliquots were removed every 5 min for 45 min and analyzed for **11b** and starting material by GLC (column A, 160 °C, after an initial 4 min at 140 °C). After each aliquot was removed the system was flushed with carbon monoxide and repressurized. After 45 min, aliquots were taken and analyzed at appropriate intervals for 2.25 h.

Cyclocarbonylation of 7b Catalyzed by [17 + 2SnCl$_2$]. A solution of 0.016 mmol of $[(Ph_3P)_4Pd_2Cl_2]^{2+}(BF_4^-)_2$, 0.032 mmol of anhydrous stannous chloride, and 0.15 mmol of naphthalene (as a GLC standard) in 5.6 mL of acetonitrile was stirred for 2 h under 7.8 atm of carbon monoxide at 75 °C. To that solution was then added 1.7 mmol of 3-butyn-1-ol. The rate of reaction was determined as above. The results are in Table IV.

Cyclocarbonylation of 7b Catalyzed by [17 + 2 Equiv of Tetramethylammonium Trichlorostannate]. A solution of 0.016 mmol of **17,** 0.032 mmol of tetramethylammonium trichlorostannate, and 0.34 mmol of naphthalene in 5.9 mL of acetonitrile was stirred for 2 h under 7.8 atm of carbon monoxide at 75 °C. To that solution was added 1.8 mmol of 3-butyn-1-ol. The rate of reaction was determined as stated above. The results are in Table IV.

Cyclocarbonylation of 7b Catalyzed by [17 + 2 Equiv of Anhydrous Stannous Chloride + 2 Equiv of Tetrabutylammonium Chloride]. A solution of 0.016 mmol of **17,** 0.032 mmol of anhydrous stannous chloride, and 0.34 mmol of naphthalene in 6.1 mL of acetronitrile was stirred for 2 h at 75 °C under 7.8 atm of carbon monoxide. To that solution was added 0.032 mmol of tetrabutylammonium chloride, the reaction vessel repressurized, and the solution stirred for 5 min. To that solution was then added 1.9 mmol of 3-butyn-1-ol and the vessel repressurized to 7.8 atm. The rate of reaction was determined as stated above. The results are in Table IV.

Conductivity Measurements. Conductivity measurements were made with a Beckmann conductivity cell (K = 0.500) and a Barnstead conductivity bridge. The cell was placed inside a 34/45 mm vacuum trap with the leads threaded through a septum on the head of the trap. The side arm of the trap was connected to a vacuum rack to allow purging with nitrogen. Carbon monoxide, when used, was introduced by a syringe needle through the septum. Measurements of the catalyst mixture were taken at 60 °C to simulate reaction conditions. The conductivity of a 3.75 × 10^{-4} M solution of tetrabutylammonium bromide was determined as a calibration of the system. The results are presented in Table III.

Cyclocarbonylation of 7b by System II in the Presence of Added 1-Heptyne. To a carbon monoxide saturated solution of 0.58 mmol of $PdCl_2$, 1.16 mmol of triphenylphosphine, 0.58 mmol of anhydrous stannous chloride, and 2.12 g of 1-heptyne in 8 mL of acetonitrile was added 14 mmol of **7b** and that solution stirred at 75 °C under 7.8 atm of carbon monoxide for 17 h. The reaction solution was then reduced in volume and passed through a 5 × 1 in. Forisil column (300 mL of Et_2O). The solvent was removed in vacuo from the eluent and analyzed by GLC (column A). The two observed products were separated by preparative GLC (column C) and identified as **11b** and the acrylic ester **22:** ^1H NMR ($CDCl_3$) δ 0.7–1.5 (m, 11 H), 1.85 (t, J = 6 Hz, 2 H), 5.48–5.65 (m, 1 H), 6.10–6.30 (m, 1 H); IR (CH_2Cl_2) 3300, 2120, 1750, 1630 cm^{-1}. Anal. ($C_{12}H_{18}O_2$) C, H. In a separate experiment, under conditions identical with the above, a solution equimolar in 1-heptyne and 3-butyn-1-ol gave a 35% yield (by GLC) of each.

5,6-Dihydro-2-pyrone (27). To a carbon monoxide saturated solution of 0.68 mmol of palladium dichloride, 0.68 mmol of anhydrous stannous chloride, and 1.36 mmol of tri-*n*-butylphosphine in 5 mL of ac-

etonitrile at 75 °C was added 23.2 mmol of 3-butyn-1-ol and that solution stirred for 16 h at 75 °C under 7.8 atm of carbon monoxide. The reaction solution was then reduced in volume and passed through a 5 × ½ in. silica gel column (250 mL of Et_2O). The diethyl ether was removed from the eluent in vacuo. The resulting yellow oil was largely **11b,** but preparative GLC (column C) permitted the isolation of 0.41 mmol of the known[70] **27.**

Destruction of 1a by Knifton Catalyst System. A solution of 0.26 mmol of bis(triphenylphosphine)palladium dichloride, 1.0 mmol of stannous chloride dihydrate, and 2.5 mL of methanol in 35 mL of methyl isobutyl ketone was stirred for 3 h at 75 °C under 7.8 atm of carbon monoxide. The pressure was briefly released, 118 mg of **1a** added, and the solution stirred for 20 h at 75 °C under 7.8 atm of carbon monoxide. The reaction mixture was reduced in volume and passed through a 6 × ½ in. silica gel column (300 mL of Et_2O). The diethyl ether was removed on a rotary evaporator. The resulting yellow oil was analyzed by NMR, which showed that all of the starting **1a** had been destroyed. GLC analysis (column A, 190 °C) revealed three products in approximate ratio of 5:4:1. The second most prominent peak coinjected on two columns (columns A and B) with **2a** isolated from the isomerization of **1a** by $Rh(H)(CO)(PPh_3)_3$.

Carbomethoxylation of 1-Heptyne by Knifton Catalyst System. A solution of 0.16 mmol of bis(triphenylphosphine)palladium dichloride, 0.79 mmol of stannous chloride dihydrate, and 1.8 mL of methanol in 21 mL of methyl isobutyl ketone was stirred for 3 h at 75 °C under 7.8 atm of carbon monoxide. Then 3.5 mmol of 1-heptyne was added to the solution and reacted at 75 °C under 7.8 atm of carbon monoxide for 16 h. Solvent was removed and the reaction mixture passed through a 4 × ½ in. Florisil column (500 mL of 50:50 Et_2O/acetone). The eluent was reduced in volume and the products were isolated by preparative GLC (column C, 180 °C). Two products, **24** and **26,** were isolated (0.79 mmol of **24** and 1.86 mmol of **26,** 3:7). The known methyl octenoate **26** was characterized by comparison of its NMR and IR spectra with reported values.[71] The only other product was the 2-substituted methyl acrylate **24:** NMR ($CDCl_3$) δ 0.8–1.6 (m, 9 H), 2.22 (m, 2 H, allylic CH_2), 3.67 (s, 3 H, OCH_3), 5.45 (m, 1 H, vinyl H trans to carbomethoxy group and cis to alkyl chain), 6.05 (m, 1 H, vinyl H cis to carbomethoxy); IR (neat) 1735, 1630 cm^{-1}. Anal. ($C_9H_{16}O_2$), C, H.

Carbomethoxylation of 1-Heptyne with System II. To a carbon monoxide saturated solution of 0.515 mmol of palladium dichloride, 0.515 mmol of anhydrous stannous chloride, and 1.03 mmol of triphenylphosphine in 10 mL of acetonitrile were added 20.1 mmol of 1-heptyne and 19 mmol of anhydrous methanol. This solution was stirred for 16 h at 75 °C under 7.8 atm of carbon monoxide. Then the solution was removed from the apparatus, reduced in volume on a rotary evaporator to ca. 5 mL, and passed through a 6 × 1 in. Florisil column (500 mL of Et_2O). The eluent was reduced in volume, then the products, **24** (3.6 mmol), **25** (1.0 mmol), and **26** (0.7 mmol), were isolated by preparative GLC (column C, 180 °C).

The new unsaturated ester **25** was tentatively identified by NMR and IR. NMR ($CDCl_3$): δ 0.9–1.8 (m, 22 H, alkyl side chains), 3.67 (s, 3 H, OMe), 5.43 (m, 1 H, vinyl H (geminal)), 6.03 (m, 1 H, vinyl H (geminal)), 6.77 (m, 1 H, vinyl H of trisubstituted double bond trans to carbomethoxy). The assignment of the geminal protons was by their nearly exact correspondence to the pattern and chemical shift of the geminal vinyls in **26.** The assignment of trans stereochemistry about the trisubstituted double bond with respect to the carbomethoxy group was based on the correspondence of the chemical shift of that multiplet (6.77 ppm) with that calculated (6.56 ppm) for such a vinyl from standard tables;[72] the chemical shift calculated for cis stereochemistry is 7.05 ppm.

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$$C_L = C_g\alpha\frac{(3.66 \times 10^{-3})}{T}$$

C_L is [CO] in mol/L in solution and C_g is the [CO] in mol/L in atmosphere above the solution.
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Enthalpies of Formation and Solution of Macrocyclic and Noncyclic Tetraaza Ligands. Origins of the Enthalpy Term in the Macrocyclic Effect

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Abstract: The heats of combustion of 1,4,8,11-tetraazacyclotetradecane and 1,4,8,11-tetraazaundecane have been determined by bomb calorimetry and the standard enthalpies of formation derived (-27.7 ± 0.5 and -23.9 ± 0.5 kcal mol^{-1}, respectively). The enthalpies of solution of the same two compounds have been determined (-2.5 and -15.8 kcal mol^{-1}, respectively) in 0.5 M NaOH. The gas-phase $\Delta H_f°$ values of the ligands have been estimated and the macrocyclic enthalpy term, which has been determined previously for both Cu(II) (-4.7 kcal mol^{-1}) and Ni(II) (-4.9 kcal mol^{-1}) with these ligands, has been compared with the estimated difference in solvation energies of the two ligands (4.6 kcal mol^{-1}). A general discussion on the terms contributing to the macrocyclic enthalpy is presented.

Introduction

The macrocyclic effect, in which the stability of metal complexes is enhanced by coordination to macrocyclic as opposed to analogous noncyclic ligands, was first reported in 1969.[3] Since then, a great deal of interest has been shown in the thermodynamic origins of this extra stability, particularly with tetraaza ligands. Early conflicting studies assigned the extra stability to wholly entropy[4] or wholly enthalpy[5] terms based on enthalpy values obtained from temperature-dependent stability constant studies. More recently,[6-9] direct calorimetric determinations of enthalpy values have shown that the entropy term is always favorable and that the enthalpy term is dependent on the matching of the size of the macrocyclic ligand aperture to that of the metal ion. For octahedral complexes of copper(II) and nickel(II) with the title ligands L_1 and L_2, ΔH values for the metathetical reaction

$$ML_2(aq)^{2+} + L_1(aq) \rightarrow ML_1(aq)^{2+} + L_2(aq) \quad (1)$$

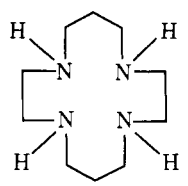
which represents the macrocyclic effect are -4.7[8] and -4.9[9] kcal mol^{-1}, respectively.

Calorimetrically one determines the enthalpy change associated with the formation reaction

$$M^{2+}(aq) + L(aq) \rightarrow ML^{2+}(aq) \quad (2)$$

and the difference between these enthalpy values for different ligands (L_1 and L_2) gives the macrocyclic enthalpy associated with reaction 1. It can therefore be seen that this macrocyclic enthalpy contains terms associated with *both* the metal complexes *and* the free ligands in solution.

If there is no enthalpy difference between the free ligands in solution, the macrocyclic enthalpy is only a measure of the energy difference between the macrocyclic and the noncyclic



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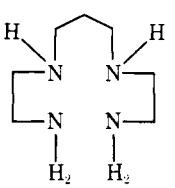

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