Acylpalladation of Internal Alkynes and Palladium-Catalyzed Carbonylation of (*Z*)-β-Iodoenones and Related Derivatives Producing γ-Lactones and γ-Lactams†

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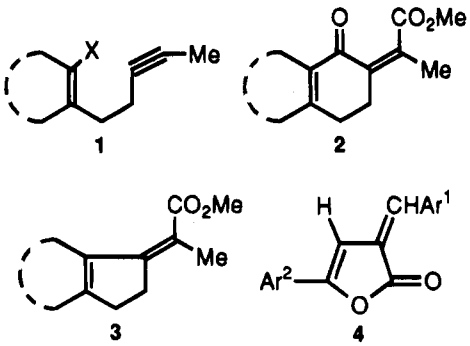
Received December 19, 1994®

Abstract: The reaction of either an internal alkyne−organic halide mixture or (*Z*)-β-iodoenones with CO in the presence of a Pd−phosphine catalyst, *e.g.*, $Cl_2Pd(PPh_3)_2$, can give one of the three discrete types of compounds as the major products depending on the substrate structure and the reaction conditions. Those substrates which are convertible to (*Z*)-γ-oxo-α,β-unsaturated acylpalladium derivatives lacking δ-H atoms are converted to the corresponding 2-butenolides (**13**) in the presence of water, which serves as a H donor. Carbon monoxide most likely is the source of two electrons. Either in the absence of water (or any other suitable H source) or in the presence of some factors disfavoring the butenolide formation, the same reaction gives the corresponding dimeric product (**16**). Even in cases where there is an α-H atom in the α-substitutent, 1,4-elimination products (**11**), reported to be the major products in a related Pd-catalyzed reaction of terminal alkyne−aryl iodide mixtures with CO, were not detected. In sharp contrast, those substrates which can give rise to (*Z*)-γ-oxo-α,β-unsaturated acylpalladium derivatives containing δ-H atoms give, under comparable reaction conditions, enol lactones (**12**), *i.e.*, (*Z*)-3-alkylidene-2-butenolides, contaminated with only very minor amounts of **22** even in cases where an excess (4 equiv) of water was present. The required (*Z*)-β-iodoenones can be readily prepared in one pot via $ZrCp_2$-promoted cyclization of alkynes with nitriles. The ready availability of the starting compounds and the high *Z* stereoselectivity make the overall sequence an attractive synthetic route to **12**. The courses of the Pd-catalyzed carbonylation reactions of (*Z*)-β-iodo-α,β-unsaturated imines **23** closely parallel the reactions of enones and produce the corresponding lactams, *i.e.*, **24** and **25**.

Over the past decade, acylpalladation[1] of alkenes[2] has been developed as a useful method for preparing cyclic compounds.[3,4] In our own studies, three competitive acylpalladation reactions which are thought to proceed as shown in Scheme 1 have been discovered and developed.[3]

On the other hand, relatively little is known about acylpalladation of alkynes.[5] We have recently found that, under Pd-catalyzed carbonylation conditions in the presence of MeOH,[3b] **1** does not produce **2**.[6] The only monomeric cyclization product was **3**, the formation of which does not involve acylpalladation. A Pd-catalyzed carbonylation reaction of a special class of terminal alkynes, *i.e.*, benzylethynes, with aryl iodides was recently reported to give **4**.[7] This reaction however is thought



to proceed not via acylpalladation but via 1-benzyl-2-benzoylethynes formed by Pd-catalyzed carbonylative coupling. Thus, the feasibility of acylpalladation of alkynes has remained undemonstrated.[8]

In order to probe the feasibility of acylpalladation of alkynes, we chose to investigate the reaction of internal alkynes with organic halides, *e.g.*, iodides, and CO in the presence of catalytic amounts of Pd−phosphine complexes, *e.g.*, $Pd(PPh_3)_4$. One crucial question to be answered was whether or not acylpalladium species that can be generated *in situ* via oxidative addition of organic halides to Pd followed by CO insertion would

†Presented in a preliminary form at IUPAC Symposium OMCOS-7 in Kobe, Japan, September 1993.

® Abstract published in *Advance ACS Abstracts,* March 1, 1995.

(1) Acylpalladation may be defined as addition of acylpalladium bonds to alkenes and alkynes.

(2) For earlier papers on polymerization via acylpalladation, see: (a) Tsuji, J.; Hosaka, S. *J. Polym. Lett.* **1965**, *3*, 705. (b) Sen, A.; Lai, T. *J. Am. Chem. Soc.* **1982**, *104*, 3520.

(3) (a) Negishi, E.; Miller, J. A. *J. Am. Chem. Soc.* **1983**, *105*, 6761. (b) Tour, J. M.; Negishi, E. *J. Am. Chem. Soc.* **1985**, *107*, 8289. (c) Negishi, E.; Tour, J. M. *Tetrahedron Lett.* **1986**, *27*, 4869. (d) Negishi, E.; Sawada, H.; Tour, J. M.; Wei, Y. *J. Org. Chem.* **1988**, *53*, 913. (e) Zhang, Y.; O'Connor, B.; Negishi, E. *J. Org. Chem.* **1988**, *53*, 5588. (f) Negishi, E.; Wu, G.; Tour, J. M. *Tetrahedron Lett.* **1988**, *29*, 6745. (g) Wu, G.; Shimoyama, I.; Negishi, E. *J. Org. Chem.* **1991**, *56*, 6506.

(4) For related papers by other workers, see: (a) Brewis, S.; Hughes, P. R. *J. Chem. Soc., Chem. Commun.* **1965**, 489. (b) Oppolzer, W.; Keller, T. H.; Bedoya-Zurita, M.; Stone, C. *Tetrahedron Lett.* **1989**, *30*, 5883. (c) Oppolzer, W. *Pure Appl. Chem.* **1990**, *62*, 1941. (d) Oppolzer, W.; Keller, T. H.; Kuo, D. L.; Pachinger, W. *Tetrahedron Lett.* **1990**, *31*, 1265. (e) Oppolzer, W.; Xu, J.; Stone, C. *Helv. Chim. Acta* **1991**, *74*, 465. (f) Ihle, N. C.; Heathcock, C. H. *J. Org. Chem.* **1993**, *58*, 560. (g) For related Ni-catalyzed carbonylative cyclization, see: Camps, F.; Coll, J.; Llebaria, A.; Moretó, J. M. *Tetrahedron Lett.* **1988**, *29*, 5811. Camps, F.; Coll, J.; Moretó, J. M.; Toras, J. *J. Org. Chem.* **1989**, *54*, 1969. Llebania, A.; Camps, F.; Moretó, J. M. *Tetrahedron Lett.* **1993**, *44*, 1283.

(5) Related studies with Pd and Rh complexes. (a) Pd: Tsuji, J.; Nogi, T. *J. Am. Chem. Soc.* **1966**, *88*, 1289. (b) Rh: Hong, P.; Mise, T.; Yamazaki, H. *Chem. Lett.* **1981**, 989. (c) Rh: Doyama, K.; Joh, T.; Onitsuka, K.; Shiohara, T.; Takahashi, S. *J. Chem. Soc., Chem. Commun.* **1987**, 649.

(6) Zhang, Y.; Negishi, E. *J. Am. Chem. Soc.* **1989**, *111*, 3454.

(7) Huang, Y.; Alper, H. *J. Org. Chem.* **1991**, *56*, 4534.

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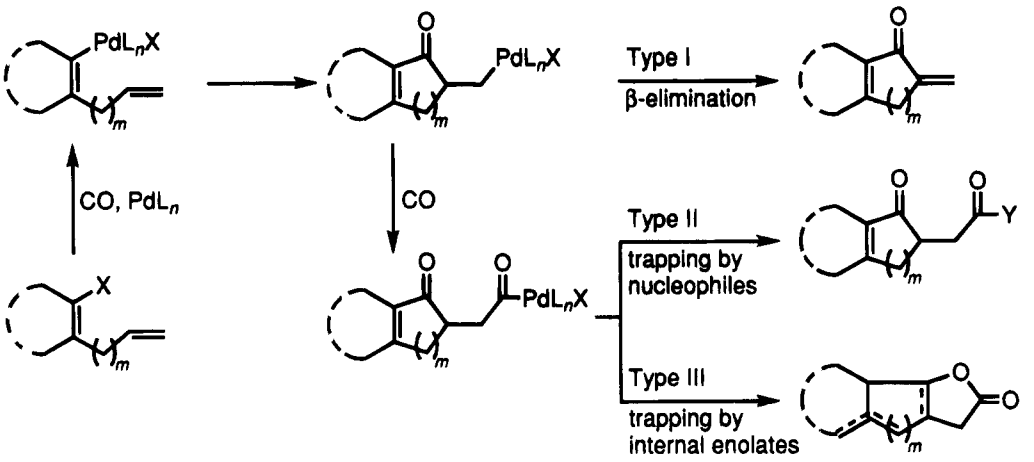
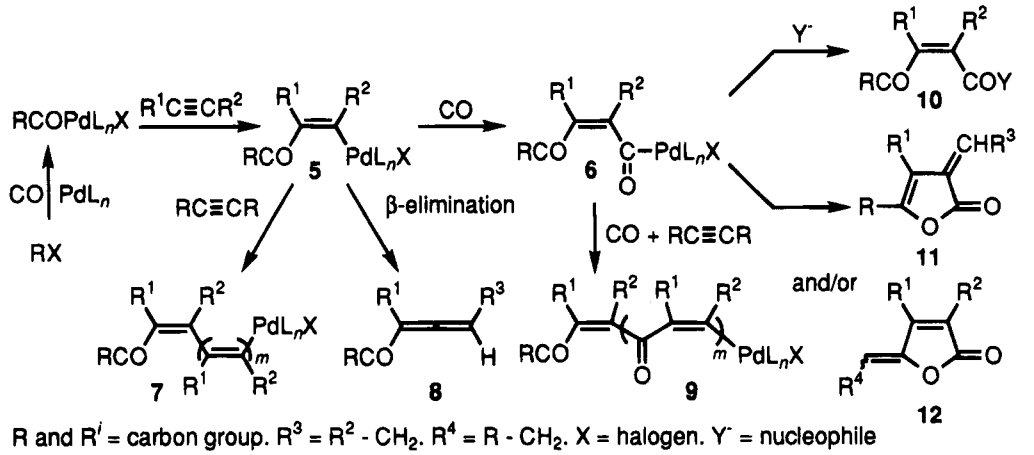
Scheme 1



Scheme 2



R and R^i = carbon group. R^3 = R^2 - CH$_2$. R^4 = R - CH$_2$. X = halogen. Y$^-$ = nucleophile

undergo acylpalladation to give **5**. If **5** could indeed be generated, it could then undergo insertion of the second molecule of CO to produce **6**. Alternatively, **5** could also be converted to oligo- and polyacetylenes (**7**) via cascade carbopalladation.[6,9] In cases where **5** contains a β-hydrogen which can be *syn*-coplanar with Pd, their dehydropalladation could give acylallenes **8**. However, our recent results[6,9] indicate that such a process is generally unfavorable. More likely under the carbonylation conditions is a polymerization process producing **9**, in which acylpalladation and CO insertion take place alternately. In order to obtain monomeric products via **6**, it would have to be trapped by external or internal nucleophiles including enolates[3c,g,10] to produce **10**–**12** (Scheme 2). Trapping by other reagents, such as alkenes, is also conceivable.

Results and Discussion

With the goal of obtaining monomeric compounds via **6**, we initially attempted trapping of such intermediates by alcohols to produce **10**. However, the reaction of iodobenzene with 4-octyne (1 equiv) and CO (1–40 atm) in the presence of 5 mol % of $Cl_2Pd(PPh_3)_2$, MeOH (4 equiv), and NEt_3 (1.5–2 equiv) in benzene or DMF at 100 °C merely gave methyl benzoate in 80–100% yields without incorporation of 4-octyne. The use of hydroxy-containing alkynes, *i.e.*, 3-pentyn-1-ol and *o*-((trimethylsilyl)ethynyl)phenol, in place of a combination of 4-octyne and MeOH also led to the formation of the corresponding esters in 85–100% yields.[11] We conclude that alcoholysis of acylpalladium species is generally faster than intermolecular acylpalladation of alkynes[12] to produce **5**.

Interestingly, the reaction of 4-octyne with PhI and CO (10–40 atm) in the absence of any alcohol under otherwise comparable conditions as above, *i.e.*, in the presence of 5 mol % of $Cl_2Pd(PPh_3)_2$ and NEt_3 (2 equiv) in DMF at 100–140 °C for 12–24 h, gave **13a** in varying yields. This product contains two more hydrogen atoms than the corresponding **11** or **12**. The use of an internal alkyne, *i.e.*, 4-octyne, precludes the mechanism involving carbonylative cross coupling proposed for the reaction of terminal alkynes.[7] On the other hand, those that proceed via **5** and **6** appear plausible, even though the presumed conversion of **6a** (R = Ph, R^1 = R^2 = *n*-Pr) into **13a** requiring incorporation of an external hydrogen atom presents a puzzle to be solved. The intermediacy of **6** was strongly supported by conversion of **14a**[13] into **13a** in nearly quantitative yield under essentially the same conditions as those mentioned above.

(8) In our concurrent study on cyclic carbopalladation of alkynes, we have recently observed a few examples of cyclic acylpalladation of alkynes [Sugihara, T.; Copéret, C.; Owczarezyk, Z.; Harring, L. S.; Negishi, E. *J. Am. Chem. Soc.* **1994**, *116*, 7923].

(9) (a) Zhang, Y.; Wu, G.; Agnel, G.; Negishi, E. *J. Am. Chem. Soc.* **1990**, *112*, 8590. (b) Negishi, E. *Pure Appl. Chem.* **1992**, *74*, 323.

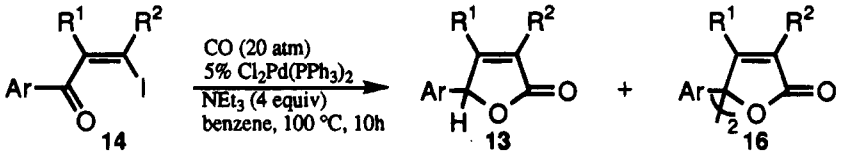
(10) (a) Roberto, D.; Catellani, M.; Chiusoli, G. P. *Tetrahedron Lett.* **1988**, *29*, 2115. (b) Negishi, E.; Zhang, Y.; Shimoyama, I.; Wu, G. *J. Am. Chem. Soc.* **1989**, *111*, 8018. (c) Shimoyama, I.; Zhang, Y.; Wu, G.; Negishi, E. *Tetrahedron Lett.* **1990**, *31*, 2841. (d) Uozumi, Y.; Mori, E.; Mori, M.; Shibasaki, M. *J. Organomet. Chem.* **1990**, *399*, 93. (e) Negishi, E.; Copéret, C.; Sugihara, T.; Shimoyama, I.; Zhang, Y.; Wu, G.; Tour, J. M. *Tetrahedron* **1994**, *50*, 425.

(11) These experiments were performed by Y. V. Gulevich in our laboratories.

(12) For some rare examples of intramolecular acylpalladation of alkynes followed by alcoholysis, see ref 8.

(13) Takahashi, T.; Kageyama, M.; Denisov, V.; Hara, R.; Negishi, E. *Tetrahedron Lett.* **1993**, *34*, 687.

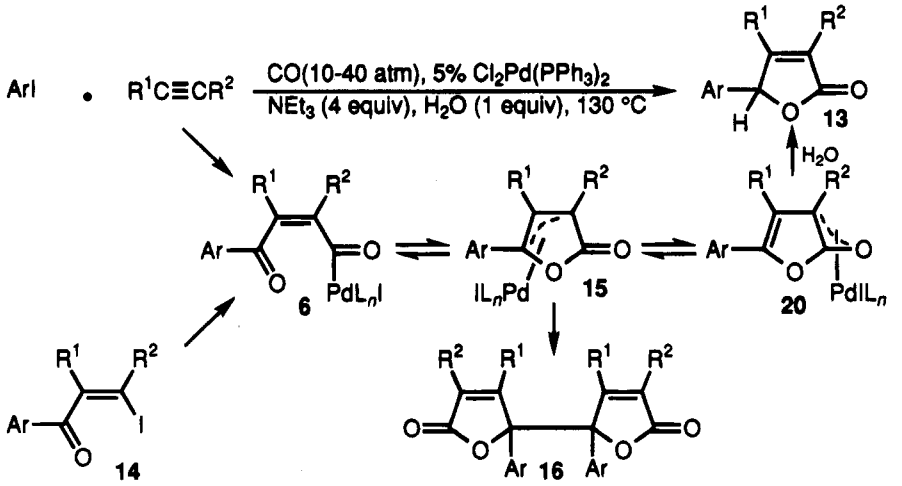
Table 1. Pd-Catalyzed Carbonylation of (*Z*)-β-Iodoalkenyl Aryl Ketones in the Presence of a Base[a]



	β-iodoenone				monomer		dimer	
	Ar	R^1	R^2	base	**13**	yield,[b,c] %	**16**	yield,[b] %
14a	Ph	*n*-Pr	*n*-Pr	NEt_3	**13a**	99	**16a**	<1
14a	Ph	*n*-Pr	*n*-Pr	K_2CO_3	**13a**	<1	**16a**	53
14c	Ph	Ph	Ph	NEt_3	**13c**	55	**16c**	<1
14d	*p*-Tol	H	*p*-$TolCH_2$	NEt_3	**13d**	49	**16d**	<5

[a] All reactions were run using 20 atm of CO, 5 mol % of $Cl_2Pd(PPh_3)_2$, and 4 equiv of a base at 100 °C for 10 h. [b] By NMR spectroscopy. [c] In each case, **11** was not detected (<2–3%) except in the reaction of **14d** in the presence of $NaHCO_3$ where **11d** was formed in 3% yield.

Scheme 3



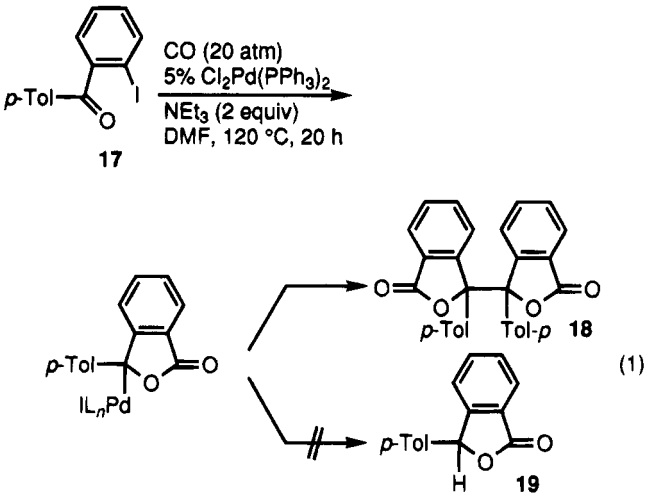
Having established the interchangeability between a 4-octyne–PhI mixture and **14a**, further mechanistic studies were conducted mainly with **14**, whose reaction was cleaner (Table 1). It is striking that the putative intermediate **6a** did not suffer from its trapping by an internal enolate to give **11a** (R = Ph, R^1 = *n*-Pr, R^3 = Et) in a detectable yield.[3c] One likely path may involve conversion of **6a** into **15a** (Scheme 3). Transformations similar to that of **6a** into **15a** have been implicated in both stoichiometric and catalytic reactions involving Rh,[5b,c] Co,[14a] and Ni.[14b,c]

In search for the source of H required for the presumed conversion of **15** into **13**, bis(α,α-dideuteriobenzyl)ethyne was prepared. This acetylene and *m*-tolyl iodide produced a tetradeuterio derivative of **13b** in 35% yield under otherwise the same conditions as before without a sign of detectable H–D scrambling. Furthermore, the reaction of **14c** gave **13c** in 55% NMR yield, which conclusively demonstrated that the formation of **13** does not require the presence of H in the allylic position of the β-substituent in **14**. This, in turn, rules out the possibility that **13** might arise via **11**. Conversion of **14a** into **13a** was also achieved in a comparable yield in benzene (95–99%) instead of DMF, indicating that neither of these solvents is responsible for the γ-H of **13a**. Tertiary amines containing α-hydrogen atoms, *e.g.*, NEt_3, are known to reduce Pd(II) complexes via α-H abstraction.[15] We therefore prepared $PhCD_2NEt_2$ and used it in place of NEt_3 in the conversion of **14a** and **13a**, but there was no indication of D incorporation into **13a**. Futhermore, the use of pyridine, which does not contain a readily abstractable α-H atom, led to the formation of **13a** in 59% yield. Highly informative was the reaction of **14a** carried out using K_2CO_3 in place of NEt_3, which produced **16a** (Ar = Ph, R^1 = R^2 = *n*-Pr) in 53% yield and only a trace quantity, if any, of **13a**. Since K_2CO_3 is a known dehydrating agent, adventitious water was suspected as the source of hydrogen.[5c] We therefore treated **14a** with CO (14 atm) in the presence of 2 equiv of NEt_3, 5 mol % of $Cl_2Pd(PPh_3)_2$, and *4 equiv of* D_2O. The expected product **13a** produced in 96% yield was ca. 85% deuterated in the γ position. These results prompted us to rerun the initial experiment for the conversion of 4-octyne and PhI to **13a** in the presence of 1 equiv of added water. As expected, the yield of **13a** was significantly improved to 66%. Although certain C–Pd bonds, *e.g.*, acyl–Pd, are known to be hydrolyzed,[16] it must be a relatively slow process which does not usually compete with a variety of known Pd-catalyzed reactions[3,4,7,8] in cases where a limited amount of H_2O is present. On this basis, the high sensitivity of the reaction producing **13** to H_2O is somewhat puzzling, even though the C–Pd bond in **15** is simultaneously allylic, benzylic, and α-acyloxy substituted. In this connection, the reaction of **17** is informative. Its carbonylation with CO (20 atm), in the presence of 5 mol % of $Cl_2Pd(PPh_3)_2$, 4 equiv of H_2O, and 2 equiv of NEt_3 in benzene at 100 °C for 20 h, gave **18** in 94% yield as a 1:1 mixture of the two possible diastereomers without producing **19** (eq 1).

(14) (a) Krafft, M. E.; Pankowski, J. *Tetrahedron Lett.* **1990**, *31*, 5139. (b) Ryang, M.; Sawa, Y.; Somasundaram, S. N.; Murai, S.; Tsutsumi, S. *J. Organomet. Chem.* **1972**, *46*, 375. (c) Carmona, E.; Gutiérrez-Puebla, E.; Monge, A.; Marín, J. M.; Paneque, M.; Poveda, M. L. *Organometallics* **1989**, *8*, 967.

(15) Murahashi, S.; Hirano, T.; Yano, T. *J. Am. Chem. Soc.* **1978**, *100*, 348.

(16) Heck, R. F. *Palladium Reagents in Organic Synthesis*; Academic Press: New York, 1985.

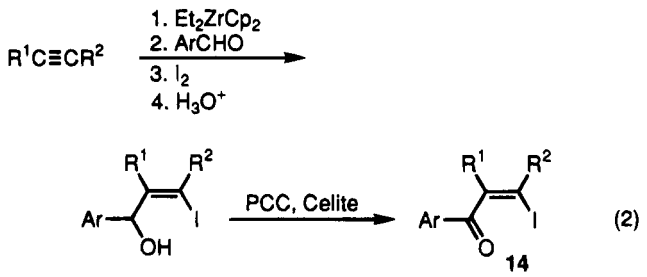


(1)

We suggest that, in Scheme 3, **15** probably undergoes migration of Pd to give **20**, which then is hydrolyzed to give **13**. This metallotropic process in the case of the reaction of **17** would involve temporary destruction of the aromatic *o*-phenylene group.

In the formation of **13** via hydrolysis shown in Scheme 3 the Pd-containing byproduct is a Pd(II) species which must be reduced for recycling Pd species as catalysts. This process requires the stoichiometric (rather than catalytic) amount of a reducing agent. This stoichiometry rules out the starting alkynes and PPh_3 present in the catalyst as the major reagent for reduction. The lack of specificity with respect to bases and solvents also rules them out as reducing agents.[16] Although aryl halides were used in excess, they are known to oxidize Pd rather than reduce it.[16] Consequently, CO is the only reasonable candidate for the reducing agent. Indeed, reduction of Pd(II) complexes by CO and proton donors, *e.g.*, EtOH, is well documented.[17]

Having clarified aspects of the reaction mechanism and the role of water, we then turned our attention to some synthetic aspects of the reaction. In addition to delineating its synthetic scope, we investigated the regiochemistry of the reaction of unsymmetrically substituted alkynes with aryl iodides (4 equiv) in benzene in the presence of CO (20 atm), 5 mol % of $Cl_2Pd(PPh_3)_2$, NEt_3, or $NaHCO_3$, and 1 molar equiv of added water. The experimental results summarized in Table 2 reveal the following features. First, the yield of the butenolide **13** is higher in cases where ArI contains an electron-donating group, *e.g.*, *p*-An. Second, alkynes containing an alkyl and an aryl substituents display the expected regioselectivity, corresponding to the intermediacy of benzylic organopalladium species. Third, the ≥94% regioselectivity observed with 1-(trimethylsilyl)-1-pentyne is opposite to that observed recently in the corresponding carbopalladation where Pd was attached to the Si-bearing carbon.[18] Although those cases in Table 2 where unsymmetrically substituted alkynes are used are quite regioselective, the use of a mixture of an alkyne and an aryl halide does not offer, in a more general sense, a high degree of flexibility in terms of regiochemistry and regioselectivity. This aspect needs to be further developed in the future. It may be pointed out, however, that the conversion of **14** into **13** (Table 1) is strictly regiospecific and that the overall regioselectivity is limited only by the availability of regiodefined precursors **14**. Some of those (*Z*)-β-iodoenones that are α-substituted are readily prepared in one pot via the reaction of the corresponding alkynes with Et_2ZrCp_2 followed by treatment with nitriles or aldehydes[13] (eq 2). In



(2)

cases where β-iodoenones are α-unsubstituted, *e.g.*, **14d**, they can be prepared by (i) reduction of propargyl alcohols with Red-Al or $LiAlH_4$ followed by iodinolysis with I_2, (ii) oxidation with PCC, (iii) addition of a Grignard reagent, and (iv) reoxidation with PCC.

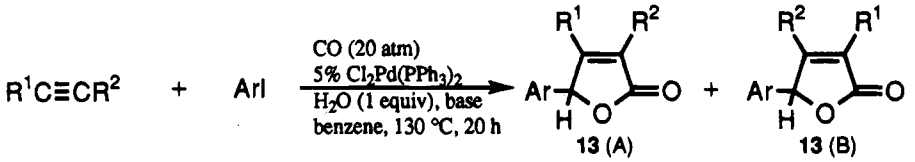
In striking contrast with those cases discussed above the corresponding reaction of (*Z*)-β-iodoenones containing α′-H atoms (**21**) has proceeded as initially expected, *i.e.*, **5** to **12** in Scheme 2, to provide **12** as the major product in high yields[3c,9,10] along with very minor amounts of **22** corresponding to **13**. The experimental results are summarized in Table 3, and the following features are noteworthy. First, all of the reactions listed in Table 3 gave compounds **12**, which were >98% *Z*. The *E* isomers were not detectable by NMR spectroscopy. Second, none of the reactions listed in Table 3 produced the γ-H abstraction product **11** in detectable yield. Third, even when 4 equiv of water was deliberately added, the reaction of **21c** under otherwise the same conditions gave **12c** in 68% along with only a 14% yield of **22c**. Clearly, conversion of **21** into **12** presumably via trapping of acylpalladium intermediates represented by **6** with internal enolates must be considerably faster than the formation of **22** via hydrolysis. This, in turn, suggests that the "effective" kinetic acidity of the α′ C−H bond in **21** is considerably higher than that of the γ C−H bond. The high yields and high stereo- and regioselectivities coupled with the ready accessibility of the starting **21** via transformations analogous to that shown in eq 2 lead to an attractive synthetic route to **12**.

The corresponding reaction of (*Z*)-β-iodoalkenyl alkyl ketones lacking a substituent in the α position appears to be less stereoselective. Thus, for example, the reaction of **21g** under the same conditions as those shown in Table 3 gave an 81:19 mixture of the *Z* and *E* isomers of **12g** in 80% combined yield along with an 8% yield of **22g** (eq 3). Presumably, the steric requirements in the α position are influential to the *Z*/*E* ratio. The fact that the same reaction run in benzene produced a 62:38 mixture in 75% combined yield indicates that the *Z*/*E* ratio may be subject to some reaction parameters, such as solvents. To further pursue the feasibility of observing γ-H abstraction, **21h** was prepared and subjected to the standard conditions shown in Table 3. The main products of the reaction were **12h** (52%), its *E* isomer (17%), and **11h** (25%) (eq 4). These results clearly indicate that the formation of **11** is, in principle, feasible but that it is less favorable than that of **12** or **22** in the other cases described herein. The possibility that **11h** is a product formed via isomerization of **12h** and its stereoisomer cannot be ruled out at this time. Although no rigorous examination was performed, it is very likely that the amount of **22** is a function of the amount of adventitious water, which probably is introduced to the reaction system as an impurity in CO.

In the reaction of alkynes with Et_2ZrCp_2 followed by treatment with nitriles and I_2, the products obtained before

(17) (a) Fenton, D. M.; Steinwand, P. J. *J. Org. Chem.* **1974**, *39*, 701. (b) Rivetti, F.; Romano, U. *J. Organomet. Chem.* **1979**, *174*, 221.
(18) Negishi, E.; Ay, M.; Sugihara, T. *Tetrahedron* **1993**, *49*, 5471.
(19) Lardelli, G.; Dcjkstra, G.; Harkes, P. D.; Boldingh, J. *Recl. Trav. Chim. Pays-Bas.* **1966**, *85*, 43.

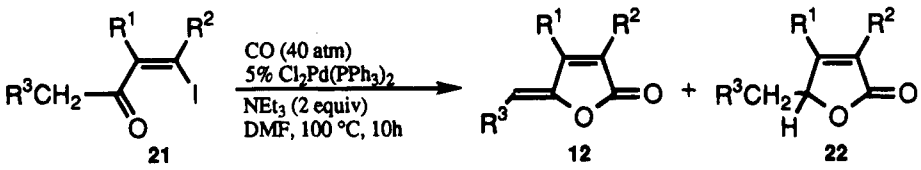
Table 2. Pd-Catalyzed Carbonylation of a Mixture of Internal Alkynes and Aryl Iodides



alkyne							
R^1	R^2	Ar of ArI	base[a]	product	combined yield,[b] %	A/B	recovered alkyne,[b] %
n-Pr	*n*-Pr	*p*-An	NEt_3	**13e**	66 (51)	*c*	*d*
n-Pr	*n*-Pr	*p*-An	$NaHCO_3$	**13e**	54	*c*	*d*
n-Pr	*n*-Pr	*m*-Tol	NEt_3	**13f**	50 (39)	*c*	*d*
n-Pr	*n*-Pr	*p*-ClC_6H_4	NEt_3	**13g**	40 (35)	*c*	*d*
Bn	Bn	*m*-Tol	NEt_3	**13b**	42 (35)	*c*	17
n-Bu	*p*-An	Ph	$NaHCO_3$	**13h**	65 (64)	89/11	20
n-Bu	*p*-An	*p*-An	$NaHCO_3$	**13i**	65 (56)	91/9	32
n-Bu	*p*-An	*p*-$MeO_2CC_6H_4$	$NaHCO_3$	**13j**	35 (21)	91/9	45
Me_3Si	*n*-Pr	Ph	NEt_3	**13k**	39 (31)	94/6	30
Me_3Si	*n*-Pr	*p*-An	NEt_3	**13l**	37 (34)	94/6	*d*

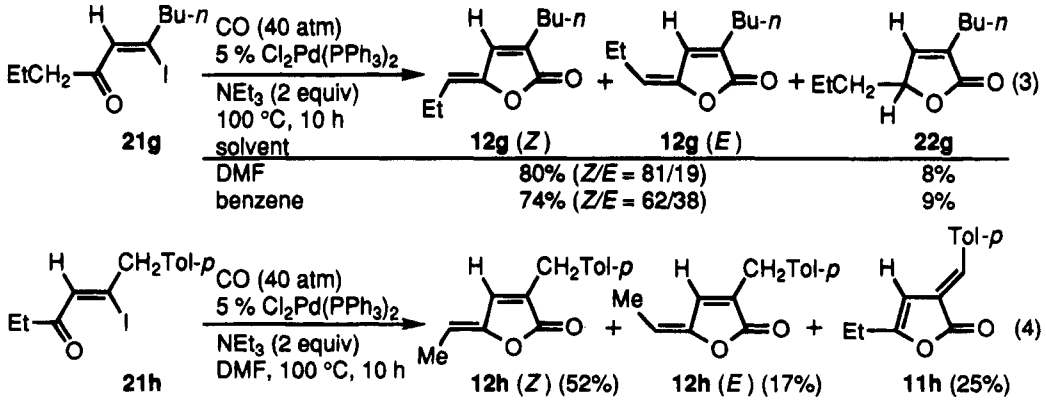
[a] Either 8 equiv of NEt_3 or 4 equiv of $NaHCO_3$ was used. [b] By NMR. The numbers in parentheses are isolated yields. [c] Not applicable. [d] Not determined.

Table 3. Pd-Catalyzed Carbonylation of (*Z*)-β-Iodoalkenyl Alkyl Ketones in the Presence of Base[a]



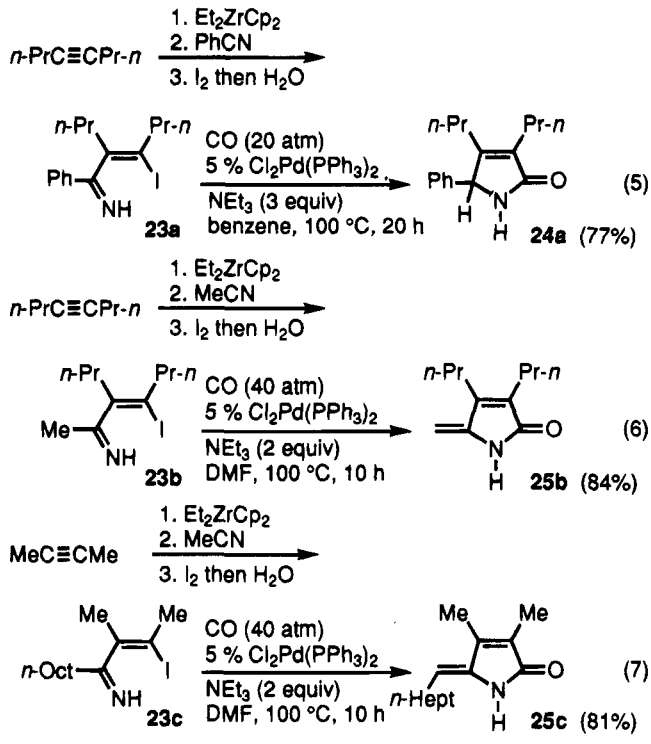
β-iodoenone				product yield,[b] %	
	R^1	R^2	R^3	**12**	**22**
21a	*n*-Pr	*n*-Pr	H	66 (66)	<2
21b	*n*-Pr	*n*-Pr	*n*-Pent	75 (70)	4
21c	*n*-Pr	Ph	Me	72 (70)	8
21d	*n*-Pr	Ph	Ph	68 (63)	6
21e	Me	Me	*n*-Hept	84 (80)	4
21f[19]	Me	Me	*n*-Bu	82 (80)	4

[a] All reactions were run at 40 atm of CO in the presence of 5 mol % of $Cl_2Pd(PPh_3)_2$ and 2 equiv of NEt_3 in DMF at 100 °C for 10 h. [b] By NMR. The numbers in parentheses are isolated yields.



prolonged treatment with 10% HCl were the corresponding imines. As expected, their carbonylation under the same conditions as those used above cleanly produced lactams. The reaction of **23a** lacking an α′-H atom gave **24a**, while **23b** and **23c** provided **25b** and **25c**, respectively (eqs 5–7). The amounts of byproducts are <2–3% each, if any. These results closely parallel those observed with the corresponding enones.

In summary, the reaction of a mixture of either an internal alkyne and an aryl halide or a (*Z*)-β-iodoenone with CO in the presence of a Pd–phosphine catalyst, *e.g.*, $Cl_2Pd(PPh_3)_2$, can give rise to an acylpalladium derivative that can be represented by **6** as an intermediate. In cases where **6** contains a δ-H, the formation of **12** is the most favorable process. In the absence of the δ-H, **6** is converted to either **13** or its dimer **16** depending on the substrate structure and whether or not water is present. The formation of **11**, which was the major product in a related reaction of terminal alkynes reported recently,[7] is generally not competitive with any of the three processes mentioned above, even though it was observed to a minor extent in the reaction of **21h** (eq 4). Finally, ((*Z*)-β-iodoalkenyl)imines **23** react similarly to give either lactams **24** or **25**. This study clearly indicates that, unlike the Pd-catalyzed carbonylation of alkenes



that can lead to the formation of polymers,[2] the predominant courses of the Pd-catalyzed carbonylation of internal alkynes are the three cyclization processes found in this study and that high-yield formation of polymers, such as **7** and **9**, may not be readily realized by this reaction. On the other hand, the Pd-catalyzed carbonylative cyclization reactions, especially those of β-haloalkenyl enones and the corresponding imines, promise to provide efficient and selective routes to γ-lactones and γ-lactams.

Experimental Section

General Procedures. All reactions were conducted under a dry Ar atmosphere. Gas chromatographic measurements were performed on SE-30 (Chromosorb W) columns with appropriate saturated hydrocarbon standards. ^{1}H and ^{13}C NMR were recorded on Varian Gemini-200, VXR-500, and GE QE-300 NMR spectrometers. All commercially available reagents were used without further purification unless otherwise noted. THF was distilled from sodium benzophenone ketyl. Benzene, CH_3CN, DMF, and NEt_3 were dried over molecular sieves 4A. The preparation of $Cl_2Pd(PPh_3)_2$ was performed as reported in the literature.[20]

Carbonylation of Organic Halides. Pd-Catalyzed high-pressure carbonylation experiments were carried out in a 22-mL autoclave (Parr Instrument Co.).

Pd-Catalyzed Carbonylation of a Mixture of Internal Alkynes and Aryl Iodides in the Presence of a Trapping Agent. (a) Reaction of Iodobenzene with 4-Octyne in the Presence of Methanol. A mixture of iodobenzene (112 μL, 204 mg, 1.0 mmol), 4-octyne (0.15 mL, 0.11 g, 1.0 mmol), Et_3N (0.28 mL, 0.22 g, 2.0 mmol), MeOH (160 μL, 128 mg, 4.0 mmol), $Cl_2Pd(PPh_3)_2$ (35 mg, 0.05 mmol), and benzene (4.0 mL) was stirred at 100 °C under CO pressure (20 atm) for 12 h. GC analysis of the crude reaction mixture showed the formation of methyl benzoate in 99% along with 51% of 4-octyne recovered.

(b) Reaction of *m*-Iodotoluene with 3-Pentyn-1-ol. A mixture of *m*-iodotoluene (0.13 mL, 218 mg, 1.0 mmol) with 3-pentyn-1-ol (101 μL, 92 mg, 1.1 mmol), Et_3N (0.21 mL, 0.15 g, 1.5 mmol), $Cl_2Pd(PPh_3)_2$ (35 mg, 0.05 mmol), and CH_3CN (4.0 mL) was stirred at 80 °C under CO pressure (20 atm) for 40 h. The reaction mixture was subsequently evaporated *in vacuo*, diluted with Et_2O, washed with H_2O, dried over $MgSO_4$, and evaporated. Analysis of the crude reaction mixture showed the formation of 3-pentynyl *m*-toluate in 85% NMR yield: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 1.76 (t, J = 2.5 Hz, 3 H), 2.35 (s, 3 H), 2.5–2.7 (m, 2 H), 4.34 (t, J = 7.0 Hz, 2 H), 7.2–7.3 (m, 2 H), 7.8–8.0 (m, 2 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 12.40, 13.10, 20.18, 21.61, 62.88, 75.58, 76.30, 125.77, 127.21, 129.04, 129.12, 132.69, 137.04, 165.42.

(c) Reaction of *m*-Iodotoluene with *o*-((Trimethylsilyl)ethynyl)phenol. A mixture of *m*-iodotoluene (0.13 mL, 218 mg, 1.0 mmol), *o*-((trimethylsilyl)ethynyl)phenol (0.245 g, 1.2 mmol), Et_3N (0.21 mL, 0.15 g, 1.5 mmol), $Cl_2Pd(PPh_3)_2$ (35 mg, 0.05 mmol), and CH_3CN (4.0 mL) was stirred at 80 °C under CO pressure (20 atm) for 12 h and then submitted to usual workup. Analysis of the crude reaction mixture showed the formation of *o*-((trimethylsilyl)ethynyl)phenyl *m*-toluate in 89% NMR yield: ^{1}H NMR ($CDCl_3$, Me_4Si) δ −0.25 (s, 9 H), 2.14 (s, 3 H), 6.8–7.25 (m, 6 H), 7.8–8.0 (m, 2 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ −0.44, 21.31, 100.03, 100.23, 117.68, 122.75, 126.12, 127.89, 128.80, 129.80, 130.06, 131.13, 133.34, 134.77, 138.64, 153.05, 165.16.

Pd-Catalyzed Carbonylation of a Mixture of Internal Alkynes and Aryl Iodides. (a) 2,3-Di-(*n*-propyl)-4-(*p*-anisyl)-2-buten-4-olide (13e). Representative Procedure (Method A). A mixture of *p*-iodoanisole (0.94 g, 4.0 mmol), 4-octyne (0.15 mL, 0.11 g, 1.0 mmol), benzene (4.0 mL), Et_3N (1.12 mL, 0.81 g, 8.0 mmol), H_2O (18 μL, 18 mg, 1.0 mmol), and $Cl_2Pd(PPh_3)_2$ (35 mg, 0.05 mmol) was stirred at 130 °C under CO pressure (20 atm) for 24 h and then treated with H_2O, extracted with CH_2Cl_2, dried over $MgSO_4$, and evaporated. Analysis of the crude reaction mixture by ^{1}H NMR showed the formation of **13e** in 66% yield along with the *p*-anisic anhydride (28%) and *N,N*-diethylanisamide (37%). Chromatography on silica gel (90/10 pentane/Et_2O) afforded 140 mg (51%) of **13e**: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.88 (t, J = 7.5 Hz, 3 H), 0.96 (t, J = 7.5 Hz, 3 H), 1.2–1.6 (m, 2 H), 1.60 (sex, J = 7.5 Hz, 2 H), 1.97 (ddd, J = 14.4, 9.0, 5.4 Hz, 1 H), 2.2–2.4 (m, 3 H), 3.79 (s, 3 H), 5.65 (s, 1 H), 6.88 (d, J = 8.5 Hz, 2 H), 7.11 (d, J = 8.5 Hz, 2 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 13.78, 13.91, 21.03, 21.45, 21.46, 28.46, 55.12, 83.40, 114.14, 126.77, 127.09, 128.26, 160.11, 163.13, 174.41; high-resolution MS calcd for $C_{17}H_{22}O_3$ 274.1569, found 274.1570.

Representative Procedure (Method B). The above reaction was performed using $NaHCO_3$ (336 mg, 4.0 mmol) in place of NEt_3 under otherwise the same conditions described above. Analysis of the crude reaction mixture by ^{1}H NMR showed the formation of **13e** in 54% yield.

(b) 2,3-Dibenzyl-4-(*m*-tolyl)-2-buten-4-olide (13b). Using method A, **13b** was formed in 42% NMR yield along with 17% of the starting alkyne. Chromatography on silica gel (90/10 pentane/Et_2O) afforded 124 mg (35%) of **13b**: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 2.31 (s, 3 H), 3.12 (d, J = 14.0 Hz, 1 H), 3.71 (d, J = 14.0 Hz, 1 H), 3.82 (d, J = 14 Hz, 1 H), 3.88 (d, J = 14 Hz, 1 H), 5.50 (s, 1 H), 6.75–6.95 (m, 4 H), 7.0–7.4 (m, 10 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 21.33, 29.67, 32.87, 83.68, 124.36, 126.66, 127.11, 127.61, 128.55 (2C), 128.72 (2C), 128.83 (3C), 130.10, 134.44, 135.96, 138.13, 138.77, 162.51, 174.22; IR (neat) 1756 (s), 1672 (w) cm^{-1}; high-resolution MS calcd for $C_{25}H_{22}O_2$ 354.1620, found 354.1613.

(c) 2,3-Bis(α,α-dideuteriobenzyl)-4-(*m*-tolyl)-2-buten-4-olide. Using method A, the butenolide was formed in 35% NMR yield: H–D scrambling <2%, ^{1}H NMR ($CDCl_3$, Me_4Si) δ 2.31 (s, 3 H), 5.50 (bs, 1 H), 6.75–6.95 (m, 4 H), 7.0–7.4 (m, 10 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 21.24, 29.02 (pent, J = 18 Hz), 32.20 (pent, J = 18 Hz), 83.62, 124.29, 126.59, 127.04, 127.55, 128.49 (2C), 128.54 (2C), 128.66 (3C), 130.03, 134.40, 135.82, 138.02, 138.70, 162.38, 174.16; IR (neat) 1754, 1664 cm^{-1}; high-resolution MS calcd for $C_{25}H_{18}D_4O$ 359.1949, found 359.1941.

(d) 2,3-Di-(*n*-propyl)-4-(*m*-tolyl)-2-buten-4-olide (13f). Using method A, **13f** was formed in 50% NMR yield. Chromatography on silica gel (90/10 pentane/Et_2O) afforded 100 mg (39%) of **13f**: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.90 (t, J = 7.4 Hz, 3 H), 0.97 (t, J = 7.4 Hz, 3 H), 1.25–1.6 (m, 2 H), 1.61 (sex, J = 7.5 Hz, 2 H), 1.97 (ddd, J = 14.4, 9.0, 5.4 Hz, 1 H), 2.2–2.45 (m, 5 H), 5.64 (s, 1 H), 6.9–7.05 (m, 2 H), 7.1–7.35 (m, 3 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 13.94, 14.07, 21.31, 31.38, 21.61, 25.26, 28.58, 83.86, 124.11, 127.19, 127.46, 128.78, 129.99, 135.04, 138.74, 163.33, 174.67; IR (neat) 1750 cm^{-1}; high-resolution MS calcd for $C_{17}H_{22}O_2$ 258.1620, found 258.1621.

(20) Jenkins, J. M.; Verkade, J. G. *Inorg. Synth.* **1968**, *11*, 108.

(e) 2,3-Di-(*n*-propyl)-4-(*p*-chlorophenyl)-2-buten-4-olide (13g). Using method A, **13g** was formed in 40% NMR yield. Chromatography on silica gel (90/10 pentane/Et_2O) afforded 97 mg (35%) of **13g**: ^1H NMR ($CDCl_3$, Me_4Si) δ 0.90 (t, J = 7.3 Hz, 3 H), 0.96 (t, J = 7.4 Hz, 3 H), 1.2−1.5 (m, 2 H), 1.60 (sex, J = 7.5 Hz, 2 H), 1.95 (ddd, J = 14.4, 9.0, 5.4 Hz, 1 H), 2.2−2.4 (m, 3 H), 5.66 (s, 1 H), 7.13 (d, J = 8.5 Hz, 2 H), 7.36 (d, J = 8.5 Hz, 2 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 13.87, 14.00, 21.23, 21.50, 25.57, 28.43, 82.82, 127.48, 128.23, 129.13, 133.66, 135.06, 162.77, 174.22; IR (neat) 1750 (s), 1670 (s) cm^{-1}; high-resolution MS calcd for $C_{16}H_{19}ClO_2$ 278.1074, found 278.1073.

(f) 2-(*p*-Anisyl)-3-butyl-4-phenyl-2-buten-4-olide (13h). Using method B, **13h** was formed in 65% NMR yield along with 20% of the starting alkyne. Chromatography on silica gel (80/20 pentane/Et_2O) afforded 206 mg (64%) of an 89/11 regioisomeric mixture of **13h** and 3-(*p*-anisyl)-2-butyl-4-phenyl-2-buten-4-olide. The spectral data for **13h** are as follows: ^1H NMR ($CDCl_3$, Me_4Si) δ 0.81 (t, J = 7.1 Hz, 3 H), 1.10−1.60 (m, 4 H), 2.08 (ddd, J = 14.3, 9.4, 5.4 Hz, 1 H), 2.60 (ddd, J = 14.2, 9.8, 6.0 Hz, 1 H), 3.83 (s, 3 H), 5.83 (s, 1 H), 6.98 (d, J = 8.7 Hz, 2 H), 7.20−7.35 (m, 2 H), 7.35−7.50 (m, 3 H), 7.46 (d, J = 8.8 Hz, 2 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 13.62, 22.65, 26.87, 29.94, 55.21, 83.59, 114.02, 122.29, 126.05, 127.10, 129.02, 129.39, 130.27, 134.95, 159.73, 163.37, 173.27; IR (neat) 1750 cm^{-1}; high-resolution MS calcd for $C_{21}H_{22}O_3$ 322.1569, found 322.1563.

(g) 2,4-Di-(*p*-anisyl)-3-butyl-2-buten-4-olide (13i). Using method B, **13i** was formed in 65% NMR yield along with 32% of the starting alkyne. Thick layer chromatography on silica gel (50/50 pentane/CH_2Cl_2) afforded 197 (56%) of an 91/9 regioisomeric mixture of **13i** and 3,4-Di-(*p*-anisyl)-2-butyl-2-buten-4-olide. The spectral data for **13i** are as follows: ^1H NMR ($CDCl_3$, Me_4Si) δ 0.83 (t, J = 7.2 Hz, 3 H), 1.15−1.60 (m, 4 H), 2.08 (ddd, J = 14.4, 9.2, 5.2 Hz, 1 H), 2.61 (ddd, J = 14.4, 9.8, 6.2 Hz, 1 H), 3.82 (s, 3 H), 3.86 (s, 3 H), 5.79 (s, 1 H), 6.93 (d, J = 8.7 Hz, 2 H), 6.99 (d, J = 8.7 Hz, 2 H), 7.20 (d, J = 8.7 Hz, 2 H), 7.46 (d, J = 8.7 Hz, 2 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 13.61, 22.65, 26.93, 29.84, 55.29 (2C), 83.36, 113.99, 114.40, 122.40, 126.76, 127.63, 128.60, 130.27, 159.70, 160.38, 163.34, 173.20; IR (neat) 1750 (s), 1670 (s) cm^{-1}; high-resolution MS calcd for $C_{22}H_{24}O_4$ 352.1675, found 352.1671.

(h) 2-(*p*-Anisyl)-3-butyl-4-(*p*-(methoxycarbonyl)phenyl)-2-buten-4-olide (13j). Using method B, **13j** was formed in 35% NMR yield along with 45% of the starting alkyne. Thick layer chromatography on silica gel (80/20 pentane/CH_2Cl_2) afforded 80 mg (21%) of an 91/9 regioisomeric mixture of **13j** and 3-(*p*-anisyl)-2-butyl-4-(*p*-(methoxycarbonyl)phenyl)-2-buten-4-olide. The spectral data for **13j** are as follows: ^1H NMR ($CDCl_3$, Me_4Si) δ 0.82 (t, J = 7.1 Hz, 3 H), 1.1−1.6 (m, 4 H), 2.05 (ddd, J = 14.4, 9.3, 5.3 Hz, 1 H), 2.61 (ddd, J = 14.3, 9.8, 6.0 Hz, 1 H), 3.85 (s, 3 H), 3.94 (s, 1 H), 5.87 (s, 1 H), 6.99 (d, J = 8.8 Hz, 2 H), 7.38 (d, J = 8.3 Hz, 2 H), 7.45 (d, J = 8.8 Hz, 2 H), 8.09 (d, J = 8.3 Hz, 2 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 13.59, 22.66, 26.82, 30.00, 52.34, 55.34, 82.84, 114.10 (2C), 126.32, 127.04 (2C), 129.88, 130.29 (4C), 131.18, 140.00, 159.89, 162.75, 166.42, 173.00; IR (neat) 1750 cm^{-1}; high-resolution MS calcd for $C_{23}H_{24}O_5$ 380.1624, found 380.1632.

(i) 4-Phenyl-3-(*n*-propyl)-2-(trimethylsilyl)-2-buten-4-olide (13k). Using method A, **13k** was formed in 39% NMR yield, regioisomeric ratio >94% along with 30% of the starting alkyne. Chromatography on silica gel (97/3 pentane/Et_2O) afforded 85 mg (31%) of a >99/1 regioisomeric mixture of **13k** and 4-phenyl-2-(*n*-propyl)-3-(trimethylsilyl)-2-buten-4-olide. The spectral data for **13k** are as follows: ^1H NMR ($CDCl_3$, Me_4Si) δ −0.01 (s, 9 H), 1.01 (t, J = 7.4 Hz, 3 H), 1.55−1.75 (m, 2 H), 2.35−2.50 (m, 2 H), 5.78 (s, 1 H), 7.10−7.20 (m, 2 H), 7.30−7.40 (m, 3 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ −1.10, 14.17, 22.54, 28.24, 86.78, 127.89, 128.71, 129.33, 135.31, 141.44, 162.02, 174.37; IR (neat) 1752 (s) cm^{-1}; high-resolution MS calcd for $C_{16}H_{22}O_2Si$ 274.1389, found 274.1386.

(j) 4-(*p*-Anisyl)-3-(*n*-propyl)-2-(trimethylsilyl)-2-buten-4-olide (13l). Using method B, **13l** was formed in 37% NMR yield, regioisomeric ratio >94%. Chromatography on silica gel (90/10 pentane/Et_2O) afforded 103 mg (34%) of a >99/1 regioisomeric mixture of **13l** and 4-(*p*-anisyl)-2-(*n*-propyl)-3-(trimethylsilyl)-2-buten-4-olide. The spectral data for **13l** are as follows: ^1H NMR ($CDCl_3$, Me_4Si) δ 0.03 (s, 9 H), 1.02 (t, J = 7.4 Hz, 3 H), 1.55−1.75 (m, 2 H), 2.35−2.55 (m, 2 H), 3.80 (s, 3 H), 5.77 (s, 1 H), 6.80−6.90 (m, 2 H), 7.05−7.10 (m, 2 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ −1.03, 14.23, 22.58, 28.31, 55.28, 86.55, 114.20, 127.27, 129.30, 141.45, 160.33, 162.09, 174.42; IR (neat) 1750 (s) cm^{-1}; high-resolution MS calcd for $C_{17}H_{24}O_3Si$ 304.1495, found 304.1495.

Synthesis of Bis(α,α-dideuteriobenzyl)ethyne. To a solution of 1-phenyl-1-propyne (1.16 g, 10 mmol) in hexane (10 mL) was added 2.6 M *n*-BuLi in hexane (24 mL, 60 mmol). The reaction mixture was refluxed for 16 h, treated very carefully with D_2O (20 mL), extracted with pentane, washed with water, dried over $MgSO_4$, filtered, and evaporated. Distillation afforded 0.89 g (75%) of 3-phenyl-1,3,3-trideuterio-1-propyne: >98% D incorporation; ^1H NMR ($CDCl_3$, Me_4Si) δ 7.0−7.6 (m, 5 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 24.76 (t, J = 22 Hz), 70.42 (t, J = 10 Hz), 81.90 (bs), 126.64, 127.78, 128.48, 136.02. A solution of 3-phenyl-1,3,3-trideuterio-1-propyne (0.41 g, 3.26 mmol) in THF (3.0 mL) was treated with 2.6 M *n*-BuLi (1.33 mL, 3.45 mmol, −78 °C) followed 30 min later by a solution of α-deuteriobenzaldehyde[21] (274 mg, 2.55 mmol) in THF (1.0 mL). The reaction mixture was warmed to 25 °C, treated with aqueous NH_4Cl, extracted with Et_2O, washed with brine, dried over $MgSO_4$, filtered, and evaporated. Chromatography on silica gel (97/3 pentane/ethyl acetate) afforded 0.43 g (74%) of 1,4-diphenyl-1,4,4-trideuterio-2-butyn-1-ol: >98% D incorporation; ^1H NMR ($CDCl_3$, Me_4Si) δ 3.3 (bs, 1 H), 7.0−7.6 (m, 10 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 24.2 (pent, J = 20 Hz), 63.9 (t, J = 22.5 Hz), 82.1, 84.4, 126.35, 126.40 (2C), 127.62, 127.82, 128.18 (2C), 128.25 (2C), 136.0 (t, J = 5 Hz), 140.8; IR (neat) 3340 cm^{-1}. To a mixture of 1,4-diphenyl-1,4,4-trideuterio-2-butyn-1-ol (408 mg, 1.78 mmol), deuteriotriethylsilane (271 mg, 2.31 mmol), and NH_4F (85 mg, 2.31 mmol) in CH_2Cl_2 (2.0 mL) was added at 0 °C a solution of CF_3COOH (0.69 mL, 1.01 g, 8.90 mmol) in CH_2Cl_2 (1.0 mL) over a 10 min period.[22] The reaction mixture was stirred for 2 h at 25 °C, treated with aqueous $NaHCO_3$, extracted with Et_2O, dried over $MgSO_4$, filtered, evaporated, and purified by chromatography on silica gel (99/1 pentane/ethyl acetate) to give 321 mg (86%) of bis(α,α-dideuteriobenzyl)ethyne: ^1H NMR ($CDCl_3$, Me_4Si) δ 7.0−7.5 (m, 10 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 24.6 (pent, J = 20 Hz), 80.17, 126.78, 128.20, 128.76, 137.60; IR (neat) 710 cm^{-1}.

Preparation of (*Z*)-β-Iodoenones and (*Z*)-β-Iodoenimines. (a) (*Z*)-3-Iodo-1-phenyl-2-(*n*-propyl)-2-hexen-1-one (14a). Representative Procedure.[13] A solution of Cp_2ZrCl_2 (1.46 g, 5.0 mmol) in THF (20 mL) was successively treated with 1.0 M EtMgBr in THF (10 mL, 10 mmol, −78 °C, 1 h), 4-octyne (0.73 mL, 0.50 g, 5.0 mmol, −78 to 0 °C, 1 h), benzaldehyde (0.61 mL, 0.64 g, 6.0 mmol, 60 °C, 3 h), I_2 (2.54 g, 10 mmol, 0 °C, 12 h) in THF (5.0 mL), and 1 M HCl. The reaction mixture was extracted with Et_2O, washed successively with 1 M HCl, aqueous $NaHCO_3$, $Na_2S_2O_3$, and NaCl, dried over $MgSO_4$, filtered, and evaporated. Chromatography on silica gel (97/3 pentane/ethyl acetate) afforded 0.70 g (41%) of (*Z*)-3-iodo-1-phenyl-2-(*n*-propyl)-2-hexen-1-ol: stereoselectivity >98%; ^1H NMR ($CDCl_3$, Me_4Si) δ 0.76 (t, J = 7.3 Hz, 3 H), 0.8−1.1 (m, 4 H), 1.1−1.5 (m, 1 H), 1.63 (sex, J = 7.4 Hz, 2 H), 1.9−2.05 (m, 1 H), 2.05−2.25 (m, 2 H), 2.2−2.5 (m, 2 H), 5.9−6.0 (m, 1 H), 7.2−7.4 (m, 3 H), 7.4−7.5 (m, 2 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 13.06, 14.43, 23.10, 23.87, 30.80, 43.07, 82.48, 108.60, 125.25, 127.15, 128.09, 141.55, 145.12; IR (neat) 3340 cm^{-1}. Oxidation of this alcohol with pyridinium chlorochromate (PCC)[23] (25 °C, 2 h) afforded 0.68 g (99%) of **14a**: ^1H NMR ($CDCl_3$, Me_4Si) δ 0.90 (t, J = 7.5 Hz, 3 H), 1.03 (t, J = 7.5 Hz, 3 H), 1.45 (sex, J = 7.5 Hz, 2 H), 1.68 (sex, J = 7.5 Hz, 2 H), 2.3−2.5 (m, 2 H), 2.6−2.7 (m, 2 H), 7.4−7.55 (m, 2 H), 7.55−7.7 (m, 1 H), 7.9−8.0 (m, 2 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 13.07, 13.88, 21.73, 22.63, 34.46, 41.66, 102.95, 128.73, 129.78, 133.40, 133.86, 146.24, 198.37; IR (neat) 1668 cm^{-1}.

(b) (*Z*)-3-Iodo-1,2,3-triphenyl-2-propen-1-one (14c). (*Z*)-3-Iodo-1,2,3-triphenyl-2-propen-1-ol was prepared using the procedure described for **14a**. Chromatography on silica gel (97/3 pentane/ethyl acetate) afforded 615 mg (30%) of (*Z*)-3-iodo-1,2,3-triphenyl-2-propen-1-ol: stereoselectivity >98%; ^1H NMR ($CDCl_3$, Me_4Si) δ 2.33 (d, J = 7 Hz, 1 H), 6.37 (d, J = 7 Hz, 1 H), 6.7−6.9 (m, 2 H), 6.9−7.3 (m, 7 H), 7.3−7.5 (m, 4 H), 7.5−7.7 (m, 2 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 81.55, 102.65 (2C), 125.63 (2C), 127.09, 127.29, 127.42 (2C),

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127.45, 127.55 (2C), 128.21 (2C), 129.21 (2C), 130.26 (2C), 135.29, 141.05, 143.81, 149.21; IR (neat) 3300 cm^{-1}. Oxidation with PCC[23] of (*Z*)-3-iodo-1,2,3-triphenyl-2-propen-1-ol (615 mg, 1.5 mmol) gave 512 mg (84%) of **14c**: ^1H NMR ($CDCl_3$, Me_4Si) δ 7.0−7.6 (m, 13 H), 7.5−7.7 (m, 2 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 98.59, 127.92, 128.12, 128.31, 128.38 (2C), 128.81 (2C), 128.90 (2C), 129.69 (2C), 130.14 (2C), 133.61, 133.70, 135.46, 141.78, 148.22, 196.17.

(c) (*Z*)-4-Iodo-5-(*n*-propyl)-4-dodecen-6-one (21b). (*Z*)-4-Iodo-5-(*n*-propyl)-4-dodecen-6-ol was prepared using the procedure described above for **14a**. Chromatography on silica gel (97/3 pentane/ethyl acetate) afforded 334 mg (19%) of (*Z*)-4-iodo-5-(*n*-propyl)-4-do-decen-6-ol: stereoselectivity >98%; ^1H NMR ($CDCl_3$, Me_4Si) δ 0.8−1.0 (m, 9 H), 1.2−1.65 (m, 14 H), 1.8−1.95 (br, 1 H), 2.0−2.15 (m, 1 H), 2.15−2.3 (m, 1 H), 2.4−2.6 (m, 2 H), 4.5−4.65 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 12.89, 14.06, 14.50, 22.58, 23.04, 24.08, 25.79, 29.21, 30.49, 31.76, 35.11, 42.93, 81.60, 106.36, 145.22; IR (neat) 3382 cm^{-1}. Oxidation with PCC[23] of (*Z*)-4-iodo-5-(*n*-propyl)-4-dodecen-6-ol (334 mg, 0.95 mmol) gave 249 mg (75%) of **21b**: ^1H NMR ($CDCl_3$, Me_4Si) δ 0.8−1.0 (m, 9 H), 1.2−1.5 (m, 8 H), 1.5−1.7 (m, 4 H), 2.2−2.3 (m, 2 H), 2.45−2.55 (m, 2 H), 2.6−2.7 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 12.82, 13.72, 13.98, 21.68, 22.46, 23.20, 28.72, 31.56, 33.39, 41.05, 41.54, 100.43, 148.84, 208.31; IR (neat) 1700 cm^{-1}.

(d) (*Z*)-1-Imino-3-iodo-1-phenyl-2-(*n*-propyl)-2-hexene (23a). This compound was prepared according to the procedure described for **14a** except that benzonitrile (0.63 mL, 0.63 g, 5.5 mmol, 0−25 °C, 1.5 h) was used in place of benzaldehyde. Chromatography on silica gel (2/1 pentane/Et_2O) afforded 1.14 g (67%) of **23a**: ^1H NMR ($CDCl_3$, Me_4Si) δ 0.88 (t, J = 7.3 Hz, 3 H), 1.02 (t, J = 7.3 Hz, 3 H), 1.40 (sex, J = 7.4 Hz, 2 H), 1.69 (sex, J = 7.4 Hz, 2 H), 2.2−2.4 (m, 2 H), 2.65 (t, J = 7.4 Hz, 2 H), 7.35−7.5 (m, 3 H), 7.75−7.9 (m, 2 H), 9.1 (bs, 1 H); ^{13}C NMR ($CDCl_3$) δ 13.15, 13.86, 21.93, 22.82, 34.19, 42.09, 105.05, 127.80 (2C), 128.60 (3C), 130.94, 135.00, 180.36; IR (neat) 3238, 1632 cm^{-1}.

(e) (*Z*)-2-Imino-4-iodo-3-(*n*-propyl)-3-heptene (23b). This compound was prepared according to the procedure described for **14a** except that acetonitrile (0.29 mL, 205 mg, 5.5 mmol, 0−25 °C, 1.5 h) was used in place of benzaldehyde. Chromatography on silica gel (50/50 pentane/Et_2O) afforded 0.85 g (61%) of **23b**: ^1H NMR ($CDCl_3$, Me_4Si) δ 0.8−1.0 (m, 6 H), 1.35−1.5 (m, 2 H), 1.5−1.7 (m, 2 H), 2.15 (d, J = 3.0 Hz, 3 H), 2.2−2.35 (m, 2 H), 2.45−2.6 (m, 2 H), 8.05 (bs, 1 H); ^{13}C NMR ($CDCl_3$) δ 12.64, 13.55, 21.46, 22.37, 24.78, 33.03, 41.52, 101.19, 148.33, 182.55; IR (neat) 3238, 1632 cm^{-1}.

(f) (*Z*)-3-(*n*-Propyl)-4-iodo-3-hepten-2-one (21a). A solution of **23b** (160 mg, 0.50 mmol) in a 5/1 mixture of THF/3 N HCl (4 mL) was stirred 3 h at 25 °C, diluted with Et_2O, washed with aqueous $NaHCO_3$, dried over $MgSO_4$, and evaporated. Chromatography on silica gel (98/2 pentane/Et_2O) afforded 122 mg (76%) of **21a**: ^1H NMR ($CDCl_3$, Me_4Si) δ 0.93 (t, J = 7.1 Hz, 3 H), 0.95 (t, J = 7.2 Hz, 3 H), 1.35−1.5 (m, 2 H), 1.5−1.7 (m, 2 H), 2.25−2.35 (m, 2H), 2.37 (s, 3H), 2.45−2.55 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 12.84, 13.70, 21.62, 22.47, 28.9, 33.28, 41.58, 100.19, 148.89, 206.15; IR (neat) 1702 cm^{-1}.

(g) (*Z*)-4-Imino-2-iodo-3-methyl-2-dodecene (23c). This compound was prepared according to the procedure described for **14a** except that 2-butyne (0.39 mL, 270 mg, 5.0 mmol) and octyl cyanide (0.97 mL, 0.77 g, 5.5 mmol, 0−25 °C, 1.5 h) were used in place of 4-octyne and benzaldehyde, respectively. Chromatography on silica gel (3/7 pentane/Et_2O) afforded 882 mg (55%) of **23c**: ^1H NMR ($CDCl_3$, Me_4Si) δ 0.88 (t, J = 7.1 Hz, 3 H), 1.1−1.5 (m, 12 H), 1.88 (s, 3 H), 2.35−2.45 (m, 2 H), 2.50 (s, 3 H), 8.03 (br, 1 H); ^{13}C NMR ($CDCl_3$) δ 13.87, 17.13, 22.40, 24.77, 28.94, 29.04, 29.16, 29.35, 31.59, 36.63, 91.05, 142.99, 186.07; IR (neat) 1622 cm^{-1}.

(h) (*Z*)-2-Iodo-3-methyl-2-dodecen-4-one (21e). Hydrolysis of **23c** (178 mg, 0.50 mmol), using the procedure described for the preparation of **21a**, afforded **21e** in 160 mg (90%) after chromatography on silica gel (95/5 pentane/Et_2O): ^1H NMR ($CDCl_3$, Me_4Si) δ 0.88 (t, J = 6.6 Hz, 3 H), 1.2−1.4 (m, 10 H), 1.5−1.7 (m, 2 H), 1.84 (s, 3 H), 2.51 (s, 3 H), 2.65 (t, J = 7.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 14.06, 16.43, 22.56, 23.32, 23.36, 28.64, 28.89, 29.55, 31.61, 40.13, 115.53, 143.49, 208.59; IR (neat) 1706 cm^{-1}.

(i) (*Z*)-2-Iodo-3-methyl-2-nonen-4-one (21f). This compound was prepared according to the procedure described for **14a** except that 2-butyne (0.39 mL, 270 mg, 5.0 mmol) and hexanenitrile (0.66 mL, 0.53 g, 5.5 mmol, 0−25 °C, 1.5 h) were used in place of 4-octyne and benzaldehyde, respectively. After iodinolysis, the reaction mixture was treated with a 3 M HCl (25 °C, 3 h). After workup, chromatography on silica gel (95/5 pentane/Et_2O) afforded 0.84 g (60%) of **21f**: ^1H NMR ($CDCl_3$, Me_4Si) δ 0.91 (t, J = 6.7 Hz, 3 H), 1.25−1.45 (m, 4 H), 1.55−1.7 (m, 2 H), 1.85 (s, 3 H), 2.51 (s, 3 H), 2.65 (t, J = 7.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 13.91, 16.50, 22.45, 23.05, 23.10, 31.29, 40.16, 115.13, 143.55, 208.68; IR (neat) 1702 cm^{-1}.

(Z)-1,4-Bis(*p*-tolyl)-3-iodo-2-buten-1-one (14d). A mixture of 2,3-butadien-1-ol[24] (140 mg, 2.0 mmol), CuI (38 mg, 0.2 mmol), and Et_2O (2.0 mL) was successively treated with 1.0 M *p*-TolMgBr[25] in THF (5.0 mL, 5.0 mmol, 0 °C, 15 h), I_2 (0.77 g, 3.0 mol, 2 h) in THF (10 mL), 1 M HCl, aqueous $NaHCO_3$, and $Na_2S_2O_3$, dried over $MgSO_4$, and evaporated. Chromatography on silica gel (9/1 pentane/Et_2O) gave 251 mg (43%) of (*Z*)-3-iodo-4-(*p*-tolyl)-2-buten-1-ol: ^1H NMR ($CDCl_3$, Me_4Si) δ 2.30 (s, 3 H), 2.67 (bs, 1 H), 3.78 (s, 2 H), 4.16 (d, J = 5.7 Hz, 2 H), 5.86 (t, J = 5.7 Hz, 1 H), 7.0−7.15 (m, 4 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 21.04, 50.93, 67.04, 108.13, 128.84, 129.09, 134.74, 134.78, 136.36; IR (neat) 3320 (bs), 1644 (s) cm^{-1}. Oxidation of (*Z*)-3-iodo-4-(*p*-tolyl)-2-buten-1-ol (109 mg, 0.38 mmol) with PCC[23] (0 °C, 3 h) and chromatography on silica gel (90/10 pentane/Et_2O) yielded 85 mg (78%) of (*Z*)-3-iodo-4-(*p*-tolyl)-2-buten-1-al: ^1H NMR ($CDCl_3$, Me_4Si) δ 2.33 (s, 3 H), 4.04 (s, 2 H), 6.18 (t, J = 6.4 Hz, 1 H), 7.07 (d, J = 7.95 Hz, 2 H), 7.15 (d, J = 7.95 Hz, 2 H), 9.55 (d, J = 6.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 21.11, 53.19, 129.13, 129.53 (2C), 132.69, 133.13, 137.34, 197.71. (*Z*)-3-Iodo-4-(*p*-tolyl)-2-buten-1-al (85 mg, 0.30 mmol) in THF (1.0 mL) was treated with 1.0 M TolMgBr in THF (0.76 mL, 0.76 mmol, 0 °C, 1 h), diluted with Et_2O, washed with 1 M HCl and aqueous $NaHCO_3$, dried over $MgSO_4$, and evaporated. Chromatography on silica gel (90/10 pentane/Et_2O) yielded 94 mg (82%) of (*Z*)-1,4-bis(*p*-tolyl)-3-iodo-2-buten-1-ol. A mixture of (*Z*)-1,4-bis(*p*-tolyl)-3-iodo-2-buten-1-ol (94 mg, 0.25 mmol) and DDQ[26] (114 mg, 0.50 mmol) in dioxane (2.0 mL) was stirred for 48 h at 25 °C and evaporated. Chromatography on silica gel (90/10 pentane/CH_2Cl_2) yielded 59 mg (63%) of **14d**: ^1H NMR ($CDCl_3$, Me_4Si) δ 2.34 (s, 3 H), 2.39 (s, 3 H), 4.05 (d, J = 1.1 Hz, 2 H), 7.10 (t, J = 1.1 Hz, 1 H), 7.16 (s, 4 H), 7.24 (d, J = 8.2 Hz, 2 H), 7.79 (d, J = 8.2 Hz, 2 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 21.16, 21.72, 53.44, 115.22, 128.79, 129.17, 129.35, 129.47, 131.15, 134.21, 134.31, 136.97, 144.29, 190.49; IR (neat) 1664 (s) cm^{-1}.

***o*-Iodophenyl *p*-Tolyl Ketone (17).** A solution of *o*-iodobenzaldehyde[27] (3.90 g, 16.8 mmol) in THF (15 mL) was successively treated with 1 M *p*-TolMgBr in THF (20 mL, 20 mmol, 0 °C, 30 min) and 1 M HCl, extracted with Et_2O, washed with brine, dried over $MgSO_4$, filtered, and evaporated to give (*o*-iodophenyl)-*p*-tolylmethanol which was directly oxidized with PCC[23] (3 h, 25 °C). Chromatography on silica gel (90/10 pentane/Et_2O) afforded 2.0 g (62%) of **17**: ^1H NMR ($CDCl_3$, Me_4Si) δ 2.42 (s, 3 H), 7.1−7.2 (m, 1 H), 7.2−7.35 (m, 3 H), 7.43 (dt, J = 7.5, 1.0 Hz, 1 H), 7.70 (dd, J = 6.5, 1.7 Hz, 2 H), 7.91 (dd, J = 8.0, 1.8 Hz, 1 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 21.81, 92.18, 127.74, 128.28, 129.38, 130.60, 130.92, 133.05, 139.56, 144.62, 144.77, 196.86; IR (neat) 1668 (s), 1602 (s) cm^{-1}.

(Z)-1-Iodo-1-phenyl-2-(*n*-propyl)-1-penten-3-one (21c). Oxidation[23] of (*Z*)-2-(*n*-propyl)-3-iodo-3-phenyl-2-propen-1-ol (1.26 g, 4.17 mmol) with PCC[23] afforded 0.93 g (74%) of (*Z*)-2-(*n*-propyl)-3-iodo-3-phenyl-2-propen-1-al: ^1H NMR ($CDCl_3$, Me_4Si) δ 0.73 (t, J = 7.3 Hz, 3 H), 1.2−1.4 (m, 2 H), 2.1−2.25 (m, 2 H), 7.2−7.45 (m, 5 H), 9.76 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 13.79, 22.06, 30.69, 118.97, 126.77, 128.29, 128.82, 142.96, 143.44, 198.62; IR (neat) 1680 cm^{-1}. (*Z*)-2-(*n*-Propyl)-3-iodo-3-phenyl-2-propen-1-al (405 mg, 1.35 mmol) in THF (4 mL) was treated with 1 M EtMgCl (2.0 mL, 2.0 mmol, 0 °C, 1 h) in THF and 1 M HCl, diluted with Et_2O, washed with $NaHCO_3$, dried over $MgSO_4$, and evaporated. The crude oil was oxidized with PCC[23] (0 °C, 8 h) to give 164 mg (37%) of **21c**: ^1H NMR ($CDCl_3$, Me_4Si) δ 0.78 (t, J = 7.3 Hz, 3 H), 1.22 (t, J = 7.3 Hz, 3 H), 1.3−1.45 (m, 2 H), 2.1−2.25 (m, 2 H), 2.80 (q, J = 7.3 Hz, 2 H), 7.2−7.4 (m, 5 H);

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^{13}C NMR ($CDCl_3$) δ 7.55, 13.53, 21.41, 34.35, 34.58, 92.06, 128.07, 128.11, 128.23, 141.97, 151.05, 208.52; IR (neat) 1702 cm^{-1}.

(Z)-1,4-Diphenyl-3-(*n*-propyl)-4-iodo-3-buten-2-one (21d). (*Z*)-2-(*n*-Propyl)-3-iodo-3-phenyl-2-propen-1-al (see **21c** for preparation) (405 mg, 1.35 mmol) in THF (4 mL) was treated with 2.0 M $PhCH_2$-MgCl in THF (0.81 mL, 1.62 mmol, 0 °C, 1 h) and 1 M HCl, diluted with Et_2O, washed with $NaHCO_3$, dried over $MgSO_4$, and evaporated. Chromatography on silica gel (95/5 pentane/Et_2O) afforded 148 mg (36%) of (*Z*)-2-(*n*-propyl)-3-iodo-3-phenyl-2-propen-1-ol as a byproduct and 125 mg (24%) of (*Z*)-1,4-diphenyl-3-(*n*-propyl)-4-iodo-3-buten-2-ol: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.71 (t, J = 7.3 Hz, 3 H), 1.3−1.5 (m, 2 H), 1.83 (d, J = 2.2 Hz, 1 H), 2.0−2.3 (m, 2 H), 2.80 (dd, J = 10.0, 13.6 Hz, 1 H), 3.11 (dd, J = 3.3, 13.6 Hz, 1 H), 4.85−4.95 (m, 1 H), 7.15−7.45 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 14.28, 23.44, 31.56, 41.92, 81.84, 96.76, 126.70, 127.57, 128.12, 128.20, 128.57, 129.51, 138.05, 144.52, 148.07; IR (neat) 3360 cm^{-1}. Oxidation of (*Z*)-1,4-diphenyl-3-(*n*-propyl)-4-iodo-3-buten-2-ol (125 mg, 0.32 mmol) with PCC[23] (25 °C, 10 h) afforded after chromatography on silica gel (95/5 pentane/Et_2O) 78.8 mg (63%) of **21d**: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.73 (t, J = 7.3 Hz, 3 H), 1.2−1.4 (m, 2 H), 2.0−2.1 (m, 2 H), 4.12 (s, 2 H), 7.2−7.4 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 13.56, 21.39, 34.89, 47.93, 93.10, 127.19, 128.09, 128.26, 128.33, 128.49, 129.95, 133.06, 142.02, 150.56, 204.83; IR (neat) 1702 cm^{-1}.

(Z)-6-Iodo-5-decen-4-one (21g). (*Z*)-3-Iodo-2-hepten-1-al (1.11 g, 4.69 mmol) in THF (5.0 mL) was treated with 2.0 M *n*-PrMgCl in Et_2O (2.80 mL, 5.60 mmol, 0 °C, 1 h) and then 1 M HCl, diluted with Et_2O, washed with $NaHCO_3$, dried over $MgSO_4$, and evaporated. Chromatography on silica gel afforded 1.06 g (86%) of (*Z*)-6-iodo-5-decen-4-ol, which was oxidized with PCC[23] (25 °C, 6 h) to give 0.72 g (86%) of **21g**: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.93 (t, J = 7.3 Hz, 3 H), 0.94 (t, J = 7.3 Hz, 3 H), 1.33 (sex, J = 7.4 Hz, 2 H), 1.5−1.8 (m, 4 H), 2.47 (t, J = 7.3 Hz, 2 H), 2.68 (t, J = 7.3 Hz, 2 H), 6.68 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 13.56, 13.67, 17.06, 21.26, 31.25, 46.05, 47.51, 116.98, 130.32, 198.25; IR (neat) 1698 (s), 1464 (s) cm^{-1}.

(Z)-5-Iodo-6-(*p*-tolyl)-4-hexen-3-one (21h). (*Z*)-2-(*n*-Propyl)-3-iodo-3-phenyl-2-propen-1-al (656 mg, 2.29 mmol) in THF (10 mL) was treated with 2 M EtMgCl in THF (1.37 mL, 2.74 mmol, 0 °C, 1 h), quenched with 1 M HCl, diluted with Et_2O, washed with $NaHCO_3$, dried over $MgSO_4$, and evaporated. Chromatography on silica gel (9/1 pentane/Et_2O) afforded 694 mg (86%) of (*Z*)-5-iodo-6-(*p*-tolyl)-4-hexen-3-ol, which was directly oxidized with PCC[23] to give 617 mg (86%) of **21h**: stereoselectivity >98%; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 1.08 (t, J = 7.3 Hz, 3 H), 2.32 (s, 3 H), 2.49 (q, J = 7.2 Hz, 2 H), 3.97 (s, 2 H), 6.63 (s, 1 H), 7.0−7.15 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 7.80, 21.34, 37.67, 53.87, 114.91, 129.29, 129.57, 131.66, 134.33, 137.07, 199.21; IR (neat) 1702 (s) cm^{-1}.

Pd-Catalyzed Carbonylation of (*Z*)-β-Iodoalkenyl Aryl Ketones. (a) 2,3-Di-(*n*-propyl)-4-phenyl-2-buten-4-olide (13a). Representative Procedure. (i) With Triethylamine as a Base (Method C). A mixture of **14a** (86 mg, 0.25 mmol), Et_3N (0.14 mL, 0.10 g, 1.0 mmol), H_2O (18 μL, 18 mg, 1.0 mmol), $Cl_2Pd(PPh_3)_2$ (8 mg, 0.012 mmol, 5 mol %), and benzene (1.0 mL) was stirred at 120 °C under CO pressure (20 atm) for 12 h. The reaction mixture was treated with H_2O, extracted with Et_2O, dried over $MgSO_4$, filtered, and evaporated. Analysis by ^{1}H NMR spectroscopy of the crude reaction mixture showed the formation of **13a** in 95−99% yield. Chromatography on silica gel (97/3 pentane/ethyl acetate) yielded 51 mg (84%) of **13a**: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.89 (t, J = 7.5 Hz, 3 H), 0.96 (t, J = 7.5 Hz, 3 H), 1.2−1.6 (m, 2 H), 1.61 (sex, J = 7.5 Hz, 2 H), 1.96 (ddd, J = 14.4, 9.0, 5.4 Hz, 1 H), 2.2−2.4 (m, 3 H), 5.68 (s, 1 H), 7.4−7.55 (m, 2 H), 7.55−7.7 (m, 1 H), 7.9−8.0 (m, 2 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 13.93, 14.05, 21.27, 21.58, 25.62, 28.53, 83.73, 126.90, 127.23, 128.90, 129.19, 135.11, 163.20, 174.55; IR (neat) 1756, 1670 cm^{-1}; high-resolution MS calcd for $C_{16}H_{20}O_2$ 244.1463, found 244.1470.

(ii) With Pyridine. Method C was modified by replacing NEt_3 with pyridine (81 μL, 79 mg, 1.0 mmol) and omitting the addition of H_2O and used to convert **14a** to **13a** in 58% NMR yield, with 21% of **14a** remaining.

(iii) With *N,N*-Diethyl-α,α-dideuteriobenzylamine. Using *N,N*-diethyl-α,α-dideuteriobenzylamine (165 mg, 1.0 mmol) in place of NEt_3 and omitting the addition of H_2O in method C, **14a** was converted to **13a** in 72% NMR yield. Incorporation of D at the γ position was <2%.

(b) 2,3,4-Triphenyl-2-buten-4-olide (13c). Using method C, **13c** was formed in 50% NMR yield. Chromatography on silica gel (93/7 pentane/ethyl acetate) afforded 27 mg (35%) of **13c**: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 6.26 (s, 1 H), 7.0−7.6 (m, 15 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 83.65, 126.84, 127.60 (2C), 128.21, 128.29 (2C), 128.52 (2C), 128.66 (2C), 128.81, 128.89 (2C), 129.33, 129.38 (2C), 129.84, 131.10, 134.74, 159.29, 172.41; IR (neat) 1756 (s), 1670 (s) cm^{-1}; high-resolution MS calcd for $C_{22}H_{16}O_2$ 312.1150, found 312.1158.

(c) 4-Deuterio-2,3-di-(*n*-propyl)-4-phenyl-2-buten-4-olide. The use of D_2O (20 μL, 20 mg, 1.0 mmol) in place of H_2O in the representative procedure led to the formation of **13a** in 95−99% yield with incorporation of D at the γ position to the extent of 85%. Chromatography on silica gel (93/7 pentane/ethyl acetate) yielded 51 mg (83%) of the 4-deuterio derivative of **13a**: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.89 (t, J = 7.5 Hz, 3 H), 0.96 (t, J = 7.5 Hz, 3 H), 1.2−1.6 (m, 2 H), 1.61 (sex, J = 7.5 Hz, 2 H), 1.96 (ddd, J = 14.4, 9.0, 5.4 Hz, 1 H), 2.2−2.4 (m, 3 H), 7.4−7.55 (m, 2 H), 7.55−7.7 (m, 1 H), 7.9−8.0 (m, 2 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 13.93, 14.05, 21.27, 21.58, 25.62, 28.53, 83.73 (t, J = 22.5 Hz), 126.90, 127.23, 128.90, 129.19, 135.11, 163.20, 174.55; IR (neat) 1756, 1670 cm^{-1}; high-resolution MS calcd for $C_{16}H_{19}DO_2$ 245.1526, found 245.1529.

(d) 3-(*p*-Tolylmethyl)-4-(*p*-tolyl)-2-buten-4-olide (13d). Using method C, **13d** was obtained from **14d** in 50% NMR yield. Chromatography on silica gel (93/7 pentane/ethyl acetate) afforded 30 mg (43%) of **13d**: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 2.32 (s, 3 H), 2.34 (s, 3 H), 3.55 (m, 2 H), 5.82 (q, J = 1.9 Hz, 1 H), 6.88 (q, J = 1.8 Hz, 1 H), 7.0−7.2 (m, 8 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 21.03, 21.18, 31.31, 82.37, 126.43 (2C), 128.77 (2C), 129.43 (2C), 129.57 (2C), 131.37, 134.02, 134.13, 136.41, 139.07, 148.83, 173.57; IR (neat) 1750 cm^{-1}; high-resolution MS calcd for $C_{19}H_{18}O_2$ 277.1228, found 277.1191.

Synthesis of *N,N*-Diethyl-α,α-dideuteriobenzylamine. A solution of α,α-dideuteriobenzyl alcohol (2.55 g, 25.0 mmol) and NEt_3 (4.9 mL, 3.56 g, 35 mmol) in CH_2Cl_2 (50 mL) was treated with CH_3SO_2Cl (2.3 mL, 3.45 g, 30.0 mmol, 0 °C, 2h), diluted with Et_2O, washed with H_2O, dried over $MgSO_4$, and evaporated to give 2.70 g (62%) of a colorless oil. A solution of this crude oil in THF was added at 0 °C to a solution of $LiNEt_2$, prepared by addition of 2.5 M *n*-BuLi in hexane (6.4 mL, 16.0 mmol) to $HNEt_2$ (1.17g, 16.0 mmol, 0 °C, 15 min) in THF (10 mL), stirred for 12h at 23 °C, diluted with ether, washed with H_2O, dried over $MgSO_4$, and evaporated. Distillation over $LiAlH_4$ afforded 0.82 g (35%) of *N,N*-diethyl-α,α-dideuteriobenzylamine: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 1.03 (t, J = 7.2 Hz, 6 H), 2.50 (q, J = 7.2 Hz, 4 H), 7.2−7.4 (m, 5 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 11.47, 46.45, 63.25 (pent, J = 20 Hz), 127.31, 128.32, 128.97, 139.26.

Pd-Catalyzed Carbonylation of (*Z*)-β-Iodoalkenyl Alkyl Ketones. (a) (*Z*)-2,3-Di-(*n*-propyl)-4-methylene-2-buten-4-olide (12a). Representative Procedure (Method D). A mixture of **21a** (140 mg, 0.50 mmol), $Cl_2Pd(PPh_3)_2$ (17 mg, 25 μmol), Et_3N (0.14 mL, 0.11 g, 1.0 mmol), and DMF (1.0 mL) was stirred at 100 °C under CO pressure (40 atm) for 10 h, treated with H_2O, extracted with CH_2Cl_2, dried over $MgSO_4$, and evaporated. Analysis of the crude reaction mixture by ^{1}H NMR spectroscopy showed the formation of **12a** in 66% yield. Chromatography on silica gel (99/1 pentane/Et_2O) afforded 59 mg (66%) of **12a**: stereoisomeric purity >98%; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.95 (t, J = 7.2 Hz, 3 H), 0.99 (t, J = 7.4 Hz, 3 H), 1.5−1.7 (m, 4 H), 2.25−2.35 (m, 2 H), 2.4−2.5 (m, 2 H), 4.82 (d, J = 2.7 Hz, 1 H), 5.07 (d, J = 2.7 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 13.96, 14.06, 21.45, 22.86, 25.82, 26.63, 92.51, 130.16, 150.64, 155.16, 170.26; IR (neat) 1772 cm^{-1}; high-resolution MS calcd for $C_{11}H_{16}O_2$ 180.1151, found 180.1156.

(b) (*Z*)-2,3-Di-(*n*-propyl)-4-hexylidene-2-buten-4-olide (12b). Using method D, **12b** was formed in 75% NMR yield. Chromatography on silica gel (99/1 pentane/Et_2O) afforded 80 mg (70%) of **12b**: stereoisomeric purity >98%; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.8−1.1 (m, 9 H), 1.2−1.7 (m, 10 H), 2.2−2.5 (m, 6 H), 5.22 (t, J = 7.8 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 13.92, 14.05, 21.55, 22.34, 23.07, 25.70, 25.95, 26.50 (2C), 28.83, 31.41, 111.29, 127.79, 149.14, 150.94, 170.64; IR (neat) 1762 cm^{-1}; high-resolution MS calcd for $C_{16}H_{26}O_2$ 250.1934, found 250.1914.

(c) (*Z*)-2-Phenyl-3-(*n*-propyl)-4-ethylidene-2-buten-4-olide (12c). Using method D, **12c** was formed in 72% NMR yield. Chromatography on silica gel (97/3 pentane/Et_2O) afforded 80 mg (70%) of **12c**: stereoisomeric purity >98%; ^1H NMR ($CDCl_3$, Me_4Si) δ 0.96 (t, J = 7.4 Hz, 3 H), 1.55−1.7 (m, 2 H), 2.00 (d, J = 7.4 Hz, 3 H), 2.5−2.65 (m, 2 H), 5.46 (q, J = 7.4 Hz, 1 H), 7.3−7.55 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 11.77, 14.19, 23.32, 26.88, 107.93, 126.23, 128.45 (2C), 128.74, 129.99, 149.84, 151.07, 169.18; IR (neat) 1756 cm^{-1}; high-resolution MS calcd for $C_{15}H_{16}O_2$ 228.1151, found 228.1156.

(d) (*Z*)-2-Phenyl-3-(*n*-propyl)-4-benzylidene-2-buten-4-olide (12d). Using method D, **12d** was formed in 68% NMR yield. Chromatography on silica gel (97/3 pentane/Et_2O) afforded 91 mg (63%) of **12d**: stereoisomeric purity >98%; ^1H NMR ($CDCl_3$, Me_4Si) δ 1.03 (t, J = 7.4 Hz, 3 H), 1.6−1.8 (m, 2 H), 2.65−2.75 (m, 2 H), 6.16 (s, 1 H), 7.3−7.6 (m, 8 H), 7.85 (d, J = 7.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 14.31, 23.51, 27.00, 110.07, 125.97, 128.63, 128.69, 128.78 (2C), 128.87, 130.01, 130.55, 133.12, 148.16, 152.46, 169.24; IR (neat) 1758 cm^{-1}; high-resolution MS calcd for $C_{20}H_{18}O_2$ 290.1307, found 290.1315.

(e) (*Z*)-2,3-Dimethyl-4-octylidene-2-buten-4-olide (12e). Using method D, **12e** was formed in 84% NMR yield. Chromatography on silica gel (99/1 pentane/Et_2O) afforded 89 mg (80%) of **12e**: stereoisomeric purity >98%; ^1H NMR ($CDCl_3$, Me_4Si) δ 0.88 (t, J = 6.6 Hz, 3 H), 1.2−1.5 (m, 10 H), 1.89 (s, 3 H), 2.03 (s, 3 H), 2.3−2.45 (m, 2 H), 5.25 (t, J = 7.9 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 8.47, 9.67, 13.99, 22.54, 25.91, 28.98, 29.17 (2C), 31.69, 110.91, 123.85, 146.82, 149.88, 170 91; IR (neat) 1768 cm^{-1}; high-resolution MS calcd for $C_{14}H_{22}O_2$ 222.1621, found 222.1628.

(f) (*Z*)-2,3-Dimethyl-4-pentylidene-2-buten-4-olide (12f). Using method D, **12f** was formed in 82% NMR yield. Chromatography on silica gel (99/1 pentane/Et_2O) afforded 108 mg (80%) of **12f**: stereoisomeric purity >98%, ^1H NMR ($CDCl_3$, Me_4Si) δ 0.92 (t, J = 6.9 Hz, 3 H), 1.2−1.55 (m, 4 H), 1.90 (s, 3 H), 2.03 (s, 3 H), 2.3−2.55 (m, 2 H), 5.22 (t, J = 7.9 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 8.44, 9.72, 13.69. 22.24, 25.56, 31.20, 110.80, 123.79, 146.81, 149.86, 170.84; IR (neat) 1766 cm^{-1}; high-resolution MS calcd for $C_{11}H_{16}O_2$ 180.1151, found 180.1149.

(g) 2-(*n*-Butyl)-4-(*n*-propylidene)-2-buten-4-olide (12g). Using method D, **12g** was formed in 80% NMR yield as an 81/19 *Z*/*E* mixture along with an 8% of 2-(*n*-butyl)-4-(*n*-propyl)-2-butenolide. The spectral data are as follows: *Z*-**12g**: ^1H NMR ($CDCl_3$, Me_4Si) δ 0.95 (t, J = 7.2 Hz, 3 H), 1.08 (t, J = 7.2 Hz, 3 H), 1.3−1.8 (m, 4 H), 2.3−2.5 (m, 4 H), 5.15 (t, J = 6.2 Hz, 1 H), 6.97 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 13.79, 13.83, 19.76, 22.37, 24.92, 29.78, 115.40, 135.28, 137.00, 148.14, 170.94. The following signals were discernible for the *E*-isomer: ^1H NMR ($CDCl_3$, Me_4Si) δ 5.59 (t, J = 5.0 Hz, 1 H), 7.28 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 22.52, 25.29, 116.28, 135.28, 137.00, 148.14, 170.94. Under the same conditions except that benzene was used in place of DMF, **12g** was formed in 74% NMR yield as a 62/38 *Z*/*E* mixture along with a 9% of 2-(*n*-butyl)-4-(*n*-propyl)-2-butenolide.

(h) (*E*)- and (*Z*)-4-Ethylidene-2-(*p*-tolylmethyl)-2-buten-4-olide (12h). Using method D, **12h** was formed in 69% NMR yield as a 75/25 *Z*/*E* mixture along with a 25% of (*E*)-2-(*p*-tolylmethylene)-4-ethyl-3-buten-4-olide (**11h**). Chromatography on silica gel (6/1 pentane/Et_2O) afforded 131 mg (51%) of **12h** (*Z*), 38.7 mg of **12h** (*E*), and 64.3 mg (25%) of **11h**. The spectral data for (*Z*)-**12h** are as follows: ^1H NMR ($CDCl_3$, Me_4Si) δ 1.91 (d, J = 7.4 Hz, 3 H), 2.33 (s, 3 H), 3.61 (s, 2 H), 5.15 (q, J = 7.4 Hz, 1 H), 6.79 (s, 1 H), 7.12 (s, 4 H); ^{13}C NMR ($CDCl_3$) δ 11.67, 20.95, 31.04, 109.99, 128.66, 129.33, 133.08, 134.10, 136.31, 137.66, 149.09, 170.27; IR (neat) 1764 cm^{-1}; high-resolution MS calcd for $C_{14}H_{14}O_2$ 214.0994, found 214.0995. (*E*)-**12h**: ^1H NMR ($CDCl_3$, Me_4Si) δ 1.81 (d, J = 7.7 Hz, 3 H), 2.35 (s, 3 H), 3.64 (s, 2 H), 5.66 (q, J = 7.4 Hz, 1 H), 7.07 (s, 1 H), 7.14 (s, 4 H); ^{13}C NMR ($CDCl_3$) δ 11.67, 21.04, 31.37, 109.32, 128.79, 129.48, 133.34, 134.08, 134.33, 136.48, 149.19, 170.29; IR (neat) 1760 cm^{-1}. **11h**: ^1H NMR ($CDCl_3$, Me_4Si) δ 1.24 (t, J = 7.4 Hz, 3 H), 2.39 (s, 3 H), 2.51 (q, J = 7.4 Hz, 2 H), 6.25 (s, 1 H), 7.23 (d, J = 8.0 Hz, 2 H), 7.28 (s, 1 H), 7.45 (d, J = 8.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 10.16, 21.50, 22.15, 100.23, 129.70, 129.90, 132.30, 134.18, 140.49, 162.80, 170.07; IR (neat) 1768 cm^{-1}.

Pd-Catalyzed Carbonylation of β-Iodoenones Producing Butenolide Dimers. (a) 1,1′-Bis(*p*-tolyl)-3,3′-dioxo-1,1′-bis(1*H*,1′*H*-isobenzofuran) (18). Using method C where 4 equiv of H_2O (18 μL, 18 mg, 1.0 mmol) was used, **18** was formed in 95% NMR yield. Chromatography on silica gel (95/5 pentane/ethyl acetate) afforded 190 mg (85%) of **18** as a 1.2:1 mixture of two diastereomers. The following signals correspond to the mixture of diastereomers denoted as a and b: ^1H NMR ($CDCl_3$, Me_4Si) δ 2.14[a] (s, 6 H), 2.23[b] (s, 6 H), 6.90[a] (d, J = 8.1 Hz, 4 H), 7.02[b] (d, J = 8.1 Hz, 4 H), 7.2−7.8 (m, 20 H), 7.88[b] (d, J = 7.8 Hz, 2 H), 8.32[a] (d, J = 7.8 Hz, 2 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 20.84, 20.92, 90.21, 90.92, 124.36, 125.02, 125.50, 125.56, 126.18, 126.69, 128.46, 128.77, 129.53, 129.58, 134.06, 134.44, 138.04, 138.23, 149.34, 149.38, 168.83, 169.35; IR (CCl_4) 1778 cm^{-1}; high-resolution MS calcd for $C_{30}H_{22}O_4$ (M + 1) 447.1596, found 447.1597.

(b) 2,2′-Diphenyl-3,3′,4,4′-tetra-(*n*-propyl)-5,5′-dioxo-2,2′-bis-(2*H*,2*H*′-furan) (16a). Using method C where NEt_3 was replaced with K_2CO_3 (140 mg, 1.0 mmol), **13d** was formed in <3% NMR yield, if any. Chromatography on silica gel (99/1 pentane/ethyl acetate) afforded 31 mg (51%) of **16a** as 1:1 mixture diastereomeric mixture: ^1H NMR ($CDCl_3$, Me_4Si) δ 0.4−3.1 (m, 28 H), 7.0−7.7 (m, 10 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 13.96, 14.20 (2C), 14.75, 20.40, 21.15, 22.71, 22.74, 26.103, 26.52, 29.71, 30.03, 91.07, 93.02, 126.20 (2C), 126.30 (2C), 128.11, 128.25 (2C), 128.45 (2C), 128.77, 129.16, 130.78, 135.37, 135.75, 165.25, 168.15, 172.43, 173.13; IR (CCl_4) 1765, 1654 cm^{-1}; high-resolution MS calcd for $C_{32}H_{38}O_4$ (M + 1) 487.2848, found 487.2833.

Pd-Catalyzed Carbonylation of (*Z*)-β-Iodoenimines. (a) (*Z*)-3,4-Di-(*n*-propyl)-5-phenyl-3-pyrrolin-2-one (25a). Using method C, **25a** was formed in 77% NMR yield. Chromatography on silica gel (80/20 pentane/Et_2O) afforded 121 mg (65%) of **25a**: ^1H NMR ($CDCl_3$, Me_4Si) δ 0.84 (t, J = 7.4 Hz, 3 H), 0.92 (t, J = 7.4 Hz, 3 H), 1.1−1.65 (m, 4 H), 1.82 (ddd, J = 14, 9, 6 Hz, 1 H), 2.1−2.4 (m, 3 H), 4.92 (s, 1 H), 7.10−7.40 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 13.84 (2C), 21.84, 21.86, 25.28, 28.28, 62.39, 126.83, 128.00, 128.10, 128.61, 131.72, 137.40, 157.08, 175.19; IR (neat) 1700 cm^{-1}; high-resolution MS calcd for $C_{16}H_{21}NO$ 243.1623, found 243.1625.

(b) (*Z*)-3,4-Di-(*n*-propyl)-5-methylene-3-pyrrolin-2-one (25b). Using method D, **25b** was formed in 84% NMR yield. Chromatography on silica gel (80/20 pentane/Et_2O) afforded 102 mg (81%) of **25b**: ^1H NMR ($CDCl_3$, Me_4Si) δ 0.95 (t, J = 7.2 Hz, 3 H), 0.96 (t, J = 7.2 Hz, 3 H), 1.4−1.65 (m, 4 H), 2.2−2.5 (m, 4 H), 4.80 (s, 1 H), 4.92 (d, J = 1.0 Hz, 1 H), 9.15 (bs, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.05 (2C), 22.03, 23.72, 25.64, 26.34, 93.23, 133.77, 144.04, 144.38, 173.05; IR (neat) 3224, 1696 cm^{-1}; high-resolution MS calcd for $C_{11}H_{17}NO$ 179.1310, found 179.1316.

(c) (*Z*)-3,4-Dimethyl-5-octylidene-3-pyrrolin-2-one (25c). Using method D, **25c** was formed in 81% NMR yield. Chromatography on silica gel (40/60 pentane/Et_2O) afforded 175 mg (79%) of **25c**: ^1H NMR ($CDCl_3$, Me_4Si) δ 0.87 (t, J = 7.0 Hz, 3 H), 1.0−1.5 (m, 10 H), 1.85 (s, 3 H), 1.98 (s, 3 H), 2.25−2.35 (m, 2 H), 5.15−5.25 (m, 1 H), 8.80 (bs, 1 H); ^{13}C NMR ($CDCl_3$) δ 8.18, 9.52, 13.96, 18.87, 22.50, 27.30, 28.99, 29.12, 31.67, 110.82, 135.04, 138.44, 140.31, 172.78; IR (neat) 3220, 1694 cm^{-1}; high-resolution; MS calcd for $C_{14}H_{23}NO$ 221.1781, found 221.1785.

Acknowledgment. We thank the National Institutes of Health (GM 36792) for support of this work. C.C. and T.S. thank the Purdue Research Foundation and the Uehara Memorial Foundation, respectively, for fellowships. We also thank Johnson Matthey for a loan of $PdCl_2$. Dr. Y. N. Gulevich provided some experimental results described herein. Professor P. L. Fuchs provided a useful mechanistic suggestion. Professor K. Nozaki of Kyoto University has kindly informed us of their related study.

JA944059F