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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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.*, Cl₂Pd(PPh₃)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 ZrCp₂-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
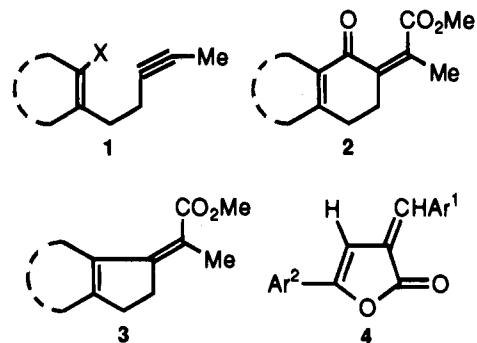
to proceed not via acylpalladation but via 1-benzyl-2-benzoylethynes formed by Pd-catalyzed carbonylative coupling. Thus, the feasibility of acylpalladation of alkynes has remained undemonstrated.[8]

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(PPh₃)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

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(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.
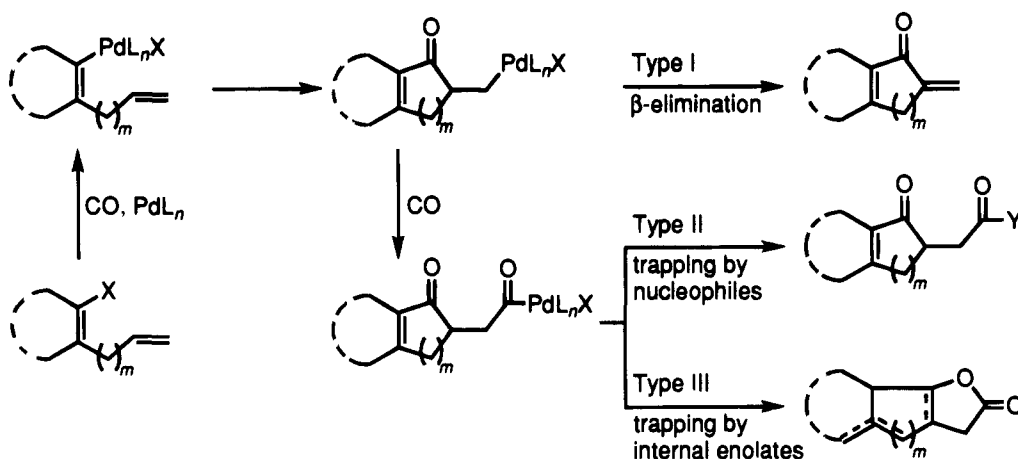(4) For related papers by other workers, see: (a) Brewis, S.; Hughes, P. R. *J. Chem. Soc., Chem. Commun.* **1965**, 489. (b) Oppolzer, W.; Keller, T. H.; Bedoya-Zurita, M.; Stone, C. *Tetrahedron Lett.* **1989**, *30*, 5883. (c) Oppolzer, W. *Pure Appl. Chem.* **1990**, *62*, 1941. (d) Oppolzer, W.; 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. Llebaria, 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.
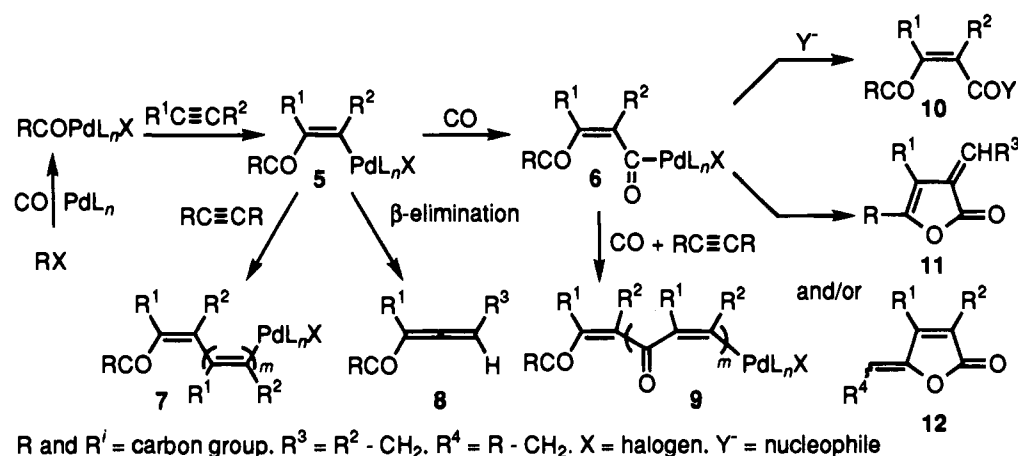(6) Zhang, Y.; Negishi, E. *J. Am. Chem. Soc.* **1989**, *111*, 3454.
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Scheme 1

Scheme 2

R and R' = 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

(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.

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.

(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.

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

		β-iodoenone			monomer		dimer	
	Ar	R¹	R²	base	13	yield,[b,c] %	16	yield,[b] %
14a	Ph	n-Pr	n-Pr	NEt₃	13a	99	16a	<1
14a	Ph	n-Pr	n-Pr	K₂CO₃	13a	<1	16a	53
14c	Ph	Ph	Ph	NEt₃	13c	55	16c	<1
14d	p-Tol	H	p-TolCH₂	NEt₃	13d	49	16d	<5

[a] All reactions were run using 20 atm of CO, 5 mol % of Cl₂Pd(PPh₃)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 NaHCO₃ where **11d** was formed in 3% yield.

Scheme 3
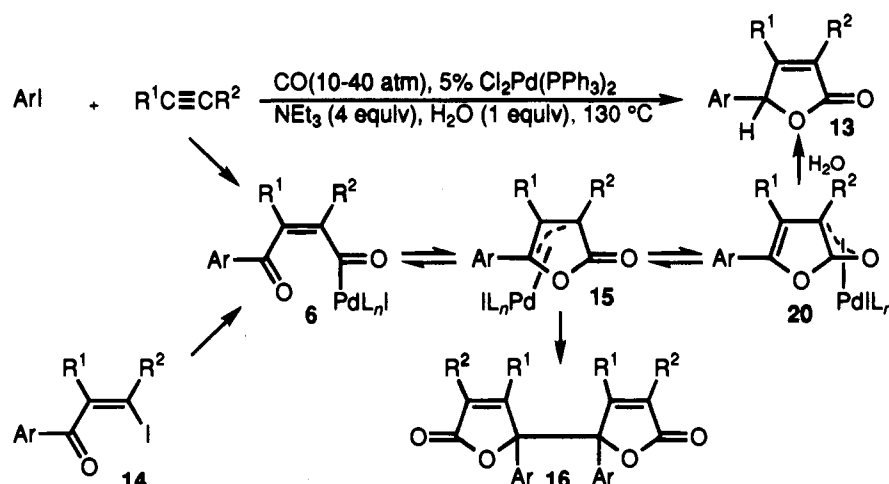
Having established the interchangeability between a 4-octyne−PhI mixture and **14a**, further mechanistic studies were conducted mainly with **14**, whose reaction was cleaner (Table 1). It is striking that the putative intermediate **6a** did not suffer from its trapping by an internal enolate to give **11a** (R = Ph, R¹ = n-Pr, R³ = 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., NEt₃, are known to reduce Pd(II) complexes via α-H abstraction.[15] We therefore prepared PhCD₂-NEt₂ and used it in place of NEt₃ 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 K₂CO₃ in place of NEt₃, which produced **16a** (Ar = Ph, R¹ = R² = n-Pr) in 53% yield and only a trace quantity, if any, of **13a**. Since K₂CO₃ 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 NEt₃, 5 mol % of Cl₂Pd(PPh₃)₂, and 4 equiv of D₂O. 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 H₂O is present. On this basis, the high sensitivity of the reaction producing **13** to H₂O 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 Cl₂Pd(PPh₃)₂, 4 equiv of H₂O, and 2 equiv of NEt₃ 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.
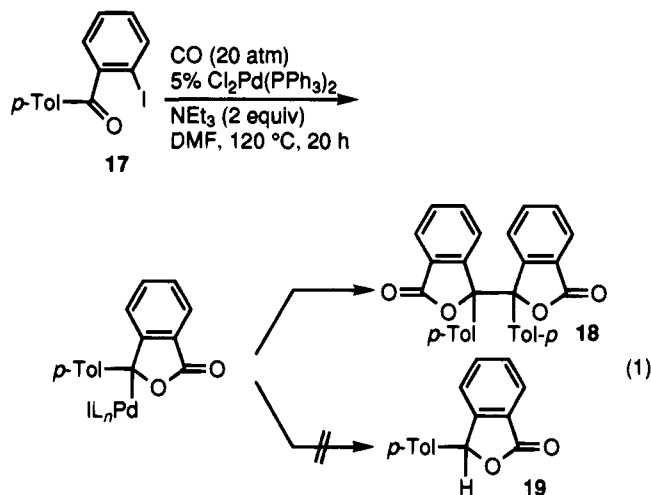
We suggest that, in Scheme 3, **15** probably undergoes migration of Pd to give **20**, which then is hydrolyzed to give **13**. This metallotropic process in the case of the reaction of **17** would involve temporary destruction of the aromatic *o*-phenylene group.

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$_2$-Pd(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$_2$ZrCp$_2$ followed by treatment with nitriles or aldehydes[13] (eq 2). In
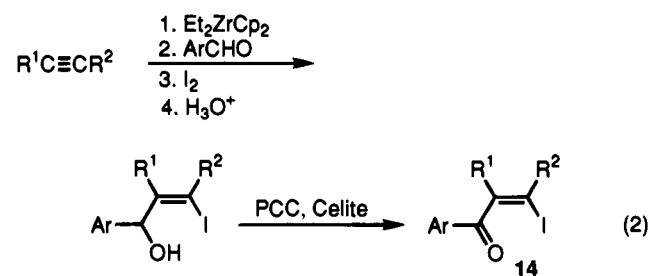
cases where *β*-iodoenones are α-unsubstituted, *e.g.*, **14d**, they can be prepared by (i) reduction of propargyl alcohols with Red-Al or LiAlH$_4$ followed by iodinolysis with I$_2$, (ii) oxidation with PCC, (iii) addition of a Grignard reagent, and (iv) reoxidation with PCC.

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$_2$ZrCp$_2$ 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.
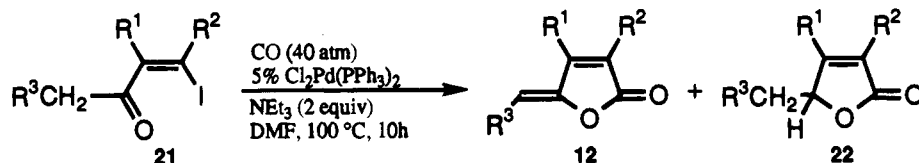
(18) Negishi, E.; Ay, M.; Sugihara, T. *Tetrahedron* **1993**, *49*, 5471.

(19) Lardelli, G.; Dcjkstra, G.; Harkes, P. D.; Boldingh, J. *Recl. Trav. Chim. Pays-Bas.* **1966**, *85*, 43.

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

$$R^1C\equiv CR^2 + ArI \xrightarrow[\substack{H_2O \text{ (1 equiv), base}\\ \text{benzene, 130 °C, 20 h}}]{\substack{CO \text{ (20 atm)}\\ 5\% \text{ Cl}_2\text{Pd(PPh}_3)_2}} \quad \text{13 (A)} + \text{13 (B)}$$
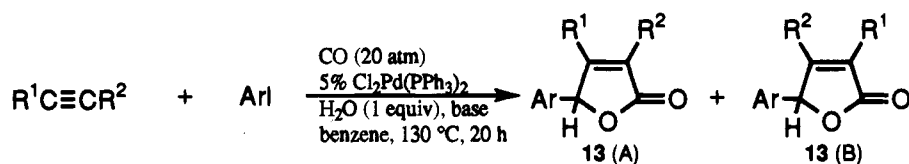
alkyne							
R^1	R^2	Ar of ArI	base[a]	product	combined yield,[b] %	A/B	recovered alkyne,[b] %
n-Pr	*n*-Pr	*p*-An	NEt₃	**13e**	66 (51)	c	d
n-Pr	*n*-Pr	*p*-An	NaHCO₃	**13e**	54	c	d
n-Pr	*n*-Pr	*m*-Tol	NEt₃	**13f**	50 (39)	c	d
n-Pr	*n*-Pr	*p*-ClC₆H₄	NEt₃	**13g**	40 (35)	c	d
Bn	Bn	*m*-Tol	NEt₃	**13b**	42 (35)	c	17
n-Bu	*p*-An	Ph	NaHCO₃	**13h**	65 (64)	89/11	20
n-Bu	*p*-An	*p*-An	NaHCO₃	**13i**	65 (56)	91/9	32
n-Bu	*p*-An	*p*-MeO₂CC₆H₄	NaHCO₃	**13j**	35 (21)	91/9	45
Me₃Si	*n*-Pr	Ph	NEt₃	**13k**	39 (31)	94/6	30
Me₃Si	*n*-Pr	*p*-An	NEt₃	**13l**	37 (34)	94/6	d

[a] Either 8 equiv of NEt₃ or 4 equiv of NaHCO₃ 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]

$$\text{21} \xrightarrow[\substack{\text{NEt}_3 \text{ (2 equiv)}\\ \text{DMF, 100 °C, 10h}}]{\substack{CO \text{ (40 atm)}\\ 5\% \text{ Cl}_2\text{Pd(PPh}_3)_2}} \quad \text{12} + \text{22}$$

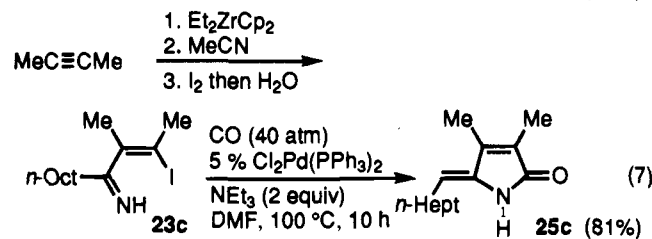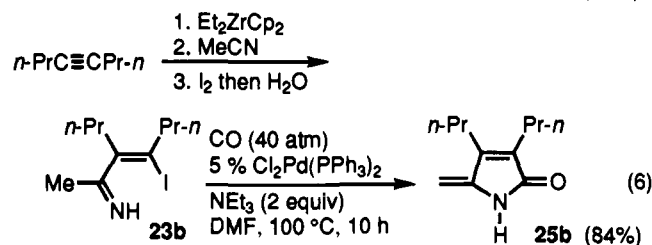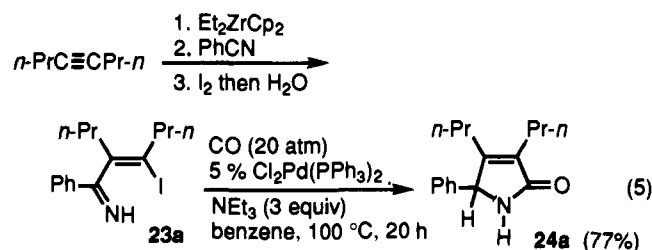|	β-iodoenone			product yield,[b] %	
	R^1	R^2	R^3	**12**	**22**
21a	*n*-Pr	*n*-Pr	H	66 (66)	<2
21b	*n*-Pr	*n*-Pr	*n*-Pent	75 (70)	4
21c	*n*-Pr	Ph	Me	72 (70)	8
21d	*n*-Pr	Ph	Ph	68 (63)	6
21e	Me	Me	*n*-Hept	84 (80)	4
21f[19]	Me	Me	*n*-Bu	82 (80)	4

[a] All reactions were run at 40 atm of CO in the presence of 5 mol % of Cl₂Pd(PPh₃)₂ and 2 equiv of NEt₃ in DMF at 100 °C for 10 h. [b] By NMR. The numbers in parentheses are isolated yields.

	12g (Z)	**12g (E)**	**22g**
DMF	80% (Z/E = 81/19)		8%
benzene	74% (Z/E = 62/38)		9%

$$\text{21g} \xrightarrow[\substack{\text{NEt}_3 \text{ (2 equiv)}\\ 100 \text{ °C, 10 h}\\ \text{solvent}}]{\substack{CO \text{ (40 atm)}\\ 5\% \text{ Cl}_2\text{Pd(PPh}_3)_2}} \quad \text{12g (Z)} + \text{12g (E)} + \text{22g} \quad (3)$$

$$\text{21h} \xrightarrow[\substack{\text{NEt}_3 \text{ (2 equiv)}\\ \text{DMF, 100 °C, 10 h}}]{\substack{CO \text{ (40 atm)}\\ 5\% \text{ Cl}_2\text{Pd(PPh}_3)_2}} \quad \text{12h (Z) (52%)} + \text{12h (E) (17%)} + \text{11h (25%)} \quad (4)$$
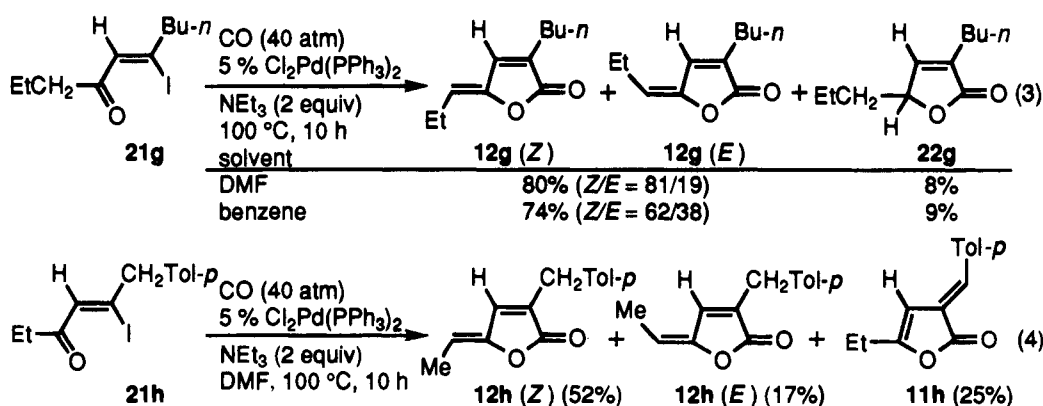
prolonged treatment with 10% HCl were the corresponding imines. As expected, their carbonylation under the same conditions as those used above cleanly produced lactams. The reaction of **23a** lacking an α'-H atom gave **24a**, while **23b** and **23c** provided **25b** and **25c**, respectively (eqs 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., Cl₂Pd(PPh₃)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

n-PrC≡CPr-n → 1. Et₂ZrCp₂ 2. PhCN 3. I₂ then H₂O

$$(5)$$

23a

24a (77%)

n-PrC≡CPr-n → 1. Et₂ZrCp₂ 2. MeCN 3. I₂ then H₂O

$$(6)$$

23b

25b (84%)

MeC≡CMe → 1. Et₂ZrCp₂ 2. MeCN 3. I₂ then H₂O

$$(7)$$

23c

25c (81%)

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. ¹H and ¹³C 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, CH₃CN, DMF, and NEt₃ were dried over molecular sieves 4A. The preparation of Cl₂Pd(PPh₃)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), Et₃N (0.28 mL, 0.22 g, 2.0 mmol), MeOH (160 μL, 128 mg, 4.0 mmol), Cl₂Pd(PPh₃)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), Et₃N (0.21 mL, 0.15 g, 1.5 mmol), Cl₂Pd(PPh₃)₂ (35 mg, 0.05 mmol), and CH₃CN (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 Et₂O, washed with H₂O, dried over

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

MgSO₄, and evaporated. Analysis of the crude reaction mixture showed the formation of 3-pentynyl m-toluate in 85% NMR yield: ¹H NMR (CDCl₃, Me₄Si) 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); ¹³C NMR (CDCl₃, Me₄Si) 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), Et₃N (0.21 mL, 0.15 g, 1.5 mmol), Cl₂Pd(PPh₃)₂ (35 mg, 0.05 mmol), and CH₃CN (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: ¹H NMR (CDCl₃, Me₄Si) 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); ¹³C NMR (CDCl₃, Me₄Si) 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), Et₃N (1.12 mL, 0.81 g, 8.0 mmol), H₂O (18 μL, 18 mg, 1.0 mmol), and Cl₂Pd(PPh₃)₂ (35 mg, 0.05 mmol) was stirred at 130 °C under CO pressure (20 atm) for 24 h and then treated with H₂O, extracted with CH₂Cl₂, dried over MgSO₄, and evaporated. Analysis of the crude reaction mixture by ¹H 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/Et₂O) afforded 140 mg (51%) of 13e: ¹H NMR (CDCl₃, Me₄Si) 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); ¹³C NMR (CDCl₃, Me₄Si) 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 C₁₇H₂₂O₃ 274.1569, found 274.1570.

Representative Procedure (Method B). The above reaction was performed using NaHCO₃ (336 mg, 4.0 mmol) in place of NEt₃ under otherwise the same conditions described above. Analysis of the crude reaction mixture by ¹H 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/Et₂O) afforded 124 mg (35%) of 13b: ¹H NMR (CDCl₃, Me₄Si) 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); ¹³C NMR (CDCl₃, Me₄Si) 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 C₂₅H₂₂O₂ 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%, ¹H NMR (CDCl₃, Me₄Si) 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); ¹³C NMR (CDCl₃, Me₄Si) 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 C₂₅H₁₈D₄O 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/Et₂O) afforded 100 mg (39%) of 13f: ¹H NMR (CDCl₃, Me₄Si) 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); ¹³C NMR (CDCl₃, Me₄Si) 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 C₁₇H₂₂O₂ 258.1620, found 258.1621.

(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$_2$O) afforded 97 mg (35%) of **13g**: ^{1}H
NMR (CDCl$_3$, Me$_4$Si) 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$_4$Si) 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$_2$O)
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: ^{1}H NMR (CDCl$_3$, Me$_4$Si) 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$_4$Si) 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$_2$-
Cl$_2$) 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: ^{1}H NMR (CDCl$_3$, Me$_4$Si) 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$_4$Si) 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$_2$Cl$_2$) afforded 80 mg (21%) of an 91/9
regioisomeric mixture of **13j** and 3-(*p*-anisyl)-2-butyl-4-(*p*-(methoxy-
carbonyl)phenyl)-2-buten-4-olide. The spectral data for **13j** are as
follows: ^{1}H NMR (CDCl$_3$, Me$_4$Si) 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$_4$Si) 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$_2$O) afforded 85 mg (31%) of a >99/1
regioisomeric mixture of **13k** and 4-phenyl-2-(*n*-propyl)-3-(trimethyl-
silyl)-2-buten-4-olide. The spectral data for **13k** are as follows: ^{1}H
NMR (CDCl$_3$, Me$_4$Si) 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$_4$Si) 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$_2$Si 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$_2$O)
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 spec-
tral data for **13l** are as follows: ^{1}H NMR (CDCl$_3$, Me$_4$Si) 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$_4$Si) 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$_3$Si 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$_2$O (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; ^{1}H NMR (CDCl$_3$,
Me$_4$Si) δ 7.0–7.6 (m, 5 H); ^{13}C NMR (CDCl$_3$, Me$_4$Si) 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-deuteriobenzalde-
hyde[21] (274 mg, 2.55 mmol) in THF (1.0 mL). The reaction mixture
was warmed to 25 °C, treated with aqueous NH$_4$Cl, extracted with Et$_2$O,
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; ^{1}H NMR (CDCl$_3$, Me$_4$Si) δ 3.3 (bs, 1 H), 7.0–7.6 (m,
10 H); ^{13}C NMR (CDCl$_3$, Me$_4$Si) 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$_4$F
(85 mg, 2.31 mmol) in CH$_2$Cl$_2$ (2.0 mL) was added at 0 °C a solution
of CF$_3$COOH (0.69 mL, 1.01 g, 8.90 mmol) in CH$_2$Cl$_2$ (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$_2$O, 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-dideuterio-
benzyl)ethyne: ^{1}H NMR (CDCl$_3$, Me$_4$Si) δ 7.0–7.5 (m, 10 H); ^{13}C
NMR (CDCl$_3$, Me$_4$Si) 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$_2$ZrCl$_2$ (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$_2$O, washed successively with 1
M HCl, aqueous NaHCO$_3$, Na$_2$S$_2$O$_3$, 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%; ^{1}H NMR (CDCl$_3$, Me$_4$-
Si) 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$_4$Si) 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**: ^{1}H NMR (CDCl$_3$,
Me$_4$Si) 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$_4$Si) 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 de-
scribed 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%; ^{1}H NMR (CDCl$_3$, Me$_4$Si) 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$_4$Si) 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 (CDCl₃, Me₄Si) δ 7.0−7.6 (m, 13 H), 7.5−7.7 (m, 2 H); ¹³C NMR (CDCl₃, Me₄Si) 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 (CDCl₃, Me₄Si) 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); ¹³C NMR (CDCl₃) 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 (CDCl₃, Me₄Si) 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); ¹³C NMR (CDCl₃) 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/Et₂O) afforded 1.14 g (67%) of **23a**: ¹H NMR (CDCl₃, Me₄-Si) 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); ¹³C NMR (CDCl₃) 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/Et₂O) afforded 0.85 g (61%) of **23b**: ¹H NMR (CDCl₃, Me₄-Si) 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); ¹³C NMR (CDCl₃) 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 Et₂O, washed with aqueous NaHCO₃, dried over MgSO₄, and evaporated. Chromatography on silica gel (98/2 pentane/Et₂O) afforded 122 mg (76%) of **21a**: ¹H NMR (CDCl₃, Me₄Si) 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); ¹³C NMR (CDCl₃) 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/ Et₂O) afforded 882 mg (55%) of **23c**: ¹H NMR (CDCl₃, Me₄Si) 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); ¹³C NMR (CDCl₃) 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/Et₂O): ¹H NMR (CDCl₃, Me₄Si) 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); ¹³C NMR (CDCl₃) 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/Et₂O) afforded 0.84 g (60%) of **21f**: ¹H NMR (CDCl₃, Me₄Si) 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); ¹³C NMR (CDCl₃) 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 Et₂O (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), I₂ (0.77 g, 3.0 mol, 2 h) in THF (10 mL), 1 M HCl, aqueous NaHCO₃, and Na₂S₂O₃, dried over MgSO₄, and evaporated. Chromatography on silica gel (9/1 pentane/Et₂O) gave 251 mg (43%) of (Z)-3-iodo-4-(p-tolyl)-2-buten-1-ol: ¹H NMR (CDCl₃, Me₄Si) 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); ¹³C NMR (CDCl₃, Me₄Si) 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/Et₂O) yielded 85 mg (78%) of (Z)-3-iodo-4-(p-tolyl)-2-buten-1-al: ¹H NMR (CDCl₃, Me₄Si) 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); ¹³C NMR (CDCl₃, Me₄Si) 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 Et₂O, washed with 1 M HCl and aqueous NaHCO₃, dried over MgSO₄, and evaporated. Chromatography on silica gel (90/10 pentane/Et₂O) 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/CH₂-Cl₂) yielded 59 mg (63%) of **14d**: ¹H NMR (CDCl₃, Me₄Si) 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); ¹³C NMR (CDCl₃, Me₄Si) 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 Et₂O, washed with brine, dried over MgSO₄, 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/Et₂O) afforded 2.0 g (62%) of **17**: ¹H NMR (CDCl₃, Me₄Si) 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); ¹³C NMR (CDCl₃, Me₄Si) 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 (CDCl₃, Me₄Si) 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); ¹³C NMR (CDCl₃) 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 Et₂O, washed with NaHCO₃, dried over MgSO₄, and evaporated. The crude oil was oxidized with PCC[23] (0 °C, 8 h) to give 164 mg (37%) of **21c**: ¹H NMR (CDCl₃, Me₄Si) 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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¹³C NMR (CDCl₃) 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 PhCH₂-MgCl in THF (0.81 mL, 1.62 mmol, 0 °C, 1 h) and 1 M HCl, diluted with Et₂O, washed with NaHCO₃, dried over MgSO₄, and evaporated. Chromatography on silica gel (95/5 pentane/Et₂O) 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: ¹H NMR (CDCl₃, Me₄Si) 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); ¹³C NMR (CDCl₃) 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 PCC²³ (25 °C, 10 h) afforded after chromatography on silica gel (95/5 pentane/Et₂O) 78.8 mg (63%) of **21d**: ¹H NMR (CDCl₃, Me₄Si) 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); ¹³C NMR (CDCl₃) 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 Et₂O (2.80 mL, 5.60 mmol, 0 °C, 1 h) and then 1 M HCl, diluted with Et₂O, washed with NaHCO₃, dried over MgSO₄, and evaporated. Chromatography on silica gel afforded 1.06 g (86%) of (Z)-6-iodo-5-decen-4-ol, which was oxidized with PCC²³ (25 °C, 6 h) to give 0.72 g (86%) of **21g**: ¹H NMR (CDCl₃, Me₄Si) 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); ¹³C NMR (CDCl₃) 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 Et₂O, washed with NaHCO₃, dried over MgSO₄, and evaporated. Chromatography on silica gel (9/1 pentane/Et₂O) afforded 694 mg (86%) of (Z)-5-iodo-6-(p-tolyl)-4-hexen-3-ol, which was directly oxidized with PCC²³ to give 617 mg (86%) of **21h**: stereoselectivity >98%; ¹H NMR (CDCl₃, Me₄Si) 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); ¹³C NMR (CDCl₃) 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), Et₃N (0.14 mL, 0.10 g, 1.0 mmol), H₂O (18 μL, 18 mg, 1.0 mmol), Cl₂Pd(PPh₃)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 H₂O, extracted with Et₂O, dried over MgSO₄, filtered, and evaporated. Analysis by ¹H 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**: ¹H NMR (CDCl₃, Me₄Si) 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); ¹³C NMR (CDCl₃, Me₄Si) 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 C₁₆H₂₀O₂ 244.1463, found 244.1470.

(ii) With Pyridine. Method C was modified by replacing NEt₃ with pyridine (81 μL, 79 mg, 1.0 mmol) and omitting the addition of H₂O 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 NEt₃

and omitting the addition of H₂O 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**: ¹H NMR (CDCl₃, Me₄Si) δ 6.26 (s, 1 H), 7.0−7.6 (m, 15 H); ¹³C NMR (CDCl₃, Me₄Si) 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 C₂₂H₁₆O₂ 312.1150, found 312.1158.

(c) 4-Deuterio-2,3-di-(n-propyl)-4-phenyl-2-buten-4-olide. The use of D₂O (20 μL, 20 mg, 1.0 mmol) in place of H₂O 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**: ¹H NMR (CDCl₃, Me₄Si) 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); ¹³C NMR (CDCl₃, Me₄Si) 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 C₁₆H₁₉DO₂ 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**: ¹H NMR (CDCl₃, Me₄Si) 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); ¹³C NMR (CDCl₃, Me₄Si) 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 C₁₉H₁₈O₂ 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 NEt₃ (4.9 mL, 3.56 g, 35 mmol) in CH₂Cl₂ (50 mL) was treated with CH₃SO₂Cl (2.3 mL, 3.45 g, 30.0 mmol, 0 °C, 2h), diluted with Et₂O, washed with H₂O, dried over MgSO₄, 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 LiNEt₂, prepared by addition of 2.5 M n-BuLi in hexane (6.4 mL, 16.0 mmol) to HNEt₂ (1.17g, 16.0 mmol, 0 °C, 15 min) in THF (10 mL), stirred for 12h at 23 °C, diluted with ether, washed with H₂O, dried over MgSO₄, and evaporated. Distillation over LiAlH₄ afforded 0.82 g (35%) of N,N-diethyl-α,α-dideuteriobenzylamine: ¹H NMR (CDCl₃, Me₄Si) 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); ¹³C NMR (CDCl₃, Me₄Si) 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), Cl₂Pd(PPh₃)₂ (17 mg, 25 μmol), Et₃N (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 H₂O, extracted with CH₂Cl₂, dried over MgSO₄, and evaporated. Analysis of the crude reaction mixture by ¹H NMR spectroscopy showed the formation of **12a** in 66% yield. Chromatography on silica gel (99/1 pentane/Et₂O) afforded 59 mg (66%) of **12a**: stereoisomeric purity >98%; ¹H NMR (CDCl₃, Me₄Si) 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); ¹³C NMR (CDCl₃) 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 C₁₁H₁₆O₂ 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/Et₂O) afforded 80 mg (70%) of **12b**: stereoisomeric purity >98%; ¹H NMR (CDCl₃, Me₄Si) 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); ¹³C NMR (CDCl₃) 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 C₁₆H₂₆O₂ 250.1934, found 250.1914.

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(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$_2$O) afforded 80 mg (70%) of **12c**: stereoisomeric purity >98%; ^{1}H NMR (CDCl$_3$, Me$_4$Si) 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$_2$O) afforded 91 mg (63%) of **12d**: stereoisomeric purity >98%; ^{1}H NMR (CDCl$_3$, Me$_4$Si) 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$_2$O) afforded 89 mg (80%) of **12e**: stereoisomeric purity >98%; ^{1}H NMR (CDCl$_3$, Me$_4$Si) 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$_2$O) afforded 108 mg (80%) of **12f**: stereoisomeric purity >98%, ^{1}H NMR (CDCl$_3$, Me$_4$Si) 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**: ^{1}H NMR (CDCl$_3$, Me$_4$Si) 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: ^{1}H NMR (CDCl$_3$, Me$_4$Si) 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$_2$O) 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: ^{1}H NMR (CDCl$_3$, Me$_4$Si) 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**: ^{1}H NMR (CDCl$_3$, Me$_4$Si) 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**: ^{1}H NMR (CDCl$_3$, Me$_4$Si) 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(1H,1′H-isobenzofuran) (18). Using method C where 4 equiv of H$_2$O (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: ^{1}H NMR (CDCl$_3$, Me$_4$Si) 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$_4$Si) 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-(2H,2H′-furan) (16a). Using method C where NEt$_3$ was replaced with K$_2$CO$_3$ (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: ^{1}H NMR (CDCl$_3$, Me$_4$Si) δ 0.4−3.1 (m, 28 H), 7.0−7.7 (m, 10 H); ^{13}C NMR (CDCl$_3$, Me$_4$Si) 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$_2$O) afforded 121 mg (65%) of **25a**: ^{1}H NMR (CDCl$_3$, Me$_4$Si) 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$_2$O) afforded 102 mg (81%) of **25b**: ^{1}H NMR (CDCl$_3$, Me$_4$Si) 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$_2$O) afforded 175 mg (79%) of **25c**: ^{1}H NMR (CDCl$_3$, Me$_4$Si) 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.