Palladacycles with a Metal-Bonded sp^3-Hybridized Carbon as Intermediates in the Synthesis of 2,2,3,4-Tetrasubstituted 2*H*-1-Benzopyrans and 1,2-Dihydroquinolines. Effects of Auxiliary Ligands and Substitution at a Palladium-Bonded Tertiary Carbon

Genliang Lu, Janelle L. Portscheller, and Helena C. Malinakova*

Department of Chemistry, University of Kansas, 1251 Wescoe Hall Drive, Lawrence, Kansas 66045

Received October 30, 2004

Prompted by the failure to prepare stable oxapalladacycles L_2Pd-1-C_6H_4-2-$OC(R^1)COOEt$ with PPh_3 ligands (L = PPh_3) and substituents R^1 other than hydrogen, systematic studies on the effects of steric and electronic properties of auxiliary ligands L and substituents R^1 (alkyl, aryl) on the feasibility of formation, stability, and reactivity of the oxapalladacycles were performed. Using *N,N,N′,N′*-tetramethyl-1,2-ethylenediamine bidentate ligand (L−L = TMEDA), stable palladacycles featuring substituents R^1 (Me, Et, *i*-Pr, and Ph) were prepared, and the presence of palladium-bonded tertiary sp^3-hybridized carbons was confirmed by X-ray crystallographic analyses on palladacycles with *i*-Pr and Ph substituents R^1. Relying on ^{31}P NMR analyses of crude reaction mixtures, ligand displacement reactions of palladacycles (TMEDA)Pd-1-C_6H_4-2-$OC(R^1)COOEt$ with monodentate phosphines (PPh_3 and PPh_2Me) were studied, as well as base-mediated ring-closure reactions of arylpalladium(II) iodo complexes $(PPh_3)_2Pd$(-1-C_6H_4-2-$OCHR^1COOEt$)I and $(PPh_2Me)_2Pd$(-1-C_6H_4-2-$OCHR^1$-COOEt)I. In both series, higher conversions to corresponding palladacycles L_2Pd-1-C_6H_4-2-$OC(R^1)COOEt$ were achieved with PPh_2Me ligands, and both the transformations were negatively affected by an increase in the steric bulk of substituents R^1. Although the palladacycles with monodentate phosphines could not be isolated as stable entities, IR spectroscopic analyses supported the presence of a Csp^3−Pd bond. On the basis of these studies, a one-pot conversion of stable arylpalladium(II) iodo complexes with PPh_2Me ligands into 2,2,3,4-tetrasubstituted 2*H*-1-benzopyrans and 1,2-dihydroquinolines via the insertion of unsymmetrical alkynes into in situ formed palladacycles was developed, providing the heterocycles in good yields (44−80%) as single regioisomers.

Introduction

σ-Alkyl organometallic complexes of palladium represent key intermediates of the versatile cross-coupling reactions.[1] However, potentially powerful methods for catalytic asymmetric construction of stereogenic carbon centers exploiting organopalladium compounds with a metal-bonded sp^3-hybridized stereogenic carbon remain rare,[2] since the majority of synthetically viable intermediates feature primary sp^3-hybridized metal-bonded carbons.[3] Additional studies on the preparation, stability,[4] and reactivity of transition metal organometallics with secondary and tertiary sp^3-hybridized metal-bonded carbons will be needed to facilitate the design of new synthetic methodologies.[5] The choice of auxiliary ligands, frequently represented by monodentate or bidentate phosphines, has a profound effect on the reactivity of organometallic species.[6] A kinetic study of thermal decomposition of *trans*-$[PdR'_2(PR_3)_2]$ complexes revealed destabilization of the Pd−alkyl bond due to the interaction between bulky phosphine ligands and the alkyl groups.[7] Structures, reactivity, and stability of arylpalladium *σ*-alkyl complexes bearing an electron-withdrawing group at the transition metal-bonded sp^3-hybridized carbon,[4d,8,9] specifically palladium ketone enolates, α-cyano alkyl complexes, and malonates, that

(1) Diederich, F., Stang, P. J., Eds. *Metal-Catalyzed Cross-Coupling Reactions*; Willey-VCH Verlag GmbH: Wenheim, 1998.

(2) Palladium-catalyzed asymmetric arylation of ketone, ester, and amide enolates demonstrates the synthetic utility of such strategies, see: (a) Buchwald, S. L.; Hamada, T. *Org. Lett.* **2002**, *4*, 999−1001. (b) Hamada, T.; Chieffi, A.; Åhman, J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 1261−1268. (c) Spielvolgel, D. J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 3500−3501. (d) Lee, S.; Hartwig, J. F. *J. Org. Chem.* **2001**, *66*, 3402−3415. (e) Åhman, J.; Wolfe, J. P.; Troutman, M. V.; Palucki, M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1998**, *120*, 1918−1919.

(3) To date, *palladium-catalyzed* coupling reactions of alkyl electrophiles have remained limited to coupling of primary alkyl halides, most likely proceeding via intermediates with primary sp^3-hybridized palladium-bonded carbons, see: (a) Wiskur, S. L.; Korte, A.; Fu, G. C. *J. Am. Chem. Soc.* **2004**, *126*, 82−83. (b) Nethernton, M. R.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 3910−3912. (c) Luh, T.-Y.; Leung, M.-K.; Wong, K.-T. *Chem. Rev.* **2000**, *100*, 3187−3204. (d) Cardenas, D. J. *Angew. Chem., Int. Ed.* **1999**, *38*, 3018−3020. A kinetic study indicated that, in contrast to *primary* akyl bromides, oxidative addition of a *secondary* alkyl bromide to $Pd(P(t\text{-}Bu)_2Me)_2$ failed to occur, see: (e) Hills, I. D.; Netherton, M. R.; Fu, G. C. *Angew. Chem., Int. Ed.* **2003**, *42*, 5749−5752. However, *nickel-catalyzed* coupling to secondary alkyl halides is known, see: (f) Zhou, J.; Fu, G. C. *J. Am. Chem. Soc.* **2004**, *126*, 1340−1341. (g) Zhou, J.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 14726−14727.

10.1021/om0491544 CCC: $30.25
Publication on Web 01/27/2005

operate as intermediates of established catalytic reactions,[2] have been investigated by Hartwig and coworkers.[9] An increase in the steric bulk of the auxiliary phosphine ligands, and the presence of additional substituents at the palladium-bonded carbon in the alkyl groups were found to promote alternative coordination modes, e.g., formation of O-bonded ketone enolates.[10] Furthermore, the thermodynamic stability of such complexes was compromised by an increase in the steric demands of the alkyl group.[9a] To date, less attention has been devoted to comparable studies on the ligand and substituent effects in palladium ester enolates, and particularly those featuring di- and trisubstituted metal-bonded carbons.[8,9,10c]

As a part of our program exploring applications of palladacycles with a metal-bonded sp^3-hybridized stereogenic carbon in asymmetric organic synthesis,[11] we have been studying the reactivity of stable cyclic arylpalladium ester enolates **II** (Figure 1). Notably, attempts

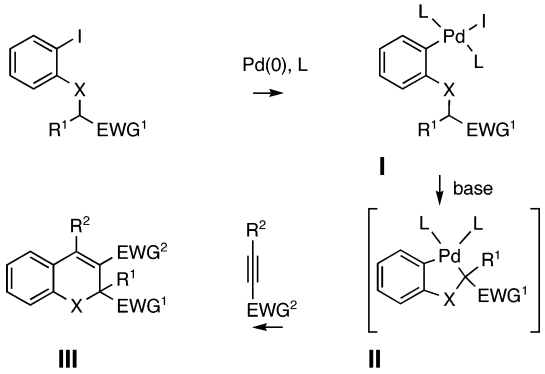


Figure 1. Synthetic strategy.

to utilize strategies previously developed[11] for the synthesis of stable palladacycles **II** and heterocycles **III** lacking substituents R^1 (R^1 = H) for preparation of analogous targets **II** and **III** with fully substituted stereogenic carbons (R^1 = alkyl, aryl) proved unsuccessful, as a result of the failure to prepare stable palladacycles **II** (R^1 = alkyl, aryl) with triphenylphosphine ligands L.

Described herein are systematic studies of the effect of steric and electronic properties of auxiliary ligands L and substituents R^1 on the formation, stability, and reactivity of palladacycles **II** (R^1 = alkyl, aryl). Palladacycles **II** (X = O, R^1 = alkyl, phenyl) with sterically unencumbered *N,N,N′,N′*-tetramethyl-1,2-ethylenediamine auxiliary ligands (L−L = TMEDA) and palladium-bonded sp^3-hybridized tertiary carbons were isolated and fully characterized. In contrast, palladacycles **II** (R^1 = alkyl, phenyl) possessing monodentate phosphine ligands (L = $PR'_xR''_y$) were detected only in situ (^{1}H and ^{31}P NMR) in crude product mixtures arising from auxiliary ligand displacements on palladacycles **II** (L−L = TMEDA), or from base-mediated ring-closure reactions of the corresponding arylpalladium(II) iodo complexes **I** (Figure 1). Notably the steric properties of both the auxiliary ligands (L = $PR'_xR''_y$) and the substituents R^1 significantly affected the progress of these transformations. Utilizing data from these experiments, a convergent synthetic approach to diverse, medicinally relevant[12] 2,2,3,4-tetrasubstituted 2*H*-1-benzopyrans **III** (X = O, R^1, R^2 = alkyl, aryl) and 2,2,3,4-tetrasubstituted 1,2-dihydroquinolies **III** (X = NCOOMe, R^1, R^2 = alkyl, aryl) was developed. Heterocycles **III**, which are not easily obtained by traditional synthetic protocols,[13] have been prepared in good to excellent

(4) *σ*-Alkyl organometallic complexes are prone to decomposition via *β*-hydride elimination, see: (a) Collman, J. P.; Hegedus, L. S.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987; Chapter 5. However, a stable alkyl palladium(II) complex featuring *β*-hydrogens ($Ph(CH_2)_3$-$Pd[P(t\text{-}Bu)_2Me]_2Br$ has been isolated and shown to undergo *β*-hydride elimination only upon warming to 50 °C, see: (b) Kirchhoff, J. H.; Netherton, M. R.; Hills, I. D.; Fu, G. C. *J. Am. Chem. Soc.* **2002**, *124*, 13662−13663. Thermodynamic stability of alkyl ligands in organometallic complexes decreases in the order methyl > primary > secondary ≫ tertiary, and isomerization of secondary alkyl complexes into primary ones was observed, see: (c) Siegbahn, P. E. M. *J. Phys. Chem.* **1995**, *99*, 12723−12729. (d) Reger, D. L.; Garza, D. G.; Baxter, J. C. *Organometallics* **1990**, *9*, 873−874. Although steric hindrance between the metal with its coordination sphere and substituents at the metal-bonded sp^3-hybridized carbon has been invoked to rationalize these observations, a recent theoretical study pointed to a significant contribution from electronic factors, demonstrating stabilization of alkyl organometallics arising from the presence of an electron-withdrawing group at the metal-bonded carbon, see: (e) Harvey, J. N. *Organometallics* **2001**, *20*, 4887−4895.

(5) Malinakova, H. C. *Chem. Eur. J.* **2004**, *10*, 2636−2646.

(6) Crabtree, R. H. *The Organometallic Chemistry of the Transition Metals,* 3rd ed., John Wiley and Sons: New York, 2001; Chapter 4.

(7) (a) Ozawa, F.; Ito, T.; Yamamoto, A. *J. Am. Chem. Soc.* **1980**, *102*, 6457−6463. A computational study reported P−Pd−P angles for *cis*-$Pd(Et)_2[P(t\text{-}Bu)_2]_2$ and *cis*-$Pd(Et)_2[P(i\text{-}Pr)_2]_2$ to be 129.6° and 101.5°, respectively. Thus, the distortion of the square planar geometry (deviation from P−Pd−P angle 90°) appears to arise from the notable steric bulk of the phosphine ligands, see: (b) Cardenas, D. J. *Angew. Chem., Int. Ed.* **2003**, *42*, 384−387.

(8) For representative examples of preparations of stable late transition metal enolates and other complexes bearing an electron-withdrawing substituent at the metal-bonded carbon, see: (a) Heathcock, C. H. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: Oxford, U. K., 1991; Vol. 2, Chapter 1.9. (b) Naota, T.; Tannna, A.; Kamuro, S.; Murahashi, S.-I. *J. Am. Chem. Soc.* **2002**, *124*, 6842−6843. (c) Ryabov, A. D.; Panyashkina, I. M.; Polyakov, V. A.; Fisher, A. *Organometallics* **2002**, *21*, 1633−1636. (d) Kujime, M.; Hikichi, S.; Akita, M. *Organometallics* **2001**, *20*, 4049−4060. (e) Hashmi, S. K. A.; Naumann, F.; Bolte, M. *Organometallics* **1998**, *17*, 2385−2387. (f) Vicente, J.; Abad, J. A.; Chicote, M.-T.; Abrisqueta, M.-D.; Lorca, J.-A.; Ramirez de Arelano, M. C. *Organometallics* **1998**, *17*, 1564−1568. (g) Rasley, B. T.; Rapta, M.; Kulawiec, R. J. *Organometallics* **1996**, *15*, 2852−2854. (h) Garcia-Ruano, J. L.; Gonzalea, A. M.; Barcena, A. I.; Camazon, M. J.; Navarro-Ranninger, C. *Tetrahedron: Asymmetry* **1996**, *7*, 139−148. (i) Hartwig, J. F.; Andersen, R. A.; Bergman, R. G. *J. Am. Chem. Soc.* **1990**, *112*, 5670−5671. (j) Burkhardt, E. R.; Doney, J. J.; Slough, G. A.; Stack, J. M.; Heathcock, C. H.; Bergman, R. G. *Pure Appl. Chem.* **1988**, *60*, 1−6. (k) Weinstock, I.; Floriani, C.; Chiesi-Villa, A.; Guastini, C. *J. Am. Chem. Soc.* **1986**, *108*, 8298−8299.

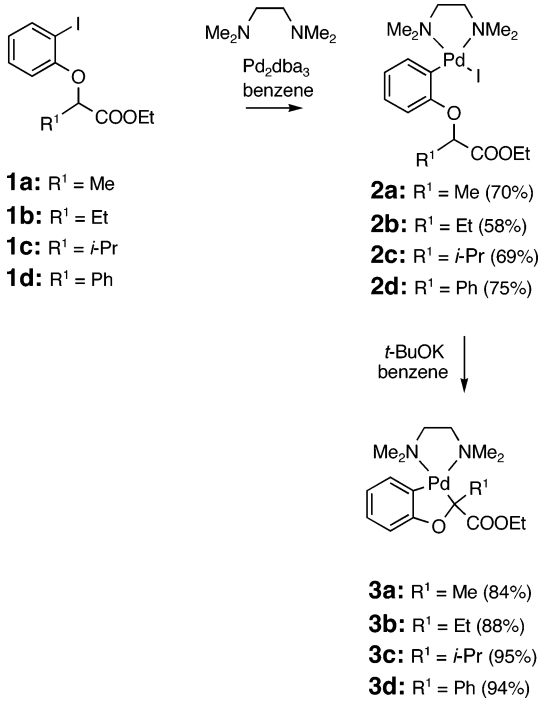
(9) (a) Culkin, D. A.; Hartwig, J. F. *Organometallics* **2004**, *23*, 3398−3416. (b) Culkin, D. A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2001**, *123*, 5816−5817.

(10) For the discussion of the different bonding modes available to palladium enolates, see: (a) Tian, G.; Boyle, P. D.; Novak, B. M. *Organometallics* **2002**, *21*, 1462−1465. (b) Albeniz, A. C.; Catalina, N. M.; Espinet, P.; Redon, R. *Organometallics* **1999**, *18*, 5571−5576. Reference 9a, and references therein. (c) In general, for late transition metal enolates, coordination to palladium through the carbon atom is preferred, see ref 10b.

(11) (a) Lu, G.; Malinakova, H. C. *J. Org. Chem.* **2004**, *69*, 8266−8279. (b) Lu, G.; Malinakova, H. C. *J. Org. Chem.* **2004**, *69*, 4701−4715. (c) Portscheller, J. L.; Lilley, S. E.; Malinakova, H. C. *Organometallics* **2003**, *22*, 2961−2971. (d) Portscheller, J. L.; Malinakova, H. C. *Org. Lett.* **2002**, *4*, 3679−3681.

(12) For examples of biologically active 2,2-disubstituted 2*H*-1-benzopyrans, see: (a) Yu, L. *J. Agric. Food Chem.* **2003**, *51*, 2344−2347. (b) Shin, H. S.; Seo, H. W.; Yoo, S. E.; Lee, B. H. *Pharmacology* **1998**, *56*, 111−124. (c) Rovnyak, G. C.; Ahmed, S. Z.; Ding, C. Z.; Dzwonczyk, S.; Ferrara, F. N.; Humphreys, W. G.; Grover, G. J.; Santafianos, D.; Atwal, K. S.; Baird, A. J.; McLaughlin, L. G.; Normandin, D. E.; Sleph, P. G.; Traeger, S. C. *J. Med. Chem.* **1997**, *40*, 24−34. For examples of biologically active 2,2-disubstituted 1,2-dihydroquinolines, see: (d) Elmore, S. W.; Pratt, J. K.; Coghlan, M. J.; Mao, Y.; Green, B. E.; Anderson, D. D.; Stashko, M. A.; Lin, C. W.; Falls, D.; Nakane, M.; Miller, L.; Tyree, C. M.; Miner, J. N.; Lane, B. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 1721−1727.

Scheme 1



yields (44−80%), and with a complete regiocontrol, in one step from stable arylpalladium(II) iodo complexes **I** bearing carefully optimized monodentate phosphine ligands (L). Results described herein contribute to expanding fundamental understanding of the effects of auxiliary phosphine ligands on the stability and reactivity of highly substituted palladium ester enolates, providing a foundation for future development of asymmetric and catalytic variants of this synthetic protocol.

Results and Discussion

Preparation of Stable Palladacycles with TMEDA Auxiliary Ligands. Utilizing sterically unencumbered *N,N,N′,N′*-tetramethyl-1,2-ethylenediamine ligand (TMEDA), a series of stable palladacycles **3a**−**d** featuring substituents R^1 (R^1 = Me, Et, *i*-Pr, Ph) was prepared (Scheme 1). Aryl iodides **1a**−**d**, available via O-alkylation of 2-iodophenol with appropriate α-bromo esters,[14] smoothly participated in oxidative addition with palladium(0) (Pd_2dba_3) in the presence of TMEDA, providing arylpalladium(II) iodo complexes **2a**−**d**. ^{1}H and ^{13}C NMR spectra of complexes **2a** and **2d** indicated the presence of diastereomers, presumably arising from a hindered rotation about the Csp^2−Pd bond.[11b] For the base-mediated (*t*-BuOK, 1.2−1.6 mol equiv) conversion of complexes **2a**−**d** into stable palladacycles **3a**−**d**, the protocol previously designed for palladacycle **3** lacking R^1 substituent (R^1 = H)[11d] had to be modified by replacing THF solvent with benzene. Under these conditions, the residual *t*-BuOK was efficiently removed from the crude reaction mixtures by filtration through a layer of Celite, preventing decomposition of palladacycles **3a**−**d** during the removal of solvents under reduced pressure. Palladacycles **3a**−**d** were isolated as moisture- and air-stable bright yellow solids in excellent yields (84−95%), unaffected by steric properties of R^1 substituents (Scheme 1). The enolate connectivity in complexes **3a**−**d** was assigned on the basis of the ^{1}H, ^{13}C NMR, and IR spectroscopic evidence. Thus, palladacycle **3a** displayed a ^{1}H NMR signal for the methyl (Pd−C−CH_3) resonance at δ 1.75, a ^{13}C NMR signal for the Pd-bonded sp^3-hybridized tertiary carbon (Pd−Csp^3) at δ 93.5, and the ν(C=O) band in the IR spectrum at 1677 cm^{-1}. Similar data were recorded for complex **3b** (R^1 = Et, ^{1}H NMR signal for the methylene (Pd−C−CH_2−) resonance at δ 2.3 (1 H) and δ 2.0 (1 H), ^{13}C NMR signal for Pd−Csp^3 at δ 99.5, and ν(C=O) band in the IR spectrum at 1670 cm^{-1}), **3c** (R^1 = *i*-Pr, ^{1}H NMR signal for the methine (Pd−C−CH−) resonance at δ 2.6−2.5 (1 H), ^{13}C NMR signal for Pd−Csp^3 at δ 103.4, and ν(C=O) band in the IR spectrum at 1664 cm^{-1}), and **3d** (R^1 = Ph, ^{13}C NMR signal Pd−Csp^3 at δ 97.5, and ν(C=O) band in the IR spectrum at 1676 cm^{-1}).[15a] Furthermore, the assigned C-bonded connectivities in complexes **3c** and **3d** were confirmed by X-ray crystallographic analyses (Figure 2).[15b]

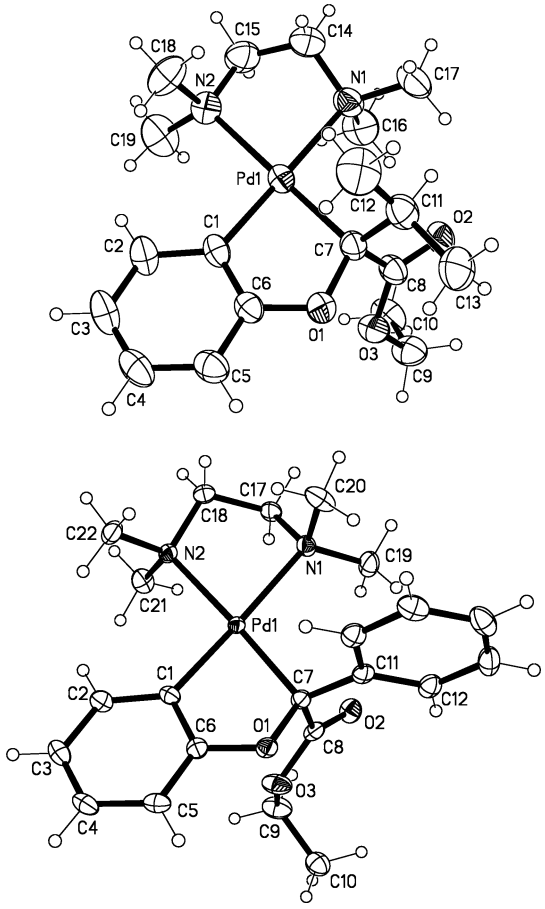


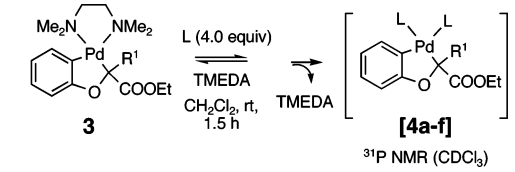
Figure 2. Thermal ellipsoid diagrams of complexes **3c** (top) and **3d** (bottom). The ellipsoids are drawn at the 50% probability level.

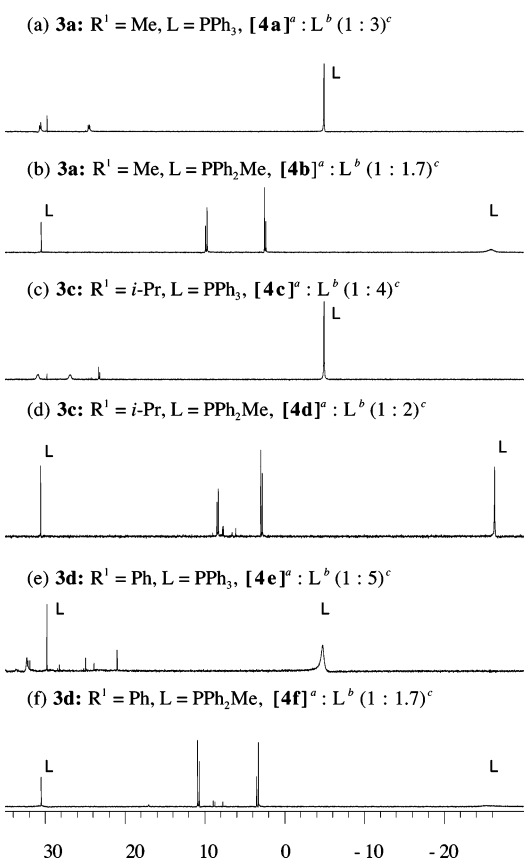
(13) Gribble, G. W., Gilchrist, T. L. Eds. *Progress in Heterocyclic Chemistry*; Pergamon: Oxford, 2001; Vol. 13.

(14) Ramakrishnan, V. R.; Kagan, J. *J. Org. Chem.* **1970**, *35*, 2901−2904.

(15) (a) For comparison, the known complex **3** lacking the R^1 substituent (R^1 = H) displayed similar spectral characteristics, e.g., ^{13}C NMR signal for the palladium-bonded sp^3-hybridized carbon (Pd−Csp^3) at δ 87.2 and ν(C=O) band in the IR spectrum at 1670 cm^{-1}, see ref 11d. (b) Both palladacycles possess square planar geometry about the palladium atom without any distortions from planarity. The sum of the angles around the palladium atom was 360.1° for both **3c** (R^1 = *i*-Pr) and **3d** (R^1 = Ph).

Scheme 2





[a] For the listing of ^{31}P NMR signals for the in situ detected complexes **[4a−f]** see Table 1. [b] Combined integration of ^{31}P NMR signals for ligands L including signals for PPh_3 and $P(=O)Ph_3$, or PPh_2Me and $P(=O)Ph_2Me$, see Table 1. [c] Molar ratio of complexes **[4]** to free ligands L based on integration of ^{31}P NMR spectra (Table 1).

Exchange of Auxiliary Ligands in Palladacycles 3a−d. Repeated attempts to prepare the palladacycle **II** bearing triphenylphosphine ligands (L = PPh_3, X = O, Figure 1) and substituent R^1 = Me via the displacement of the TMEDA ligand in palladacycle **3a** with excess PPh_3 failed.[16] Aiming to qualitatively assess the effects of steric and electronic properties of auxiliary monodentate phosphine ligands L and the nature of substituents R^1 on the ligand displacement process, methylene chloride solutions of palladacycles **3a**, **3c**, and **3d** were treated with PPh_3 or PPh_2Me (4.0 equiv) at room temperature under argon for a set time period of 1.5 h. Subsequently, volatile components (TMEDA, methylene chloride) were removed under reduced pressure, and crude products were analyzed by ^1H and ^{31}P NMR in $CDCl_3$ (Scheme 2). Utilizing PPh_3 ligands, new organopalladium complexes possessing palladium-bonded phosphine ligands were indeed formed according to ^{31}P NMR analyses (spectra a, c, and e, Scheme 2 and Table 1). Reactions involving substrates **3a** and **3c** gave rise to crude mixtures containing complexes **[4a]** and **[4c]** with characteristic ^{31}P NMR signals suggesting the presence of two palladium-bonded phosphine ligands in *cis* orientation (**[4a]**: δ 30.0 (d, J = 24.3 Hz, 1 P), 24.5 (d, J = 25.7 Hz, 1 P), spectrum a, and **[4c]**: δ 30.8 (d br, J = 35−40 Hz, 1 P), 26.7 (d br, J = 35−40 Hz, 1 P), spectrum c, Scheme 2 and Table 1). Due to a notable broadening of signals for complex **[4c]**, the coupling constants could not be precisely measured. In contrast, ligand displacement on palladacycle **3d** (R^1 = Ph) afforded complex **[4e]**, likely possessing a single palladium-bonded phosphine ligand,[17] as indicated by a single broad singlet signal at δ 32.1 (spectrum e, Scheme 2 and Table 1). The line broadening, also observed for the signal of PPh_3, might point to the existence of a dynamic exchange process involving palladacycle **[4e]** and the free ligand. Integration of the ^{31}P NMR spectra of the crude reaction mixtures revealed that the ratios of molar equivalents of complexes **[4a]**, **[4c]**, and **[4e]** to combined molar equivalents of free ligands L (a combined integration of signals for PPh_3 and $P(=O)Ph_3$) were 1:3, 1:4, and 1:5, respectively, indicating that only a partial conversion of substrates **3a**, **3c**, and **3d** occurred.[18] Accordingly, integration of ^1H NMR spectra confirmed the presence of unreacted complexes **3a** (16%), **3c** (11%), and **3d** (40%). The disproportionately low content of detected palladacycle **3c** (60% would correspond to the observed **[4c]**:L ratio) may reflect instability of complex **3c**, leading to decomposition in solution. Attempts to isolate complexes **[4a]**, **[4c]**, and **[4e]** from the crude mixtures were unsuccessful, and for this reason the enolate connectivity could not be unequivocally established (the brackets in **[4a−f]** designation of the palladacycles indicate the failure to completely characterize these entities).

Replacement of PPh_3 with PPh_2Me, a ligand with stronger donor abilities and a smaller cone angle,[19] resulted in practically complete conversions of the selected substrates **3a**, **3c**, and **3d** (spectra b, d, and f, Scheme 2), as indicated by ^1H NMR data.[20] The pairs of doublet signals expected for palladacycles **[4b]**, **[4d]**, and **[4f]** featuring two phosphine ligands in *cis* disposition were detected in the ^{31}P NMR spectra regardless of the nature of the R^1 substituents (^{31}P NMR signals for the in situ detected complexes **[4b]**: R^1 = Me: δ 9.5

(16) In contrast, an analogous procedure applied to complex **3** lacking the R^1 substituent has previously provided quantitative yields of the corresponding palladacycle **II** (X = O, EWG^1 = COOEt, R^1 = H, L = PPh_3), see ref 11d.

(17) For the synthesis of stable three-coordinate arylpalladium halide and arylpalladium amido complexes featuring one sterically demanding phosphine ligand, see: (a) Yamashita, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2004**, *126*, 5344−5345. (b) Stambuli, J. P.; Bühl, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 9346−9347. Involvement of dimeric arylpalladium halide complexes with a single sterically demanding phosphine ligand as intermediates in palladium-catalyzed cross-coupling reactions has been proposed, see: (c) Galardon, E.; Ramdeehul, J. M.; Brown, J. M.; Cowley, A.; Kuok, K. H.; Jutand, A. *Angew. Chem., Int. Ed.* **2002**, *41*, 1760−1763.

(18) Considering that palladacycles **3** were treated with 4.0 equiv of PPh_3 or PPh_2Me ligands, the molar ratio of palladacycles **[4]** to the combined free ligands L (a combined integration for $P(=O)R_3 + PR_3$), e.g., **[4]**:L = 1:2, would be expected for a complete conversion to palladacycles **[4]** with two phosphine ligands per palladium atom (complexes **[4a]** and **[4c]**), and a ratio of **[4]**:L = 1:3 would be expected for a complete conversion to palladacycle **[4e]** with a single phosphine ligand per palladium.

(19) Tollman, C. A. *Chem. Rev.* **1977**, *77*, 313−348.

(20) Integration of ^1H NMR spectra confirmed the presence of 0%, 3%, and 4% of unreacted complexes **3a**, **3c**, and **3d**, in the crude reaction mixtures corresponding to spectra b, d, and f in Scheme 2, respectively.

Table 1. Summary of ^{31}P NMR Data Reported in Scheme 2

spectrum	chemical shift δ (ppm)	multiplicity	assignment	relative integration
a	30.0	d, J = 24.3 Hz	**[4a]**	1 P
R^1 = Me	24.5	d, J = 25.7 Hz	**[4a]**	1 P
L = PPh_3	−4.9	s	PPh_3	3 P
b	30.5	s	$P(=O)Ph_2Me$	0.4 P
R^1 = Me	9.5	d, J = 30.8 Hz	**[4b]**	1 P
L = PPh_2Me	2.2	d, J = 30.8 Hz	**[4b]**	1 P
	−25.3	s, br	PPh_2Me	1.3 P
c	30.8	d, br, J = 35−40 Hz	**[4c]**	1 P
R^1 = *i*-Pr	26.7	d, br, J = 35−40 Hz	**[4c]**	1 P
L = PPh_3	−4.9	s	PPh_3	4 P
d	30.5	s	$P(=O)Ph_2Me$	0.3 P
R^1 = *i*-Pr	8.3	d, J = 29.6 Hz	**[4d]**	1 P
L = PPh_2Me	2.9	d, J = 29.5 Hz	**[4d]**	1 P
	−25.3	s	PPh_2Me	1.7 P
e	32.1	s, br	**[4e]**	1 P
R^1 = Ph	29.7	s	$P(=O)Ph_3$	0.5 P
L = PPh_3	−4.9	s, br	PPh_3	4.5 P
f	30.5	s	$P(=O)Ph_2Me$	0.6 P
R^1 = Ph	10.8	d, J = 34.3 Hz	**[4f]**	1 P
L = PPh_2Me	3.4	d, J = 34.3 Hz	**[4f]**	1 P
	−25.3	s, br	PPh_2Me	1.1 P

(d, J = 30.8 Hz, 1 P), 2.2 (d, J = 30.8 Hz, 1 P), **[4d]**: R^1 = *i*-Pr: δ 8.3 (d, J = 29.6 Hz, 1 P), 2.9 (d, J = 29.5 Hz, 1 P), **[4f]**: R^1 = Ph: δ 10.8 (d, J = 34.3 Hz, 1 P), 3.4 (d, J = 34.3 Hz, 1 P), Scheme 2 and Table 1). Furthermore, the observed ratios of molar equivalents of palladacycles **[4b]**, **[4d]**, and **[4f]** to the combined molar equivalents of free ligands L (a combined integration of signals for PPh_2Me and $P(=O)Ph_2Me$) were 1:1.7, 1:2, and 1:1.7, respectively, as anticipated within experimental error for complete conversions of complexes **3a**, **3c**, and **3d**.[18,21] Disappointingly, isolation and complete characterization of complexes **[4b]**, **[4d]**, and **[4f]** were thwarted by the persistent presence of $P(=O)Ph_2Me$ in products. The failure to isolate pure palladacycles **[4b]**, **[4d]**, and **[4f]** likely arises from a relatively weak bonding of phosphine ligands to sterically crowded palladium centers.

Data summarized in Scheme 2 and Table 1 demonstrate that a complete displacement of TMEDA ligands in palladacycles **3** with diverse substituents R^1 can be achieved by a proper choice of monodentate phosphine ligands, providing semistable complexes **[4]** with two phosphine ligands in *cis* disposition. Evidence supporting the involvement of carbon-bonded palladium enolates **[4b]**, **[4d]**, and **[4f]** was based on IR spectroscopic data (vide infra).

Ligand and Substituent Effects on the Intramolecular Displacement of the Anionic Ligands. Continuing to pursue the isolation of stable palladacycles **II** bearing monodentate phosphine ligands L, a complementary strategy involving an irreversible intramolecular displacement of the anionic iodide ligand by in situ generated ester enolates[22] of arylpalladium(II) iodo complexes **I** (L = $PR'_xR''_y$) (Figure 1) was examined. Arylpalladium(II) iodo complexes **5**−**8** featuring diverse groups R^1 (Me, Et, *i*-Pr, Ph) and a series of phosphine ligands L (PPh_3, PPh_2Me, $PPhMe_2$, PMe_3) were prepared via alternative protocols, relying on either oxidative addition to aryl iodides **1a**−**d** (method A),[11d] or a ligand displacement on complexes **2b**−**e** (method B)[11d] (Scheme 3). Method B was chosen in cases when chromatographic removal of dibenzylidene acetone (dba) liberated in the oxidative addition proved more convenient as a part of the preparation of complexes **2**, rather than complexes **5**−**8**. ^{31}P NMR analysis of complexes **5**−**8** indicated a *trans* disposition of two nonequivalent phosphines,[23] which was confirmed by X-ray crystallographic analyses on complexes **6a** and **7b**.[24]

To qualitatively compare the influence of steric and electronic characteristics of monodentate phosphine ligands L, and the nature of substituents R^1 on the rate of the ring-closure reactions,[22] solutions of complexes **5a**,**b**, **7a**,**b**, and **8a**,**b** in THF were treated with *t*-BuOK for 20 min at ambient temperature under an atmosphere of dry argon.[25] Following the addition of benzene,

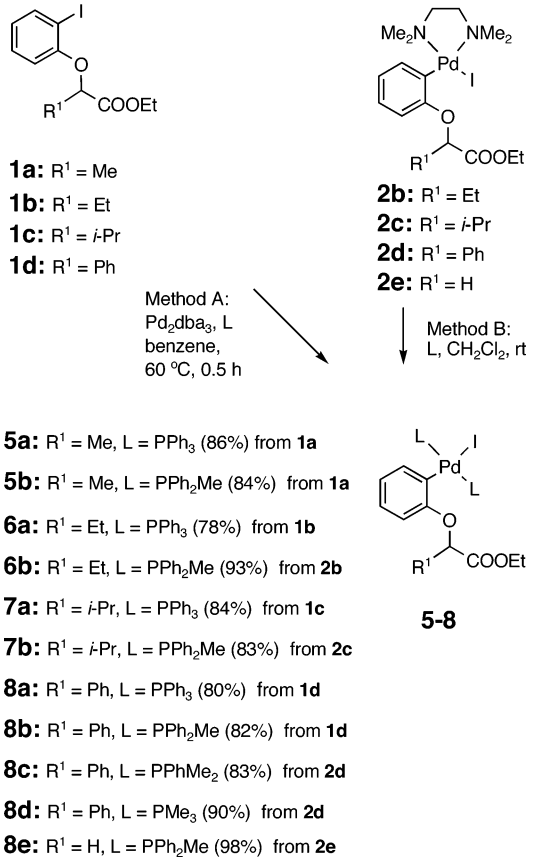
(21) A notable broadening of the signal of the free PPh_2Me ligand was detected in the products of ligand exchange reactions with palladacycles **3a** (R^1 = Me, spectrum b, Scheme 2) and **3d** (R^1 = Ph, spectrum f, Scheme 2). For comparison, the ligand displacement reaction of palladacycle **3** (R^1 = H)[11d] with PPh_2Me ligand under the conditions described in Scheme 2 afforded ^{31}P NMR spectra indicating the presence of the corresponding palladacycle **[4]** (R^1 = H) with two phosphines in *cis* orientation (**[4]**: δ 9.52 (d, J = 31.4 Hz, 1 P), 4.55 (d, J = 31.2 Hz, 1 P), and **[4]**:L ratio of 1:1.85), corresponding to a complete conversion of substrate **3**. The signal for excess PPh_2Me ligand showed little peak broadening in $CDCl_3$ solution.

(22) The relative thermodynamic stabilities of the iodide (pK_{aHI} < 1) and potassium ester enolate (A^-, pK_{aHA} = 23) anionic ligands would be expected to provide a sufficient driving force for the ring closure of complexes **I** to yield palladacycles **II** (Figure 1). However, the nature of substituents R^1 and ligands L could have a profound effect on the kinetics of the ligand displacement. For the estimate of the pK_a for esters of 2-phenoxycarboxylic acids, see: Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456−463.

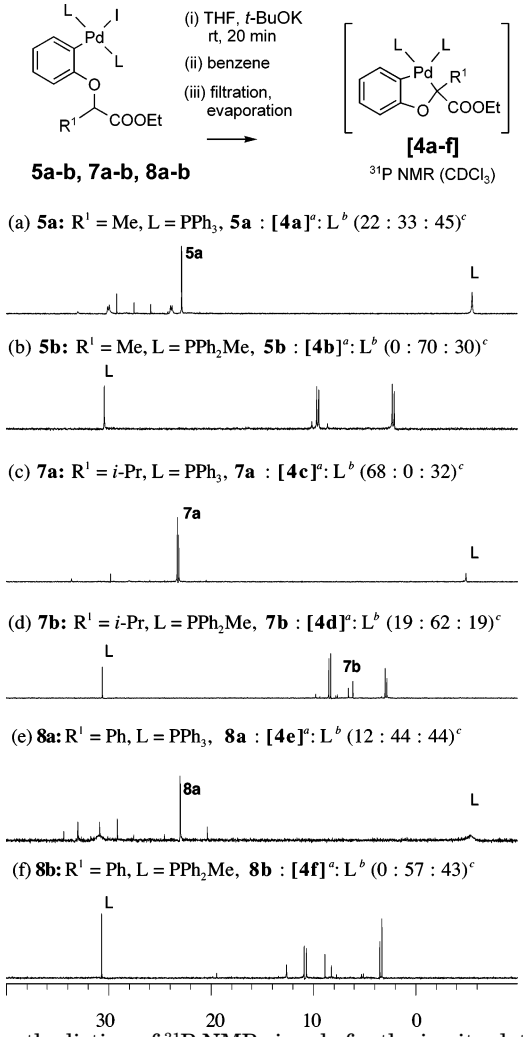
(23) As a result of the presence of a stereogenic carbon in complexes **5**−**8**, the two phosphorus atoms are nonequivalent (diastereotopic), each giving rise to a doublet signal with $J(^{31}P-^{31}P)$ = 430−480 Hz, consistent with *trans* disposition of the phosphine ligands, see: Pregosin, P. S.; Kunz, T. W. *^{31}P and ^{13}C NMR of Transition Metal Phosphine Complexes in NMR 16. Basic Principles and Progress*; Diehl, P., Fluck, E., Kosfeld, R., Eds.; Springer-Verlag: Berlin, 1979. ^{31}P NMR spectra of complexes **5**−**8** reveal second-order AB patterns for the two nonequivalent and strongly coupled phosphorus atoms with a significant "roofing effect". As a consequence, in the spectra of complexes **5a**, **6a**, and **8a**, the weak "outer" signals could not be detected, and only two singlet signals could be reported.

(24) Both complexes possess square planar geometry about the palladium atom without any distortions from planarity. The sum of the angles around the palladium atom was 360.1° and 359.6° for **6a** (R^1 = Et, L = PPh_3), and **7b** (R^1 = *i*-Pr, L = PPh_2Me), respectively.

Scheme 3



Scheme 4



[a] For the listing of ^{31}P NMR signals for the in situ detected complexes **[4a−f]** and unreacted complexes **5**−**8**, see Table 2. [b] Combined integration of ^{31}P NMR signals for ligands L including signals for PPh_3 and $P(=O)Ph_3$, or PPh_2Me and $P(=O)Ph_2Me$, see Table 2. [c] Ratios of molar percent of substrates **5**−**8**, complexes **[4]**, and free ligands L based on integration of ^{31}P NMR spectra (Table 2).

filtration, and removal of volatiles (*t*-BuOH, THF and benzene) under reduced pressure,[26] the crude products were analyzed by ^{31}P NMR in $CDCl_3$ (Scheme 4 and Table 2). Integration of ^{31}P NMR signals in spectra a−f (Scheme 4) was used to establish the molar ratios of unreacted complexes **5**−**8** to palladacycles **[4]** and to the combined integral of free ligands L (L represents a combined integration for both phosphines ($PR'_xR''_y$) and phosphine oxides ($P(=O)R'_xR''_y$) (Scheme 4 and Table 2).

Complexes **[4a−f]**, identical to products of the ligand displacement process (Scheme 2 and Table 1), were generated as shown by signals in the ^{31}P NMR spectra (spectra a−f, Scheme 4 and Table 2). Notably, the ring closure on complex **8a** (R^1 = Ph, L = PPh_3) gave rise to a single broad signal at δ 30.9 for complex **[4e]**, possibly bearing a single phosphine ligand,[17,18] and a significantly broadened signal for free PPh_3 ligand. These observations suggested the involvement of the previously observed dynamic equilibrium in the $CDCl_3$ solution (compare spectra e in Schemes 2 and 4). Utilizing substrates **5a** (R^1 = Me), **7a** (R^1 = *i*-Pr), and **8a** (R^1 = Ph), bearing sterically demanding PPh_3 ligands, only partial conversions were achieved, leaving significant amounts of unreacted complexes **5a** (δ 23.12 (s, 1 P), 23.09 (s, 1 P), 22%),[23] **7a** (δ 23.30 (d, J = 434.1 Hz, 1 P), 22.42 (d, J = 434.1 Hz, 1 P), 68%),[27] and **8a** (δ 23.28 (s, 1 P), 23.25 (s, 1 P), 12%)[23,27] in the crude product mixtures (spectra a, c, and e, Scheme 4 and Table 2). The corresponding palladacycles **[4a]** and **[4e]** were detected in 33% and 44%, respectively (spectra a and e, Scheme 4), while only traces of palladacycle **[4c]**, featuring the most sterically demanding *i*-Pr substituent (spectrum c, Scheme 4), were present.[27] Unexpectedly, free PPh_3 (32−45%) was generated by the ring-closure reactions of complexes **5a**, **7a**, and **8a** (spectra a, c, and e, Scheme 4 and Table 2). The free phosphine ligands could arise from a partial decomposition of palladacycles **[4a]**, **[4c]**, and **[4e]**, caused by destabilization due to steric crowding around the palladium centers. The amounts of unreacted complexes **5a**, **7a**, and **8a**, and

(25) For comparison, the treatment of arylpalladium(II) iodo complex **I** lacking the R^1 substituent (X = O, EWG^1 = COOEt, R^1 = H, L = PPh_3) under the same conditions afforded the corresponding palladacycle **II** (X = O, EWG^1 = COOEt, R^1 = H, L = PPh_3) as a stable fully characterized product in 86% yield, see ref 11d.

(26) Addition of benzene induced a complete precipitation of residual *t*-BuOK and KI, which were removed by filtration and thus allowed for the acquisition of high-quality ^{31}P NMR spectra in $CDCl_3$. However, a partial oxidation of air-sensitive phosphine ligands and/or partial decomposition of the semistable organopalladium complexes could not be avoided under these conditions.

(27) In contrast to alkyl substituents R^1 (Me and *i*-Pr) that are expected to cause an increasing destabilization of palladacycles **[4]** due to the increase in their steric bulk, the phenyl substituent R^1 (Ph) could partially offset the unfavorable steric factors by its electron-withdrawing effects, see refs 4d and 9a.

Table 2. Summary of ^{31}P NMR Data Reported in Scheme 4

spectrum	chemical shift δ (ppm)	multiplicity	assignment	relative integration	molar percent (%)
a	30.0	d, J = 28.0 Hz	**[4a]**	1 P	33
R^1 = Me	23.9	d, J = 28.0 Hz	**[4a]**	1 P	
L = PPh_3	23.12	s	**5a**	0.7 P	22
	23.09	s	**5a**	0.7 P	
	−5.5		PPh_3	1.3 P	45
b	30.4	s	P(=O)Ph_2Me	0.4 P	30
R^1 = Me	9.5	d, J = 30.8 Hz	**[4b]**	1 P	70
L = PPh_2Me	2.2	d, J = 30.8 Hz	**[4b]**	1 P	
c	23.3	d, J = 434.1 Hz	**7a**	0.5 P	68
R^1 = *i*-Pr	22.4	d, J = 434.1 Hz	**7a**	0.5 P	
L = PPh_3	−5.5	s	PPh_3	0.23 P	32
d	30.4	s	P(=O)Ph_2Me	0.3 P	19
R^1 = *i*-Pr	8.4	d, J = 29.6 Hz	**[4d]**	1 P	62
L = PPh_2Me	2.9	d, J = 29.5 Hz	**[4d]**	1 P	
	7.2	d, J = 452.1 Hz	**7b**	0.3 P	19
	5.5	d, J = 452.0 Hz	**7b**	0.3 P	
e	30.9	s, br	**[4e]**	1.7 P	44
R^1 = Ph	23.28	s	**8a**	0.5 p	12
L = PPh_3	23.25	s	**8a**	0.5 P	
	−4.9	s, br	PPh_3	1.7 P	44
f	30.4	s	P(=O)Ph_2Me	0.8 P	43
R^1 = Ph	10.8	d, J = 34.1 Hz	**[4f]**	1 P	57
L = PPh_2Me	3.4	d, J = 34.3 Hz	**[4f]**	1 P	

the contents of palladacycles **[4a]**, **[4c]**, and **[4e]** detected in the crude mixtures correlate well with the anticipated steric and electronic effects of substituents R^1 (Me, *i*-Pr, Ph).[4d,9a,27]

In contrast, treatment of complexes **5b** (R^1 = Me) and **8b** (R^1 = Ph), possessing PPh_2Me ligands,[19] with *t*-BuOK under the standard conditions led to a complete conversion of the substrates, yielding crude products with higher contents of the corresponding palladacycles **[4b]** (70%) and **[4f]** (57%) (spectra b and f, Scheme 4 and Table 2). However, only an incomplete conversion of palladium(II) complex **7b** (R^1 = *i*-Pr) possessing an *i*-Pr substituent[27] was achieved, delivering a crude product containing palladacycle **[4d]** (62%) as well as unreacted complex **7b** (19%) (spectrum d, Scheme 4 and Table 2). A destabilization of palladacycles **[4b]**, **[4d]**, and **[4f]** was suggested by the presence of free ligands, mostly as the phosphine oxide P(=O)Ph_2Me in 30%, 19%, and 43% in spectra b, d, and f, respectively (Scheme 4 and Table 2).[28] Attempts at isolation and complete characterization of complexes **[4]** from all the ring-closure experiments (Scheme 4) were unsuccessful due to the persistent presence of significant quantities of free ligands and/or ligand oxides. To provide insight into the bonding mode of palladium enolates in complexes **[4b]**, **[4d]**, and **[4f]**, IR spectroscopic analyses were performed on the crude reaction mixtures from experiments shown in spectra b, d, and f (Scheme 4). The IR spectroscopy revealed ν(C=O) bands at 1687 cm^{-1} (spectrum b), 1676 cm^{-1} (spectrum d, ν(C=O) at 1739 cm^{-1} was observed for the remaining complex **7b**), and 1676 cm^{-1} (spectrum f), respectively.[29] The data are consistent with the ν(C=O) band observed in IR spectra recorded on palladacycles **3**,[15] and on palladacycles of type **4** lacking the R^1 substituent (R^1 = H), and featuring diverse phosphine ligands,[30] for which the existence of a palladium-bonded sp^3-hybridized carbon was unequivocally established.[11] Thus, although the involvement of O-bonded palladium enolates could not be rigorously ruled out, the presented evidence supports the conclusion that palladacycles **[4b]**, **[4d]**, and **[4f]** feature a fully substituted, sp^3-hybridized carbon bonded to palladium.

Synthesis of 2,2,3,4-Tetrasubstituted 2*H*-1-Benzopyrans and 1,2-Dihydroquinolines. As anticipated,[11] treatment of palladacycle **3a** with dimethyl acetylenedicarboxylate (dmad) (3.1 equiv, 80 °C in 1,2-dichloroethane) failed to afford the corresponding benzopyran **9** (Scheme 5), conceivably due to a relatively tight binding of the bidentate *N,N,N′,N′*-tetramethyl-1,2-ethylenediamine (TMEDA) ligand forming a five-membered chelate ring.[31] To facilitate the displacement of TMEDA ligand, and allow for the attachment of the alkyne to palladium in the presumed transition state,[32] monodentate phosphine ligands (3.0 equiv) were added to palladacycle **3a**, along with dimethyl acetylenedicarboxylate (3.1 equiv of dmad, 80 °C in 1,2-dichloroethane,

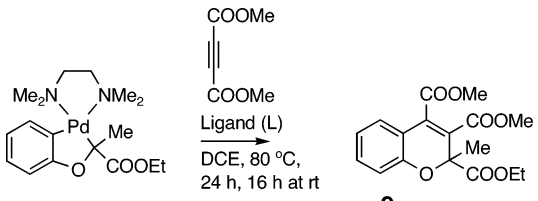
(28) For comparison, an intramolecular displacement of the iodide ligand in complex **8e** (R^1 = H, L = PPh_2Me, Scheme 3) under the conditions of the experiment described in Scheme 4 afforded ^{31}P NMR spectra indicating a complete conversion of complex **8e**, and the presence of the corresponding palladacycle **[4g]** (R^1 = H, L = PPh_2Me) along with small amounts of the ligand oxide P(=O)Ph_2Me, in the molar ratio **8e**:**[4g]**:L = 0:87:13. However, isolation and complete characterization of palladacycle **[4g]** were not attempted.

(29) The IR spectra of the crude reaction mixtures were measured in neat films generated upon evaporation of methylene chloride solvent on the surface of NaCl salt plates.

(30) IR spectra recorded on previously characterized palladacycles **4** lacking substituent R^1 (R^1 = H), indicated the presence of ν(C=O) band of the ester group at 1708 cm^{-1} for L = PPh_3, and at 1692 cm^{-1} for L−L = 1,2-bis(diphenylphosphino)ethane (dppe), see refs 11c and 11d.

(31) Attempted insertion of highly activated dimethyl acetylenedicarboxylate (dmad) into palladacycle of type **II** (R^1 = H, EWG^1 = COOEt, L-L = 1,2-bis(diphenylphosphino)butane (dppb)) with a bidentate ligand giving rise to a seven-membered chelate ring afforded only low (<30%) yields of the corresponding benzopyran, requiring forcing conditions (Portscheller, J. L., Malinakova, H. C. Unpublished results). It is notable that the replacement of the ester (COOEt) group with a sterically demanding amide ($CONEt_2$) group in the presence of the same bidentate ligand (dppb) in palladacycle of type **II** (R^1 = H, EWG^1 = $CONEt_2$, L-L = 1,2-bis(diphenylphosphino)butane (dppb)) facilitated the insertion of dmad, providing the corresponding benzopyran in a good yield (64%), see ref 11d.

Scheme 5



3a **9**

ligand	yield (%)
L = PPh_3	traces
L = PPh_2Me[a]	(31%)
L = $PPhMe_2$[a]	(42%)
L = PMe_3[a]	(52%)
L = P(*n*-Bu)$_3$[a]	(68%)

[a] Tetrafluoroborate salt HPR_3BF_4 of the ligand was used and deprotonated in situ by (*i*-Pr)$_2$EtN.

Scheme 5).[33] Testing a series of phosphines with increasing ligand strength and a decreasing cone angle,[19] the yield of benzopyran **9** was found to rise from 31% for the reaction mediated by PPh_2Me, to 68% yield obtained from the reaction mediated by the P(*n*-Bu)$_3$ ligand (Scheme 5). However, attempts to insert less activated unsymmetrical alkynes (e.g., MeC≡CCOOEt) into palladacycle **3a** under the optimized conditions (Scheme 5) proved unsuccessful.[34] Results similar to those described above were obtained with palladacycles **3b**,**c**, and further development of this protocol was abandoned.

Seeking a general method that would permit an independent variation of substituents at C-2 (R^1) and C-4 (R^2) in tetrasubstituted 2*H*-1-benzopyrans **III** (Figure 1), palladium(II) iodo complexes **5**−**8** were treated with *t*-BuOK (1.2 equiv, room temperature, THF, 20−40 min), followed by the addition of diverse alkynes (MeOOCC≡CCOOMe, MeC≡CCOOEt, or $MeOC_6H_4C$≡CCOOEt, 2.5−3.0 equiv) and 1,2-dichloroethane,[35] and heating (80 °C) for 24 h, or until significant quantities of palladium(0) precipitated (Table 3). According to ^{31}P NMR studies on the ring-closure reactions (Scheme 4), and depending on the choice of auxiliary monodentate phosphine ligand L, either partial or complete conversion of complexes **5**−**8** into palladacycles **[4]**, which would subsequently react with alkynes, was anticipated.[36] Due to the observed partial conversion of complexes **7a,b** in experiments described in Scheme 4 (spectra c and d), the time for treatment of complexes **7a,b** with *t*-BuOK was extended to 40 min (entries 11−14, Table 3).[36] Gratifyingly, the two-step one-pot protocol smoothly afforded targeted 2*H*-1-benzopyrans **9**−**17** in good yields (44−80%) as single products, and no traces of regioisomeric heterocycles[11,32] were detected by ^1H NMR analyses of crude reaction mixtures. The highly selective formation of heterocycles with the two ester substituents at carbons C-2 and C-3 is consistent with our previous studies on the insertion of unsymmetrical alkynes into stable palladacycles of type **[4]** (R^1 = H, L = PPh_3).[11] The regiochemical assignments in benzopyrans **10**, **12**, **14**, and **16** possessing a methyl substituent (R^2 = Me) in the C-4 position were based on NOE ^1H NMR experiments.[37] The structure of benzopyran **11** was established by single-crystal X-ray crystallographic analysis, and the structures of benzopyrans **13**, **15**, and **17** were assigned accordingly.[38]

The nature of auxiliary phosphine ligands in substrates **5**−**8** affected yields of benzopyrans **9**−**17**. Thus, arylpalladium(II) iodo complexes **5a**, **6a**, and **8a** possessing PPh_3 ligands afforded the corresponding benzopyrans **9**−**16** in low to moderate yields, 20−59% (entries 1, 3, 5, 7, 9, 11, 13, and 15, Table 3). The failure to obtain appreciable yields of benzopyrans **14** and **15** (entries 11 and 13, Table 3) from complex **7a** (R^1 = *i*-Pr, L = PPh_3) is in agreement with the failure to generate significant amounts of palladacycle **[4c]** via the ring-closure reaction of complex **7a** (spectrum c, Scheme 4).[39] Substrates **5b**−**8b** featuring PPh_2Me ligands afforded benzopyrans **9**−**15** and **17** in consistently better yields, 57−80% (entries 2, 4, 6, 8, 10, 12, 14, and 19, Table 3). The described auxiliary ligand effects on synthesis of benzopyrans **9**−**17** correlate closely with the previously observed ligand effects on generation of palladacycles [**4**] via the ring-closure (Scheme 4). The content of palladacycles with PPh_2Me ligands, e.g., **[4b]** (70%), **[4d]** (62%), and **[4f]** (57%) in the crude products of the ring-closure experiments, was higher than the contents of palladacycles **[4a]** (33%), **[4c]** (0%), and **[4e]** (44%) bearing the PPh_3 ligand (Scheme 4 and Table 2). In a single example involving the reaction between complex **8b** (R^1 = Ph, L = PPh_2Me) and ethyl 2-butynoate, only a low yield (44%) of benzopyran **16** was obtained (entry 16, Table 3). Interestingly, further increase in the

(32) For the discussion of the mechanism and the origins of regiocontrol in alkyne insertion reactions with group 10 metalacycles, see: (a) Bennet, M. A.; Macgregor, S. A.; Wenger, E. *Helv. Chim. Acta* **2001**, *84*, 3084−3104. (b) Campora, J.; Palma, P.; Carmona, E. *Coord. Chem. Rev.* **1999**, *193*−*195*, 207−281.

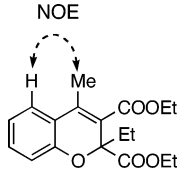
(33) The ligands were added as tetrafluoroborate salts and deprotonated in situ by (*i*-Pr)$_2$EtN, see: Netherton, M. R.; Fu, G. C. *Org. Lett.* **2001**, *3*, 4295−4298.

(34) Treatment of palladacycle **3a** with CH_3C≡CCOOEt and ligand $[HPMe_3]BF_4$ under the conditions described in Scheme 5 for 24 h did not give rise to the corresponding benzopyran in concentrations detectable by TLC.

(35) The addition of 1,2-dichloroethane (DCE) (6 mL) solvent into the THF (1 mL) solutions of the reactants allowed performing the alkyne insertion reaction under reflux at elevated temperatures. Furthermore, the decrease in overall solvent polarity in the DCE/THF mixtures would be expected to favor migratory insertion of alkynes into palladacycles of type **[4]**.

(36) The additions of alkyne solutions into the reaction mixtures containing arylpalladium(II) iodo complexes **5**−**8** were delayed 20−40 min following the introduction of *t*-BuOK, to allow for the ring closure to occur and to consume the *t*-BuOK, and thus avoid possible base-induced side-reactions between a full equivalent of base (*t*-BuOK) and the alkynes.

(37) For example, the ^1H NMR NOE analysis of benzopyran **12** indicated that irradiation of the signal for the proton in the methyl group attached to C-4 position at δ 2.26 (s) led to the NOE enhancement of the signal for the proton at C-5 in the aromatic ring at δ 7.31 (dd).

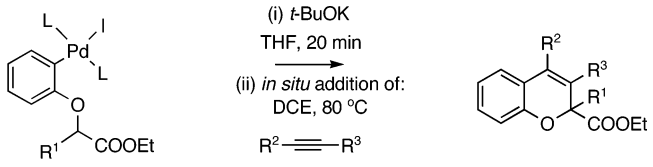


12

(38) Assignment of regiochemistry in benzopyrans **11**, **13**, **15**, and **17** via long-range $^1H-^{13}C$ correlations revealed by HMBC 2D NMR spectroscopic analysis was complicated due to the overlap of both the proton and carbon signals for protons and carbons from the two aromatic rings.

(39) Although the reaction time for the ring closure of arylpalladium(II) iodo complex **7a** was extended to 40 min (entries 11 and 13, Table 1), benzopyrans **14** and **15** were isolated in only 34% and 26% yields, respectively, as crude materials with only 85−90% purity by ^1H NMR.

Table 3. Regiocontrolled Synthesis of 2,2,3,4-Tetrasubstituted 2*H*-1-Benzopyrans



5-8 **9-17**

entry	substrate	R^1	L	time (h)	R^2	R^3	produt	yield (%)
1	**5a**	Me	PPh_3	3	COOMe	COOMe	**9**	20
2	**5b**	Me	PPh_2Me	1	COOMe	COOMe	**9**	63
3	**5a**	Me	PPh_3	8	Me	COOEt	**10**	51
4	**5b**	Me	PPh_2Me	24	Me	COOEt	**10**	59
5	**5a**	Me	PPh_3	12	*p*-$MeOC_6H_4$−	COOMe	**11**	59
6	**5b**	Me	PPh_2Me	24	*p*-$MeOC_6H_4$−	COOMe	**11**	80
7	**6a**	Et	PPh_3	11	Me	COOEt	**12**	50
8	**6b**	Et	PPh_2Me	24	Me	COOEt	**12**	63
9	**6a**	Et	PPh_3	10	*p*-$MeOC_6H_4$−	COOMe	**13**	54
10	**6b**	Et	PPh_2Me	24	*p*-$MeOC_6H_4$−	COOMe	**13**	69
11	**7a**[a]	*i*-Pr	PPh_3	18	Me	COOEt	**14**[b]	*b*
12	**7b**[a]	*i*-Pr	PPh_2Me	24	Me	COOEt	**14**	57
13	**7a**[a]	*i*-Pr	PPh_3	18	*p*-$MeOC_6H_4$−	COOMe	**15**[c]	*c*
14	**7b**[a]	*i*-Pr	PPh_2Me	24	*p*-$MeOC_6H_4$−	COOMe	**15**	72
15	**8a**	Ph	PPh_3	42	Me	COOEt	**16**	34
16	**8b**	Ph	PPh_2Me	24	Me	COOEt	**16**	44
17	**8c**	Ph	$PPhMe_2$	24	Me	COOEt	**16**	<5
18	**8d**	Ph	PMe_3	24	Me	COOEt	**16**	<5
19	**8b**	Ph	PPh_2Me	24	*p*-$MeOC_6H_4$−	COOMe	**17**	69

[a] Reaction mixture was stirred with *t*-BuOK for 40 min prior to the addition of the solution of alkyne. [b] Only 34% yield of crude product **14** in 85−90% purity by ^1H NMR was isolated. [c] Only 26% yield of crude product **15** in 85−90% purity by ^1H NMR was isolated.

strength[19] of the auxiliary ligands L in complexes **8c** (L = $PPhMe_2$) and **8d** (L = PMe_3) permitted only the isolation of traces of benzopyran **16**, likely reflecting an unfavorable position of the ligand exchange equilibrium between ligands L and the alkyne (entries 17 and 18, Table 3). Results in Table 3 did not point to pronounced effects of the nature of substituent R^1 on the yield of the corresponding benzopyrans (e.g., compare entries 16 and 19, or 4 and 12, Table 3). However, the observed correlation between the ligand effects documented by the experiments in Scheme 4, and the role of the auxiliary ligands in the preparation of benzopyrans **9**−**17** (Table 3) suggests that the formation of benzopyrans **9**−**17** proceeds via palladacycles **[4a**−**f]** as reactive intermediates, although the existence of alternative pathways could not be rigorously ruled out.[40]

The optimized synthetic protocol was successfully applied to the synthesis of 1,2-dihydroquinolines **22** and **23** (Scheme 6). N-Alkylation[41] of aryl iodide **18**[42] afforded carbamate **19**, which was converted by the established methods[11] into aryl palladium(II) complexes **20** and **21** (Scheme 6). Complexes **20** and **21** were isolated as stable, fully characterized solids. As anticipated, ^1H, ^{13}C, and ^{31}P NMR spectra of compounds **18**−**21** showed significant signal broadening due to the amide resonance. A sequential treatment of palladium(II) complex **21** with *t*-BuOK (1.2 equiv, room temperature, THF, 40 min) and solutions of alkynes (MeC≡CCOOEt and $MeOC_6H_4C$≡CCOOEt, 2.5−3.0 equiv) in 1,2-dichloroethane afforded the corresponding tetrasubstituted 1,2-dihydroquinolines **22** and **23** in moderate yields of 55% and 50%, respectively. No traces of regioisomeric products were detected in the crude reaction mixtures by ^1H NMR spectroscopic analyses. The assignment of regiochemistry for 1,2-dihydroquinoline **22** was based on the ^1H NOE experiment,[43] and the structure of 1,2-dihydroquinoline **23** was established by X-ray crystallographic analysis.

Conclusions

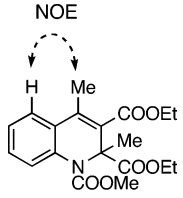
Stable oxapalladacycles **3a**−**d** with sterically unencumbered TMEDA auxiliary ligands and a tertiary sp^3-hybridized palladium-bonded carbon were prepared and fully characterized. Enolate connectivities in palladacycles **3c** and **3d** with *i*-Pr and Ph substituents R^1 were

(40) (a) An alternative pathway consisting of a migratory insertion of the alkyne into palladium(II) complexes **5**−**8** and subsequent displacement of the anionic iodide ligand providing seven-membered palladacycles, which would undergo a reductive elimination, might also account for the formation of benzopyrans **9**−**17**. Most likely, the extent of this process would be limited to the portion of complexes **5**−**8** that failed to provide palladacycles **[4]** within the initial 20−40 min period of treatment with *t*-BuOK. The formation of palladacycles **[4]** could continue after the addition of alkynes, and thus simultaneous operation of both these pathways cannot be ruled out. For examples of studies exploring insertion of unsaturated molecules into stable arylpalladium(II) halide complexes yielding heterocyclic products, see: (b) Vicente, J.; Abad, J.-A.; Lopez-Serrano, J.; Jones, P. G. *Organometallics* **2004**, *23*, 4711−4722. (c) Vicente, J.; Abad, J.-A.; Fortsch, W.; Lopez-Saez, M.-J.; Jones, P. G. *Organometallics* **2004**, *23*, 4414−4429.

(41) Bergeron, R. J.; Hoffman, P. *J. Org. Chem.* **1980**, *45*, 161−163.

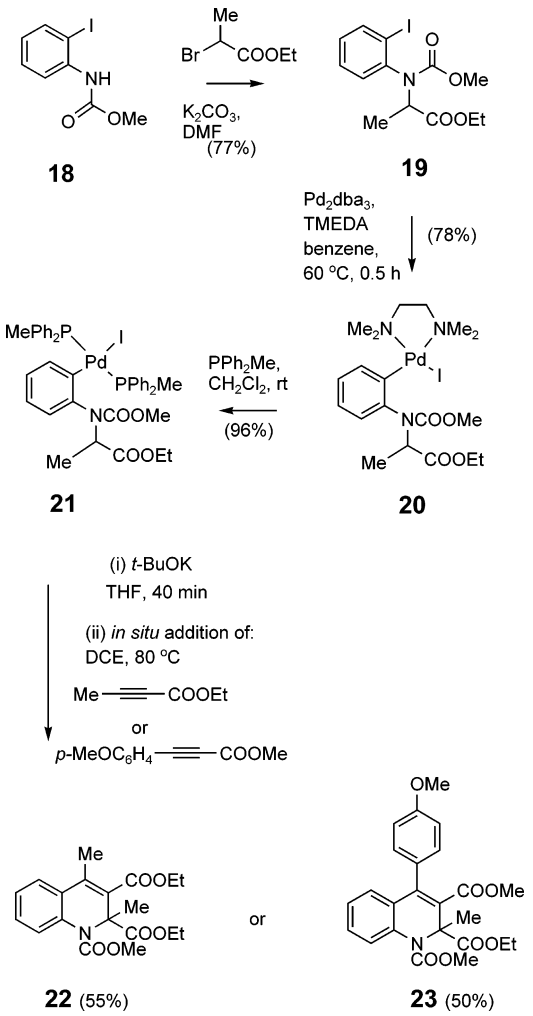
(42) (a) Crich, D.; Sannigrahi, M. *Tetrahedron* **2002**, *58*, 3319−3322. (b) Ko, S. S.; Confalone, P. N. *Tetrahedron* **1985**, *41*, 3511−3518.

(43) The ^1H NMR NOE analysis of 1,2-dihydroquinoline **22** indicated that irradiation of the signal for the proton in the methyl group attached to the C-4 position at δ 2.22 (s) led to the NOE enhancement of the signal for the proton at C-5 in the aromatic ring at δ 7.37 (d).



22

Scheme 6



confirmed by X-ray crystallographic analyses. ^{1}H and ^{31}P NMR monitoring experiments indicated that ligand exchange reactions between palladacycles **3a** (R^1 = Me), **3c** (R^1 = *i*-Pr), and **3d** (R^1 = Ph) and PPh_2Me ligands reached complete conversions to the corresponding palladacycles **[4]** possessing the two phosphines in *cis* orientation. However, the reactions with PPh_3 ligand under equivalent conditions led only to partial conversions of substrates **3**. These observations contrast with a facile displacement of the TMEDA ligand with PPh_3 in palladacycle **3** lacking an R^1 substituent (R^1 = H).[11d] The choice of monodentate phosphine ligands (L), and the nature of the substituent R^1 in arylpalladium(II) iodo complexes **I** proved critical for the successful generation of palladacycles **II** (Figure 1) from complexes **I** via an intramolecular displacement of iodide. Thus, ^{31}P NMR analyses of the crude product mixtures arising from the ring-closure reactions of arylpalladium(II) iodo complexes **5a**,**b**, **7a**,**b**, and **8a**,**b** (L = PPh_3 or PPh_2Me, R^1 = Me, *i*-Pr, and Ph) run for a set time period of 20 min revealed an incomplete conversion of complexes bearing PPh_3 ligands (**5a**, **7a**, and **8a**), and the complex **7b** (L = PPh_2Me, R^1 = *i*-Pr) possessing a sterically demanding *i*-Pr substituent,[27] while essentially complete conversions were reached with complexes **5b** and **8b** bearing PPh_2Me ligands. The mol % content of palladacycles **[4]** with PPh_3 ligands in the crude product mixtures was in the range of 0−44 mol %, while the mol % content of palladacycles **[4]** with PPh_2Me ligands varied from 57 to 70%. Although palladacycles **[4]** could not be isolated as pure entities and fully characterized, IR spectroscopic analyses of crude reaction mixtures lend support to the presence of palladium-bonded sp^3-hybridized carbon in palladacycles **[4b**,**d**,**f]**.[10c] An efficient one-pot two-step protocol for the preparation of 2,2,3,4-tetrasubstituted benzopyrans **9**−**17**, and 1,2-dihydroquinolines **22** and **23** from arylpalladium(II) complexes **5**−**8** and **21**, and alkynes was devised (Table 3 and Scheme 6), providing the heterocycles in good yields (44−80%) as single regioisomers. A correlation between the observed effects of the nature of auxiliary phosphine ligands on the yields of benzopyrans **9**−**17**, with the NMR monitoring data described above, suggested that heterocycles **9**−**17** were generated via a regiocontrolled migratory insertion of alkynes[11] into palladacycles **[4]** generated in situ from complexes **5**−**8**. The presented study provides generally useful insights into the role played by a proper balance between the nature of substituents at the palladium-bonded sp^3-hybridized carbon, and the steric and electronic properties of auxiliary phosphine ligands in palladium-mediated carbon−carbon bond-forming processes.

Experimental Section

Unless otherwise indicated, all NMR data were collected at room temperature in $CDCl_3$ with internal $CHCl_3$ as the reference (δ 7.26 ppm for ^{1}H and 77.00 ppm for ^{13}C) and external (present in a sealed capillary inserted into the NMR tube) H_3PO_4 (δ 0 ppm) as the reference for ^{31}P NMR. IR spectra were measured in KBr pellets or as thin films on salt (NaCl) plates. Melting points are uncorrected and were taken in open capillary tubes. MS were measured under fast atom bombardment (FAB) or electrospray (ES) ionization conditions. Analytical thin-layer chromatography (TLC) was carried out on commercial Merck silica gel 60 plates, 0.25 μm thickness, with fluorescent indicator (F-254) or stained with aqueous $KMnO_4$ solution. Column chromatography was performed with 40−63 μm silica gel (Merck) or basic alumina (150 mesh, Brokmann I). Tetrahydrofuran (THF) was freshly distilled from sodium/benzophenone. Benzene was distilled from CaH_2 and kept over 3 Å (8−12 mesh) molecular sieves under an atmosphere of dry argon. 1,2-Dichloroethane and methylene chloride were kept over 3 Å (8−12 mesh) molecular sieves under an atmosphere of dry argon; other solvents were used as received. Unless otherwise specified, all reactions were carried out under an atmosphere of dry nitrogen or argon in oven-dried (at least 6 h at 140 °C) glassware. Single crystals for X-ray analysis were obtained by a slow diffusion of hexanes into methylene chloride solutions of the palladium complexes, and by a slow diffusion of hexanes into ether solutions of heterocycles (a 2*H*-1-benzopyran and a 1,2-dihydroquinoline).

General Procedure for the Synthesis of Aryl Iodides 1a−**d.** To a suspension of 2-iodophenol (1.0 mmol) and K_2CO_3 (5.0 mmol) in acetone (3.3 mL) at room temperature under argon was added the corresponding α-bromo ester as neat liquid, and the resulting suspension was refluxed for 16−26 h. The reaction mixtures were filtered, and the solvents were removed under reduced pressure to provide crude products that were purified by flash chromatography over silica eluting with ether/hexane or EtOAc/hexane mixtures to afford aryl iodides **1a**−**d** as colorless or yellow oils.

Ethyl 2-(2-Iodophenoxy)propionate (1a). Treatment of 2-iodophenol (1.00 g, 4.55 mmol), K_2CO_3 (3.33 g, 24.1 mmol), and ethyl 2-bromopropionate (0.90 mL, 1.25 g, 6.91 mmol) for 17 h according to the general procedure described above eluting with ether/hexane (1:20) afforded aryl iodide **1a** (1.425

g, 98%) as a light yellow oil: $R_f = 0.48$ (EtOAc/hexane, 1:9); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (dd, $J = 7.7$ Hz, 1.5 Hz, 1 H), 7.24 (ddd, $J = 8.2$ Hz, 6.5 Hz, 1.6 Hz, 1 H), 6.75−6.69 (m, 2 H), 4.74 (q, $J = 6.8$ Hz, 1 H), 4.27−4.27 (m, 2 H), 1.69 (d, $J = 6.8$ Hz, 3 H), 1.24 (t, $J = 7.1$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.6, 156.6, 139.8, 129.3, 123.4, 113.5, 87.3, 74.2, 61.3, 18.5, 14.1; IR (neat, cm^{-1}) 1750 (s), 746 (m), 650 (m); HRMS (FAB) calcd for $C_{11}H_{14}IO_3$ (M + H$^+$), 320.9988, found 320.9971.

Ethyl 2-(2-Iodophenoxy)butyrate (1b). Treatment of 2-iodophenol (3.30 g, 15.0 mmol), K_2CO_3 (10.0 g, 72.4 mmol), and ethyl 2-bromobutyrate (4.43 mL, 5.840 g, 30.0 mmol) for 26 h according to the general procedure described above eluting with EtOAc/hexane (1:20) afforded aryl iodide **1b** (4.80 g, 96%) as a light yellow oil: $R_f = 0.52$ (EtOAc/hexane, 1:9); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (dd, $J = 7.8$ Hz, 1.6 Hz, 1 H), 7.25 (td, $J = 8.1$ Hz, 1.6 Hz, 1 H), 6.73 (td, $J = 7.6$ Hz, 1.2 Hz, 1 H), 6.66 (dd, $J = 8.2$ Hz, 1.1 Hz, 1 H), 4.60 (t, $J = 5.9$ Hz, 1 H), 4.27−4.19 (m, 2 H), 2.07 (pent, $J = 7.3$ Hz, 2 H), 1.25 (t, $J = 7.1$ Hz, 3 H), 1.17 (t, $J = 7.4$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.0, 156.6, 139.7, 129.3, 123.1, 112.6, 86.9, 78.7, 61.2, 26.2, 14.4, 9.7; IR (neat, cm^{-1}) 1746 (s), 801 (m), 735 (m); HRMS (ES) calcd for $C_{12}H_{16}IO_3$ (M + H$^+$), 335.0144, found 335.0129.

Ethyl 2-(2-Iodophenoxy)-3-methylbutyrate (1c). Treatment of 2-iodophenol (0.999 g, 4.542 mmol), and K_2CO_3 (3.18 g, 23.0 mmol) with a solution of ethyl 2-bromo-3-methylbutyrate (1.436 g, 6.868 mmol) in acetone (2.0 mL) for 19 h according to the general procedure described above was followed by the addition of a second portion of the solution of ethyl 2-bromo-3-methylbutyrate (0.959 g, 4.588 mmol) in acetone (2.0 mL), and reflux for additional 30 h. Crude product was purified according to the general procedure, eluting with ether/hexane (1:20) to afford aryl iodide **1c** (1.404 g, 89%) as a light yellow oil: $R_f = 0.55$ (EtOAc/hexane, 1:9); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, $J = 7.8$ Hz, 1.6 Hz, 1 H), 7.22 (td, $J = 7.6$ Hz, 1.6 Hz, 1 H), 6.70 (td, $J = 7.6$ Hz, 1.2 Hz, 1 H), 6.60 (dd, $J = 8.2$ Hz, 1.1 Hz, 1 H), 4.43 (d, $J = 4.7$ Hz, 1 H), 4.20 (q, $J = 7.1$ Hz, 2 H), 2.4−2.3 (m, 1 H), 1.23 (t, $J = 7.1$ Hz, 3 H), 1.16 (d, $J = 6.8$ Hz, 3 H), 1.14 (d, $J = 6.9$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.6, 156.6, 139.7, 129.2, 122.9, 112.0, 86.6, 82.1, 61.1, 31.8, 18.9, 17.6, 14.1; IR (neat, cm^{-1}) 1753 (s), 1731 (m), 748 (m); HRMS (FAB) calcd for $C_{13}H_{18}IO_3$ (M + H$^+$), 349.0301, found 349.0300.

Ethyl 2-(2-Iodophenoxy)-2-phenylacetate (1d). Treatment of 2-iodophenol (1.004 g, 4.56 mmol), K_2CO_3 (3.15 g, 22.8 mmol), and ethyl 2-bromophenylacetate (1.20 mL, 1.66 g, 6.84 mmol) for 16 h according to the general procedure described above eluting with ether/hexane (1:20) afforded aryl iodide **1b** (1.751 g, 100%) as a yellow oil: $R_f = 0.48$ (EtOAc/hexane, 1:9); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (dd, $J = 8.1$ Hz, 1.6 Hz, 1 H), 7.70−7.68 (m, 2 H), 7.44−7.35 (m, 3 H), 7.23 (td, $J = 8.2$ Hz, 1.6 Hz, 1 H), 6.76−6.72 (m, 2 H), 5.68 (s, 1 H), 4.29−4.11 (m, 2 H), 1.18 (t, $J = 7.1$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.3, 156.0, 139.9, 134.9, 129.3, 128.9, 128.7 (2 carbons) 127.5 (2 carbons), 123.5, 113.2, 87.2, 79.5, 61.7, 13.9; IR (neat, cm^{-1}) 1734 (s), 748.5 (m), 697.8 (m); HRMS (FAB) calcd for $C_{16}H_{16}IO_3$ (M + H$^+$), 382.0144, found 383.0137.

General Procedure for the Synthesis of Palladium(II) Iodo Complexes 2a−d. To a solution of tris(dibenzylideneacetone)dipalladium(0) (Pd_2dba_3) (0.500 mmol) in benzene (25 mL) at room temperature under argon was added neat *N,N,N′,N′*-tetramethyl-1,2-ethylenediamine (TMEDA) (1.5 mmol) and the solution of aryl iodides **1a−d** (1.05−1.1 mmol) in benzene (1−2 mL). The reaction mixture was stirred at 55 °C for 30 min. The resulting suspension was filtered through a plug of Celite, and solvents were removed under reduced pressure. The crude product was deposited on Celite, introduced on top of a short silica column, and eluted with EtOAc/hexane (1:5) mixture to remove excess dba, and subsequently with EtOAc/hexane (1:1) to afford a solid product, which was triturated with minimum amounts of ether, yielding pure palladium(II) iodo complexes **2a−d** as yellow solids.

{2-[1-Ethoxycarbonylethoxy]phenyl}iodo(tetramethylethylenediamine)palladium (2a). Pd_2dba_3 (1.00 g, 1.09 mmol), TMEDA (0.50 mmol, 0.385 g, 3.31 mmol), and aryl iodide **1a** (0.770 g, 2.41 mmol) were treated according to the general procedure described above to afford the palladium complex **2a** (0.830 g, 70%) as a yellow solid: mp 130−131 °C (ether); $R_f = 0.32$ (EtOAc/hexane, 1:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (dd, $J = 7.2$ Hz, 1.7 Hz, 0.2 H), 7.17 (dd, $J = 7.4$ Hz, 1.5 Hz, 0.8 H), 6.80−6.73 (m, 1.2 H), 6.68 (td, $J = 7.3$ Hz, 1.2 Hz, 0.8 H), 6.60 (d, $J = 7.5$ Hz, 0.2 H), 6.41 (dd, $J = 7.8$ Hz, 1.1 Hz, 0.8 H), 5.86 (q, $J = 6.8$ Hz, 0.2 H), 4.86 (q, $J = 6.8$ Hz, 0.8 H), 4.34−4.26 (m, 0.4 H), 4.24−4.15 (m, 1.6 H), 2.82−2.75 (m, 1 H), 2.73 (s, 2.4 H), 2.71 (s, 2.4 H), 2.70 (s, 0.6 H), 2.66 (s, 0.6 H), 2.63−2.55 (m, 3 H), 2.52 (s, 0.6 H), 2.44 (s, 2.4 H), 2.39 (s, 2.4 H), 2.34 (s, 0.6 H), 1.76 (d, $J = 6.8$ Hz, 2.4 H), 1.48 (d, $J = 6.8$ Hz, 0.6 H), 1.31 (t, $J = 7.1$ Hz, 0.6 H), 1.26 (t, $J = 7.1$ Hz, 2.4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.0, (173.6), 160.3, (159.6), (139.3), 137.9, (132.8), 131.4, 123.7, (123.6), (122.6), 121.4, (120.9), 113.7, (74.6), 73.7, 62.1, 60.7, (60.6), 58.6, 50.6, (50.5), 50.2, 49.9, 49.4, (49.3), 20.1, (17.9), (14.4), 14.2 (signals for the minor isomer arising from a hindered rotation about the Csp^2−Pd bond are shown in parentheses); IR (KBr, cm^{-1}) 1724 (s), 800 (m), 748 (m); HRMS (FAB) calcd for $C_{17}H_{30}N_2O_5IPd$ (M + H$^+$), 543.0336, found 543.0327.

{2-[1-Ethoxycarbonylpropoxy]phenyl}iodo(tetramethylethylenediamine) palladium (2b). Pd_2dba_3 (1.00 g, 1.09 mmol), TMEDA (0.50 mmol, 0.385 g, 3.31 mmol), and aryl iodide **1b** (0.807 g, 2.41 mmol) were treated according to the general procedure described above to afford the palladium complex **2b** (0.707 g, 58%) as a yellow solid: mp 102−104 °C (ether); $R_f = 0.29$ (EtOAc/hexane, 1:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17 (d, $J = 7.3$ Hz, 1 H), 6.77 (t, $J = 7.2$ Hz, 1 H), 6.66 (t, $J = 7.2$ Hz, 1 H), 6.25 (d, $J = 7.8$ Hz, 1 H), 4.63 (t, $J = 6.3$ Hz, 1 H), 4.20 (q, $J = 7.1$ Hz, 2 H), 2.81−2.75 (m, 1 H), 2.71 (s, 6 H), 2.66−2.54 (m, 3 H), 2.47 (s, 3 H), 2.42 (s, 3 H), 2.17−2.13 (m, 1 H), 2.12−2.04 (m, 1 H), 1.26 (td, $J = 7.0$ Hz, 2.0 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.3, 159.9, 137.7, 130.3, 123.7, 120.8, 111.2, 77.3, 62.1, 60.6, 58.5, 50.6, 50.2, 49.8, 49.2, 27.2, 14.3, 10.2; IR (KBr, cm^{-1}) 1739 (s), 802 (m), 746 (m); HRMS (ES) calcd for $C_{18}H_{32}N_2O_3IPd$ (M + H$^+$), 557.0500, found 557.0511.

{2-[1-Ethoxycarbonyl-2-methylpropoxy]phenyl}iodo(tetramethylethylenediamine)palladium (2c). Pd_2dba_3 (0.962 g, 1.05 mmol), TMEDA (0.47 mmol, 0.362 g, 3.11 mmol), and aryl iodide **1c** (0.771 g, 2.21 mmol) were treated according to the general procedure described above to afford the palladium complex **2c** (0.833 g, 69%) as a yellow solid: mp 168−170 °C (ether); $R_f = 0.45$ (EtOAc/hexane, 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (dd, $J = 7.3$ Hz, 1.6 Hz, 1 H), 6.77 (td, $J = 7.2$ Hz, 1.6 Hz, 1 H), 6.64 (td, $J = 7.3$ Hz, 1.2 Hz, 1 H), 6.16 (dd, $J = 7.9$ Hz, 1.0 Hz, 1 H), 4.44 (d, $J = 4.3$ Hz, 1 H), 4.19 (q, $J = 7.2$ Hz, 2 H), 2.82−2.75 (m, 1 H), 2.72 (s, 6 H), 2.66−2.51 (m, 3 H), 2.47 (s, 3 H), 2.43 (s, 3 H), 2.40−2.32 (m, 1 H), 1.27 (d, $J = 2.6$ Hz, 3 H), 1.26 (t, $J = 7.2$ Hz, 3 H), 1.25 (d, $J = 2.0$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.6, 159.8, 137.7, 129.5, 123.7, 120.4, 109.5, 80.2, 62.1, 60.5, 58.6, 50.6, 50.3, 49.7, 49.3, 32.3, 19.8, 18.1,14.3; IR (KBr, cm^{-1}) 1737 (s), 802 (m), 746 (m); HRMS (ES) calcd for $C_{19}H_{34}N_2O_3IPd$ (M + H$^+$), 571.0657, found 571.0679.

{2-[(Ethoxycarbonyl)phenylmethoxy]phenyl}iodo(tetramethylethylenediamine)palladium (2d). Pd_2dba_3 (1.00 g, 1.09 mmol), TMEDA (0.50 mmol, 0.385 g, 3.31 mmol), and aryl iodide **1d** (0.916 g, 2.40 mmol) were treated according to the general procedure described above to afford the palladium complex **2d** (0.997 g, 75%) as a yellow solid: mp 168−170 °C (ether); $R_f = 0.39$ (EtOAc/hexane, 1:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, $J = 7.4$ Hz, 1 H), 7.61 (d, $J = 8.1$ Hz, 0.6 H), 7.39−7.25 (m, 4.4 H), 6.80 (td, $J = 7.4$ Hz, 1.5 Hz, 0.6 H), 6.73 (td, $J = 7.3$ Hz, 1.3 Hz, 0.6 H), 6.70 (td, $J = 7.3$ Hz,

1.3 Hz, 0.4 H), 6.64 (dd, J = 7.9 Hz, 1.2 Hz, 0.6 H), 6.62 (td, J = 7.5 Hz, 1.3 Hz, 0.4 H), 6.30 (s, 0.4 H), 6.17 (dd, J = 7.8 Hz, 1.3 Hz, 0.4 H), 6.05 (s, 0.6 H), 4.20−4.12 (m, 2 H), 2.82−2.78 (m, 0.6 H), 2.73 (s, 1.2 H), 2.72 (s, 1.2 H), 2.65 (s, 1.8 H), 2.64−2.50 (m, 3.4 H), 2.49 (s, 1.2 H), 2.41 (s, 1.8 H), 2.39 (s, 1.2 H), 2.37 (s, 1.8 H), 2.36 (s, 1.8 H), 1.20 (t, J = 7.1 Hz, 1.8 H), 1.18 (t, J = 7.1 Hz, 1.2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.8, (171.5), 160.2, (159.9), (138.6), 138.5, (137.9), 137.7, (132.7), 132.1, 128.3, (128.2), 128.1 (2 carbons), 128.0, (127.9), 127.4, 123.8, (123.5), (122.5), 122.1, (118.8), 115.7, (80.5), 79.3, (62.2), 62.1, 61.0, (60.9), (58.6), 58.5, (50.6), 50.5, (50.3), 50.2, 49.9, (49.2), 49.0, (14.2), 14.1 (signals for the minor isomer arising from a hindered rotation about the Csp^2−Pd bond are shown in parentheses); IR (KBr, cm^{-1}) 1751 (s), 800 (m), 769 (m); HRMS (ES) calcd for $C_{22}H_{35}N_3O_3IPd$ (M + NH_4^+), 622.0758, found 622.0766.

General Procedure for the Synthesis of Stable Palladacycles 3a−d. To a solution of palladium(II) iodo complexes **2a−d** (1.0 mmol) in benzene (14−30 mL) under argon at room temperature was added *t*-BuOK (1.2−1.6 mmol, 1.0 M in THF). The resulting suspension was stirred for 15−20 min, filtered through Celite, and the solvents were removed under reduced pressure to afford palladacycles **3a−d** as yellow solids.

[1-Ethoxycarbonyl-1-ethinoxy-1,2-phenylene][tetramethylethylenediamine]palladium (3a). A solution of palladium(II) complex **2a** (0.800 g, 1.47 mmol) in benzene (20 mL) was treated with *t*-BuOK (2.2 mL, 2.2 mmol, 1.0 M in THF) according to the general procedure described above to afford palladacycle **3a** (0.514 g, 84%) as a yellow solid: mp 154−156 °C dec (benzene); R_f = 0.34 (EtOAc/hexane, 3:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.03 (d, J = 7.5 Hz, 1 H), 6.93 (t, J = 7.2 Hz, 1 H), 6.69 (d, J = 7.8 Hz, 1 H), 6.60 (t, J = 7.3 Hz, 1 H), 4.18−4.07 (m, 2 H), 2.78 (s, 3 H), 2.77 (s, 3 H), 2.73−2.62 (m, 2 H), 2.67 (s, 3 H), 2.52 (s, 3 H), 2.48−2.38 (m, 2 H), 1.75 (s, 3 H), 1.21 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.9, 172.2, 136.5, 133.4, 125.5, 117.2, 108.5, 93.5, 61.6, 61.2, 59.7, 50.4, 49.3 (2 carbons), 47.9, 25.7, 14.5; IR (KBr, cm^{-1}) 1677 (s), 802 (m), 750 (m); HRMS (ES) calcd for $C_{17}H_{29}N_2O_3Pd$ (M + H^+), 415.1220, found 415.1210.

[1-Ethoxycarbonyl-1-prophinoxy-1,2-phenylene][tetramethylethylenediamine]palladium (3b). A solution of palladium(II) complex **2b** (0.600 g, 1.08 mmol) in benzene (15 mL) was treated with *t*-BuOK (1.7 mL, 1.7 mmol, 1.0 M in THF) according to the general procedure described above to afford palladacycle **3b** (0.407 g, 88%) as a yellow solid: mp 132−134 °C dec (benzene); R_f = 0.44 (EtOAc/hexane, 3:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.03 (d, J = 7.6 Hz, 1 H), 6.93 (td, J = 7.5 Hz, 0.8 Hz, 1 H), 6.70 (dd, J = 7.5 Hz, 0.8 Hz, 1 H), 6.57 (td, J = 7.7 Hz, 0.8 Hz, 1 H), 4.18−4.09 (m, 2 H), 2.79 (s, 3 H), 2.78 (s, 3 H), 2.74−2.67 (m, 2 H), 2.65 (s, 3 H), 2.50 (s, 3 H), 2.46−2.42 (m, 1 H), 2.38−2.35 (m, 1 H), 2.29 (sext, J = 7.4 H, 1 H), 1.99 (sext, J = 7.1 Hz, 1 H), 1.23 (t, J = 7.1 Hz, 3 H), 1.13 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.1, 173.1, 136.3, 133.3, 125.5, 116.8, 108.2, 99.5, 61.6, 61.2, 59.6, 50.6, 49.4, 49.1, 47.5, 31.7, 14.5, 12.4; IR (KBr, cm^{-1}) 1670 (s), 802 (m), 756 (m); HRMS (FAB) calcd for $C_{18}H_{31}N_2O_3Pd$ (M + H^+), 429.1377, found 429.1353.

[1-Ethoxycarbonyl-2-methyl-1-prophinoxy-1,2-phenylene][tetramethylethylenediamine]palladium (3c). A solution of palladium(II) complex **2c** (0.500 g, 0.855 mmol) in benzene (25 mL) was treated with *t*-BuOK (1.0 mL, 1.0 mmol, 1.0 M in THF) according to the general procedure described above to afford palladacycle **3c** (0.371 g, 95%) as a yellow solid: mp 152−154 °C dec (benzene); R_f = 0.56 (EtOAc/hexane, 3:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.02 (dd, J = 7.6 Hz, 1.0 Hz, 1 H), 6.92 (td, J = 7.3 Hz, 1.2 Hz, 1 H), 6.70 (dd, J = 7.8 Hz, 1.2 Hz, 1 H), 6.55 (td, J = 7.6 Hz, 1.2 Hz, 1 H), 4.23−4.07 (m, 2 H), 2.80 (s, 3 H), 2.78 (s, 3 H), 2.76−2.66 (m, 2 H), 2.64 (s, 3 H), 2.60−2.53 (m, 1 H), 2.51 (s, 3 H), 2.44 (dt, J = 13.1 Hz, 3.3 Hz, 1 H), 2.34 (dt, J = 12.9 Hz, 2.3 Hz, 1 H), 1.35 (d, J = 6.9 Hz, 3 H), 1.22 (t, J = 7.1 Hz, 3 H), 1.03 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.5, 174.3, 135.6, 133.2, 125.4, 116.4, 107.8, 103.4, 61.5, 61.2, 59.5, 50.6, 49.6, 49.2, 47.5, 35.8, 24.5, 17.3, 14.6; IR (KBr, cm^{-1}) 1664 (s), 800 (m), 746 (m); HRMS (ES) calcd for $C_{19}H_{33}N_2O_3Pd$ (M + H^+), 443.1534, found 443.1546.

[1-Ethoxycarbonyl-1-phenylmethinoxy-1,2-phenylene][tetramethylethylenediamine]palladium (3d). A solution of palladium(II) complex **2d** (0.600 g, 0.992 mmol) in benzene (30 mL) was treated with *t*-BuOK (1.6 mL, 1.6 mmol, 1.0 M in THF) according to the general procedure described above to afford palladacycle **3d** (0.446 g, 94%) as a yellow solid: mp 164−166 °C dec (benzene); R_f = 0.67 (EtOAc/hexane, 3:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (dd, J = 8.4 Hz, 1.2 Hz, 2 H), 7.28−7.20 (m, 2 H), 7.12 (t, J = 7.3 Hz, 1 H), 7.05 (dd, J = 7.6 Hz, 1.2 Hz, 1 H), 6.95 (td, J = 7.8 Hz, 1.3 Hz, 1 H), 6.75 (dd, J = 7.8 Hz, 1.3 Hz, 1 H), 6.65 (td, J = 7.5 Hz, 1.3 Hz, 1 H), 4.16−4.07 (m, 2 H), 2.82 (s, 3 H), 2.75 (s, 3 H), 2.73−2.55 (m, 3 H), 2.37 (s, 3 H), 2.22−2.19 (m, 1 H), 1.48 (s, 3 H), 1.09 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.1, 172.8, 143.9, 136.6, 133.3, 128.7 (2 carbons), 127.6 (2 carbons), 125.8, 125.3, 117.4, 108.6, 97.5, 61.2, 61.1, 59.5, 51.1, 49.3, 49.1, 47.4, 14.1; IR (KBr, cm^{-1}) 1676 (s), 800 (m), 757 (m), 702 (m); HRMS (ES) calcd for $C_{22}H_{31}N_2O_3Pd$ (M + H^+), 477.1378, found 477.1382.

General Procedure for the Synthesis of Palladium(II) Iodo Complexes with Monodentate Phosphine Ligands. Method A. To a solution of tris(dibenzylideneacetone)dipalladium(0) (Pd_2dba_3) (0.50 mmol) and phosphine (2.0 mmol) in benzene (20 mL) at room temperature under argon was added a solution of aryl iodides **1a−d** (1.1 mmol) in benzene (1−2 mL). The mixture was stirred at 60 °C for 30 min. The resulting suspension was filtered through a plug of Celite, and solvents were removed under reduced pressure. The crude product was purified by flash chromatography over silica, eluting with with EtOAc/hexane (1:10) to remove excess dibenzylideneacetone (dba), and subsequently with EtOAc/hexane (1:3) to afford palladium (II) complexes **5−8** as yellow or white solids.

Method B. To a solution of arylpalladium(II) complexes **2b−e** (1.0 mmol) in CH_2Cl_2 (10 mL) under argon at room temperature was added the corresponding phosphine (2.4−2.5 mmol) or trimethylphosphonium tetrafluoroborate (2.3 mmol) and diisopropylethylamine (4.6 mmol). The mixture was stirred at room temperature for the indicated time, solvents were removed under reduced pressure, and the crude product was purified by flash chromatography over silica eluting with EtOAc/hexane (1:20) to remove excess phosphine, and subsequently with EtOAc/hexane (1:3) to afford palladium(II) complexes **6−8** as yellow or white solids.

***trans*-{2-[1-Ethoxycarbonylethoxy]phenyl}iodobis(triphenylphosphine)palladium (5a).** Pd_2dba_3 (0.916 g, 1.00 mmol), PPh_3 (1.049 g, 4.00 mmol), and aryl iodide **1a** (0.704 g, 2.200 mmol) were treated according to method A described above to afford the arylpalladium(II) iodo complex **5a** (1.639 g, 86%) as a yellow solid: mp 156−158 °C dec (EtOAc/hexane, 1:3); R_f = 0.54 (EtOAc/hexane, 1:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (q, J = 5.4 Hz, 6 H), 7.50 (q, J = 5.4 Hz, 6 H), 7.32−7.20 (m, 18 H), 6.76 (d, J = 6.3 Hz, 1 H), 6.35 (t, J = 7.4 Hz, 1 H), 6.05 (t, J = 7.2 Hz, 1 H), 5.49 (d, J = 7.9 Hz, 1 H), 4.15−4.07 (m, 1 H), 3.98−3.90 (m, 1 H), 3.67 (q, J = 6.6 Hz, 1 H), 1.38 (d, J = 6.6 Hz, 3 H), 1.07 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 157.4, 146.8, 136 (t, $J(^{13}C-^{31}P)$ = 4.2 Hz), 134.9 (t, $J(^{13}C-^{31}P)$ = 5.6 Hz), 132.8, 132.5 (d, $J(^{13}C-^{31}P)$ = 6.1 Hz), 132.3 (d, $J(^{13}C-^{31}P)$ = 6.7 Hz), 132.2, 129.5 (d, $J(^{13}C-^{31}P)$ = 16.8 Hz), 127.4 (q, $J(^{13}C-^{31}P)$ = 5.3 Hz), 123.5, 120.9, 110.3, 71.8, 60.7, 18.9, 13.9, several signals account for more than one carbon; ^{31}P NMR (162 MHz, $CDCl_3$) δ 23.12 (s, 1 P), 23.09 (s, 1 P);[23] IR (KBr, cm^{-1}) 1751 (s), 1730 (s), 1433 (s), 740 (m), 692 (s), 509 (s); HRMS (ES) calcd for $C_{47}H_{43}O_3P_2Pd$ (M − I^+), 823.1722, found 823.1703.

***trans*-{2-[1-Ethoxycarbonylethoxy]phenyl}iodobis(methyldiphenylphosphine)palladium (5b).** Pd_2dba_3 (1.374 g, 1.500 mmol), PPh_2Me (1.1 mL, 1.184 g, 6.00 mmol), and aryl iodide **1a** (1.056 g, 3.300 mmol) were treated according to method A described above to afford the palladium complex **5b** (2.075 g, 84%) as a yellow solid: mp 78−80 °C (EtOAc/hexane, 1:3); R_f = 0.58 (EtOAc/hexane, 1:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88−7.84 (m, 2 H), 7.65−7.62 (m, 2 H), 7.58−7.54 (m, 2 H), 7.42−7.39 (m, 4 H), 7.33−7.24 (m, 8 H), 7.19 (t, J = 7.2 Hz, 2 H), 6.81 (dq, J = 7.3 Hz, 1.7 Hz, 1 H), 6.62 (t, J = 7.2 Hz, 1 H), 6.34 (t, J = 7.2 Hz, 1 H), 5.87 (dd, J = 8.1 Hz, 1.0 Hz, 1 H), 4.19−4.01 (m, 3 H), 1.95 (d, J = 6.0 Hz, 3 H), 1.49 (s br, 3 H), 1.48 (t br, J = 1.3 Hz, 3 H), 1.14 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.9, 158.1 (t, $J(^{13}C-^{31}P)$ = 2.4 Hz), 144.6 (t, $J(^{13}C-^{31}P)$ = 4.7 Hz), 143.3, 136.1 (t, $J(^{13}C-^{31}P)$ = 17.7 Hz), 135.8 (t, $J(^{13}C-^{31}P)$ = 4.2 Hz), 134.8 (d, $J(^{13}C-^{31}P)$ = 5.0 Hz), 134.7, 134.5 (d, $J(^{13}C-^{31}P)$ = 13.7 Hz), 133.9 (dd, $J(^{13}C-^{31}P)$ = 8.6 Hz, 4.2 Hz), 133.7 (d, $J(^{13}C-^{31}P)$ = 13.5 Hz), 133.4 (dd, $J(^{13}C-^{31}P)$ = 8.9 Hz, 4.2 Hz), 133.2, 133.1, 132.9, 132.8 (dd, $J(^{13}C-^{31}P)$ = 8.2 Hz, 4.0 Hz), 132.5 (dd, $J(^{13}C-^{31}P)$ = 7.8 Hz, 3.8 Hz), 132.0 (d, $J(^{13}C-^{31}P)$ = 18.4 Hz), 130.5, 129.9 (d, $J(^{13}C-^{31}P)$ = 28.0 Hz), 129.3 (d, $J(^{13}C-^{31}P)$ = 9.4 Hz), 128.9, 128.4, 128.1 (dd, $J(^{13}C-^{31}P)$ = 7.2 Hz, 2.7 Hz), 127.9 (dd, $J(^{13}C-^{31}P)$ = 7.4 Hz, 2.7 Hz), 127.5 (td, $J(^{13}C-^{31}P)$ = 7.8 Hz, 2.6 Hz), 125.4, 123.9, 120.9, 110.0, 71.6, 60.9, 19.2, 17.0 (dd, $J(^{13}C-^{31}P)$ = 21.5 Hz, 9.1 Hz), 14.5 (dd, $J(^{13}C-^{31}P)$ = 22.7 Hz, 9.2 Hz), 14.1, several signals account for more than one carbon; ^{31}P NMR (162 MHz, $CDCl_3$) δ 6.84 (d, J = 451.1 Hz, 1 P), 5.71 (d, J = 451.0 Hz, 1 P); IR (KBr, cm^{-1}) 1749 (s), 1726 (m), 891 (s), 740 (m), 692 (s); HRMS (FAB) calcd for $C_{37}H_{39}O_3P_2Pd$ (M − I$^+$), 699.1409, found 699.1391.

***trans*-{2-[1-Ethoxycarbonylpropoxy]phenyl}iodobis(triphenylphosphine)palladium (6a).** Pd_2dba_3 (0.916 g, 1.00 mmol), PPh_3 (1.049 g, 4.00 mmol), and aryl iodide **1b** (0.735 g, 2.20 mmol) were treated according to method A described above to afford the arylpalladium (II) iodo complex **6a** (1.510 g, 78%) as a yellow solid: mp 144−146 °C dec (EtOAc/hexane, 1:3); R_f = 0.53 (EtOAc/hexane, 1:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62−7.57 (m, 6 H), 7.51−7.47 (m, 6 H), 7.33−7.26 (m, 6 H), 7.23−7.20 (m, 12 H), 6.74−6.72 (m, 1 H), 6.35 (t, J = 7.4 Hz, 1 H), 6.02 (t, J = 7.3 Hz, 1 H), 5.53 (t, J = 7.9 Hz, 1 H), 4.21−4.03 (m, 1 H), 3.99−3.88 (m, 1 H), 3.57 (dd, J = 7.0 Hz, 4.3 Hz, 1 H), 1.90−1.71 (m, 2 H), 1.04 (td, J = 7.1 Hz, 1.3 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 157.7 (t, $J(^{13}C-^{31}P)$ = 2.5 Hz), 146.8 (t, $J(^{13}C-^{31}P)$ = 3.3 Hz), 136.6 (t, $J(^{13}C-^{31}P)$ = 4.3 Hz), 134.9 (t, $J(^{13}C-^{31}P)$ = 5.7 Hz), 132.7 (d, $J(^{13}C-^{31}P)$ = 19.4 Hz), 132.5 (d, $J(^{13}C-^{31}P)$ = 5.3 Hz), 132.3 (d, $J(^{13}C-^{31}P)$ = 4.5 Hz), 132.1 (d, $J(^{13}C-^{31}P)$ = 18.8 Hz), 129.6 (d, $J(^{13}C-^{31}P)$ = 20.0 Hz), 127.5 (t, $J(^{13}C-^{31}P)$ = 5.7 Hz), 123.5, 120.8, 110.6, 76.6, 60.5, 26.0, 14.0, 8.9, several signals account for more than one carbon; ^{31}P NMR (162 MHz, $CDCl_3$) δ 22.78 (s, 1 P), 22.73 (s, 1 P);[23] IR (KBr, cm^{-1}) 1749 (s), 1730 (m), 740 (m), 692 (s), 509 (m), 491 (m); HRMS (ES) calcd for $C_{38}H_{45}O_3P_2Pd$ (M − I$^+$), 837.1896, found 837.1936.

***trans*-{2-[1-Ethoxycarbonylpropoxy]phenyl}iodobis(methyldiphenylphosphine)palladium (6b).** Palladium(II) complex **2b** (0.779 g, 1.400 mmol) and PPh_2Me (0.65 mL, 0.70 g, 3.50 mmol) were treated according to method B described above to afford the arylpalladium(II) iodo complex **6b** (1.111 g, 93%) as a pale yellow solid: mp 60−62 °C (EtOAc/hexane, 1:3); R_f = 0.54 (EtOAc/hexane, 1:3); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88−7.85 (m, 2 H), 7.67−7.63 (m, 2 H), 7.58 (td, J = 8.5 Hz, 1.5 Hz, 2 H), 7.43−7.38 (m, 3 H), 7.33−7.25 (m, 9 H), 7.19 (t, J = 6.9 Hz, 2 H), 6.76 (dd, J = 7.3 Hz, 1.6 Hz, 1 H), 6.66 (t, J = 7.5 Hz, 1 H), 6.38 (t, J = 7.2 Hz, 1 H), 5.94 (d, J = 7.8 Hz, 1 H), 4.20−4.05 (m, 2 H), 4.02 (t, J = 5.9 Hz, 1 H), 1.91−1.84 (m, 5 H), 1.44 (d, J = 6.6 Hz, 3 H), 1.17 (t, J = 7.1 Hz, 3 H), 1.12 (t, J = 7.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.3, 158 (t, $J(^{13}C-^{31}P)$ = 2.6 Hz), 144.4 (t, $J(^{13}C-^{31}P)$ = 4.9 Hz), 136.2 (d, $J(^{13}C-^{31}P)$ = 13.1 Hz), 135.9 (d, $J(^{13}C-^{31}P)$ = 12.9 Hz), 135.7 (t, $J(^{13}C-^{31}P)$ = 4.2 Hz), 134.9 (d, $J(^{13}C-^{31}P)$ = 12.1 Hz), 134.6 (d, $J(^{13}C-^{31}P)$ = 12.1 Hz), 133.9 (dd, $J(^{13}C-^{31}P)$ = 8.9 Hz, 3.8 Hz), 133.7 (d, $J(^{13}C-^{31}P)$ = 11.4 Hz), 133.5 (dd, $J(^{13}C-^{31}P)$ = 9.1 Hz, 4.0 Hz), 133.2 (d, $J(^{13}C-^{31}P)$ = 12.1 Hz), 132.8 (dd, $J(^{13}C-^{31}P)$ = 8.5 Hz, 3.8 Hz), 132.5 (dd, $J(^{13}C-^{31}P)$ = 8.0 Hz, 3.2 Hz), 129.9 (d, $J(^{13}C-^{31}P)$ = 23.8 Hz), 129.3 (d, $J(^{13}C-^{31}P)$ = 13.4 Hz), 128.3, 128.1 (dd, $J(^{13}C-^{31}P)$ = 7.5 Hz, 2.4 Hz), 127.8 (dd, $J(^{13}C-^{31}P)$ = 7.8 Hz, 2.5 Hz), 127.5 (d, $J(^{13}C-^{31}P)$ = 7.6 Hz), 124.0, 120.9, 110.1, 76.4, 60.8, 26.5, 16.5 (dd, $J(^{13}C-^{31}P)$ = 22.4 Hz, 8.2 Hz), 14.1 (dd, $J(^{13}C-^{31}P)$ = 24.1 Hz, 13.2 Hz), 14.2, 9.6, several signals account for more than one carbon; ^{31}P NMR (202 MHz, $CDCl_3$) δ 7.27 (d, J = 451.0 Hz, 1 P), 5.88 (d, J = 451.0 Hz, 1 P); IR (KBr, cm^{-1}) 1749 (s), 1730 (m), 892 (s), 740 (m), 729 (m), 692 (s), 503 (m); HRMS (ES) calcd $C_{38}H_{41}O_3P_2Pd$ (M − I$^+$), 713.1580, found 713.1572.

***trans*-{2-[1-Ethoxycarbonyl-2-methylpropoxy]phenyl}iodobis(triphenylphosphiine)palladium (7a).** Pd_2dba_3 (1.282 g, 1.400 mmol), PPh_3 (1.469 g, 5.600 mmol), and aryl iodide **1c** (1.079 g, 3.100 mmol) were treated according to method A described above to afford the arylpalladium(II) complex **7a** (2.290 g, 84%) as a yellow solid: mp 140−142 °C dec (EtOAc/hexane, 1:3); R_f = 0.51 (EtOAc/hexane, 1:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65−7.55 (m, 6 H), 7.54−7.39 (m, 6 H), 7.33−7.20 (m, 18 H), 6.66 (d, J = 5.5 Hz, 1 H), 6.36 (t, J = 7.0 Hz, 1 H), 5.96 (t, J = 7.2 Hz, 1 H), 5.60 (d, J = 7.8 Hz, 1 H), 4.16−4.10 (m, 1 H), 3.87−3.83 (m, 1 H), 3.45 (d, J = 4.2 Hz, 1 H), 2.18−2.05 (m, 1 H), 1.14 (d, J = 6.7 Hz, 3 H), 1.01 (d, J = 5.1 Hz, 3 H), 1.00 (t, J = 5.1 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.9, 158.1 (t, $J(^{13}C-^{31}P)$ = 2.4 Hz), 146.7 (t, $J(^{13}C-^{31}P)$ = 3.2 Hz), 137.2 (t, $J(^{13}C-^{31}P)$ = 4.4 Hz), 134.9 (dd, $J(^{13}C-^{31}P)$ = 8.1 Hz, 4.2 Hz), 132.7 (d, $J(^{13}C-^{31}P)$ = 15.4 Hz), 132.5 (d, $J(^{13}C-^{31}P)$ = 15.4 Hz), 132.3 (d, $J(^{13}C-^{31}P)$ = 14.6 Hz), 132.1 (d, $J(^{13}C-^{31}P)$ = 14.7 Hz), 129.5 (d, $J(^{13}C-^{31}P)$ = 29.0 Hz), 127.5 (pent, $J(^{13}C-^{31}P)$ = 3.5 Hz), 123.5, 120.8, 110.8, 80.5, 60.3, 31.6, 18.6, 17.5, 14.1 several signals account for more than one carbon; ^{31}P NMR (162 MHz, $CDCl_3$) δ 23.30 (d, J = 434.1 Hz, 1 P), 22.42 (d, J = 434.1 Hz, 1 P); IR (KBr, cm^{-1}) 1747 (m), 1733 (m), 738 (s), 692 (s), 520 (m), 511 (m); HRMS (ES) calcd for $C_{49}H_{47}O_3P_2Pd$ (M − I$^+$), 851.2053, found 851.2016.

***trans*-{2-[1-Ethoxycarbonyl-2-methylpropoxy]phenyl}iodobis(methyldiphenylphosphine)palladium (7b).** Palladium(II) complex **2c** (0.799 g, 1.400 mmol) and PPh_2Me (0.65 mL, 0.70 g, 3.50 mmol) were treated according to method B described above to afford the aryl palladium(II) iodo complex **7b** (0.981 g, 83%) as a pale yellow solid: mp 150−151 °C (EtOAc/hexane, 1:3); R_f = 0.61 (EtOAc/hexane, 1:3); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (t, J = 6.9 Hz, 2 H), 7.67−7.64 (m, 2 H), 7.58 (t, J = 7.3 Hz, 2 H), 7.43−7.25 (m, 12 H), 7.20 (t, J = 7.4 Hz, 2 H), 6.71−6.67 (m, 2 H), 6.39 (t, J = 7.2 Hz, 1 H), 6.03 (d, J = 7.9 Hz, 1 H), 4.22−4.10 (m, 2 H), 3.97 (d, J = 5.3 Hz, 1 H), 2.19−2.12 (m, 1 H), 1.77 (d, J = 6.5 Hz, 3 H), 1.41 (d, J = 7.0 Hz, 3 H), 1.19 (t, J = 7.1 Hz, 3 H), 1.14 (d, J = 6.9 Hz, 3 H), 1.12 (d, J = 6.9 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.6, 158.8, 144.1, 135.9 (t, $J(^{13}C-^{31}P)$ = 4.3 Hz), 135.1 (d, $J(^{13}C-^{31}P)$ = 11.4 Hz). 133.9 (dd, $J(^{13}C-^{31}P)$ = 9.4 Hz, 3.4 Hz), 133.6 (dd, $J(^{13}C-^{31}P)$ = 9.5 Hz, 3.6 Hz), 133.0 (dd, $J(^{13}C-^{31}P)$ = 8.7 Hz, 3.4 Hz), 132.7 (dd, $J(^{13}C-^{31}P)$ = 8.1 Hz, 2.9 Hz), 129.9 (d, $J(^{13}C-^{31}P)$ = 18.1 Hz), 129.4 (d, $J(^{13}C-^{31}P)$ = 14.6 Hz), 128.1 (dd, $J(^{13}C-^{31}P)$ = 9.8 Hz, 2.0 Hz), 127.9 (d, $J(^{13}C-^{31}P)$ = 8.2 Hz), 127.6 (td, $J(^{13}C-^{31}P)$ = 8.2 Hz, 1.9 Hz), 124.2, 120.9, 110.1, 80.4, 60.6, 31.9, 18.8, 18.5, 16.1 (dd, $J(^{13}C-^{31}P)$ = 23.6 Hz, 7.2 Hz), 14.2, 13.8 (dd, $J(^{13}C-^{31}P)$ = 25.0 Hz, 7.1 Hz), several signals account for more than one carbon; ^{31}P NMR (202 MHz, $CDCl_3$) δ 7.20 (d, J = 452.1 Hz, 1 P), 5.54 (d, J = 452.0 Hz, 1 P); IR (KBr, cm^{-1}) 1739 (s), 748 (m), 730 (m), 692 (s), 501 (m), 484 (m); HRMS (FAB) calcd for $C_{39}H_{43}O_3P_2Pd$ (M − I$^+$), 727.1737, found 727.1746.

***trans*-{2-[(Ethoxycarbonyl)phenylmethoxy]phenyl}iodobis(triphenylphosphine)palladium (8a).** Pd_2dba_3 (1.282 g, 1.400 mmol), PPh_3 (1.469 g, 5.600 mmol), and aryl iodide **1d** (1.185 g, 3.100 mmol) were treated according to method A

described above to afford the arylpalladium(II) iodo complex **8a** (2.266 g, 80%) as a yellow solid: mp 126−128 °C dec (EtOAc/hexane, 1:3); R_f = 0.44 (EtOAc/hexane, 1:3); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69−7.66 (m, 6 H), 7.54−7.49 (m, 6 H), 7.39−7.26 (m, 17 H), 7.12−7.10 (m, 6 H), 6.82 (d, J = 6.5 Hz, 1 H), 6.38 (t, J = 7.5 Hz, 1 H), 6.1 (t, J = 7.2 Hz, 1 H), 5.56 (d, J = 7.9 Hz, 1 H), 4.38 (s br, 1 H), 4.19−4.13 (m, 1 H), 3.95−3.87 (m, 1 H), 1.02 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 157.7 (t, $J(^{13}C-^{31}P)$ = 2.5 Hz), 147.7 (t, $J(^{13}C-^{31}P)$ = 3.4 Hz), 136.5, 135.0 (t, $J(^{13}C-^{31}P)$ = 5.4 Hz), 134.7 (t, $J(^{13}C-^{31}P)$ = 6.3 Hz), 132.6 (d, $J(^{13}C-^{31}P)$ = 19.1 Hz), 132.4 (d, $J(^{13}C-^{31}P)$ = 9.5 Hz), 132.3 (d, $J(^{13}C-^{31}P)$ = 9.0 Hz), 132.1 (d, $J(^{13}C-^{31}P)$ = 18.9 Hz), 129.5 (d, $J(^{13}C-^{31}P)$ = 20.8 Hz), 128.7 (d, $J(^{13}C-^{31}P)$ = 24.8 Hz), 127.9, 127.5 (t, $J(^{13}C-^{31}P)$ = 5.1 Hz), 127.3 (t, $J(^{13}C-^{31}P)$ = 5.0 Hz), 123.5, 121.1, 110.8, 78.5, 61.1, 13.8, several signals account for more than one carbon; ^{31}P NMR (162 MHz, $CDCl_3$) δ 23.28 (s, 1 P), 23.25 (s, 1 P);[23] IR (KBr, cm^{-1}) 1751 (m), 1733 (m), 740 (m), 692 (s), 509 (s), 493 (m); HRMS (ES) calcd for $C_{52}H_{45}O_3P_2Pd$ (M − I$^+$), 885.1898, found 885.1898.

***trans*-{2-[(Ethoxycarbonyl)phenylmethoxy]phenyl}-iodobis(methyldiphenylphosphine)palladium (8b).** Pd_2-dba_3 (0.916 g, 1.000 mmol), PPh_2Me (0.74 mL, 0.796 g, 4.00 mmol), and aryl iodide **1d** (0.840 g, 2.200 mmol) were treated according to method A described above to afford the arylpalladium(II) complex **8b** (1.460 g, 82%) as a yellow solid: mp 72−74 °C (EtOAc/hexane, 1:3); R_f = 0.53 (EtOAc/hexane, 1:3); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89−7.86 (m, 2 H), 7.76 (d, J = 7.0 Hz, 2 H), 7.72−7.68 (m, 2 H), 7.48−7.39 (m, 10 H), 7.32 (t, J = 7.0 Hz, 2 H), 7.17 (t, J = 7.4 Hz, 3 H), 6.98−6.94 (m, 4 H), 6.85 (dd, J = 7.3 Hz, 1.6 Hz, 1 H), 6.64 (t, J = 7.3 Hz, 1 H), 6.41 (t, J = 7.2 Hz, 1 H), 5.94 (d, J = 8.0 Hz, 1 H), 4.90 (s, 1 H), 4.23−4.08 (m, 2 H), 1.87 (d, J = 5.5 Hz, 3 H), 1.56 (d, J = 7.1 Hz, 3 H), 1.15 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.9, 157.9 (t, $J(^{13}C-^{31}P)$ = 2.8 Hz), 145.3 (t, $J(^{13}C-^{31}P)$ = 4.7 Hz), 143.3, 136. 2, 136.1 (d, $J(^{13}C-^{31}P)$ = 15.9 Hz), 135.9 (d, $J(^{13}C-^{31}P)$ = 15.8 Hz), 134.9 (d, $J(^{13}C-^{31}P)$ = 8.1 Hz), 134.7 (d, $J(^{13}C-^{31}P)$ = 15.5 Hz), 133.9 (dd, $J(^{13}C-^{31}P)$ = 8.2 Hz, 4.4 Hz), 133.7 (d, $J(^{13}C-^{31}P)$ = 14.7 Hz), 133.5 (dd, $J(^{13}C-^{31}P)$ = 8.6 Hz, 4.6 Hz), 132.9 (dd, $J(^{13}C-^{31}P)$ = 7.8 Hz, 4.2 Hz), 132.7 (d, $J(^{13}C-^{31}P)$ = 15.1 Hz), 132.1 (dd, $J(^{13}C-^{31}P)$ = 7.3 Hz, 3.8 Hz), 130.5, 130.0, 129.7, 129.5, 128.9, 128.8, 128.7, 128.5, 128.3, 128.2 (dd, $J(^{13}C-^{31}P)$ = 6.9 Hz, 3.1 Hz), 127.8 (dd, $J(^{13}C-^{31}P)$ = 7.1 Hz, 3.2 Hz), 127.6 (dd, $J(^{13}C-^{31}P)$ = 7.0 Hz, 3.0 Hz), 127.1 (dd, $J(^{13}C-^{31}P)$ = 6.6 Hz, 2.9 Hz), 126.9, 125.4, 124.1, 121.3, 110.1, 77.7, 61.4, 16.4 (dd, $J(^{13}C-^{31}P)$ = 20.6 Hz, 9.9 Hz), 14.1 (dd, $J(^{13}C-^{31}P)$ = 22.9 Hz, 9.9 Hz), 14.1, several signals account for more than one carbon; ^{31}P NMR (202 MHz, $CDCl_3$) δ 6.94 (d, J = 450.6 Hz, 1 P), 6.00 (d, J = 450.5 Hz, 1 P); IR (KBr, cm^{-1}) 1751 (m), 891 (s), 729 (m), 692 (s), 503 (m), 484 (m); HRMS (ES) calcd for $C_{24}H_{41}O_3P_2Pd$ (M − I$^+$), 761.1581, found 761.1569.

***trans*-{2-[(Ethoxycarbonyl)phenylmethoxy]phenyl}-iodobis(dimethylphenylphosphine)palladium (8c).**[44] Palladium(II) complex **2d** (0.605 g, 1.000 mmol) and $PPhMe_2$ (0.34 mL, 0.329 g, 2.38 mmol) were treated according to method B described above to afford arylpalladium(II) complex **8c** (0.764 g, 83%) as a white solid: mp 62−64 °C (EtOAc/hexane, 1:3); R_f (two rotamers) = 0.56 and 0.38 (EtOAc/hexane, 1:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73−7.66 (m, 4 H), 7.44−7.37 (m, 3 H), 7.33−7.32 (m, 3 H), 7.21−7.14 (m, 3 H), 7.0 (t, J = 6.7 Hz, 2 H), 6.93 (dd, J = 7.3 Hz, 1.5 Hz, 1 H), 6.85 (t, J = 7.3 Hz, 1 H), 6.61 (t, J = 7.2 Hz, 1 H), 6.28 (d, J = 7.3 Hz, 1 H), 5.26 (s, 1 H), 4.23−4.10 (m, 2 H), 1.82 (d, J = 6.6 Hz, 3 H), 1.47 (d, J = 6.4 Hz, 3 H), 1.42 (d, J = 6.6 Hz, 3 H), 1.35 (d, J = 6.5 Hz, 3 H), 1.19 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.9, 158.2 (t, $J(^{13}C-^{31}P)$ = 2.8 Hz), 144.5 (t, $J(^{13}C-^{31}P)$ = 5.5 Hz), 136.2 (t, $J(^{13}C-^{31}P)$ = 4.1 Hz), 135.8, 135.7 (d, $J(^{13}C-^{31}P)$ = 13.0 Hz), 135.4 (d, $J(^{13}C-^{31}P)$ = 12.4 Hz), 135.1 (d, $J(^{13}C-^{31}P)$ = 12.4 Hz), 131.3 (dd, $J(^{13}C-^{31}P)$ = 8.1 Hz, 3.6 Hz), 130.6 (dd, $J(^{13}C-^{31}P)$ = 7.8 Hz, 3.5 Hz), 129.3 (d, $J(^{13}C-^{31}P)$ = 1.3 Hz), 128.9 (d, $J(^{13}C-^{31}P)$ = 1.4 Hz), 128.7, 128.5, 127.9 (dd, $J(^{13}C-^{31}P)$ = 7.3 Hz, 2.3 Hz), 127.6 (dd, $J(^{13}C-^{31}P)$ = 7.2 Hz, 2.3 Hz), 126.6, 124.1, 121.6, 110.1, 77.6, 61.4, 16.9 (dd, $J(^{13}C-^{31}P)$ = 22.3 Hz, 9.0 Hz), 15.9 (dd, $J(^{13}C-^{31}P)$ = 21.9 Hz, 8.5 Hz), 14.9 (dd, $J(^{13}C-^{31}P)$ = 22.4 Hz, 8.6 Hz), 14.1, 13.7 (dd, $J(^{13}C-^{31}P)$ = 22.6 Hz, 8.4 Hz), several signals account for more than one carbon; ^{31}P NMR (162 MHz, $CDCl_3$) δ −8.80 (d, J = 466.1 Hz, 1 P), −10.50 (d, J = 465.9 Hz, 1 P); IR (neat, cm^{-1}) 1747 (s), 908 (s), 740 (m), 715 (w), 694 (m); HRMS (ES) calcd for $C_{32}H_{37}O_3P_2Pd$ (M − I$^+$), 637.1265, found 637.1279.

***trans*-{2-[(Ethoxycarbonyl)phenylmethoxy]phenyl}-iodobis(trimethylphosphine)palladium (8d).** Palladium(II) complex **2d** (0.605 g, 1.000 mmol), $[HPMe_3]BF_4$ (0.377 g, 2.30 mmol), and diisopropylethylamine (0.80 mL, 0.594 g, 4.60 mmol) were treated according to method B described above to afford arylpalladium(II) iodo complex **8d** (0.575 g, 90%) as a pale yellow solid: mp 154−156°C dec (EtOAc/hexane, 1:3); R_f = 0.56 (EtOAc/hexane, 1:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 7.4 Hz, 2 H), 7.42 (t, J = 7.2 Hz, 2 H), 7.34 (t, J = 7.2 Hz, 1 H), 7.21 (dd, J = 7.1 Hz, 1.0 Hz, 1 H), 6.95 (t, J = 7.2 Hz, 1 H), 6.79 (t, J = 7.1 Hz, 1 H), 6.49 (d, J = 7.6 Hz, 1 H), 5.59 (s, 1 H), 4.23−4.11 (m, 2 H), 1.36 (d, J = 6.6 Hz, 9 H), 1.21 (t, J = 7.1 Hz, 3 H), 1.09 (d, J = 6.4 Hz, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 158 (t, $J(^{13}C-^{31}P)$ = 2.7 Hz), 144.9 (t, $J(^{13}C-^{31}P)$ = 6.0 Hz), 136.3 (t, $J(^{13}C-^{31}P)$ = 4.2 Hz), 135.7, 128.7, 128.6, 126.5, 124.0, 121.9, 110.2, 77.4, 61.5, 16.2 (d, $J(^{13}C-^{31}P)$ = 9.3 Hz), 16.0 (dd, $J(^{13}C-^{31}P)$ = 9.0 Hz, 1.7 Hz), 15.8 (d, $J(^{13}C-^{31}P)$ = 9.0 Hz), 14.1, several signals account for more than one carbon; ^{31}P NMR (162 MHz, $CDCl_3$) δ −17.79 (d, J = 480.6 Hz, 1 P), −19.41 (d, J = 480.5 Hz, 1 P); IR (neat, cm^{-1}) 1749 (m), 948 (s), 856 (w), 736 (m), 696 (w); HRMS (ES) calcd for $C_{22}H_{33}O_3P_2Pd$ (M − I$^+$), 513.0949, found 513.0931.

***trans*-[2-(Ethoxycarbonylmethoxy)phenyl]iodobis(methyldiphenylphosphine)palladium (8e).** Palladium(II) complex **2e**[11d] (0.200 g, 0.379 mmol) and PPh_2Me (0.23 mL, 0.247 g, 1.25 mmol) were treated according to method B described above to afford arylpalladium(II) complex **8e** (0.301 g, 98%) as a yellow solid: mp 86−88 °C (EtOAc/hexane, 1:3); R_f = 0.44 (EtOAc/hexane, 1:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58−7.49 (m, 8 H), 7.34−7.23 (m, 12 H), 6.73 (dd, J = 7.3 Hz, 1.3 Hz, 1 H), 6.58 (t, J = 7.8 Hz, 1 H), 6.23 (t, J = 7.3 Hz, 1 H), 5.78 (d, J = 8.1 Hz, 1 H), 4.25 (q, J = 7.1 Hz, 2 H), 4.00 (s, 2 H), 1.86 (t, J = 3.3 Hz, 6 H), 1.29 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.5, 158.0 (t, $J(^{13}C-^{31}P)$ = 2.6 Hz), 144.4 (t, $J(^{13}C-^{31}P)$ = 4.6 Hz), 135.7 (t, $J(^{13}C-^{31}P)$ = 4.2 Hz), 135.1 (t, $J(^{13}C-^{31}P)$ = 23.1 Hz), 133.5 (t, $J(^{13}C-^{31}P)$ = 22.9 Hz), 133.1 (t, $J(^{13}C-^{31}P)$ = 6.4 Hz), 133.0 (t, $J(^{13}C-^{31}P)$ = 6.0 Hz), 129.5 (d, $J(^{13}C-^{31}P)$ = 14.7 Hz), 127.8 (t, $J(^{13}C-^{31}P)$ = 5.1 Hz), 127.6 (t, $J(^{13}C-^{31}P)$ = 4.9 Hz), 123.9, 121.0, 109.4, 64.4, 60.9, 16.0 (t, $J(^{13}C-^{31}P)$ = 108.9 Hz), 14.2; ^{31}P NMR (162 MHz, $CDCl_3$) δ 6.78 (s, 2 P); IR (neat, cm^{-1}) 1753 (s), 891 (m), 692 (m); HRMS (ES) calcd for $C_{36}H_{37}O_3P_2Pd$ (M − I$^+$), 685.1253, found 685.1241.

2-Ethoxycarbonyl-3,4-bis(methoxycarbonyl)-2-methyl-2*H*-1-benzopyran (9). To a solution of palladacycle **3a** (0.050 g, 0.120 mmol) and trimethylphosphonium tetrafluoroborate $[HPMe_3]BF_4$ (0.060 g, 0.366 mmol) in dichloroethane (3.0 mL) were added diisopropylethylamine (0.065 mL, 0.373 mmol) and dimethyl acetylenedicarboxylate (dmad) (0.050 mL, 0.407

(44) Chromatographic analyses of complex **8c** indicated the presence of two portions of the product with distinct retention factors in TLC. Preparative TLC separation of these two portions provided samples with essentially equivalent spectral features in ^{1}H, ^{13}C, and ^{31}P NMR spectroscopy. However, while well-resolved sharp signals were observed for one portion (material with R_f = 0.56 in TLC (EtOAc/hexanes, 1:3), broad, poorly resolved signals were detected in the spectra of the second portion (material with R_f = 0.38 in TLC (EtOAc/hexanes, 1:3). It is conceivable that as a result of a restricted rotation, complex **8c** exists as two chromatographically separable conformational isomers. The observed difference in the appearance of NMR spectra of the two conformational isomers reflects the difference in the degree of rotational freedom in each isomer.

mmol). The mixture was stirred at 80 °C for 24 h, and for an additional 20 h at room temperature. Solvents were removed under reduced pressure, and the crude product was separated by flash chromatography over silica eluting with EtOAc/hexane (1:9) to afford benzopyran **9** (0.021 g, 52%) as a colorless oil: R_f = 0.30 (EtOAc/hexane, 1:3); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (td, J = 8.2 Hz, 1.5 Hz, 1 H), 7.06 (dd, J = 7.7 Hz, 1.3 Hz, 1 H), 6.95 (t, J = 7.5 Hz, 1 H), 6.89 (d, J = 8.1 Hz, 1 H), 4.33−4.26 (m, 1 H), 4.24−4.17 (m, 1 H), 3.94 (s, 3 H), 3.76 (s, 3 H), 1.74 (s, 3 H), 1.25 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 166.8, 163.6, 151.8, 136.9, 132.9, 126.4, 122.9, 122.2, 117.2, 117.0, 80.1, 62.0, 52.7, 52.3, 21.6, 13.9; IR (neat, cm^{-1}) 1741 (s), 1718 (s), 1267 (m), 1245 (m), 1222 (w), 1209 (w); HRMS (ES) calcd for $C_{17}H_{19}O_7$ (M + H$^+$), 335.1131, found 335.1119.

General Procedure for the Synthesis of 2,2-Disubstituted 2*H*-1-Benzopyrans. To a solution of arylpalladium(II) iodo complexes **5**−**8** (0.200 mmol) in THF (1 mL) at room temperature under argon was added *t*-BuOK (1.0 M in THF, 0.24 mL, 0.24 mmol). The reaction mixture was stirred for 20 min at room temperature, unless a different time period is indicated. Subsequently, the appropriate alkyne (0.50−0.60 mmol) and 1,2-dichloroethane (6 mL) were added, and the reaction mixtures were heated to 80 °C for the indicated time period under argon, and in several cases for an additional 16 h at room temperature in air. Solvents were removed under reduced pressure, and the crude product was separated by flash chromatography over silica, eluting with EtOAc/hexane or ether/hexane mixtures to afford 2,2-disubstitued 2*H*-1-benzopyrans **9**−**17** as colorless or yellow oils or solids.

2-Ethoxycarbonyl-3,4-bis(methoxycarbonyl)-2-methyl-2*H*-1-benzopyran (9). Treatment of complex **5b** (0.165 g, 0.200 mmol), *t*-BuOK (1.0 M in THF, 0.24 mL, 0.24 mmol), and dimethyl acetylenedicarboxylate (dmad) (0.074 mL, 0.086 g, 0.60 mmol) for 1 h at 80 °C according to the general procedure described above, eluting with EtOAc/hexane (5:1), afforded 2*H*-1-benzopyran **9** (0.042 g, 63%) as a yellow oil: R_f = 0.30 (EtOAc/hexane, 1:3).

2,3-Bis(ethoxycarbonyl)-2,4-bis(methyl)-2*H*-1-benzopyran (10). Treatment of complex **5b** (0.165 g, 0.200 mmol), *t*-BuOK (1.0 M in THF, 0.24 mL, 0.24 mmol), and ethyl 2-butynoate (0.070 mL, 0.068 g, 0.60 mmol) for 24 h at 80 °C and subsequently for 16 h at room temperature in air according to the general procedure described above, eluting with EtOAc/hexane (10:1), afforded 2*H*-1-benzopyran **10** (0.036 g, 59%) as a yellow oil: R_f = 0.53 (EtOAc/hexane, 1:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (dd, J = 7.8 Hz, 1.5 Hz, 1 H), 7.24 (t, J = 7.2 Hz, 1 H), 6.97 (td, J = 7.7 Hz, 1.2 Hz, 1 H), 6.87 (dd, J = 8.0 Hz, 1.0 Hz, 1 H), 4.26−4.15 (m, 4 H), 2.39 (s, 3 H), 1.69 (s, 3 H), 1.30 (t, J = 7.1 Hz, 3 H), 1.25 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 165.6, 151.8, 137.8, 131.2, 125.2, 123.8, 122.2, 121.7, 116.9, 80.5, 61.7, 60.9, 21.9, 15.0, 14.0, 13.9; IR (neat, cm^{-1}) 1751 (s), 1718 (s), 1247 (s), 1051 (m), 1033 (m); HRMS (FAB) calcd for $C_{17}H_{21}O_5$ (M + H$^+$), 305.1389, found 305.1406.

2-Ethoxycarbonyl-3-methoxycarbonyl-4-(4-methoxyphenyl)-2-methyl-2*H*-1-benzopyran (11). Treatment of complex **5b** (0.165 g, 0.200 mmol), *t*-BuOK (1.0 M in THF, 0.24 mL, 0.24 mmol), and methyl (*p*-methoxy)phenylpropiolate (0.095 g, 0.50 mmol) for 24 h at 80 °C and subsequently for 19 h at room temperature in air according to the general procedure described above, eluting with EtOAc/hexane (10:1), afforded 2*H*-1-benzopyran **11** (0.061 g, 80%) as a yellow solid: mp 102−104 °C (CH_2Cl_2); R_f = 0.53 (EtOAc/hexane, 1:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (td, J = 7.6 Hz, 1.8 Hz, 1 H), 7.12 (d br, J = 7.7 Hz, 2 H), 6.93 (d, J = 8.3 Hz, 3 H), 6.81 (td, J = 7.1 Hz, 1.0 Hz, 1 H), 6.76 (dd, J = 13.4 Hz, 1.7 Hz, 1 H), 4.31−4.09 (m, 2 H), 3.85 (s, 3 H), 3.45 (s, 3 H), 1.82 (s, 3 H), 1.23 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 166.3, 159.4, 152.4, 141.0, 131.4, 129.9 (2 carbons), 128.5, 128.0, 124.2, 122.5, 121.6, 116.8, 113.6 (2 carbons), 80.6, 61.8, 55.2, 51.4, 21.9, 13.9; IR (KBr, cm^{-1}) 1753 (s), 1730 (s), 1245 (s), 1130 (m), 1026 (m); HRMS (FAB) calcd for $C_{22}H_{23}O_6$ (M + H$^+$), 383.1495, found 383.1506.

2,3-Bis(ethoxycarbonyl)-2-ethyl-4-methyl-2*H*-1-benzopyran (12). Treatment of complex **6b** (0.168 g, 0.200 mmol), *t*-BuOK (1.0 M in THF, 0.24 mL, 0.24 mmol), and ethyl 2-butynoate (0.070 mL, 0.068 g, 0.60 mmol) for 24 h at 80 °C and subsequently for 16 h at room temperature in air according to the general procedure described above, eluting with EtOAc/hexane (10:1), afforded 2*H*-1-benzopyran **12** (0.040 g, 63%) as a yellow oil: R_f = 0.30 (EtOAc/hexane, 1:9); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (dd, J = 7.7 Hz, 1.5 Hz, 1 H), 7.22 (td, J = 8.0 Hz, 1.5 Hz, 1 H), 6.94 (td, J = 7.6 Hz, 1.2 Hz, 1 H), 6.89 (dd, J = 8.1 Hz, 1.0 Hz, 1 H), 4.27−4.12 (m, 4 H), 2.26 (s, 3 H), 2.21−2.08 (m, 2 H), 1.32 (t, J = 7.1 Hz, 3 H), 1.21 (t, J = 7.1 Hz, 3 H), 0.99 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 166.3, 152.6, 135.9, 130.9, 124.8, 123.5, 121.7, 121.4, 116.3, 82.6, 61.5, 60.9, 29.4, 15.4, 14.0, 13.9, 8.1; IR (neat, cm^{-1}) 1742 (s), 1718 (s), 1253 (s), 754 (m); HRMS (FAB) calcd for $C_{18}H_{23}O_5$ (M + H$^+$), 319.1545, found 319.1547.

2-Ethoxycarbonyl-2-ethyl-3-methoxycarbonyl-4-(4-methoxyphenyl)-2*H*-1-benzopyran (13). Treatment of complex **6b** (0.168 g, 0.200 mmol), *t*-BuOK (1.0 M in THF, 0.24 mL, 0.24 mmol), and methyl (*p*-methoxy)phenylpropiolate (0.095 g, 0.50 mmol) for 24 h at 80 °C and subsequently for 16 h at room temperature in air according to the general procedure described above, eluting with EtOAc/hexane (6:1), afforded 2*H*-1-benzopyran **13** (0.055 g, 69%) as a yellow oil that solidified on standing at room temperature: mp 50−52 °C (CH_2Cl_2); R_f = 0.50 (EtOAc/hexane, 1:3); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 (td, J = 7.3 Hz, 1.8 Hz, 1 H), 7.14 (dd, J = 6.7 Hz, 1.9 Hz, 2 H), 6.95 (dd, J = 8.2 Hz, 0.7 Hz, 1 H), 6.92 (d, J = 8.7 Hz, 2 H), 6.81 (td, J = 7.3 Hz, 0.9 Hz, 1 H), 6.77 (dd, J = 7.7 Hz, 1.8 Hz, 1 H), 4.27−4.15 (m, 2 H), 3.84 (s, 3 H), 3.43 (s, 3 H), 2.30−2.16 (m, 2 H), 1.21 (t, J = 7.1 Hz, 3 H), 1.07 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.2, 166.6, 159.4, 153.1, 140.5, 131.1, 130.1 (2 carbons), 128.4, 127.6, 123.9, 121.9, 121.3, 116.3, 113.6 (2 carbons), 82.9, 61.6, 55.2, 51.4, 29.2, 14.0, 8.1; IR (neat, cm^{-1}) 1739 (s), 1249 (s), 1031 (m); HRMS (ES) calcd for $C_{23}H_{24}O_6Na$ (M + Na$^+$), 419.1471, found 419.1489.

2,3-Bis(ethoxycarbonyl)-4-methyl-2-isopropyl-2*H*-1-benzopyran (14). According to the general procedure described above, complex **7b** (0.171 g, 0.200 mmol) and *t*-BuOK (1.0 M in THF, 0.24 mL, 0.24 mmol) were treated for 40 min at room temperature prior to the addition of 1,2-dichloroethane (6 mL) and ethyl 2-butynoate (0.070 mL, 0.068 g, 0.60 mmol). The reaction mixture was heated for 24 h at 80 °C and subsequently for 16 h at room temperature in air. The crude product was separated by chromatography over silica, eluting with EtOAc/hexane (10:1), to afford 2*H*-1-benzopyran **14** (0.038 g, 57%) as a yellow oil that solidified on standing at room temperature: mp 56−58 °C (CH_2Cl_2); R_f = 0.39 (EtOAc/hexane, 1:9); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26−7.18 (m, 2 H), 6.91 (td, J = 7.1 Hz, 0.8 Hz, 1 H), 6.88 (dd, J = 7.5 Hz, 1.1 Hz, 1 H), 4.52−4.05 (m, 4 H), 2.65−2.55 (m, 1 H), 2.11 (s, 3 H), 1.36 (t, J = 7.1 Hz, 3 H), 1.20 (t, J = 7.1 Hz, 3 H), 1.10 (d, J = 6.7 Hz, 3 H), 1.03 (d, J = 6.8 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 166.8, 153.3, 133.8, 130.8, 124.4, 123.8, 121.0, 120.7, 115.8, 84.5, 61.3, 60.9, 34.4, 17.2, 16.8, 15.9, 14.0, 13.9; IR (neat, cm^{-1}) 1747 (m), 1720 (s), 1255 (m), 1244 (m), 1035 (m), 754 (s); HRMS (FAB) calcd for $C_{19}H_{25}O_5$ (M + H$^+$), 333.1702, found 333.1702.

2-Ethoxycarbonyl-3-methoxycarbonyl-4-(4-methoxyphenyl)-2-isopropyl-2*H*-1-benzopyran (15). According to the general procedure described above, complex **7b** (0.171 g, 0.200 mmol) and *t*-BuOK (1.0 M in THF, 0.24 mL, 0.24 mmol) were treated for 40 min at room temperature prior to the addition of dichloroethane (6 mL) and methyl (*p*-methoxy)-phenylpropiolate (0.095 g, 0.50 mmol). The reaction mixture was heated for 24 h at 80 °C and for 16 h at room temperature

in air. The crude product was separated by chromatography over silica, eluting with EtOAc/hexane (10:1), to afford 2*H*-1-benzopyran **15** (0.059 g, 72%) as a yellow oil: $R_f = 0.50$ (EtOAc/hexane, 1:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22−7.17 (m, 1 H), 7.13 (d, $J = 8.4$ Hz, 2 H), 6.97 (d, $J = 8.0$ Hz, 1 H), 6.91 (d, $J = 8.8$ Hz, 2 H), 6.77−6.75 (m, 2 H), 4.23−4.16 (m, 2 H), 3.83 (s, 3 H), 3.37 (s, 3 H), 2.76−2.66 (m, 1 H), 1.23 (t, $J = 7.1$ Hz, 3 H), 1.16 (d, $J = 6.8$ Hz, 3 H), 1.08 (d, $J = 6.8$ Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 166.8, 159.3, 153.7, 139.5, 131.0, 130.1 (2 carbons), 128.2, 127.2, 124.1, 120.9, 120.7, 115.8, 113.6 (2 carbons), 85.2, 61.5, 55.2, 51.5, 34.5, 17.1, 16.6, 14.0; IR (neat, cm^{-1}) 1724 (s), 1247 (s), 1176 (m), 1033 (m); HRMS (ES) calcd for $C_{24}H_{27}O_6$ (M + H$^+$), 411.1808, found 411.1804.

2,3-Bis(ethoxycarbonyl)-4-methyl-2-phenyl-2*H*-1-benzopyran (16). Treatment of complex **8b** (0.178 g, 0.200 mmol), *t*-BuOK (1.0 M in THF, 0.24 mL, 0.24 mmol), and ethyl 2-butynoate (0.070 mL, 0.068 g, 0.60 mmol) for 24 h at 80 °C and subsequently for 24 h at room temperature in air according to the general procedure described above, eluting with EtOAc/hexane (10:1), afforded 2*H*-1-benzopyran **16** (0.032 g, 44%) as a yellow oil: $R_f = 0.49$ (EtOAc/hexane, 1:3); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (dd, $J = 8.3$ Hz, 1.7 Hz, 2 H), 7.33 (dd, $J = 7.8$ Hz, 1.3 Hz, 1 H), 7.29−7.23 (m, 3 H), 7.20 (td, $J = 8.2$ Hz, 1.4 Hz, 1 H), 6.97 (dd, $J = 8.1$ Hz, 0.9 Hz, 1 H), 6.93 (td, $J = 7.8$ Hz, 1.0 Hz, 1 H), 4.31−4.25 (m, 1 H), 4.22−4.17 (m, 1 H), 4.15 (q, $J = 7.1$ Hz, 2 H), 2.41 (s, 3 H), 1.23 (t, $J = 7.1$ Hz, 3 H), 1.17 (t, $J = 7.1$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.8, 166.3, 151.9, 138.5, 138.1, 131.1, 128.4, 127.9 (2 carbons), 127.6 (2 carbons), 125.2, 124.0, 123.1, 122.1, 117.3, 83.5, 62.1, 60.9, 15.6, 13.9, 13.8; IR (neat, cm^{-1}) 1755 (m), 1718 (s), 1251 (s), 1031 (m), 756 (w); HRMS (FAB) calcd for $C_{22}H_{23}O_5$ (M + H$^+$), 367.1545, found 367.1544.

2-Ethoxycarbonyl-3-methoxycarbonyl-4-(4-methoxyphenyl)-2-phenyl-2*H*-1-benzopyran (17). Treatment of complex **8b** (0.178 g, 0.200 mmol), *t*-BuOK (1.0 M in THF, 0.24 mL, 0.24 mmol), and methyl (*p*-methoxy)phenylpropiolate (0.095 g, 0.50 mmol) for 24 h at 80 °C and subsequently for 18 h at room temperature in air according to the general procedure described above, eluting with EtOAc/hexane (5:1), afforded 2*H*-1-benzopyran **17** (0.061 g, 69%) as a yellow solid: mp 58−60 °C (CH_2Cl_2); $R_f = 0.40$ (EtOAc/hexane, 1:3); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, $J = 10.5$ Hz, 2 H), 7.33 (t, $J = 6.8$ Hz, 2 H), 7.29−7.28 (m, 1 H), 7.23−7.19 (m, 3 H), 7.04 (d, $J = 7.9$ Hz, 1 H), 6.95 (d, $J = 8.9$ Hz, 2 H), 6.81 (td, $J = 6.9$ Hz, 0.9 Hz, 1 H), 6.78 (dd, $J = 7.8$ Hz, 1.9 Hz, 1 H), 4.33−4.27 (m, 1 H), 4.25−4.18 (m, 1 H), 3.85 (s, 3 H), 3.38 (s, 3 H), 1.22 (t, $J = 7.1$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.6, 166.7, 159.6, 152.3, 141.7, 138.1, 131.3, 130.4 (2 carbons), 128.5, 128.4, 128.0, 127.8 (2 carbons), 127.8 (2 carbons), 124.1, 123.2, 121.9, 117.2, 113.6 (2 carbons), 83.7, 62.3, 55.2, 51.5, 13.9; IR (neat, cm^{-1}) 1753 (m), 1730 (m), 1249 (s), 1054 (w), 1031 (w); HRMS (ES) calcd for $C_{27}H_{25}O_6$ (M + H$^+$), 445.1651, found 445.1635.

Ethyl 2-[*N*-(2-Iodophenyl)-*N*-methoxycarbonyl]aminopropionate (19). To a suspension of *N*-methoxycarbonyl-2-iodoaniline **18**[42] (3.878 g, 14.00 mmol) and anhydrous K_2CO_3 (10.0 g, 72.40 mmol) in DMF (40 mL) at room temperature under argon was added neat ethyl 2-bromopropionate (7.27 mL, 10.14 g, 56.0 mmol), and the resulting suspension was stirred at 100 °C for 33 h. The reaction mixture was partitioned between water (50 mL) and ether (3 × 50 mL) and dried ($MgSO_4$), and the crude product was purified by flash chromatography over silica, eluting with EtOAc/hexane (1:3), to afford aryl iodide **19** (4.04 g, 77%) as a light yellow solid: mp 78−80 °C (EtOAc/hexane, 1:3); $R_f = 0.56$ (EtOAc/hexane, 1:3); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, $J = 7.5$ Hz, 1 H), 7.63 (dd, $J = 7.8$ Hz, 1.2 Hz, 0.8 H), 7.53 (d, $J = 7.6$ Hz, 0.2 H), 7.37 (t, $J = 7.6$ Hz, 1 H), 7.04 (td, $J = 7.8$ Hz, 1.2 Hz, 0.8 Hz), 7.00 (t, $J = 7.9$ Hz, 0.2 H), 4.91 (q, $J = 7.6$ Hz, 0.8 H), 4.76 (q, $J = 7.6$ Hz, 0.2 H), 4.33−4.22 (m, 2 H), 3.78 (s, 0.6 H), 3.66 (s, 2.4 H), 1.84 (d, $J = 7.1$ Hz, 0.6 H), 1.31 (t, $J = 7.1$ Hz, 3 H), 1.10 (d, $J = 7.6$ Hz, 2.4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.3, (171.3), 155.6, (155.1, 154.5), (145.7, 141.3), 140.9, (139.6, 139.3), 139.2, (131.0), 130.6, (129.7), (129.5), 129.4, (129.2), 129.0, (128.6), 103.6, (61.5), 61.3, (61.2), (55.6), 55.5, 53.3, (53.2), (53.0), (16.8), (15.6), 15.0, (14.3), 14.1 (signals for the minor isomers arising as a result of the amide resonance are shown in parentheses); IR (neat, cm^{-1}) 1741 (s), 1712 (s), 767 (m); HRMS (FAB) calcd for $C_{13}H_{16}INO_4Li$ (M + Li$^+$), 384.0284, found 384.0278.

{*N*-[(1-Ethoxycarbonyl)ethyl]-*N*-methoxycarbonyl-2-aminophenyl}iodo(tetramethylethylenediamine)palladium (20). To a solution of tris(dibenzylideneacetone)-dipalladium(0) (Pd_2dba_3) (2.747 g, 3.00 mmol) and aryl iodide **19** (2.263 g, 6.00 mmol) in benzene (100 mL) at room temperature under argon was added neat *N,N,N′,N′*-tetramethyl-1,2-ethylenediamine (TMEDA) (1.8 mL, 1.395 g, 12.00 mmol). The resulting suspension was stirred for 30 min at 60 °C and filtered through a plug of Celite, and solvents were removed under reduced pressure. The crude product was purified by flash chromatography over silica eluting with EtOAc/hexane (1:5) to remove excess dibenzylideneacetone (dba) and subsequently with EtOAc/hexane (2:1) to afford complex **20** (2.805 g, 78%) as a yellow solid: mp 102−104 °C (EtOAc/hexane, 2:1); $R_f = 0.28$ (EtOAc/hexane, 3:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (dd, $J = 7.1$ Hz, 2.0 Hz, 0.75 H), 7.52−7.50 (m, 0.25 H), 7.17 (d br, $J = 7.0$ Hz, 0.1 H), 7.09−7.07 (m, 0.15 H), 6.87−6.79 (m, 2.35 H), 6.73 (dd, $J = 7.1$ Hz, 1.9 Hz, 0.4 H), 5.78 (pent, $J = 6.6$ Hz, 0.75 H), 5.02−4.97 (m, 0.25 H), 4.34−4.25 (m, 0.5 H), 4.23−4.20 (m, 1.5 H), 3.71 (s, 0.25 H), 3.69 (s, 0.75 H), 3.59 (s, 0.5 H), 3.58 (s, 1.5 H), 2.88−2.67 (m, 2 H), 2.71 (s, 1 H), 2.68 (s, 2 H), 2.67 (s, 1 H), 2.64 (s, 2 H), 2.61 (s, 2 H), 2.60 (s, 1 H), 2.48 (s, 0.5 H), 2.43 (s, 1.5 H), 2.36 (s, 0.25 H), 2.43 (s, 0.75 H), 2.30−2.22 (m, 2 H), 1.50 (d, $J = 6.8$ Hz, 2.05 H), 1.45 (d, $J = 6.9$ H, 0.75 H), 1.33 (t, $J = 7.1$ Hz, 2.10 H), 1.27 (t, $J = 7.1$ Hz, 0.50 H), 0.96 (d, $J = 6.6$ Hz, 0.1 H), 0.91 (d, $J = 6.6$ Hz, 0.1 H), 0.87 (t, $J = 7.0$ Hz, 0.4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.3 (172.8, 172.4), 155.9 (157.8, 157.0, 156.8), 144.9 (148.1, 147.3, 145.7), 140.2 (139.8, 139.4, 139.3), 138.7 (138.9, 138.0, 137.9), 129.2 (129.4, 128.9), 124.2 (124.8, 124.3), 122.8 (123.5, 123.3, 123.1, 122.9), 62.5 (62.7, 62.6), 60.6 (60.8), 58.6 (59.6, 59.1, 58.8, 58.6), 52.2 (52.3, 52.1), 50.9 (51.4, 51.1), 50.2 (50.5, 50.0), 49.9, 49.6 (49.7), 22.6 (21.0, 19.7), 14.4 (14.6, 14.5, 14.3, 14.2, 14.1), 13.3 (multiple signals for the minor isomers arising from the hindered rotation about the Csp^2−Pd bond and/or the amide resonance are shown in parentheses); IR (neat, cm^{-1}) 1733 (s), 1701 (s); HRMS (ES) calcd for $C_{19}H_{33}N_3O_4IPd$ (M + H$^+$), 600.0551, found 600.0555.

***trans*-{*N*-[(1-Ethoxycarbonyl)ethyl]-*N*-methoxycarbonyl-2-aminophenyl}iodobis(methyldiphenylphosphine)-palladium (21).** To a solution of arylpalladium(II) complex **20** (0.840 g, 1.400 mmol) in methylene chloride (14 mL) at room temperature under argon was added diphenylmethylphosphine (0.65 mL, 0.70 g, 3.50 mmol), and the solution was stirred at room temperature under argon for 2 h. Solvents were removed under reduced pressure, and the crude product was purified by flash chromatography over silica eluting with EtOAc/hexane (1:10) to remove excess phosphine, and subsequently with EtOAc/hexane (1:1) to afford palladium(II) complex **21** (1.066 g, 96%) as a yellow solid: mp 105−107 °C (EtOAc/hexane, 1:1); $R_f = 0.28$ (EtOAc/hexane, 1:3); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (s br, 2 H), 7.75 (s br, 2 H), 7.53−7.27 (m, 10 H), 7.25−6.95 (m, 8 H), 6.89 (s br, 1 H), 6.83 (s br, 1 H), 4.14−3.97 (m, 1.6 H), 3.36 (s br, 1 H), 3.22 (s br, 0.4 H), 2.78 (s br, 2 H), 2.21−1.95 (m, 3 H), 1.90−1.68 (m, 2 H), 1.54−1.10 (m, 8 H); ^{13}C NMR (125 MHz, $CDCl_3$) 171.7 (171.5, 171.1), 156.3, 155.2, 153.7 (153.4), 147.5, 137.3 (d, $J(^{13}C-^{31}P) = 46.6$ Hz), 134.5 (d, $J(^{13}C-^{31}P) = 62.8$ Hz), 133.8, 132.3, 130.3 (d, $J(^{13}C-^{31}P) = 50.6$ Hz), 129.5 (d, $J(^{13}C-^{31}P) = 8.1$ Hz), 128.3, 128.1 (pent, $J(^{13}C-^{31}P) = 5.0$ Hz), 126.4 (d, $J(^{13}C-^{31}P) = 7.0$ H), 124.1 (d, $J(^{13}C-^{31}P) = 19.2$ Hz), 60.9, 59.3 (58.7), 51.3 (51.2), 21.0, 17.8 (s br),

14.9 (s br), 14.3 (14.1) (multiple signals for the minor isomers arising from the amide resonance are shown in parentheses); ^{31}P NMR (161 MHz, $CDCl_3$, 55 °C) δ 4.82 (d br, J = 443.0 Hz, 1 P), 3.10 (d br, J = 443.0 Hz, 1 P) (broad signals arise from the amide resonance); IR (neat, cm^{-1}) 1735 (s), 1701 (s), 891 (m), 692 (m); HRMS (ES) calcd for $C_{39}H_{42}NO_4P_2Pd$ (M − I$^+$), 756.1624, found 756.1618.

General Procedure for the Synthesis of 2,2-Disubstituted 1,2-Dihydroquinolines. To a solution of arylpalladium(II) iodo complex **21** (0.200 mmol) in THF (1 mL) at room temperature under argon was added *t*-BuOK (1.0 M in THF, 0.24 mL, 0.24 mmol). The reaction mixture was stirred for 40 min at room temperature, the appropriate alkyne (0.50−0.60 mmol) and 1,2-dichloroethane (6 mL) were added, and the mixtures were heated to 80 °C for 12 h under argon and for an additional 16 h at room temperature in air. The solvents were removed under reduced pressure and the crude product was separated by flash chromatography over silica, eluting with EtOAc/hexane mixtures, to afford 2,2-disubstituted 1,2-dihydroquinolines as yellow solids.

2,3-Bis(ethoxycarbonyl)-*N*-methoxycarbonyl-2,4-bis-(methyl)-1,2-dihydroquinoline (22). Treatment of complex **21** (0.177 g, 0.200 mmol) and *t*-BuOK (1.0 M in THF, 0.24 mL, 0.24 mmol), and ethyl 2-butynoate (0.070 mL, 0.068 g, 0.60 mmol) for 12 h at 80 °C and subsequently for 16 h at room temperature according to the general procedure described above, eluting with EtOAc/hexane (5:1), afforded 1,2-dihydroquinoline **22** as a yellow oil (0.040 g, 55%) that solidified on standing at room temperature: mp 83−85 °C (EtOAc/hexane, 1:5); R_f = 0.38 (EtOAc/hexane, 1:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, J = 8.0 Hz, 2 H), 7.26 (td, J = 7.4 Hz, 1.5 Hz, 1 H), 7.10 (td, J = 7.7 Hz, 1.1 Hz, 1 H), 4.27−4.14 (m, 4 H), 3.76 (s, 3 H), 2.22 (s, 3 H), 1.62 (s, 3 H), 1.31 (t, J = 7.1 Hz, 3 H), 1.28 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.4, 166.2, 154.2, 134.8, 132.8, 130.2, 129.1, 126.2, 124.4, 123.9, 122.7, 66.0, 61.8, 61.0, 52.9, 20.5, 15.5, 14.0, 13.9; IR (neat, cm^{-1}) 1749 (m), 1722 (s), 1716 (s); HRMS (FAB) calcd for $C_{19}H_{23}NO_6Li$ (M + Li$^+$), 368.1685, found 368.1691.

2-Ethoxycarbonyl-3-methoxycarbonyl-*N*-methoxycarbonyl-4-(4-methoxyphenyl)-2-methyl-1,2-dihydroquinoline (23). Treatment of complex **21** (0.177 g, 0.200 mmol) and *t*-BuOK (1.0 M in THF, 0.24 mL, 0.24 mmol), and methyl (*p*-methoxy)phenylpropiolate (0.095 g, 0.50 mmol) for 12 h at 80 °C and subsequently for 16 h at room temperature in air according to the general procedure described above, eluting with EtOAc/hexane (3:1), afforded 1,2-dihydroquinoline **23** as a yellow solid (0.045 g, 50%): mp 145−147 °C (EtOAc/hexane, 1:3); R_f = 0.24 (EtOAc/hexane, 1:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (dd, J = 8.3 Hz, 0.8 Hz, 1 H), 7.25 (td, J = 7.2 Hz, 1.5 Hz, 1 H), 7.12 (s br, 2 H), 6.95 (td, J = 7.8 Hz, 1.0 Hz, 1 H), 6.91 (d br, J = 8.3 Hz, 2 H), 6.80 (dd, J = 7.8 Hz, 1.5 Hz, 1 H), 4.20 (qd, J = 7.1 Hz, 2.2 Hz, 2 H), 3.83 (s, 3 H), 3.80 (s, 3 H), 3.38 (s, 3 H), 1.75 (s, 3 H), 1.25 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 166.6, 159.4, 154.2, 138.5, 135.2, 130.2 (2 carbons), 130.0, 129.4, 128.8, 127.8, 126.4, 123.8, 122.8, 113.6 (2 carbons), 66.3, 61.9, 55.2, 53.1, 51.5, 20.7, 13.9; IR (neat, cm^{-1}) 1755 (m), 1724 (s), 1269 (s), 1247 (s), 1064 (m), 761 (m); HRMS (FAB) calcd for $C_{24}H_{25}NO_7Li$ (M + Li$^+$), 446.1791, found 446.1790.

Acknowledgment. Support for this work from The American Chemical Society Petroleum Research Fund, Kansas NSF EPSCoR, and Kansas Technology Enterprise Corporation, and the National Science Foundation via CAREER Award (CHE-0239123) to H.C.M. is gratefully acknowledged. We thank Dr. S. Kumara Vadivel for contributions to earlier stages of this research, and to our colleague Dr. Douglas R. Powell for his assistance with X-ray crystallography.

Supporting Information Available: Detailed description of protocols for acquisition of the ^{31}P NMR spectra shown in Schemes 2 and 4 including full-scale photocopies of spectra a−f, photocopies of ^{1}H and ^{13}NMR spectra of all new compounds prepared in this study, and ^{1}H NOE difference spectra of 2*H*-1-benzopyrans **10**, **12**, **14**, and **16**, and 1,2-dihydroquinoline **22**. Includes X-ray crystallographic studies on organopalladium complexes **3c**, **3d**, **6a**, and **7b** and heterocycles **11** and **23**. This material is available free of charge via the Internet at http://pubs.acs.org.

OM0491544