Regio- and Diastereoselective Insertion of Allenes into Stable Oxapalladacycles with a Metal-Bonded Stereogenic Carbon. Preparation of Contiguously Substituted 3,4-Dihydro-2*H*-1-Benzopyrans

Genliang Lu and Helena C. Malinakova*

Department of Chemistry, University of Kansas, 1251 Wescoe Hall Drive, Lawrence, Kansas 66045-7582,
and the Center for Chemical Methodology and Library Development at the University of Kansas,
1501 Wakarusa Drive, Lawrence, Kansas 66047

hmalina@ku.edu

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Insertion of monosubstituted allenes into stable oxapalladacycle **I** was studied. The aim of this work was to define steric and electronic parameters of allenes that would allow for a regio- and diastereoselective synthesis of 2,3-disubstituted 3,4-dihydro-2*H*-1-benzopyrans, which could not be prepared via related catalytic protocols. Allenes with electron-donating alkyl substituents R sterically unencumbered at the C-3 and C-4 carbons reacted with palladacycles **I** to afford benzopyrans **IV** in good yields (45−81%), exclusively as *cis* diastereomers. Less than 10% of the regioisomeric benzopyrans **V** was detected in the crude reaction mixtures. Methoxy 1,2-propadiene afforded benzopyran **IV** in 98% yield as the *trans* diastereomer in 92% de. In contrast, allenes with electron-withdrawing substituents yielded benzopyrans **V** with an *E* double bond exclusively. Nonracemic palladacycles featuring a palladium-bonded stereogenic carbon as the only element of asymmetry underwent the allene insertion with 63−93% retention of the stereochemical information, providing benzopyrans **IV** or **V** in 40−47% ee. These results demonstrated that O-bonded palladium enolates did not operate as predominant intermediates in the insertion process. The study highlights the configurational stability of carbon-bonded palladium ester enolates, especially notable in systems lacking chiral nonracemic auxiliary ligands.

Introduction

Palladium-catalyzed annulation reactions have been recognized as powerful tools for a rapid construction of diverse heterocyclic and carbocyclic frameworks.[1] Among these, transformations relying on carbopalladation of allenes[2] to generate π-allylpalladium intermediates, which subsequently reacted *in situ* with internal nucleophiles, proved to be extraordinarily versatile (Figure 1).[3] Utilizing heteroatoms or malonate carbanions as nucleophiles, the reactions afforded achiral heterocycles or carbocycles via pathway 1, or chiral molecules with one stereogenic center via pathway 2 (Figure 1).[3] However, with a single exception,[3j] the potential of these catalytic processes to create two adjacent stereogenic carbons has yet to be realized. The synthetic challenge consists in identifying a system that would allow for a regio- and diastereoselective attack of nonstabilized carbon nucleophiles (Nu = :CHY) at the substituted terminus of the π-allylpalladium intermediate (pathway 2, Figure 1).

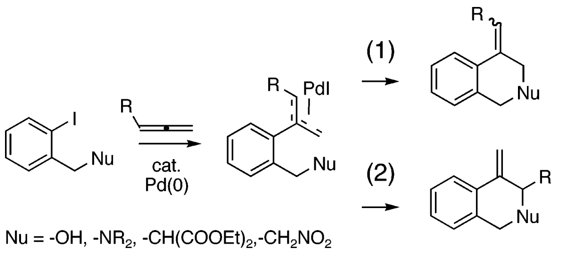

FIGURE 1. Palladium-catalyzed annulation reactions of allenes.

Studies aimed at exploration of the fundamental aspects of transition-metal-mediated transformations are essential for successful application of these methods to synthetic problems of ever-increasing complexity.[4] Toward this goal, we have initiated a program focused on

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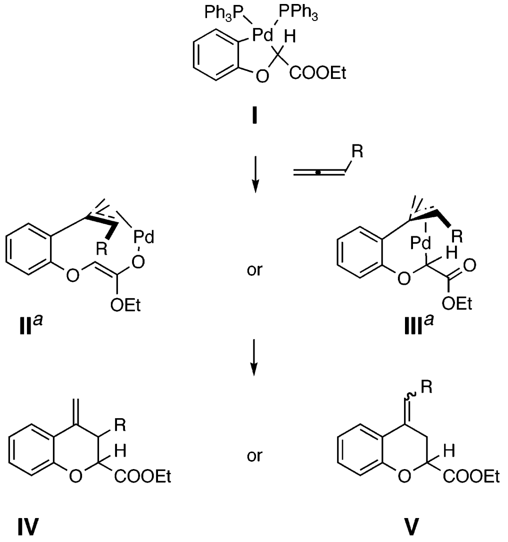

^{a} Auxiliary ligands were omitted for clarity.

FIGURE 2. General outline of the synthetic strategy.

asymmetric synthesis and reactivity of novel palladacycles, exploring the "fate" of the metal-bonded sp^3-hybridized stereogenic carbon.[5] Benzannulated oxapalladacycle **I** (Figure 2) was synthesized and shown to participate in regioselective reactions with unsymmetrical alkynes, yielding highly substituted nonracemic benzopyrans.[5] Conceivably, insertion of monosubstituted allenes[2] into oxapalladacycle **I**, occurring preferentially into the Csp^2−Pd bond,[6] would afford unique π-allylpalladium complexes of oxygen- or carbon-bonded palladium ester enolates **II** or **III**.[7] Intermediates **II** or **III** would collapse into 3,4-dihydro-2*H*-1-benzopyrans **IV** or **V** via reductive elimination (Figure 2). Complexes **II** and **III** represent intermediates of hypothetical catalytic reactions, in which *nonstabilized* ester enolates would attack the palladium metal *prior* to the carbon−carbon bond formation.[8] Thus, we envisioned that a systematic exploration of reactions between stable palladacycle **I** and allenes would provide valuable data on the steric and electronic parameters of allenes critical for achieving a regio- and diastereoselective formation of contiguously substituted benzopyrans **IV**. Furthermore, reactions with enantiomerically enriched palladacycles **I** would provide insights into the bonding modes of palladium enolates in intermediates **II** or **III**,[7e−j] and permit the assessment of feasibility of asymmetry transfer from the palladium-bonded stereogenic carbon.

Described herein is a highly regio- and diastereocontrolled preparation of 2,3-disubstituted 3,4-dihydro-4-methylene-2*H*-1-benzopyrans **IV** from the stable palladacycle **I**. Allenes featuring electron-donating alkyl substituents R, sterically unencumbered at the C-3 and C-4 carbons, reacted with palladacycles **I** to afford benzopyrans **IV** in good yields (45 − 81%), exclusively as *cis* diastereomers. Less than 10% of the regioisomeric benzopyrans **V** was detected in the crude reaction mixtures. Methoxy 1,2-propadiene afforded benzopyran **IV** in 98% yield as the *trans* diastereomer in 92% de. Reactions with enantiomerically enriched palladacycle **I** afforded several benzopyrans **IV** or **V** in 40−47% ee, corresponding to 63−93% retention of the stereochemical information embedded in the palladium-bonded stereogenic carbon, suggesting that O-bonded enolates do not operate as the predominant intermediates on the pathway to benzopyrans **IV** and **V**.

Studies described herein contribute to the rapidly expanding areas of metal-mediated reactions with allenes and the application of transition metal enolates in carbon−carbon bond formation. Although transition-metal-catalyzed cycloadditions and cyclizations involving allenes are well-known,[9] examples of insertions of allenes into stable metalacycles (C−M−C, M = Pd, Ni) are rare.[10] Reactions between allenes and stable cyclopalladated complexes of amines and imines (C−Pd−N) have been studied,[11] and applied to the construction of a library of achiral quaternized *N*-heterocycles for biological testing.[12]

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(6) Studies on the reactions of various unsaturated molecules (e.g., NO_2, TsN_3, CS_2, COS, PhNSC) with benzannulated nickelacyclopentanes provided unequivocal evidence for the insertion occurring preferentially into the Csp^2−Ni (aryl−nickel) bond, most likely as a result of a chemoselective displacement of the more labile trialkylphosphine ligand positioned *trans* to the alkyl-Ni bond. Exceptions to this regiochemical preference are known (e.g., for reactions of CO or $H_2C{=}O$). See: (a) Koo, K.; Hillhouse, G. L. *J. Am. Chem. Soc.* **1996**, *15*, 2669−2671. (b) Koo, K.; Hillhouse, G. L.; Rheingold, A. L. *Organometallics* **1995**, *14*, 456−460. (c) Koo, K.; Hillhouse, G. L. *Organometallics* **1995**, *14*, 4421−4423. (d) Campora, J.; Gutierrez, E.; Monge, A.; Palma, P.; Poveda, M. L.; Ruiz, C.; Carmona, E. *Organometallics* **1994**, *13*, 1728−1745. (e) Campora, J.; Llebaria, A.; Moreto, J. M.; Poveda, M. L.; Carmona, E. *Organometallics* **1993**, *12*, 4032−4038. (f) Carmona, E.; Gutierrea-Puebla, E.; Marin, J. M.; Monge, A.; Paneque, M.; Poveda, M. L.; Ruiz, C. *J. Am. Chem. Soc.* **1989**, *111*, 2883−2891.

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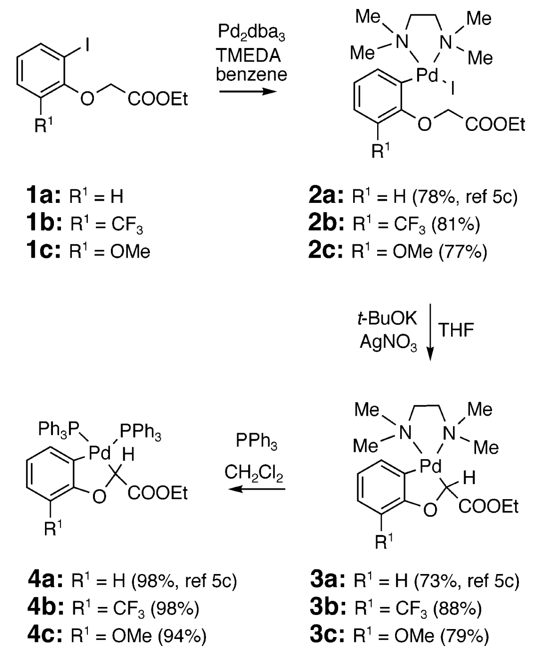
The regio- and stereochemistry of these transformations has been rationalized relying on the mechanistic work pertaining to the "classical" palladium-catalyzed allylation reaction (Tsuji−Trost reaction).[13] However, the involvement of nonstabilized palladium ester enolates[8] in the described process makes the prediction of the regiochemical outcome rather uncertain.[13d] Nonstabilized enolates, as preformed zinc or silyl enolates, were used successfully in palladium-catalyzed arylations of esters.[14]

Various synthetic strategies[15−19] have been developed for the assembly of the pharmaceutically significant 3,4-dihydro-2*H*-1-benzopyran (chroman) core.[20] Known methodologies exploit cycloaddition reactions,[15] mechanistically diverse intramolecular cyclizations terminated either via carbon−carbon[16,17]or carbon−oxygen[18] bond formations, or the elaboration of chromone substrates.[19] Notably, the described convergent strategy allows for the formation of benzopyrans with adjacent stereogenic centers at C-2 and C-3 carbons from achiral organic substrates and establishes a rational foundation for a future design of a new catalytic protocol.

SCHEME 1



Results and Discussion

Electronically differentiated palladacycles **4b,c** were prepared according to the protocol developed for palladacycle **4a** (Scheme 1).[5c] Aryl iodides **1b,c** were obtained via O-alkylation of the corresponding 2-iodophenols,[21] accessible via standard directed *ortho*-metalation protocols.[22] Oxidative addition of palladium(0) (Pd_2dba_3) in the presence of *N*,*N*,*N*,*N*′-tetramethyl-1,2-ethylenediamine ligand (TMEDA) afforded complexes **2a**−**c** (77−81%), which readily underwent an intramolecular displacement of iodide by an ester enolate upon treatment with *t*-BuOK. The ring closure afforded stable palladacycles **3a**−**c** in good yields (73−88%) after chromatography on basic alumina. Although $AgNO_3$ additive was not necessary for the success of the ring closure, its presence allowed for a more convenient product isolation.[5c] Ligand exchange reactions of palladacycles **3a**−**c** with triphenylphosphine (PPh_3) delivered palladacycles **4a**−**c** as moisture- and air-stable white crystalline solids. Although a one-pot method for a direct conversion of the aryl iodide **1a** into palladacycle **4a** was previously developed,[5c] the three-step procedure shown in Scheme 1 proved to be satisfactory, providing palladacycles **4a**−**c** in 56−70% yields from aryl iodides **1a**−**c**.

Initially, the reaction of palladacycles **4a** and **4c** with electron-deficient ethyl 2,3-butadienoate and 3,4-pentadien-2-one was studied (Scheme 2). Insertions of allenes

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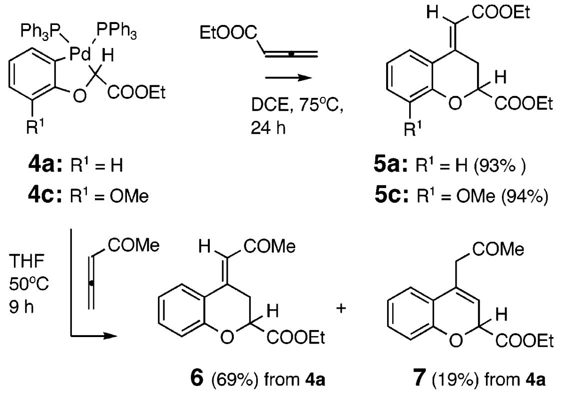
SCHEME 2



into palladacycles **4a** and **4c** required elevated temperatures to provide high yields of products **5a** (93%), **5c** (94%), **6** (69%), and **7** (19%). The carbon−carbon bond formations occurred exclusively at the internal and the unsubstituted terminal carbons of the allene, and a double bond isomerization apparently gave rise to the minor product **7**. The geometry of the double bond in benzopyrans **5a**, **5c**, and **6** was unequivocally established as *E* via NOE ^{1}H NMR experiments indicating enhancement of the signal for the C-5 aromatic proton (7.14−7.59 ppm) upon irradiation of the vinylic protons (6.36−6.76 ppm).

In contrast, the insertion of allenes featuring electron-donating substituents into palladacycles **4a**−**c** afforded benzopyrans of type **IV** preferentially. The desired 2,3-disubstituted benzopyrans **8**−**22** were produced in moderate to good yields (45−98%) with excellent diastereocontrol (Table 1). Reactions of palladacycles **4a,b** with methoxy 1,2-propadiene afforded exclusively benzopyrans **8** and **9**, as chromatographically inseparable mixtures of *trans* (major) and *cis* diastereomers in 98% and 77% yield, and with 92% and 90% de, respectively.[23] A reaction of palladacycle **4a** with methoxy 1,2-propadiene performed at room temperature afforded benzopyran **8** in a diminished yield, and the replacement of THF solvent with 1,2-dichloroethane caused a decrease in the diastereoselectivity to 68% de (83% yield). The insertion of 1,2-nonadiene into palladacycles **4a**−**c** also favored the 2,3-disubstituted benzopyrans **10**, **12**, and **13** with synthetically practical 10:1 regioselectivity (entries 3−5, Table 1).[24] Regioisomeric benzopyrans **10** and **11** were isolated as a chromatographically inseparable mixture in a combined yield of 84% and 91:9 ratio of regioisomers **10** and **11** (entry 3, Table 1).[24] Replacement of THF solvent with 1,2-dichloroethane, benzene, or DMF at 80 °C resulted in a decrease in regioselectivity, yielding products **10** and **11** in 85:15 ratio. The exclusive formation of the *cis* diastereomer **10** and *E* isomer of **11**, as shown in Table 1, was confirmed by NOE ^{1}H NMR experiments.[24] To evaluate the role of electronic effects in the palladacycles, 1,2-nonadiene was reacted with functionalized palladacycles **4b,c** (entries 4 and 5). Allene insertion into the electron deficient palladacycle **4b** proved sluggish, and the reaction time had to be extended to provide a pure 2,3-disubstituted benzopyran **12** in a moderate yield 56% (entry 4). The presence of a methoxy substituent in palladacycle **4c** did not significantly effect the reaction rate, and benzopyran **13** could be isolated as a pure single diastereomer in an excellent 78% yield after 19 h (entry 5). NOE ^{1}H NMR experiments confirmed the assignment of *cis* relative stereochemistry for benzopyrans **12** and **13**.[24] In both cases (entries 4 and 5), the regioisomeric benzopyrans of type **V** were detected in the crude reaction mixtures in less than 10% of the content of the major products **12** and **13**. However, these products could not be isolated in a sufficient purity to permit a complete characterization.

Branching in the alkyl substituents (R) in 6-methyl-1,2-heptadiene (entries 6−8) and in 5-ethyl-1,2-nonadiene (entries 9−11) did not exert any effect on regio- or diastereoselectivities. 2,3-Disubstituted benzopyrans **14** (as an inseparable mixture with 8% of regioisomer **15**), **16**, **17**, **18** (as an inseparable mixture with 10% of regioisomer **19**), **20**, and **21** were isolated in excellent yields as single diastereoisomers.[24] With the exception of entry 11,[25] isolation and a complete characterization of benzopyrans of type **V**, detected in the crude mixtures from experiments in entries 7, 8, and 10 in less than 10% of the content of the major isomer, was unsuccessful.

However, steric factors were found to affect the regioselectivity. The insertion of an allene featuring a quaternary carbon at the C-5 position into palladacycle **4a** afforded the 2,3-disubstituted benzopyran **22** in only 45% yield, along with the regioisomeric benzopyran **23** in 23% yield (entry 12). Both products were isolated as pure compounds, with stereochemistry consistent with previous experiments.[24] Disubstitution at the C-4 carbon in cyclohexyl allene reversed the regiochemical preference, and its reaction with palladacycle **4a** provided a chromatographically inseparable mixture of benzopyrans **24** and **25** in 72% yield and 22:78 ratio favoring benzopyran **25** (entry 13, Table 1).[26] The stereochemical outcome (*cis* isomer of **24**, *E* double bond in **25**) remained unaltered.[26]

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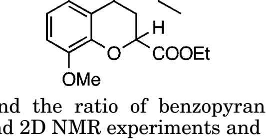
(23) Structures and the ratio of *cis*/*trans* benzopyrans **8** and **9** were established by 1D and 2D NMR data on the mixtures of *trans* and *cis* isomers **8a,b** and **9a,b**, including the examination of long-range ^{1}H−^{13}C connectivities obtained from HMBC 2D NMR experiments, and a series of NOE experiments. For details, see Supporting Information.

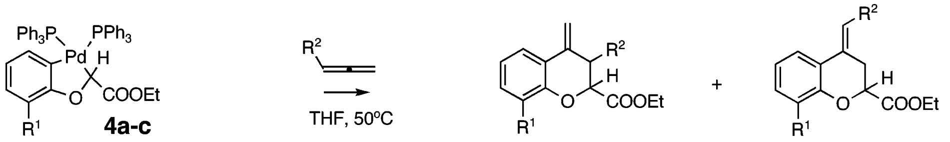
(24) Structures and the ratio of benzopyrans **10** and **11** were established by 1D and 2D NMR data acquired on the mixture of chromatographically inseparable products **10**, and **11**, including the examination of long-range ^{1}H−^{13}C connectivities obtained from HMBC 2D NMR experiments, and a series of NOE experiments. Analogous spectroscopic studies (1D and 2D NMR, NOE) were performed on the mixtures of products **14** with **15** (entry 6, Table 1), **18** with **19** (entry 9, Table 1), and pure isolated benzopyrans **12**, **13**, **16**, **17**, **20**, **21**, **22**, and **23**. For details, see Supporting Information.

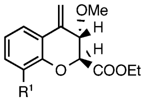
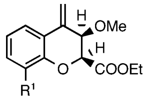
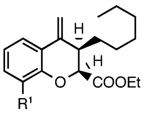
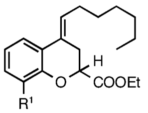
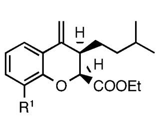
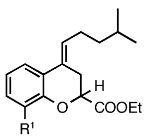
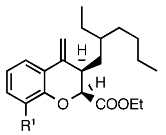
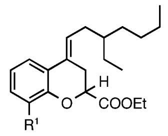
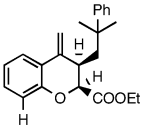
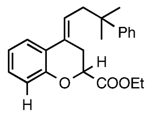
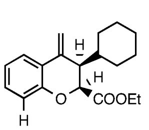
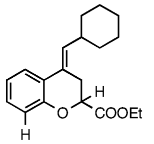
(25) From the experiment described in entry 11 (Table 1), 7% yield of (*E*)-3,4-dihydro-2-ethoxycarbonyl-4-(3-ethylheptylidene)-8-methoxy-2*H*-1-benzopyran (below) was isolated in 95% purity, and the structure assignment was confirmed by 1D and 2D NMR spectroscopic analyses and by an NOE experiment. Irradiation of the signal for the vinylic proton at δ 6.10 (t) ppm led to the NOE enhancement of the signal at δ 7.10 (dd) ppm corresponding to the aromatic proton at C-5.



(26) Structures and the ratio of benzopyrans **24** and **25** were established by 1D and 2D NMR experiments and NOE studies on the mixture of chromatographically inseparable products **24**, and **25**. For details, see Supporting Information.

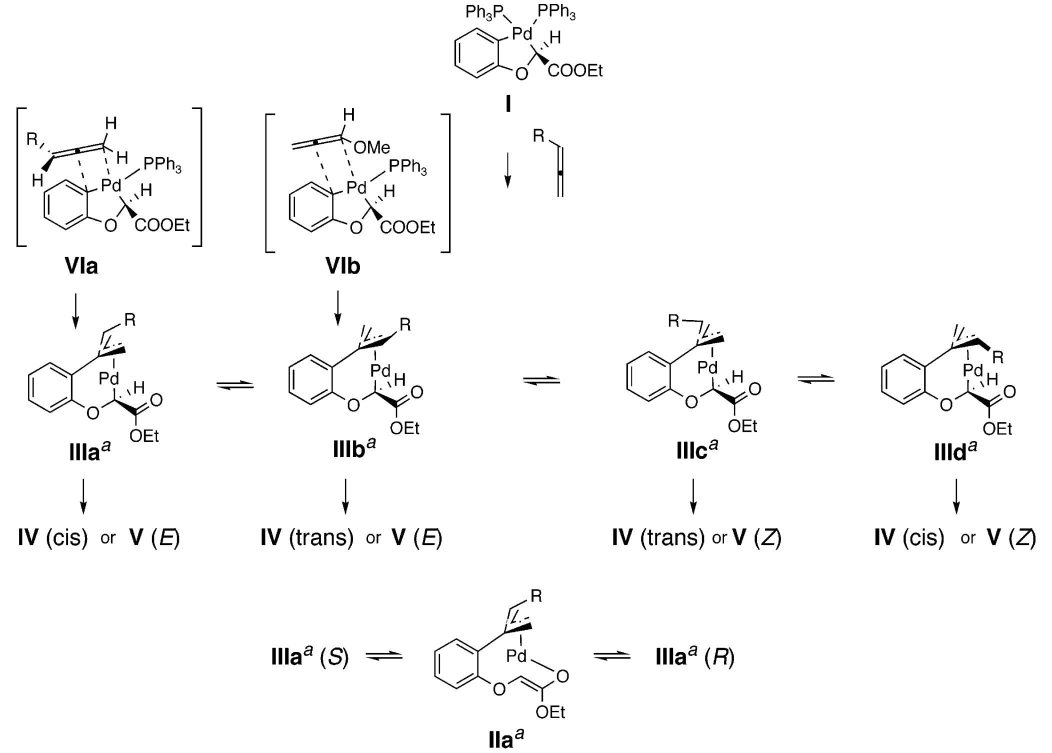
TABLE 1. Synthesis of 2,3-Disubstituted 3,4-Dihydro-2*H*-1-benzopyrans



	palladacycle	R^2 (allene)	time (h)	product(s)			yield (%)
1	**4a**: $R^1 = H$	OMe	54 h	 **8a**	+	 **8b**	98 (96 : 4)[a]
2	**4b**: $R^1 = CF_3$	OMe	94 h	**9a**	+	**9b**	77 (95 : 5)[a]
3	**4a**: $R^1 = H$	*n*-hexyl	10 h[b]	 **10**	+	 **11**	84 (91 : 9)[a]
4	**4b**: $R^1 = CF_3$	*n*-hexyl	72 h	**12**			56[c]
5	**4c**: $R^1 = OMe$	*n*-hexyl	19 h	**13**			78[c]
6	**4a**: $R^1 = H$	3-methylbutyl	22 h	 **14**	+	 **15**	84 (92 : 8)[a]
7	**4b**: $R^1 = CF_3$	3-methylbutyl	90 h	**16**			49[c]
8	**4c**: $R^1 = OMe$	3-methylbutyl	19 h	**17**			72[c]
9	**4a**: $R^1 = H$	2-ethylhexyl	20 h	 **18**	+	 **19**	64 (90 : 10)[a]
10	**4b**: $R^1 = CF_3$	2-ethylhexyl	90 h	**20**			52[c]
11	**4c**: $R^1 = OMe$	2-ethylhexyl	19 h	**21**		[d]	81[c]
12	**4a**: $R^1 = H$	(2-methyl-2-phenyl)propyl	20 h	 **22** (45%)		 **23** (23 %)	68[e]
13	**4a**: $R^1 = H$	cyclohexyl	18 h	 **24**	+	 **25**	72 (22 : 78)[a]

[a] Yield of an inseparable mixture of isomers. [b] Reaction was run under reflux of THF. [c] Yield of a pure product. [d] A 7% yield of the minor product was isolated in 95% purity (ref 25). [e] Combined yield of isolated pure products.

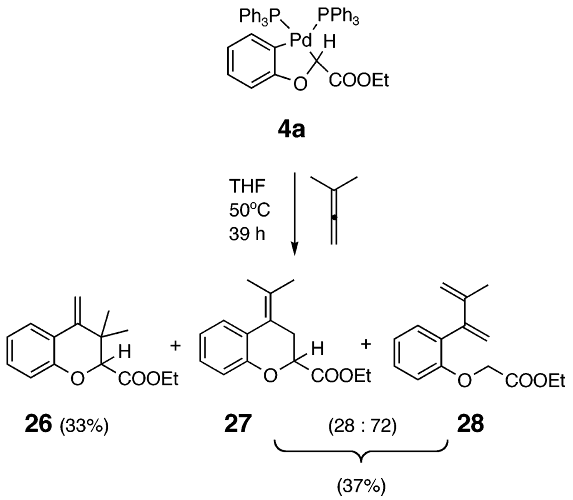
Finally, disubstitution at the C-3 terminal carbon of the allene severely reduced the efficiency of the insertion. Treatment of palladacycle **4a** with 3-methyl-1,2-butadiene led to 2,3,3-trisubstituted benzopyran **26** in 33% yield, along with an inseparable mixture of benzopyran **27** and diene **28** in a combined 37% yield and 28:72 ratio favoring diene **28** (Scheme 3).[27] Diene **28** was formed via β-hydride elimination from the intermediates **II/III**.[28]



^{a}Auxiliary ligands (PPh_3) were omitted for clarity.

FIGURE 3. Plausible mechanism.

SCHEME 3



The results outlined in Table 1 and Scheme 3 define a synthetically useful range of monosubstituted allenes that react with palladacycles **4a**−**c** to afford regio- and stereoselectively 2,3-disubstituted 3,4-dihydro-2*H*-1-benzopyrans. Monosubstituted allenes featuring an aryl substituent, 1,3- or 1,2-disubstituted allenes with a methoxy or an ester and an alkyl substituent, or symmetrical 1,3-dialkyl-substituted allenes provided complex mixtures of the insertion products.

To rationalize the regio- and stereochemical outcome of the described process, a model outlined in Figure 3 was considered. Allene insertion into palladacycle **I** would proceed with regiochemistry permitting the formation of stabilized *syn* or *anti* isomers of the diastereomeric π-allylpalladium complexes **IIIa**−**d** (Figure 3).[2,11,12] Reductive elimination at the substituted carbon of the allyl ligand in complexes **IIIa** or **IIId** would afford the observed *cis* isomers of benzopyrans **IV**. In contrast, complexes **IIIb** and **IIIc** would lead to *trans* isomers of benzopyrans **IV**. Reductive elimination at the unsubstituted allyl termini of complexes **IIIa** and **IIIb** would provide the observed *E* isomers of products **V**, while complexes **IIIc** and **IIId** would yield *Z* isomers (Figure 3). The presented results indicate that in the absence of an extreme steric hindrance, regiochemistry of the reductive elimination is controlled by the electronic nature of the substituent R (Schemes 2 and 3 and Table 1),[13c] in a manner analogous to the Tsuji−Trost reaction. Thus, nucleophiles attack allylic termini that are better able to accommodate a partial positive charge, e.g., unsubstituted carbons in allyls bearing electron-withdrawing groups,[29] and carbons bearing an electron-donating (e.g., alkoxy) group.[30] The stability of the resulting Pd(0)−alkene complexes of electron-deficient double bonds may also contribute to the regiocontrol.[31] A preferential formation of the *E* double bond in heterocycles arising

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[27] The ratio of products **27**:**28** (28:72) was determined from the integration of ^{1}H NMR signals at 4.89 (t) ppm for proton H^2 in benzopyran **27** and at 5.13 (s) ppm for one vinylic proton in product **28**.

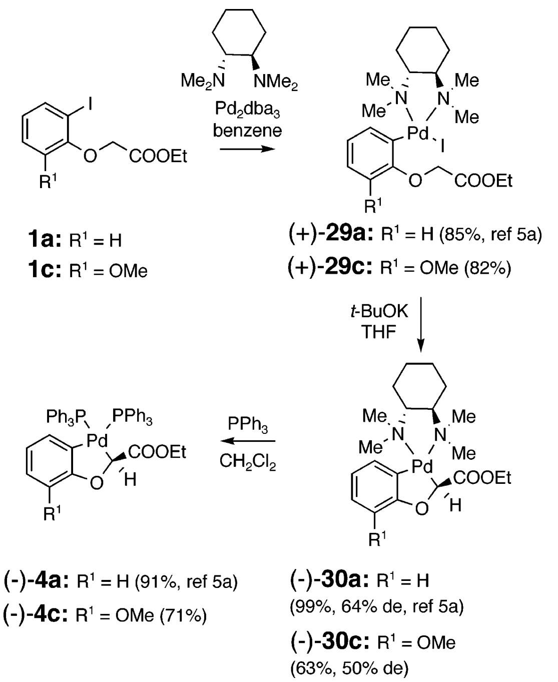
[28] Ma, S.; Negishi, E.-I. *J. Org. Chem.* **1994**, *59*, 4730−4732.

[29] For examples of a regioselective attack of nucleophiles at the unsubstituted termini of π-allylpalladium complexes bearing electron-withdrawing substituents, see: (a) Prat, M.; Ribas, J.; Moreno-Manas, M. *Tetrahedron* **1992**, *48*, 1695−1706. (b) Tanikaga, R.; Jun, T. X.; Kaji, A. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1185−1191. (c) Ono, N.; Hamamoto, I.; Kaji, A. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1439−1443. (d) Tsuji, J.; Ueno. H.; Kobayashi, Y.; Okumoto, H. *Tetrahedron Lett.* **1981**, *22*, 2573−2574.

from allene insertions into stable cyclopalladated complexes was observed,[12] while the catalytic processes yielded both *E* and *Z* products or *E*/*Z* mixtures.[3h−k] Steric interactions between the aromatic ring and the group R may destabilize *syn* allyl palladium complexes **IIIc** and **IIId**, explaining the absence of the *Z* isomers of benzopyrans **V** among the products (Figure 3).

The excellent diastereocontrol in preparation of benzopyrans **IV** could arise via two plausible pathways. Assuming the interconversion of complexes **IIIa**−**d** present in equilibrium is faster than reductive elimination,[13b,32] the differences in rates of reductive elimination from complexes **IIIa**−**d** would control the *cis/trans* selectivity. Interconversion of complexes **IIIa**−**d** would occur via the $\eta^3-\eta^1-\eta^3$ slippage mechanism.[33] Alternatively, on condition that the rate of interconversion of complexes **III** is relatively slow in comparison to the rate of reductive elimination, the rates of formation of complexes **III** would control the diastereoselectivity. Migratory insertion of allenes into the carbon−palladium bond[34] would be expected to involve insertion of the unsubstituted terminal double bond of allenes, approaching from the less sterically hindered allene face,[35] as shown by transition state **VIa**. The observed selective formation of *cis* benzopyrans from alkyl-substituted allenes suggests that complex **IIIa** might be formed preferentially (Figure 3). The reasons for a stereodivergent outcome of reactions with 1-methoxy-1,2-propadiene remain unclear. Possibly, a strong electronic effect of the methoxy substituent could cause the migratory insertion to occur into the less electron-rich internal double bond[36] of 1-methoxy-1,2-propadiene as shown in the transition state **VIb** to provide selectively intermediate **IIIb** and subsequently *trans* benzopyrans **8** and **9** (Figure 3, Table 1). At present, in the absence of kinetic data, the mechanism of stereoinduction cannot be defined more precisely.

SCHEME 4



The bonding mode of the ester enolate ligands was expected to have a significant effect on stereoinduction. Conceivably, oxygen-bonded enolate complexes **IIa**−**d** could be involved as intermediates en route to benzopyrans **IV** and **V** (Figures 1 and 3).[7] To provide an insight into the nature of the reactive intermediates, insertion of allenes into enantiomerically enriched palladacycles (−)-**4a** and (−)-**4c** was investigated, reasoning that the isolation of racemic benzopyrans would support the involvement of O-bonded palladium enolates **IIa**−**d** (Figure 3). Preparation of enantiomerically enriched palladacycle **4a** from complexes (+)-**29a** and (−)-**30a** (64% de) was previously demonstrated.[5a] The original procedure[5a] was easily adopted for the preparation of complex (+)-**29c** and palladacycle (−)-**30c** in 50% de (Scheme 4).[37] Regrettably, an analytical technique capable of an independent assignment of the enantiomeric purity of palladacycles (−)-**4a** and (−)-**4c**, arising via ligand exchange reaction on diastereomerically enriched palladacycles (−)-**30a** and (−)-**30c**, could not be identified.[38] In analogy to our earlier study,[5a] palladacycles (−)-

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[30] For examples of a regioselective attack of nucleophiles at the substituted termini of π-allylpalladium complexes bearing electron-donating substituents, see: (a) Trost, B. M.; Jakel, C.; Plietker, B. *J. Am. Chem. Soc.* **2003**, *125*, 4438−4439 (b) Vicart, N.; Cazes, B.; Gore, J. *Tetrahedron Lett.* **1995**, *36*, 535−538. (c) Chaptal, N.; Colovray-Gotteland, V.; Grandjean, C.; Cazes, B.; Gore, J. *Tetrahedron Lett.* **1991**, *32*, 1795−1798. (c) Åkermark, B.; Hansson, S.; Krakenberger, B.; Vitagliano, A.; Zetterberg, K. *Organometallics* **1984**, *3*, 679−682.

[31] For the discussion of the potential significance of the stability of the Pd(0)−alkene complexes, formed upon alkylation, for the regiocontrol of the nucleophilic attack at unsymmetrically substituted π-allylpalladium complexes in the Tsuji−Trost reactions, see: (a) Trost, B. M.; Verhoeven, T. R. *J. Am. Chem. Soc.* **1980**, *102*, 4730−4743. (b) Trost, B. M.; Weber, L.; Strege, P.; Fullerton, T. J.; Dietsche, T. J. *J. Am. Chem. Soc.* **1978**, *100*, 3426−3435.

[32] For studies demonstrating the stereocontrol of palladium-catalyzed allylic alkylation by controling the relative rates of *anti-syn* isomerization of π-allylpalladium intermediates and the rate of the nucleophilic attack, see: (a) Sjogren, M. P. T.; Hansson, S.; Åkermark, B. *Organometallics* **1994**, *13*, 1963−1971. (b) Åkermark, B.; Hansson, S.; Vitagliano, A. *J. Am. Chem. Soc.* **1990**, *112*, 4587−4588.

[33] For the discussion of the of $\eta^3-\eta^1-\eta^3$ slippage mechanism and relevant mechanistic studies, see: (a) Breutel, C.; Pregosin, P. S.; Salzmann, Togni, A. *J. Am. Chem. Soc.* **1994**, *116*, 4067−4068. (b) Pregosin, P. S.; Ruegger, H.; Salzmann, R.; Albinati, A.; Lianza, F.; Kunz, R. W. *Organometallics* **1994**, *13*, 83−90. (c) Consiglio, G.; Waymouth, R. M. *Chem. Rev.* **1989**, *89*, 257−276.

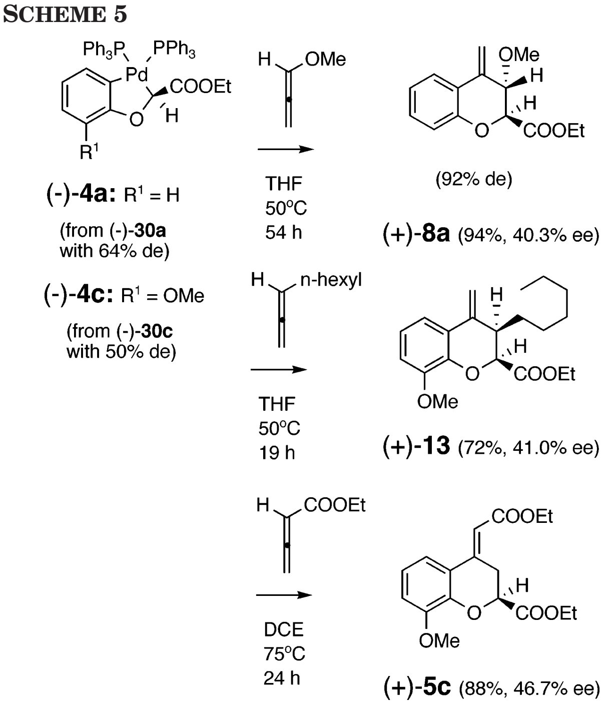
[34] For studies on the mechanistic aspects of the migratory insertion of allenes into carbon−transition metal bonds, see: (a) Canovese, L.; Visentin, F.; Chessa, G.; Santo, C.; Ugliagliati, P.; Bandoli, G. *J. Organomet. Chem.* **2002**, *650*, 43−56. (b) Canovese, L.; Visentin, F.; Chessa, G.; Uguagliati, P.; Bandoli, G. *Organometallics* **2000**, *19*, 1461−1463. (c) Delis, J. G. P.; Groen, J. H.; Vrieze, K.; van Leeuwen, W. N. M. P. *Organometallics* **1997**, *16*, 551−562. (d) Ankersmit, H. A.; Veldman, N.; Spek, A. L.; Eriksen, K.; Goubitz, K.; Vriese, K.; van Koten, G. *Inorg. Chim. Acta* **1996**, *252*, 203−219. (e) Groen, J. H.; Elsevier: C. J.; Vrieze, K.; Smeets, W. J. J.; Spek, A. L. *Organometallics* **1996**, *15*, 3445−3455. (f) Ruelke, R. E.; Kliphuis, D.; Elsevier, C. J.; Fraanje, J.; Goubitz, K.; van Leeuwen, P. W. N. M.; Vrieze, K. *J. Chem. Soc., Chem. Commun.* **1994**, 1817−1819. (g) Cazes, B. *Pure Appl. Chem.* **1990**, 62, 1867−1878. (h) Reference 2a and references cited within.

[35] An analogous transition state has been proposed in a study investigating the stereocontrol in carbopalladation of chiral nonracemic allenes; see: (a) Kato, F.; Hiroi, K. *Chem. Pharm. Bull.* **2004**, *52*, 95−103. (b) Kato, F.; Hiratsuka, Y.; Mitsui, T.; Watanabe, T.; Hiroi, K. *Heterocycles* **1999**, *50*, 83−87.

[36] Hartley, F. R. *Chem. Rev.* **1969**, *69*, 799−844.

[37] The diastereomeric composition of palladacycle (−)-**30c** was established by integration of ^{1}H NMR signals corresponding to the methine protons attached to the palladium-bonded sp^3-hybridized carbon: a singlet at 5.75 (s) ppm for the major diastereomer of (−)-**30c** and a singlet at 5.35 (s) ppm for the minor diastereomer of **30c**. Absolute configuration (*S*) of the palladium-bonded stereogenic carbon in palladacycle (−)-**30a** was unequivocally established as described in ref 5a. In analogy, the absolute configuration of the palladium-bonded stereogenic carbon in palladacycle (−)-**30c** was tentatively assigned as (*S*).

SCHEME 5



4a and (−)-**4c** were presumed to be obtained in enantiomeric excesses equal or lower than 64% ee and 50% ee, respectively (Scheme 4).[39] Insertion of 1-methoxy-2,3-propadiene, 1,2-nonadiene, and ethyl-2,3-butadienoate into palladacycles (−)-**4a** (presumably 64% ee)[39] and (−)-**4c** (presumably 50% ee)[39] afforded nonracemic benzopyrans (+)-**8a** (40.3% ee), (+)-**13** (41.0% ee), and (+)-**5c** (46.7% ee),[40] indicating 63%, 82%, and 93% retention of the stereochemical information, respectively (Scheme 5).[41] Isolation of enantiomerically enriched benzopyrans **IV** and **V** demonstrates that, at least to the extent indicated by the percentage of retention of the stereochemical information (63−93%), O-bonded palladium enolates **IIa**−**d** are not involved as intermediates on the pathway leading to benzopyrans **IV** and **V**.

Efforts at extending the described protocol to reactions with azapalladacycles analogous to **I** (NTf or NTs group instead of O in **I**)[5a] have failed.[42] Initial attempts at catalytic reactions between aryl iodide **1a** and 1-methoxy-2,3-propadiene or 1,2-nonadiene, either utilizing reagents developed for the known corresponding catalytic reactions[43] or employing somewhat stronger bases,[44] have not succeeded. Realization of a catalytic protocol will likely require the application of preformed metal (Zn) or silyl ester enolates under mild reaction conditions.[14]

Conclusions

A new avenue for a rapid and convergent construction of synthetically valuable 2,3-disubstituted 3,4-dihydro-2*H*-1-benzopyrans, which could not be prepared via established palladium-catalyzed annulations, has been demonstrated. The protocol generates two adjacent stereogenic centers and allows for a rapid generation of diverse potentially medicinally relevant benzopyrans. The insertion of monosubstituted allenes possessing methoxy or sterically unencumbered alkyl substituents into unique palladacycles with a metal-bonded stereogenic carbon proceeded with a high regiocontrol (>10:1) and with complete diastereocontrol to afford benzopyrans **IV** (Figure 2) in 45−98% yields. Allenes bearing electron-withdrawing substituents afforded benzopyrans **V**, exclusively with *E* double bond geometry (Figure 2). Nonracemic benzopyrans featuring a palladium-bonded stereogenic carbon as the only element of asymmetry reacted with 63−93% retention of the stereochemical information to afford benzopyrans **IV** or **V** (three examples) in 40−47% ee, implying that C-bonded palladium ester enolates **III**, rather than O-bonded enolates **II** (Figure 3), were operating as the predominant intermediates. These studies, along with our earlier work,[5] point to a high configurational stability of carbon-bonded palladium ester enolates, especially notable in a system lacking chiral nonracemic auxiliary ligands.[7] Results described herein highlight the synthetic potential of high enantiopurity organometallics with a metal-bonded sp^3-hybridized stereogenic carbon[45] and currently are being applied toward the design of a catalytic protocol.

Experimental Section

General Procedure for Synthesis of Phenoxyacetates 1b and 1c. To a suspension of the phenols (10 mmol) and K_2CO_3 (10.0 g, 72.5 mmol) in acetone (50 mL) at room temperature under argon was added ethyl bromoacetate (1.55 mL, 2.338 g, 14.00 mmol), and the suspension was refluxed.

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[38] All attempts at resolving chromatographic signals for the enantiomers of complexes (−)-**4a** and (−)-**4c** via HPLC on CHIRALPAK AD, AS and CHIRACEL OD chiral stationary phases failed. Furthermore, ^{1}H NMR and ^{31}P NMR of complexes (−)-**4a** and (−)-**4c** run in the presence of Eu(hfc)$_3$ chiral shift reagent did not provide a sufficient resolution to ascertain the enantiomeric excess.

[39] The ligand exchange reaction has been shown to proceed without affecting the configurational integrity of the metal-bonded stereocenter. Stability of a Pd−C bond during a ligand exchange process has been previously established; see: (a) Pfeffer, M.; Spencer, J.; Maassarani, F.; DeCian, A.; Fisher, J. *Tetrahedron: Asymmetry* **1994**, *5*, 321−324. It has been used for the preparation of enantiomerically enriched transition metal complexes with achiral ligands; see: (b) Ryabov, A. D.; Panyashkina, I. M.; Polyakov, V. A.; Howard, J. A. K.; Kuzmina, L. G.; Datt, M. S.; Sacht, C. *Organometallics* **1998**, *17*, 3615−3618. (c) Garcia-Ruano, J. L.; Gonzalez, A. N.; Barcena, A. I.; Camazon, M. J.; Navarro-Ranninger, C. *Tetrahedron: Asymmetry* **1996**, *7*, 139−148. However, partial racemization of palladacycles (−)-**4a** and (−)-**4c** during the reaction or an alteration of the enantiomeric composition during isolation cannot be completely ruled out. For studies evaluating the stability of palladacycle (−)-**4a** against racemization, see ref 5a.

[40] Enantiomeric excess of heterocycles (+)-**8a**, (+)-**13**, and (+)-**5c** was measured by chiral phase HPLC analysis on CHIRALPAK AD chiral stationary phase.

[41] The insertion reaction likely proceeded with the retention of the absolute configuration at the palladium-bonded stereogenic carbon. However, the absolute configuration of the nonracemic benzopyrans (+)-**8a**, (+)-**13**, and (+)-**5c** was not established. It is generally accepted that migratory insertion reactions proceed with a retention of the absolute configuration at the metal-bonded carbon; see: (a) Flood, T. C. In *Topics in Inorganic and Organometallic Stereochemistry*; Geoffroy, G., Allinger, N. L., Eliel, E. L., Eds.; Wiley-Interscience: New York, 1981; Vol. 12, pp 37−117. (b) Bock, P. L.; Boschetto, D. J.; Rasmussen, J. R.; Demers, J. P.; Whitesides, G. M. *J. Am. Chem. Soc.* **1974**, *96*, 2814−2824.

[42] Reasoning that the presence of relatively electron-deficient groups (NSO_2R) in palladacycle **I** might significantly disfavor the reductive elimination event (see ref 7e), preparation and reactivity of azapalladacycles with diverse N-protecting groups is being investigated.

[43] The following experimental conditions were employed: 5 mol % Pd(OAc)$_2$, 5 mol % PPh$_3$, Na_2CO_3, *n*-Bu$_4$NCl, DMF, 80 °C (see ref 3j).

[44] The following experimental conditions were employed. Conditions A: Pd$_2$dba$_3$, PPh$_3$, *t*-BuOK, THF, 65 °C. Conditions B: Pd$_2$dba$_3$, PPh$_3$, KHMDS, THF, 65 °C.

[45] Malinakova, H. C. *Chem. Eur. J.* **2004**, *10*, 2636−2646.

The reaction mixtures were filtered, and solvents were removed under reduced pressure to afford the crude products. The crude products were separated by flash chromatography over silica eluting with mixtures of EtOAc/hexane to afford aryl iodides **1b** and **1c** as colorless oils.

Ethyl (2-Iodo-6-(trifluoromethyl)phenoxy)acetate (1b). 2-Iodo-6-(trifluoromethyl)phenol[22a] (2.880 g, 10.00 mmol) was treated according to the procedure described above, refluxing the reaction mixture for 24 h and eluting with EtOAc/hexane (1:15) mixture to afford aryl iodide **1b** (3.555 g, 95%) as a colorless oil: $R_f = 0.43$ (EtOAc/hexane 1:9); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, $J = 7.9$ Hz, 1 H), 7.60 (d, $J = 7.8$ Hz, 1 H), 7.00 (t, $J = 7.9$ Hz, 1 H), 4.61 (s, 2 H), 4.33 (q, $J = 7.1$ Hz, 2 H), 1.34 (t, $J = 7.1$ Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 155.7, 143.8, 127.4 (q, J ($^{13}C-^{19}F$) = 5.0 Hz), 126.7, 125.4 (q, J ($^{13}C-^{19}F$) = 31.2 Hz), 122.5 (q, J ($^{13}C-^{19}F$) = 271.6 Hz), 92.7, 70.6, 61.4, 14.1; IR (neat, cm^{-1}) 1765 (s), 1450 (s), 1434 (s); HRMS (FAB) calcd for $C_{11}H_{14}NO_3F_3I$ ($M + NH_4^+$) 391.9971, found 391.9976.

Ethyl (2-Iodo-6-methoxyphenoxy)acetate (1c). 2-Iodo-6-methoxyphenol[22b] (2.500 g, 10.00 mmol) was treated according to the procedure described above, refluxing the reaction mixture for 20 h and eluting with EtOAc/hexane (1:10) mixture to afford aryl iodide **1c** (3.161 g, 94%) as a colorless oil: $R_f = 0.19$ (EtOAc/hexane 1:9); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (dd, $J = 7.9$ Hz, 1.5 Hz, 1 H), 6.87 (dd, $J = 8.20$ Hz, 1.5 Hz, 1 H), 6.79 (t, $J = 7.9$ Hz, 1 H), 4.59 (s, 2 H), 4.29 (q, $J = 7.1$ Hz, 2 H), 3.81 (s, 3 H), 1.32 (t, $J = 7.1$ Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 152.1, 147.0, 130.7, 126.1, 112.7, 91.9, 69.2, 61.1, 55.9, 14.2; IR (neat, cm^{-1}) 1761 (s), 1029 (s); HRMS (FAB) calcd for $C_{11}H_{14}O_4I$ ($M + H^+$) 336.9937, found 336.9929.

General Procedure for Synthesis of Palladium(II) Complexes 2b,c. To a solution of tris(dibenzylideneacetone)-dipalladium(0) (Pd_2dba_3) (1.0 mmol) in benzene (30 mL) at room temperature under argon was added *N,N,N′,N′*-tetramethyl-1,2-ethylenediamine (TMEDA) (4.0 mmol) and a solution of the aryl iodide (2.20 mmol) in benzene (5.0 mL). The reaction mixture was stirred at 55 °C for 30 min. The suspension was filtered through a plug of Celite, and solvents were removed under reduced pressure to afford a crude product. The crude product was purified by flash chromatography over silica, eluting with EtOAc/hexane (1:10) to remove excess dibenzylideneacetone (dba) and subsequently with EtOAc/hexane (1:1) to afford palladium(II) complexes **2b,c** as yellow solids.

[2-(Ethoxycarbonylmethoxy)-3-(trifluoromethyl)phenyl]iodo(tetramethylethylenediamine)palladium (2b). Treatment of Pd_2dba_3 (1.832 g, 2.0 mmol), TMEDA (1.20 mL, 0.930 g, 8.0 mmol), and aryl iodide **1b** (1.646 g, 4.4 mmol) according to the procedure described above afforded palladium(II) complex **2b** (1.926 g, 81%) as a yellow solid: mp 125−127 °C (EtOAc/hexane 1:1); $R_f = 0.21$ (EtOAc/hexane 1:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, $J = 7.3$ Hz, 1 H), 7.09 (d, $J = 7.3$ Hz, 1 H), 6.83 (t, $J = 7.5$ Hz, 1 H), 5.68 (d, $J = 16.1$ Hz, 1 H), 4.54 (d, $J = 16.1$ H, 1 H), 4.34−4.27 (m, 1 H), 4.24−4.12 (m, 1 H), 2.95−2.85 (m, 1 H), 2.72 (s, 3 H), 2.67 (s, 3 H), 2.65−2.61 (m, 3 H), 2.59 (s, 3 H), 2.28 (s, 3 H), 1.31 (t, $J = 7.1$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.1, 158.2, 143.8, 136.2, 123.8 (q, J ($^{13}C-^{19}F$) = 272.1 Hz), 122.8 (q, J ($^{13}C-^{19}F$) = 29.1 Hz), 122.1, 121.5 (q, J ($^{13}C-^{19}F$) = 5.1 Hz), 69.9, 62.2, 60.5, 58.8, 50.8, 50.4, 50.3, 49.5, 14.3; IR (KBr, cm^{-1}) 1754 (s), 1745 (s), 1314 (s), 802 (m), 784 (m), 678 (m); HRMS (FAB) calcd for $C_{17}H_{30}N_3O_3O_5IF_3Pd$ ($M + NH_4^+$) 614.0319, found 614.0314.

[2-(Ethoxycarbonylmethoxy)-3-methoxyphenyl]iodo(tetramethylethylenediamine)palladium (2c). Treatment of Pd_2dba_3 (2.289 g, 2.50 mmol), TMEDA (1.60 mL, 1.162 g, 10.0 mmol), and aryl iodide **1c** (1.849 g, 5.50 mmol) according to the procedure described above afforded palladium(II) complex **2c** (2.150 g, 77%) as a yellow solid: mp 154−156 °C (EtOAc/hexane 1:1); $R_f = 0.12$ (EtOAc/hexane 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.86 (d, $J = 7.6$ Hz, 1 H), 6.72 (t, $J = 7.7$ Hz, 1 H), 6.45 (d, $J = 7.8$ Hz, 1 H), 5.10 (d, $J = 15.7$ Hz, 1 H), 4.69 (d, $J = 15.7$ Hz, 1 H), 4.31−4.19 (m, 2 H), 3.75 (s, 3 H), 2.85−2.75 (m, 1 H), 2.68 (s, 3 H), 2.67 (s, 3 H), 2.65−2.55 (m, 3 H), 2.58 (s, 3 H), 2.40 (s, 3 H), 1.30 (t, $J = 7.1$ Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 151.6, 148.2, 135.5, 130.4, 122.8, 106.7, 67.7, 62.2, 60.3, 58.6, 54.9, 50.7, 50.4, 50.0, 49.5, 14.3; IR (KBr, cm^{-1}) 1729 (s), 1035 (s), 801 (m), 771 (m); HRMS (FAB) calcd for $C_{17}H_{33}N_3O_4IPd$ ($M + NH_4^+$) 576.0551, found 576.0537.

General Procedure for Synthesis of Palladacycles 3b,c. To a suspension of the palladium(II) iodo complex (1.0 mmol) and silver nitrate (2.0 mmol) in THF (20−25 mL) was added *t*-BuOK (1.0 M solution in THF, 1.20 mL, 1.20 mmol). The reaction mixture was stirred for 10 min at room temperature and subsequently filtered through a plug of Celite and basic alumina, eluting with EtOAc/hexane (2:1). Solvents were removed under reduced pressure to afford palladacycles **3b,c** as white solids.

(Ethoxycarbonylmethineoxy-3-trifluoromethyl-1,2-phenylene)(tetramethylethylenediamine)palladium (3b). Palladium(II) complex **2b** (1.740 g, 2.916 mmol), $AgNO_3$ (1.02 g, 6.0 mmol), and *t*-BuOK (3.50 mL, 3.50 mmol) were treated according to the procedure described above to afford palladacycle **3b** (1.20 g, 88%) as a white solid: mp 198−200 °C dec (EtOAc/hexane 2:1); $R_f = 0.27$ (EtOAc/hexane 3:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (t, $J = 6.8$ Hz, 2 H), 6.64 (t, $J = 7.6$ Hz, 1 H), 5.85 (s, 1 H), 4.19−4.09 (m, 1 H), 4.02−3.95 (m, 1 H), 2.92 (td, $J = 13.8$ Hz, 3.0 Hz, 1 H), 2.85 (s, 3 H), 2.85−2.78 (m, 1 H), 2.81 (s, 3 H), 2.69 (s, 3 H), 2.58 (s, 3 H), 2.45 (dt, $J = 13.5$ Hz, 3.2 Hz, 1 H), 2.33 (dt, $J = 13.0$ Hz, 3.2 Hz, 1 H), 1.15 (t, $J = 7.1$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.2, 169.9, 140.4, 136.9, 124.5 (q, J ($^{13}C-^{19}F$) = 270.1 Hz), 122.4 (q, J ($^{13}C-^{19}F$) = 4.9 Hz), 116.9, 110.9 (q, J ($^{13}C-^{19}F$) = 30.7 Hz), 88.9, 60.9, 60.4, 59.5, 51.3, 51.0, 49.5, 46.4, 14.1; IR (KBr, cm^{-1}) 1679 (s), 1328 (s), 801(m), 741 (m); HRMS (FAB) calcd for $C_{17}H_{26}N_2O_3F_3Pd$ ($M + H^+$) 469.0930, found 469.0938.

(Ethoxycarbonylmethineoxy-3-methoxy-1,2-phenylene)(tetramethylethylenediamine)palladium (3c). Palladium(II) complex **2c** (1.850 g, 3.310 mmol), $AgNO_3$ (1.125 g, 6.62 mmol), and *t*-BuOK (4.00 mL, 4.00 mmol) were treated according to the procedure described above to afford palladacycle **3c** (1.120 g, 79%) as a white solid: mp 165−167 °C (EtOAc/hexane 2:1); $R_f = 0.20$ (EtOAc/hexane 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.66−6.56 (m, 3 H), 5.82 (s, 1 H), 4.10 (qd, $J = 7.1$ Hz, 1.1 Hz, 2 H), 3.81 (s, 3 H), 2.94 (td, $J = 12.4$ Hz, 3.1 Hz, 1 H), 2.85 (s, 3 H), 2.85−2.73 (m, 1 H), 2.81 (s, 3 H), 2.71 (s, 3 H), 2.55 (s, 3 H), 2.41 (dt, $J = 13.5$ Hz, 2.9 Hz, 1 H), 2.28 (dt, $J = 12.8$ Hz, 3.1 Hz, 1 H), 1.18 (t, $J = 7.1$ Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.8, 162.2, 143.7, 137.7, 125.9, 117.3, 109.6, 87.9, 61.0, 60.5, 59.4, 56.2, 51.3, 51.1, 49.4, 46.2, 14.3; IR (KBr, cm^{-1}) 1707 (s), 1153 (s), 803 (m); HRMS (FAB) calcd for $C_{17}H_{29}N_2O_4Pd$ ($M + H^+$) 431.1162, found 431.1161.

General Procedure for Synthesis of Palladacycles 4b,c. A solution of palladacycle **3b,c** (1.0 mmol) and triphenylphosphine (PPh_3) (3.5 mmol) in methylene chloride (13.0−14.0 mL) was stirred at room temperature under argon for the indicated period of time. The solvent was removed under reduced pressure to afford a crude product. Trituration of the crude product with minimum amounts of hexane and ether afforded palladacycles **4b,c** as white solids.

(Ethoxycarbonylmethineoxy-3-trifluoromethyl-1,2-phenylene)bis(triphenylphosphine)palladium (4b). Treatment of palladacycle **3b** (1.071 g, 2.285 mmol) and PPh_3 (2.098 g, 8.0 mmol) for 1 h according to the general procedure described above afforded palladacycle **4b** (1.970 g, 98%) as a white solid: mp 216−219 °C dec (ether); $R_f = 0.63$ (EtOAc/hexane 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (dd, $J = 11.9$ Hz, 7.7 Hz, 1 H), 7.50 (t, $J = 8.7$ Hz, 6 H), 7.31−7.28 (m, 9 H), 7.23 (t, $J = 7.3$ Hz, 3 H), 7.16 (t, $J = 7.3$ Hz, 6 H), 7.05 (t, $J = 6.3$ Hz, 6 H), 6.54 (t, $J = 5.8$ Hz, 1 H), 6.06 (t, $J = 7.4$ Hz, 1 H), 5.67 (dd, $J = 10.5$ Hz, 7.6 Hz, 1 H), 4.16−4.08 (m, 1 H), 3.93−3.85 (m, 1 H), 1.01 (t, $J = 7.1$ Hz, 3 H); ^{13}C NMR (100

MHz, $CDCl_3$) δ 175.3, 169.5, 150.5 (dd, $J(^{13}C-^{31}P) = 105.5$ Hz, 10.8 Hz), 144.3 (d, $J(^{13}C-^{31}P) = 8.9$ Hz), 135.3 (d, $J(^{13}C-^{31}P) = 13.0$ Hz), 134.5 (d, $J(^{13}C-^{31}P) = 12.9$ Hz), 133.3, 133.0, 132.8, 132.4, 132.0 (d, $J(^{13}C-^{31}P) = 9.8$ Hz), 131.9 (d, $J(^{13}C-^{31}P) = 2.6$ Hz), 129.9 (d, $J(^{13}C-^{31}P) = 7.6$ Hz), 128.4 (d, $J(^{13}C-^{31}P) = 12.1$ Hz), 128.0 (d, $J(^{13}C-^{31}P) = 9.8$ Hz), 127.8 (d, $J(^{13}C-^{31}P) = 9.6$ Hz), 124.8 (d, $J(^{13}C-^{19}F) = 270.1$ Hz), 122.7 (d, $J(^{13}C-^{31}P) = 4.9$ Hz), 116.8 (dd, $J(^{13}C-^{31}P) = 8.5$ Hz, 3.3 Hz), 111.2 (d, $J(^{13}C-^{31}P) = 33.1$ Hz), 122.7 (d, $J(^{13}C-^{31}P) = 4.9$ Hz), 116.8 (dd, $J(^{13}C-^{31}P) = 8.5$ Hz, 3.3 Hz), 98.2 (dd, $J(^{13}C-^{31}P) = 83.3$ Hz, 5.7 Hz), 59.1, 14.3; ^{31}P NMR (162 MHz, $CDCl_3$) δ 25.2 (d, $J = 29.6$ Hz, 1 P), 29.9 (d, $J = 29.6$ Hz, 1 P); IR (KBr, cm^{-1}) 1680 (w), 1433 (s), 1320 (s), 695 (s); HRMS (FAB) calcd for $C_{47}H_{40}F_3O_3P_2Pd$ (M + H^+) 877.1440, found 877.1476.

(Ethoxycarbonylmethineoxy-3-methoxy-1,2-phenylene)bis(triphenylphosphine)palladium (4c). Treatment of palladacycle **3c** (0.944 g, 2.19 mmol) and PPh_3 (2.010 g, 7.669 mmol) for 2 h according to the procedure described above afforded palladacycle **4c** (1.720 g, 94%) as a white solid: mp 155−158 °C (ether); $R_f = 0.48$ (EtOAc/hexane 3:1); ^1H NMR (400 MHz, $CDCl_3$) δ 7.50 (t, $J = 9.1$ Hz, 6 H), 7.35−7.29 (m, 6 H), 7.27 (d, $J = 5.6$ Hz, 3 H), 7.20 (t, $J = 7.7$ Hz, 3 H), 7.15 (t, $J = 6.4$ Hz, 6 H), 7.04 (t, $J = 7.1$ Hz, 6 H), 6.45 (d, $J = 7.4$ Hz, 1 H), 6.04−5.95 (m, 2 H), 5.49 (dd, $J = 10.9$ Hz, 7.6 Hz, 1 H), 4.19−4.11 (m, 1 H), 3.87−3.80 (m, 1 H), 3.80 (s, 3 H), 1.01 (t, $J = 7.1$ Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.7, 161.9 (d, $J(^{13}C-^{31}P) = 4.1$ Hz), 148.8 (dd, $J(^{13}C-^{31}P) = 104.8$ Hz, 11.1 Hz), 144.2 (d, $J(^{13}C-^{31}P) = 3.9$ Hz), 135.3 (d, $J(^{13}C-^{31}P) = 13.0$ Hz), 134.5 (d, $J(^{13}C-^{31}P) = 12.8$ Hz), 133.7, 133.4, 133.2 (d, $J(^{13}C-^{31}P) = 11.5$ Hz), 132.9, 132.6, 129.7 (dd, $J(^{13}C-^{31}P) = 9.8$ Hz, 1.8 Hz), 127.9 (d, $J(^{13}C-^{31}P) = 9.7$ Hz), 127.7 (d, $J(^{13}C-^{31}P) = 9.6$ Hz), 117.3 (d, $J(^{13}C-^{31}P) = 9.9$ Hz), 108.6, 97.6 (dd, $J(^{13}C-^{31}P) = 83.7$ Hz, 6.2 Hz), 58.9, 55.9, 14.4; ^{31}P NMR (162 MHz, $CDCl_3$) δ 29.3 (d, $J = 28.4$ Hz, 1 P), 25.1 (d, $J = 28.1$ Hz, 1 P); IR (KBr, cm^{-1}) 1711 (s), 1434 (m), 695 (s), 510 (m); HRMS (FAB) calcd for $C_{47}H_{42}O_4P_2Pd$ (M^+) 838.1593, found 838.1584.

(−)-(Ethoxycarbonylmethineoxy-3-methoxy-1,2-phenylene)bis(triphenylphosphine)palladium [(−)-4c]. Treatment of palladacycle (−)- **30c** (50% de) (vide infra) (0.422 g, 0.87 mmol) and PPh_3 (1.826 g, 6.96 mmol) for 31 h according to the procedure described above afforded palladacycle (−)-**4c** (0.521 g, 71%) as a pale yellow solid: mp 152−155 °C (ether); $[\alpha]^{20}_D - 21.9$ (*c* 1.03 CH_2Cl_2).

General Procedure for Synthesis of 2*H*-1−3,4-Dihydrobenzopyrans. To a solution of the oxapalladacycle (0.185 mmol) in THF or 1,2-dichloroethane (5.0 mL) at room temperature under argon was added a solution of the allene (0.555−1.110 mmol) in THF or 1,2-dichloroethane (0.60 mL). Reaction mixtures were heated at the indicated temperature for the indicated time period. The solvent was 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*H*-1−3,4-dihydrobenzopyrans as colorless or yellow oils or solids.

(*E*)-Ethyl (2,3-Dihydro-2-ethoxycarbonyl-4*H*-1-benzopyran-4-ylidene)-acetate (5a). Treatment of oxapalladacycle **4a** (0.150 g, 0.185 mmol) and ethyl 2,3-butadiene (0.083 g, 0.74 mmol) at 75 °C in 1,2-dichloroethane for 24 h according to the procedure described above, eluting with ether/hexane (1:6), afforded benzopyran **5a** (0.050 g, 93%) as a colorless oil that solidified upon standing: mp 30−32 °C (ether/hexanes 1:6); $R_f = 0.50$ (EtOAc/hexane 1:3); ^1H NMR (500 MHz, $CDCl_3$) δ 7.56 (dd, $J = 8.0$ Hz, 1.0 Hz, 1 H), 7.30 (td, $J = 7.7$ Hz, 1.1 Hz, 1 H), 7.00 (d, $J = 8.2$ Hz, 1 H), 6.94 (t, $J = 7.3$ Hz, 1 H), 6.36 (s br, 1 H), 4.77 (dd, $J = 8.7$ Hz, 4.2 Hz, 1 H), 4.35−4.18 (m, 4 H), 3.74 (ddd, $J = 16.5$ Hz, 4.2 Hz, 1.3 Hz, 1 H), 3.53 (ddd, $J = 16.5$ Hz, 8.7 Hz, 1.6 Hz, 1 H), 1.31 (t, $J = 7.1$ Hz, 3 H), 1.26 (t, $J = 7.1$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.6, 166.4, 154.9, 144.9, 132.1, 124.3, 121.6, 120.2, 118.2, 111.5, 73.6, 61.6, 60.0, 28.6, 14.3, 14.1; IR (KBr, cm^{-1}) 1756 (m), 1707 (s), 1481 (m), 1461 (m), 1172 (s), 758 (m); HRMS (ES) calcd for $C_{16}H_{22}NO_5$ (M + NH_4^+) 308.1498, found 308.1514.

(*E*)-Ethyl (2,3-Dihydro-2-ethoxycarbonyl-8-methoxy-4*H*-1-benzopyran-4-ylidene)-acetate (5c). Treatment of oxapalladacycle **4c** (0.155 g, 0.185 mmol) and ethyl 2,3-butadiene (0.083 g, 0.74 mmol) at 75 °C in 1,2-dichloroethane for 24 h according to the procedure described above, eluting with EtOAc/hexane (1:6), afforded benzopyran **5c** (0.056 g, 94%) as a white solid: mp 96−98 °C (EtOAc/hexanes 1:6); $R_f = 0.41$ (EtOAc/hexane 3:1); ^1H NMR (400 MHz, $CDCl_3$) δ 7.14 (dd, $J = 6.3$ Hz, 3.2 Hz, 1 H), 6.94−6.81 (m, 2 H), 6.35 (s br, 1 H), 4.91 (dd, $J = 6.9$ Hz, 4.9 Hz, 1 H), 4.20 (qd, $J = 7.1$ Hz, 2.1 Hz, 4 H), 3.9 (s, 3 H), 3.77 (ddd, $J = 16.4$ Hz, 6.9 Hz, 1.4 Hz, 1 H), 3.53 (ddd, $J = 16.4$ Hz, 4.8 Hz, 1.7 Hz, 1 H), 1.30 (t, $J = 7.1$ Hz, 3 H), 1.21 (t, $J = 7.1$ Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 166.3, 148.9, 144.7, 144.5, 120.9, 120.8, 115.9, 113.2, 112.2, 73.6, 61.5, 60.0, 56.1, 28.1, 14.2, 14.0; IR (KBr, cm^{-1}) 1737 (s), 1701 (s), 1195 (s), 1037 (m), 856 (m), 779 (m); HRMS (FAB) calcd for $C_{17}H_{20}O_6$ (M^+) 320.1260, found 320.1262.

Preparation of (+)-5c. Treatment of oxapalladacycle (−)-**4c** (generated from complex (−)-**30c** with 50% de) (0.155 g, 0.185 mmol) and ethyl 2,3-butadiene (0.083 g, 0.74 mmol) at 75 °C in 1,2-dichloroethane for 24 h according to the procedure described above, eluting with EtOAc/hexane (1:6), afforded benzopyran (+)-**5c** (0.052 g, 88%) as a slightly yellow solid in 46.7% ee (by HPLC): mp 94−96 °C (EtOAc/hexanes 1:6); $[\alpha]^{20}_D$ +18.4 (*c* 1.52 CH_2Cl_2).

(*E*)-3,4-Dihydro-2-ethoxycarbonyl-4-(2-oxopropylidene)-2*H*-1-benzopyran (6) and 2-Ethoxycarbonyl-4-methylcarbonylmethyl-2*H*-1-benzopyran (7). Treatment of oxapalladacycle **4a** (0.150 g, 0.185 mmol) and 3,4-pentadiene-2-one[46] (0.046 g, 0.555 mmol) at 50 °C in THF for 9 h according to the procedure described above, eluting with EtOAc/hexane (1:4), afforded benzopyran **6** (0.033 g, 69%) and benzopyran **7** (0.009 g, 19%) as pure yellow oils that solidified on standing, providing yellow solids.

Analytical data for benzopyran 6: mp 64−66 °C (EtOAc/hexanes 1:4); $R_f = 0.34$ (EtOAc/hexane 1:3); ^1H NMR (500 MHz, $CDCl_3$) δ 7.59 (dd, $J = 8.0$ Hz, 1.2 Hz, 1 H), 7.32 (t, $J = 7.7$ Hz, 1 H), 7.00 (d, $J = 8.0$ Hz, 1 H), 6.96 (t, $J = 7.9$ Hz, 1 H), 6.76 (s br, 1 H), 4.73 (dd, $J = 8.7$ Hz, 4.4 Hz, 1 H), 4.23 (q, $J = 7.1$ Hz, 2 H), 3.68 (ddd, $J = 16.9$ Hz, 4.4 Hz, 1.5 Hz, 1 H), 3.50 (ddd, $J = 16.9$ Hz, 8.6 Hz, 1.7 Hz, 1 H), 2.31 (s, 3 H), 1.24 (t, $J = 14.2$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.2, 169.7, 155.8, 143.2, 132.4, 124.1, 121.6, 120.2, 118.4, 117.9, 73.6, 61.6, 32.3, 28.9, 14.1; IR (KBr, cm^{-1}) 1744 (s), 1677 (s), 1591 (s), 1227 (s), 756 (m); HRMS (ES) calcd for $C_{15}H_{20}NO_4$ (M + NH_4^+) 278.1392, found 278.1390.

Analytical data for benzopyran 7: mp 47−49 °C (EtOAc/hexanes 1:4); $R_f = 0.23$ (EtOAc/hexane 1:3); ^1H NMR (500 MHz, $CDCl_3$) δ 7.18 (t, $J = 7.4$ Hz, 1 H), 7.03 (d, $J = 7.6$ Hz, 1 H), 6.96 (d, $J = 8.1$ Hz, 1 H), 6.90 (t, $J = 7.5$ Hz, 1 H), 5.79 (d, $J = 4.3$ Hz, 1 H), 5.38 (d, $J = 4.3$ Hz, 1 H), 4.27−4.18 (m, 2 H), 3.51 (d, $J = 15.8$ Hz, 1 H), 3.43 (d, $J = 15.8$ Hz, 1 H), 2.16 (s, 3 H), 1.27 (t, $J = 7.1$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.7, 169.4, 152.9, 130.2, 129.7, 123.7, 121.8, 120.9, 119.6, 116.5, 73.2, 61.6, 47.4, 28.8, 14.1; IR (KBr, cm^{-1}) 1741 (s), 1736 (s), 1197 (s), HRMS (ES) calcd for $C_{15}H_{20}NO_4$ (M + NH_4^+) 278.1392, found 278.1366.

***trans*-3,4-Dihydro-2-ethoxycarbonyl-3-methoxy-4-methylene-2*H*-1-benzopyran (8a) and *cis*-3,4-Dihydro-2-ethoxycarbonyl-3-methoxy-4-methylene-2*H*-1-benzopyran (8b) (96:4).** Treatment of oxapalladacycle **4a** (0.150 g, 0.185 mmol) and 1-methoxy-1,2-propadiene[47] (0.078 g, 1.11 mmol) at 50 °C in THF for 54 h in a pressure tube according to the procedure described above, eluting with EtOAc/hexane (1:3),

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[46] For the preparation of 3,4-pentadiene-2-one, see: Constantieux, T.; Buono, G. *Org. Synth.* **2002**, *78*, 135−141.

[47] For the preparation of 1-methoxy-1,2-propadiene, see: Brandsma, L.; Verkruijsse, H. D. *Synthesis of Acetylenes, Allenes and Cumulenes*; Elsevier: New York, 1981.

afforded a chromatographically inseparable mixture of benzopyrans **8a** and **8b** (96:4 by ^{1}H NMR) (0.045 g, 98%) as a yellow oil: R_f = 0.48 (EtOAc/hexane 1:3); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.54 (dd, J = 7.8 Hz, 1.2 Hz, 0.04 H), 7.47 (dd, J = 7.8 Hz, 1.2 Hz, 0.96 H), 7.23 (td, J = 7.6 Hz, 1.5 Hz, 1 H), 7.04 (d, J = 8.2 Hz, 0.04 H), 6.98 (dd, J = 8.2 Hz, J = 0.7 Hz, 0.96 H), 6.93 (td, J = 7.8 Hz, 1.0 Hz, 1 H), 5.76 (s, 0.04 H), 5.69 (s, 0.96 H), 5.18 (s, 0.04 H), 5.12 (s, 0.96 H), 5.07 (d, J = 2.8 Hz, 0.96 H), 4.69 (d, J = 1.5 Hz, 0.04 H), 4.31 (d, J = 1.3 Hz, 0.04 H), 4.24 (d, J = 2.7 Hz, 0.96 H), 4.20−4.11 (m, 2 H), 3.35 (s, 2.88 H), 3.27 (s, 0.12 H), 1.37 (t, J = 7.1 Hz, 0.12 H), 1.18 (t, J = 7.1 Hz, 2.88 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 168.7, 152.1, 133.6, 130.2, (130.0), 125.0, (124.9), (121.6), 121.3, 119.2, (117.6), 116.9, 112.9, (112.4), 77.2, 76.8, (61.7), 61.6, 56.1, (56.0), (14.2), 14.0 (signals for the minor diastereomer are given in parentheses); IR (neat, cm^{-1}) 1756 (s), 1731 (m), 1483 (m), 1457 (m), 1191 (m), 1119 (m), 754 (m); HRMS (ES) calcd for $C_{14}H_{20}NO_4$ (M + NH$_4^+$) 266.1392, found 266.1404.

Preparation of (+)-8a. Treatment of oxapalladacycle (−)-**4a** (generated from complex (−)-**30a** with 64% de) (0.150 g, 0.185 mmol) and 1-methoxy-1,2-propadiene[47] (0.078 g, 1.11 mmol) at 50 °C in THF for 54 h according to the procedure described above, eluting with EtOAc/hexane (1:3), afforded an inseparable mixture of benzopyrans (+)-**8a** and **8b** (96:4 by ^{1}H NMR) (0.043 g, 94%) as a yellow oil in 40.3% ee for (+)-**8a** (by HPLC): $[\alpha]^{20}_D$ +18.3 (*c* 1.25 CH$_2$Cl$_2$).

***trans*-3,4-Dihydro-2-ethoxycarbonyl-3-methoxy-4-methylene-8-trifluoromethyl-2*H*-1-benzopyran (9a) and *cis*-3,4-Dihydro-2-ethoxycarbonyl-3-methoxy-4-methylene-8-trifluoromethyl-2*H*-1-benzopyran (9b) (95:5).** Treatment of oxapalladacycle **4b** (0.162 g, 0.185 mmol) and 1-methoxy-1,2-propadiene[47] (0.078 g, 1.11 mmol) at 50 °C in THF for 94 h in a pressure tube according to the procedure described above, eluting with EtOAc/hexane (1:10), afforded a chromatographically inseparable mixture of benzopyrans **9a** and **9b** (95:5 by ^{1}H NMR) (0.045 g, 77%) as a yellow oil that solidified on standing, providing a yellow solid: mp 50−52 °C (EtOAc/hexane 1:10), R_f = 0.23 (EtOAc/hexane 1:9); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.68 (d, J = 7.9 Hz, 0.05 H), 7.64 (d, J = 7.8 Hz, 0.95 H), 7.52 (d, J = 7.6 Hz, 1 H), 6.98 (t, J = 7.7 Hz, 1 H), 5.77 (s, 0.05 H), 5.73 (s, 0.95 H), 5.28 (s, 0.05 H), 5.20−5.19 (m, 1.95 H), 4.25 (d, J = 2.4 Hz, 1 H), 4.21−4.06 (m, 2 H), 3.35 (s, 2.85 H), 3.28 (s, 0.15 H), 1.35 (t, J = 7.1 Hz, 0.15 H), 1.15 (t, J = 7.1 Hz, 2.85 H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 168.0, (167.4), 150.2, (150.2), 132.6, 128.8, 127.4 (q, J (^{13}C−^{19}F) = 5.1 Hz), 123.4 (q, J (^{13}C−^{19}F) = 271.0 Hz), 120.6, 120.5, 118.3 (q, J (^{13}C−^{19}F) = 31.2 Hz), 114.7, (113.6), 77.4, 76.5, 61.7, (56.3), 56.1, (14.01), 13.9 (signals for the minor diastereomer are given in parentheses); IR (neat, cm^{-1}) 1754 (s), 1453 (m), 1115 (s), 1022 (m); HRMS (ES) calcd for $C_{15}H_{19}NO_4F_3$ (M + NH$_4^+$) 334.1266, found 334.1244.

***cis*-3,4-Dihydro-2-ethoxycarbonyl-3-(1-hexyl)-4-methylene-2*H*-1-benzopyran (10) and (*E*)-3,4-Dihydro-2-ethoxycarbonyl-4-(heptylidene)-2*H*-1-benzopyran (11) (91:9).** Treatment of oxapalladacycle **4a** (0.150 g, 0.185 mmol) and 1,2-nonadiene[48] (0.069 g, 0.555 mmol) at reflux in THF for 10 h according to the procedure described above, eluting with ether/hexane (1:6), afforded a chromatographically inseparable mixture of benzopyrans **10** and **11** (91:9 by ^{1}H NMR) (0.047 g, 84%) as a yellow oil: R_f = 0.65 (EtOAc/hexane 1:3); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.49 (dd, J = 7.9 Hz, 1.3 Hz, 0.09 H), 7.45 (dd, J = 7.8 Hz, 1.5 Hz, 0.91 H), 7.21 (td, J = 7.7 Hz, 1.5 Hz, 0.91 H), 7.14 (td, J = 7.7 Hz, 1.4 Hz, 0.09 H), 6.96 (d, J = 8.3 Hz, 0.09 H), 6.93 (d, J = 8.2 Hz, 0.91 H), 6.91 (t, J = 7.9 Hz, 1 H), 6.09 (t, J = 7.4 Hz, 0.09 H), 5.47 (s, 0.91 H), 4.87 (s, 0.91 H), 4.78 (d, J = 1.7 Hz, 0.91 H), 4.75 (dd, J = 7.4 Hz, 4.4 Hz, 0.09 H), 4.23−4.21 (m, 0.18 H), 4.13 (q, J = 7.1 Hz, 1.82 H), 2.89 (dd, J = 7.6 Hz, 4.3 Hz, 0.18 H), 2.83 (td, J = 7.6 Hz, 1.6 Hz, 0.91 H), 2.19 (qd, J = 7.3 Hz, 2.4 Hz, 0.18 H), 1.61−1.56 (m, 0.91 H), 1.51−1.43 (m, 0.91 H), 1.36 (q, J = 14.2 Hz, 7.2 Hz, 2 H), 1.31−1.25 (m, 6 H), 1.16 (t, J = 7.1 Hz, 3 H), 0.90 (t, J = 6.7 Hz, 0.27 H), 0.86 (t, J = 6.8 Hz, 2.73 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 170.7, (170.4), (152.6), 152.1, 137.7, 129.7, (128.4), (125.7), 124.9, (124.7), (123.4), (122.6), (121.2), 120.9, 120.3, (117.4), 116.6, 109.5, 77.2, (73.9), (61.4), 61.2, 42.8, 31.8, 31.7, (29.7), (29.5), (29.0), 28.9, (27.8), (27.7), 27.1, (22.6), 22.5, (14.2), 14.1, (14.06), 14.02 (signals for the minor regioisomer are given in parentheses); IR (neat, cm^{-1}) 1757 (s), 1733 (m), 1456 (m), 1188 (m), 752 (m); HRMS (ES) calcd for $C_{19}H_{30}NO_3$ (M + NH$_4^+$) 320.2226, found 320.2215.

***cis*-3,4-Dihydro-2-ethoxycarbonyl-3-(1-hexyl)-4-methylene-8-trifluoromethyl-2*H*-1-benzopyran (12).** Treatment of oxapalladacycle **4b** (0.150 g, 0.185 mmol) and 1,2-nonadiene[48] (0.069 g, 0.555 mmol) at 50 °C in THF for 72 h in a pressure tube, according to the procedure described above, eluting with EtOAc/hexane (1:20), afforded benzopyran **12** (0.038 g, 56%) as a yellow oil: R_f = 0.45 (EtOAc/hexane 1:9); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.63 (d, J = 7.3 Hz, 1 H), 7.50 (d, J = 7.7 Hz, 1 H), 6.95 (t, J = 7.7 Hz, 1 H), 5.52 (s, 1 H), 4.96 (s, 1 H), 4.91 (d, J = 1.6 Hz, 1 H), 4.21−4.04 (m, 2 H), 2.87 (ddd, J = 8.3 Hz, 6.1 Hz, 1.5 Hz, 1 H), 1.64−1.57 (m, 1 H), 1.50−1.41 (m, 1 H), 1.37−1.25 (m, 8 H), 1.15 (t, J = 9.1 Hz, 3 H), 0.86 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 169.9, 150.2, 136.6, 128.7, 127.1 (q, J(^{13}C−^{19}F) = 5.1 Hz), 123.5 (q, J (^{13}C−^{19}F) = 271.0 Hz), 121.6, 120.1, 118.2 (q, J (^{13}C−^{19}F) = 31.0 Hz), 111.3, 77.7, 61.3, 42.4, 31.7, 29.7, 28.9, 26.9, 22.5, 14.02, 14.00; IR (neat, cm^{-1}) 1758 (s), 1736 (m), 1451 (s), 1133 (m), 753 (w); HRMS (ES$^+$) calcd for $C_{20}H_{29}NO_3F_3$ (M + NH$_4^+$) 388.2100, found 388.2129.

***cis*-3,4-Dihydro-2-ethoxycarbonyl-3-(1-hexyl)-8-methoxy-4-methylene-2*H*-1-benzopyran (13).** Treatment of oxapalladacycle **4c** (0.155 g, 0.185 mmol) and 1,2-nonadiene[48] (0.069 g, 0.555 mmol) at 50 °C in THF for 19 h according to the procedure described above, eluting with EtOAc/hexane (1:5) and including an additional purification by preparative thin-layer chromatography over silica eluting with EtOAc/hexane (1:10), afforded benzopyran **13** (0.048 g, 78%) as a yellow oil: R_f = 0.48 (EtOAc/hexane 1:3); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.06 (dd, J = 7.3 Hz, 1.9 Hz, 1 H), 6.86−6.80 (m, 2 H), 5.47 (s, 1 H), 4.91 (d, J = 1.6 Hz, 1 H), 4.88 (s, 1 H), 4.17−4.05 (m, 2 H), 3.89 (s, 3 H), 2.81 (ddd, J = 8.2 Hz, 6.4 Hz, 1.4 Hz, 1 H), 1.65−1.58 (m, 1 H), 1.56−1.42 (m, 1 H), 1.37−1.31 (m, 1 H), 1.29−1.23 (m, 7 H), 1.13 (t, J = 7.1 Hz, 3 H), 0.85 (t, J = 6.9 Hz, 3 H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 170.4, 148.1, 141.6, 137.4, 120.9, 120.4, 116.8, 111.3, 110.2, 77.4, 61.1, 56.1,42.7, 31.8, 31.7, 28.9, 27.0, 22.5, 14.07, 14.02; IR (neat, cm^{-1}) 1756 (s), 1731 (m), 1579 (m), 1265 (m), 739 (m); HRMS (ES) calcd for $C_{20}H_{32}NO_4$ (M + NH$_4^+$) 350.2331, found 350.2319.

Preparation of (+)-13. Treatment of oxapalladacycle (−)-**4c** (generated from complex (−)-**30c** with 50% de) (0.155 g, 0.185 mmol) and 1,2-nonadiene[48] (0.069 g, 0.555 mmol) at 50 °C in THF for 19 h according to the procedure described above, eluting with EtOAc/hexane (1:5) and including an additional purification by preparative thin-layer chromatography over silica eluting with EtOAc/hexane (1:10), afforded benzopyran (+)-**13** (0.044 g, 72%) as a yellow oil in 41.0% ee (by HPLC): $[\alpha]^{20}_D$ +6.0 (*c* 1.50 CH$_2$Cl$_2$).

***cis*-3,4-Dihydro-2-ethoxycarbonyl-3-(3-methyl-1-butyl)-4-methylene-2*H*-1-benzopyran (14) and (*E*)-3,4-Dihydro-2-ethoxycarbonyl-4-(4-methylpentylidene)-2*H*-1-benzopyran (15) (92:8).** Treatment of oxapalladacycle **4a** (0.150 g, 0.185 mmol) and 6-methyl-1,2-heptadiene[48] (0.061 g, 0.555 mmol) at 50 °C in THF for 22 h according to the procedure described above, eluting with EtOAc/hexane (1:10), afforded a chromatographically inseparable mixture of benzopyrans **14** and **15** (92:8 by ^{1}H NMR) (0.045 g, 84%) as a yellow oil: R_f = 0.77 (EtOAc/hexane 1:3); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.48 (dd, J = 7.8 Hz, 1.4 Hz, 0.08 H), 7.45 (dd, J = 7.8 Hz, 1.5 Hz, 0.92 H), 7.21 (td, J = 7.8 Hz, 1.5 Hz, 0.92 H), 7.14 (td, J = 7.7 Hz, 1.4 Hz, 0.08 H), 6.96 (dd, J = 8.4 Hz, 0.9 Hz, 0.08 H), 6.93

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[48] For the preparation of alkyl-substituted allenes, see: Moreau, J. L.; Gaudemar, M. *J. Organomet. Chem.* **1976**, *108*, 159−164 and ref 47.

(d, J = 8.3 Hz, 0.92 H), 6.90 (td, J = 7.5 Hz, 1.0 Hz, 1 H), 6.08 (t, J = 7.4 Hz, 0.08 H), 5.47 (s, 0.92 H), 4.87 (s, 0.92 H), 4.79 (d, J = 1.7 Hz, 0.92 H), 4.75 (dd, J = 7.3 Hz, 4.5 Hz, 0.08 H), 4.28−4.20 (m, 0.16 H), 4.13 (qd, J = 7.1 Hz, 1.4 Hz, 1.84 H), 2.89 (t, J = 8.2 Hz, 0.16 H), 2.79 (ddd, J = 8.4 Hz, 6.3 Hz, 1.6 Hz, 0.92 H), 2.19 (ddd, J = 15.1 Hz, 7.4 Hz, 2.6 Hz, 0.16 H), 1.63−1.57 (m, 0.92 H), 1.52−1.43 (m, 1.92 H), 1.37−1.30 (m, 0.08 H), 1.29−1.23 (m, 1.92 H), 1.16 (t, J = 7.1 Hz, 3 H), 0.93 (d, J = 6.6 Hz, 0.48 H), 0.86 (d, J = 6.6 Hz, 2.76 H), 0.84 (d, J = 6.6 Hz, 2.76 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 170.7, (170.4), (152.6), 152.1, 137.7, 129.7, (128.4), (125.5), 124.9, (124.8), (123.4), (122.5), (121.2), 121.0, 120.2, (117.4), 116.6, 109.6, 77.3, (73.9), (61.4), 61.2, 43.1, (38.6), 36.3, 29.7, 27.8, (27.7), (27.6), (25.5), 22.6, 22.5, (22.4), (22.3), (14.1), 14.1 (signals for the minor regioisomer are given in parentheses); IR (neat, cm^{-1}) 1757 (s), 1732 (m), 1481 (m), 1457 (s), 1188 (s), 752 (m); HRMS (ES) calcd for $C_{18}H_{25}O_3$ (M + H$^+$) 289.1804, found 289.1800.

***cis*-3,4-Dihydro-2-ethoxycarbonyl-3-(3-methyl-1-butyl)-4-methylene-8-trifluoromethyl-2*H*-1-benzopyran (16).** Treatment of oxapalladacycle **4b** (0.162 g, 0.185 mmol) and 6-methyl-1,2-heptadiene[48] (0.061 g, 0.555 mmol) at 50 °C in THF for 90 h in a pressure tube according to the procedure described above, eluting with EtOAc/hexane (1:20), afforded benzopyran **16** (0.032 g, 49%) as a yellow oil: R_f = 0.44 (EtOAc/hexane 1:9); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.63 (d, J = 7.8 Hz, 1 H), 7.50 (d, J = 7.6 Hz, 1 H), 6.95 (t, J = 7.6 Hz, 1 H), 5.52 (s, 1 H), 4.95 (s, 1 H), 4.91 (d, J = 1.6 Hz, 1 H), 4.16−4.06 (m, 2 H), 2.83 (ddd, J = 8.4 Hz, 6.2 Hz, 1.48 Hz, 1 H), 1.63−1.60 (m, 1 H), 1.56−1.42 (m, 2 H), 1.27−1.22 (m, 2 H), 1.13 (t, J = 7.1 Hz, 3 H), 0.86 (d, J = 6.6 Hz, 3 H), 0.83 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 169.9, 150.2, 136.6, 128.7, 127.1 (q, $J(^{13}\text{C}-^{19}\text{F})$ = 5.1 Hz), 123.5 (q, $J(^{13}\text{C}-^{19}\text{F})$ = 270.9 Hz), 121.6, 120.1, 118.2 (q, $J(^{13}\text{C}-^{19}\text{F})$ = 31.0 Hz), 111.3, 77.7, 61.3, 42.6, 36.2, 29.5, 27.7, 22.5, 22.4,14.2; IR (neat, cm^{-1}) 1757 (s), 1739 (m), 1451 (s), 1133 (m), 1099 (m), 753 (m); HRMS (ES) calcd for $C_{19}H_{27}NO_3F_3$ (M + NH$_4^+$) 374.1943, found 374.1945.

***cis*-3,4-Dihydro-2-ethoxycarbonyl-3-(3-methyl-1-butyl)-8-methoxy-4-methylene-2*H*-1-benzopyran (17).** Treatment of oxapalladacycle **4c** (0.155 g, 0.185 mmol) and 6-methyl-1,2-heptadiene[48] (0.061 g, 0.555 mmol) at 50 °C in THF for 19 h according to the procedure described above, eluting with EtOAc/hexane (1:10) and including an additional purification by preparative thin-layer chromatography over silica eluting with EtOAc/hexane (1:10), afforded benzopyran **17** (0.042 g, 72%) as a yellow oil: R_f = 0.50 (EtOAc/hexane 1:3); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.07 (dd, J = 7.4 Hz, 2.0 Hz, 1 H), 6.86−6.80 (m, 2 H), 5.47 (s, 1 H), 4.92 (d, J = 1.7 Hz, 1 H), 4.88 (s, 1 H), 4.17−4.05 (m, 2 H), 3.89 (s, 3 H), 2.78 (ddd, J = 8.3 Hz, 6.3 Hz, 1.6 Hz, 1 H), 1.65−1.58 (m, 1 H), 1.53−1.43 (m, 2 H), 1.30−1.20 (m, 2 H), 1.13 (t, J = 7.1 Hz, 3 H), 0.85 (d, J = 6.6 Hz, 3 H), 0.82 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 170.4, 148.1, 141.7, 137.5, 120.9, 120.4, 116.8, 111.4, 110.3, 77.5, 61.2, 56.1, 43.0, 36.3, 29.8, 27.8, 22.6, 22.5, 14.1; IR (neat, cm^{-1}) 1756 (s), 1731 (m), 1481 (m), 1461 (m), 1265 (s), 739 (w); HRMS (ES) calcd for $C_{19}H_{30}NO_4$ (M + NH$_4^+$) 336.2175, found 336.2161.

***cis*-3,4-Dihydro-2-ethoxycarbonyl-3-(2-ethyl-1-hexyl)-4-methylene-2*H*-1-benzopyran (18) and (*E*)-3,4-Dihydro-2-ethoxycarbonyl-4-(3-ethylheptylidene)-2*H*-1-benzopyran (19) (90:10).** Treatment of oxapalladacycle **4a** (0.150 g, 0.185 mmol) and 5-ethyl-1,2-nonadiene[48] (0.084 g, 0.555 mmol) at 50 °C in THF for 20 h according to the procedure described above, eluting with EtOAc/hexane (1: 10), afforded a chromatographically inseparable mixture of benzopyrans **18** and **19** (90:10 by ^{1}H NMR) (0.039 g, 64%) as a yellow oil: R_f = 0.70 (EtOAc/hexane 1:3); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.49 (d, J = 7.9 Hz, 0.1 H), 7.43 (d, J = 7.8 Hz, 0.9 H), 7.20 (td, J = 7.6 Hz, 1.4 Hz, 0.9 H), 7.14 (t, J = 7.13 Hz, 0.1 H), 6.96 (d, J = 8.3 Hz, 0.1 H), 6.93 (d, J = 8.2 Hz, 0.9 H), 6.90 (t, J = 7.6 Hz, 1 H), 6.11 (t, J = 7.5 Hz, 0.1 H), 5.45 (s, 0.9 H), 4.87 (s, 0.9 H), 4.74 (s br, 0.9 H), 4.73 (t, J = 4.2 Hz, 0.1 H), 4.29−4.20 (m, 0.2 H), 4.13 (q, J = 7.1 Hz, 1.8 H), 2.94 (t, J = 7.6 Hz, 0.9 H), 2.84 (dd, J = 14.8 Hz, 7.8 Hz, 0.2 H), 2.21−2.13 (m, 0.2 H), 1.64−1.44 (m, 1.8 H), 1.43−1.26 (m, 5 H), 1.22−1.12 (m, 4 H), 1.16 (t, J = 7.1 Hz, 3 H), 0.90 (t, J = 6.7 Hz, 2 H), 0.85 (t, J = 7.3 Hz, 1 H), 0.82 (t, J = 7.3 Hz, 2 H), 0.74 (t, J = 7.4 Hz, 1 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 170.77 [170.74], (170.4), (152.6), 152.13 [152.12], 138.26 [138.19], 129.74, (128.4), (126.34 [126.31]), 124.99 [124.97], (123.6 [123.5]), (123.5), (122.6), (121.2), 120.9, 120.4, (117.4), 116.59 [116.57], 109.4 [109.4], 77.5 [77.4], (74.0), (61.4), 61.2, 40.54 [40.51], (39.9 [39.8]), 35.9 [35.8], 35.7 [35.6], (32.8 [32.8]), 32.5 [32.4], (31.5 [31.4]), (29.7), (29.2), (29.0), 28.6 [28.4], (27.9), (26.1 [25.9]), 25.7 [25.6], 23.1, 22.8, 14.1, (14.0), (11.1 [11.0]), 10.5 [10.3] (signals for the minor regioisomer are given in parentheses, and signals for a presumed conformational isomer, arising as a result of a hindered rotation are given in brackets); IR (neat, cm^{-1}) 1758 (m), 1733 (m), 1481 (m), 1457 (s), 1186 (m), 751 (s); HRMS (ES) calcd for $C_{21}H_{31}O_3$ (M + H$^+$) 331.2273, found 331.2299.

***cis*-3,4-Dihydro-2-ethoxycarbonyl-3-(2-ethyl-1-hexyl)-4-methylene-8-trifluoromethyl-2*H*-1-benzopyran (20).** Treatment of oxapalladacycle **4b** (0.162 g, 0.185 mmol) and 5-ethyl-1,2-nonadiene[48] (0.084 g, 0.555 mmol) at 50 °C in THF for 90 h in a pressure tube according to the procedure described above, eluting with EtOAc/hexane (1:20), afforded benzopyran **20** (0.038 g, 52%) as a yellow oil: R_f = 0.52 (EtOAc/hexane 1:9); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.61 (d, J = 7.8 Hz, 1 H), 7.50 (d, J = 7.6 Hz, 1 H), 6.95 (t, J = 7.8 Hz, 1 H), 5.50 (s, 1 H), 4.96 (s, 1 H), 4.88 (t, J = 1.7 Hz, 1 H), 4.19−4.05 (m, 2 H), 2.97 (td, J = 7.7 Hz, 1.5 Hz, 1 H), 1.51−1.47 (m, 1 H), 1.41−1.19 (m, 8 H), 1.14 (td, J = 7.1 Hz, 0.8 Hz, 3 H), 0.91−0.85 (m, 3 H), 0.82 (t, J = 7.3 Hz, 3 H), 0.74 (t, J = 7.2 Hz, 2 H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 170.1, (170.0), 150.2, 137.2, (137.1), 128.8, 127.1 (q, $J(^{13}\text{C}-^{19}\text{F})$ = 4.8 Hz), 123.5 (q, $J(^{13}\text{C}-^{19}\text{F})$ = 270.9 Hz), 121.8, 120.1, 118.3, (117.9), 111.2, (111.1), 77.8, (77.6), 61.4, 40.1, 35.9, (35.8), 35.5, (35.4), 32.7, (32.5), 28.6, (28.5), 25.9, (25.5), 23.0, (22.8), 14.1, (14.05), 14.02, 10.51, (10.47) (signals for a presumed conformational isomer, arising as a result of a hindered rotation, are given in parentheses); IR (neat, cm^{-1}) 1758 (s), 1736 (m), 1451 (m), 1370 (m), 1299 (s), 752 (m); HRMS (ES) calcd for $C_{22}H_{33}NO_3F_5$ (M + NH$_4^+$) 416.2413, found 416.2423.

***cis*-3,4-Dihydro-2-ethoxycarbonyl-3-(2-ethyl-1-hexyl)-8-methoxy-4-methylene-2*H*-1-benzopyran (21) and (*E*)-3,4-Dihydro-2-ethoxycarbonyl-4-(3-ethylheptylidene)-8-methoxy-2*H*-1-benzopyran.** Treatment of oxapalladacycle **4c** (0.155 g, 0.185 mmol) and 5-ethyl-1,2-nonadiene[48] (0.084 g, 0.555 mmol) at 50 °C in THF for 19 h according to the procedure described above, eluting with EtOAc/hexane (1:6) and including an additional purification by preparative thin-layer chromatography over silica eluting with EtOAc/hexane (1:5), afforded benzopyran **21** (0.054 g, 81%) as a yellow oil, and a minor product, (*E*)-3,4-dihydro-2-ethoxycarbonyl-4-(3-ethylheptylidene)-8-methoxy-2*H*-1-benzopyran (0.005 g, 7%), as a yellow oil.

Analytical data for benzopyran 21: R_f = 0.52 (EtOAc/hexane 1:3); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.05 (ddd, J = 7.0 Hz, 2.3 Hz, 1.2 Hz, 1 H), 6.87−6.74 (m, 2 H), 5.45 (s, 1 H), 4.88 (s, 1 H), 4.86 (s br, 1 H), 4.20−4.05 (m, 2 H), 3.89 (s, 3 H), 2.92 (ddd, J = 8.3 Hz, 6.8 Hz, 1.5 Hz, 1 H), 1.48−1.42 (m, 1 H), 1.35−1.04 (m, 9 H), 1.14 (td, J = 7.1 Hz, 0.7 Hz, 3 H), 0.90−0.84 (m, 4 H), 0.80 (t, J = 7.3 Hz, 1 H), 0.71 (t, J = 7.3 Hz, 2 H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 170.5, (170.4), 148.1, (148.0), 141.6, (141.6), 137.9, (137.8), 121.0, 120.4, 116.93, (116.90), 111.4, 110.2, (110.1), 77.8, (77.7) 61.2, 56.1, 44.4, (44.3), 35.75, (35.73), 35.68, (35.60), 32.3, 28.5, (28.3), 25.4, (25.4), 23.1, (23.8), (14.13), 14.10, 14.0, 10.5, (10.2) (signals for a presumed conformational isomer, arising as a result of a hindered rotation, are given in parentheses); IR (neat, cm^{-1}) 1757 (s), 1732 (m), 1481 (s), 1480 (s); HRMS (ES) calcd for $C_{22}H_{36}NO_4$ (M + NH$_4^+$) 378.2644, found 378.2622.

Analytical data for (*E*)-3,4-dihydro-2-ethoxycarbonyl-4-(3-ethylheptylidene)-8-methoxy-2*H*-1-benzopyran: R_f = 0.48 (EtOAc/hexane 1:3); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.10 (dd, J = 8.1 Hz, 1,3 Hz, 1 H), 6.84 (t, J = 7.9 Hz, 1 H), 6.76 (dd, J = 8.0 Hz, 1.3 Hz, 1 H), 6.10 (t, J = 7.5 Hz, 1 H), 4.89 (dd, J = 6.3 Hz, 4.6 Hz, 1 H), 4.30−4.06 (m, 2 H), 3.88 (s, 3 H), 2.95 (dd, J = 14.6 Hz, 5.9 Hz, 1 H), 2.85 (dd, J = 14.9 Hz, 3.4 Hz, 1 H), 2.21−2.01 (m, 2 H), 1.42−1.22 (m, 9 H), 1.23 (t, J = 7.1 Hz, 3 H), 0.90−0.86 (m, 6 H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 170.2, 148.7, 142.0, 125.9, (125.8), 124.5, (124.4), 123.4, 120.4, 115.5, 110.2, 74.1, 61.4, 56.0, 39.9, (39.8), 32.9, (32.8), 31.5, (31.4), 29.2, (28.9), 27.5, 26.1, (25.9), 23.1, (23.0), 14.1, 11.1, 10.9 (signals for a presumed conformational isomer, arising as a result of a hindered rotation, are given in parentheses).

***cis*-3,4-Dihydro-2-ethoxycarbonyl-3-(2-methyl-2-phenyl-1-propyl)-4-methylene-2*H*-1-benzopyran (22) and (*E*)-3,4-Dihydro-2-ethoxycarbonyl-4-(3-methyl-3-phenylbutylidene)-2*H*-1-benzopyran (23).** Treatment of oxapalladacycle **4a** (0.150 g, 0.185 mmol) and 5-methyl-5-phenyl-1,2-hexadiene[48] (0.096 g, 0.555 mmol) at 50 °C in THF for 20 h according to the procedure described above, eluting with EtOAc/hexane (1:30), afforded benzopyran **22** (0.029 g, 45%) and benzopyran **23** (0.015 g, 23%), both as colorless oils.

Analytical data for benzopyran 22: R_f = 0.41 (EtOAc/hexane 1:9); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.35−7.31 (m, 3 H), 7.30−7.27 (m, 2 H), 7.21−7.18 (m, 2 H), 6.90 (dd, J = 8.2 Hz, 0.9 Hz, 1 H), 6.87 (t, J = 7.0 Hz, 1.1 Hz, 1 H), 5.18 (s, 1 H), 4.47 (s, 1 H), 4.34 (d, J = 1.8 Hz, 1 H), 4.02 (q, J = 7.1 Hz, 2 H), 2.78 (td, J = 5.6 Hz, 1.8 Hz, 1 H), 2.06 (dd, J = 14.4 Hz, 6.0 Hz, 1 H), 1.74 (dd, J = 14.4 Hz, 5.5 Hz, 1 H), 1.38 (s, 3 H), 1.37 (s, 3 H), 1.1 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 170.3, 152.3, 147.9, 139.1, 129.7, 128.1 (2 carbons), 126.1 (2 carbons), 125.8, 125.2, 120.9, 120.7, 116.5, 109.1, 78.1, 61.0, 45.8, 39.3, 38.2, 29.6, 28.8. 14.0; IR (neat, cm^{-1}) 1755 (s), 1732 (m), 1456 (m), 1189 (s), 764 (m), 752 (m), 700 (m); HRMS (ES) calcd for C$_{23}$H$_{30}$NO$_3$ (M + NH$_4^+$) 368.2226, found 368.2241.

Analytical data for benzopyran 23: R_f = 0.36 (EtOAc/hexane 1:9); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.38−7.36 (m, 2 H), 7.33−7.29 (m, 3 H), 7.20 (t, J = 6.5 Hz, 1 H), 7.11 (td, J = 7.6 Hz, 1.4 Hz, 1 H), 6.93 (dd, J = 8.1 Hz, 0.9 Hz, 1 H), 6.84 (td, J = 7.4 Hz, 1.1 Hz, 1 H), 5.90 (t, J = 7.6 Hz, 1 H), 4.60 (dd, J = 8.1 Hz, 4.0 Hz, 1 H), 4.28−4.25 (m, 2 H), 2.80 (dd, J = 14.9 Hz, 3.1 Hz, 1 H), 2.72 (dd, J = 14.3 Hz, 8.1 Hz, 1 H), 2.55 (dd, J = 14.5 Hz, 8.0 Hz, 1 H), 2.45 (dd, J = 14.5 Hz, 7.3 Hz, 1 H), 1.38 (s, 3 H), 1.37 (s, 3 H), 1.28 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 170.4, 152.6, 148.7, 128.6, 128.1 (2 carbons), 127.4, 125.8 (2 carbons), 125.7, 123.5, 122.4, 121.2, 121.1, 117.4, 73.9, 61.4, 42.2, 38.7, 28.9, 28.4, 27.9, 14.2; IR (neat, cm^{-1}) 1757 (s), 1734 (m), 1481 (m), 1458 (s), 1186 (s), 753 (m), 699 (m); HRMS (ES) calcd for C$_{23}$H$_{30}$NO$_3$ (M + NH$_4^+$) 368.2226, found 368.2204.

(*E*)-3,4-Dihydro-2-ethoxycarbonyl-4-(cyclohexylmethylene)-2*H*-1-benzopyran (25) and *cis*-3,4-Dihydro-2-ethoxycarbonyl-3-(cyclohexyl)-4-methylene-2*H*-1-benzopyran (24) (78:22). Treatment of oxapalladacycle **4a** (0.150 g, 0.185 mmol) and 1-cyclohexyl-1,2-propadiene[48] (0.068 g, 0.555 mmol) at 50 °C in THF for 18 h according to the procedure described above, eluting with EtOAc/hexane (1:10), afforded a chromatographically inseparable mixture of benzopyrans **25** and **24** (78:22 by ^{1}H NMR) (0.040 g, 72%) as a colorless oil: R_f = 0.69 (EtOAc/hexane 1:3); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.47 (dd, J = 7.9 Hz, 1.3 Hz, 0.78 H), 7.41 (dd, J = 7.7 Hz, 1.4 Hz, 0.22 H), 7.20 (td, J = 7.6 Hz, 1.5 Hz, 0.22 H), 7.13 (td, J = 7.6 Hz, 1.5 Hz, 0.78 H), 6.95 (dd, J = 8.2 Hz, 0.9 Hz, 1 H), 6.92−6.88 (m, 1 H), 5.92 (d, J = 9.3 Hz, 0.78 H), 5.47 (s, 0.22 H), 5.03 (d, J = 1.5 Hz, 0.22 H), 4.81 (s, 0.22 H), 4.76 (t, J = 5.8 Hz, 0.78 H), 4.29−4.17 (m, 1.56 H), 4.15−4.04 (m, 0.44 H), 2.91 (dd, J = 5.8 Hz, 1.4 Hz, 1.56 H), 2.48 (dd, J = 10.0 Hz, 1.2 Hz, 0.22 H), 2.40−2.31(m, 0.78 H), 2.04−1.94 (m, 0.22 H), 1.76−1.61 (m, 4 H), 1.41−1.23 (m, 4 H), 1.27 (t, J = 7.1 Hz, 2.34 H), 1.22−1.06 (m, 1.78 H), 1.55 (t, J = 7.1 Hz, 0.66 H), 0.88 (qd, J = 12.4 Hz, 3.1 Hz, 0.22 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ (171.3), 170.5, 152.7, (152.6), (136.8), 130.5, (129.7), 128.5, (124.9), 123.9, 123.5, (122.6), 121.1, (120.97), 120.91, 117.4, (116.5), (110.8), (74.6), 74.0, 61.3, (61.2), (48.8), 36.7, (35.9), 33.1, 33.0, (31.2), (30.7), 27.9, (26.3), (26.1), (26.0), 25.9, 25.8 (2 carbons), 14.1 (signals for the minor regioisomer are given in parentheses); IR (neat, cm^{-1}) 1758 (s), 1734 (m), 1481 (m), 1457 (s), 1183 (s), 752 (m); HRMS (ES) calcd for C$_{19}$H$_{28}$NO$_3$ (M + NH$_4^+$) 318.2069, found 318.2068.

3,4-Dihydro-2-ethoxycarbonyl-3,3-dimethyl-4-methylene-2*H*-1-benzopyran (26), 3,4-Dihydro-2-ethoxycarbonyl-4-(2-propylidene)-2*H*-1-benzopyran (27), and 1-Ethoxycarbonylmethoxy-2-(3-methyl-1,3-butadiene-2-yl)benzene (28). Treatment of oxapalladacycle **4a** (0.150 g, 0.185 mmol) and 3-methyl-1,2-propadiene[48] (0.063 g, 0.925 mmol) at 50 °C in THF for 39 h in a pressure tube according to the procedure described above, eluting with EtOAc/hexane (1:30) afforded pure benzopyran **26** (0.015 g, 33%) as a yellow oil, and a chromatographically inseparable mixture of benzopyran **27** and diene **28** (28:72 by ^{1}H NMR) (0.017 g, 37%) as a colorless oil.

Analytical data for benzopyran 26: R_f = 0.48 (EtOAc/hexane 1:9); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.51 (d, J = 7.8 Hz, 1 H), 7.21 (td, J = 8.1 Hz, 1.6 Hz, 1 H), 6.95−6.89 (m, 2 H), 5.52 (s, 1 H), 5.06 (s, 1 H), 4.41 (s, 1 H), 4.26−4.14 (m, 2 H), 1.27 (s, 3 H), 1.25 (t, J = 7.1 Hz, 3 H), 1.24 (s, 3 H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 169.4, 152.1, 144.9, 129.4, 124.8, 121.1, 120.9, 116.8, 105.0, 82.3, 60.9, 36.1, 26.1, 22.1, 13.6; IR (neat, cm^{-1}) 1751 (s), 1733 (m), 1482 (s), 1455 (s), 752 (m), 764 (m); HRMS (ES) calcd for C$_{15}$H$_{19}$O$_3$ (M + H$^+$) 247.1334, found 247.1327.

Analytical data for the mixture of products 27 and 28 (28:72): R_f = 0.39 (EtOAc/hexane 1:9); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.27−7.22 (m, 1 H), 7.13 (dd, J = 7.4 Hz, 1.8 Hz, 0.72 H), 7.15−7.12 (m, 0.28 H), 6.98 (td, J = 7.4 Hz, 0.9 Hz, 0.72 H), 6.94 (dd, J = 8.2 Hz, 1.0 Hz, 0.28 H), 6.88 (td, J = 7.6 Hz, 1.2 Hz, 0.28 H), 6.78 (d, J = 8.2 Hz, 0.72 H), 5.46 (d, J = 0.5 Hz, 0.72 H), 5.13 (s br, 0.72 H), 5.01 (s br, 0.72 H), 4.89 (t, J = 4.8 Hz, 0.28 H), 4.67 (s br, 0.72 H), 4.57 (s, 1.44 H), 4.27−4.20 (m, 0.28 H), 4.22 (q, J = 7.1 Hz, 2.8 Hz, 1.44 H), 4.18−4.13 (m, 0.28 H), 3.00 (dd, J = 13.6 Hz, 5.6 Hz, 0.28 H), 2.72 (dd, J = 13.6 Hz, 4.4 Hz, 0.28 H), 2.04 (s, 2.16 H), 2.02 (s, 0.84 H), 1.85 (s, 0.84 H), 1.26 (t, J = 7.1 Hz, 2.16 H), 1.24 (t, J = 7.1 Hz, 0.84 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ (170.8), 169.1, 155.2, (152.9), 147.2, 142.8, (131.8), 131.2, (129.0), (128.9), 128.4, (128.0), (123.8), 121.5, (121.3), 119.7, (116.5), 115.9, 115.2, 112.5, (75.0), 66.1, (61.2), 61.1, (29.2), (22.6), (21.4), 20.4, (14.2), 14.1; IR (neat, cm^{-1}) 1759 (s), 1734 (m),1490 (m), 1450 (m), 1190 (s), 895 (m), 752 (m); HRMS (ES) calcd for C$_{15}$H$_{19}$O$_3$ (M + H$^+$) 247.1334, found 247.1334.

(+)-[2-(Ethoxycarbonylmethoxy)-3-methoxyphenyl]-iodo [(1*R*,2*R*)-*N*,*N*,*N*′,*N*′-Tetramethyl-1,2-diaminocyclohexane]palladium [(+)-29c]. To a solution of Pd$_2$dba$_3$ (1.831 g, 2.00 mmol) and (1*R*,2*R*)-*N*,*N*,*N*′,*N*′-tetramethyl-1,2-diaminocyclohexane (TMDACH)[49] (0.817 g, 4.800 mmol) in benzene (60 mL) at room temperature under argon was added a solution of aryl iodide **1c** (1.479 g, 4.4 mmol) in benzene (5 mL). The mixture was stirred at 55 °C for 30 min. The suspension was filtered through a plug of Celite, and solvents were removed under reduced pressure to afford a crude product. The crude product was purified by flash chromatography over silica, eluting with EtOAc/hexane (1:10) to remove excess dibenzylideneacetone (dba), and subsequently with EtOAc/hexane (1:1) to afford palladium(II) complex (+)-**29c** (2.007 g, 82%) as a yellow solid: mp 92−95 °C (EtOAc/hexane 1:1); R_f = 0.43 (EtOAc/hexane 1:1); $[\alpha]^{20}_{D}$ +18.7 (*c* 0.77 CH$_2$Cl$_2$); ^{1}H NMR (400 MHz, CDCl$_3$) δ 6.86 (ddd, J = 7.6 Hz, 4.7

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(49) For the preparation of TMDACH from diaminocyclohexane, see: Remenar, J. F.; Brett, B. L.; Column, D. V. *J. Am. Chem. Soc.* **1997**, *119*, 5567−5572.

Hz, 1.2 Hz, 1 H), 6.73 (td, $J = 7.8$ Hz, 1.6 Hz, 1 H), 6.45 (t, $J = 8.1$ Hz, 1 H), 5.21 (d, $J = 15.8$ Hz, 0.5 H), 5.04 (d, $J = 15.7$ Hz, 0.5 H), 4.71 (dd, $J = 15.8$ Hz, 2.4 Hz, 1 H), 4.31−4.03 (m, 2 H), 3.76 (s, 1.5 H), 3.75 (s, 1.5 H), 2.95 (td, $J = 11.3$ Hz, 3.6 Hz, 1 H), 2.87 (s, 3 H), 2.77−2.64 (m, 1 H), 2.69 (s, 1 H), 2.61 (s, 2 H), 2.59 (s, 1 H), 2.53 (s, 2 H), 2.47 (s, 2 H), 2.33 (s, 1 H), 2.08−2.01 (m, 2 H), 1.78−1.65 (m, 2 H), 1.37−1.24 (m, 2 H), 1.30 (t, $J = 7.1$ Hz, 3 H), 1.21−1.03 (m, 2 H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 171.0, (170.9), 151.7, (151.5), 148.3, (147.9), 137.8, (137.2), 131.3, (131.0), 122.9, (122.6), 106.8, (106.4), 70.3, (69.6), 67.6, (67.3), 66.9, (66.3), 60.3, 54.9, (54.8), 49.8, (49.9), 48.9, (48.1), 42.6, (41.7), 41.5, (41.1), 24.7, 24.6, 23.3, 23.2, (23.1), 14.3 (signals for a conformational isomer arising due to a hindered rotation about the aryl-palladium bond[5a] are given in parentheses); IR (KBr, cm^{-1}) 1751 (s), 1458 (s), 1195 (s), 840 (m), 767 (m); HRMS (ES) calcd for $C_{21}H_{36}N_2O_4IPd$ (M + H$^+$) 613.0755, found 613.0732.

(−)-[(Ethoxycarbonylmethineoxy-3-methoxy-1,2-phenylene)][(1*R*,2*R*)-(*N*,*N*,*N*′,*N*′-tetramethyl-1,2-diaminocyclohexane)]palladium [(−)-30c]. To a suspension of palladium(II) complex (+)-**29c** (0.613 g, 1.00 mmol) in THF (40 mL) under argon at room temperature was added *t*-BuOK (1.0 M solution in THF, 1.80 mL, 1.80 mmol). The reaction mixture was stirred for 4 h at room temperature. The suspension was filtered though a plug of Celite and basic alumina, eluting with EtOAc, and solvents were removed under reduced pressure to afford palladacycle (−)-**30c** (0.305 g, 63%) as a pale yellow solid in 50% de (ratio of diastereomeric palladacycles 75:25 was established by ^{1}H NMR): mp 143−145 °C (EtOAc); $R_f = 0.13$ (EtOAc/hexane 1:1); $[\alpha]^{20}_{D}$ −111.4 (c 0.42 CH$_2$Cl$_2$); ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.71 (dd, $J = 6.9$ Hz, 1.9 Hz, 1 H), 6.64−6.56 (m, 2 H), 5.75 (s, 0.75 H), 5.35 (s, 0.25 H), 4.13−4.05 (m, 1.5 H), 3.98 (q, $J = 2.7$ Hz, 0.5 H), 3.81 (s, 3 H), 2.95 (s, 2.25 H), 2.87 (s, 2.25 H), 2.79 (s, 0.75 H), 2.77 (s, 0.75 H), 2.76 (s, 0.75 H), 2,71 (s, 0.75 H), 2.64 (s, 2.25 H), 2.50 (s, 2.25 H), 2.24−2.07 (m, 2 H), 1.83−1.77 (m, 4 H), 1.73−1.72 (m, 2 H), 1.4−1.20 (m, 2 H), 1.16 (t, $J = 7.1$ Hz, 3 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 178.1, (177.8), 162.3, (161.0), (143.8), 143.7, (139.9), 138.6, 125.9, (125.9), 117.9, (117.3), 109.5, (109.0), 88.2, (87.6), (68.6), 68.5, (67.4), 67.3, 59.4, (59.0), 56.2, (56.0), 48.7, 48.6, (48.5), 47.7, 42.7, (41.7), (41.0), 38.2, 25.6, (25.0), 24.5, (23.5), (22.8), 21.6, 14.4, (14.1) (signals for the minor diastereomer are given in parentheses); IR (KBr, cm^{-1}) 1710 (s), 1458 (m), 1431 (m), 1145 (m), 844 (m), 594 (m); HRMS (FAB) calcd for $C_{21}H_{35}N_2O_4Pd$ (M + H$^+$) 485.1632, found 485.1628.

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Supporting Information Available: Description of experimental procedures; analytical methods for determination of the enantiomeric excess of benzopyrans (+)-**8a**, (+)-**13**, and (+)-**5c**, including chiral phase HPLC chromatograms; detailed descriptions of the structure elucidation of benzopyrans **8a**, **10**, and **11** via HMBC 2D NMR analyses and NOE ^{1}H NMR experiments; ^{1}H and ^{13}C NMR spectra for all new compounds prepared in this study, and NOE ^{1}H NMR experiments for compounds **5a**−**c**, **6**, and **8**−**25**. This material is available free of charge via the Internet at http://pubs.acs.org.

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