Synthesis and Catalytic Properties of Configurationally Stable and Non-racemic Sulfur-Containing Palladacycles

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Racemic sulfur chloro-bridged palladacycles (*rac*-**4b**−**6b**), derived from the orthopalladation of (1-*tert*-butylsulfanylethyl)benzene, (1-methylsulfanylethyl)benzene, and 2-(1-*tert*-butylsulfanylethyl)naphthalene (*rac*-**1**−**3**), have been synthesized in good yields using palladium acetate as the metalation agent and followed by reaction with LiCl. Palladacycles *rac*-**4b** and *rac*-**6b** have been isolated as single isomers, whereas *rac*-**5b** has been obtained as a mixture of two diastereoisomers (3:1). Variable-temperature ^{1}H NMR showed that the S-*t*-Bu palladacycle **4b** is configurationally stable over a large range of temperatures (from −20 to 100 °C). On the other hand, S-Me analogue **5b** undergoes facile sulfur pyramidal inversion with an energy barrier of 18 kcal/mol. Moreover, the optically active (1-alkylsufanylethyl)benzenes, (*R*)-**1** and (*R*)-**2**, respectively, have been prepared in 91% and 97% ee, respectively, from the reaction of sodium methylthiolate and sodium *tert*-butylthiolate, respectively, with non-racemic (*S*)-(−)-1-phenylethanol (93−99% ee). The reaction of (1-alkylsufanylethyl)benzenes (*R*)-**1** and (*R*)-**2** with palladium acetate in acetic acid at 90 °C affords the corresponding orthopalladated compound (*R*,*R*)-**4a** and *(R*,*R* and *R*,*S*)-**5a**, respectively. The molecular structure of the acetato-bridged dimer (*R*,*R*)-**4a** has been determined by means of an X-ray diffraction analysis. The palladacycle (*R*,*R*)-**4b** has shown to be excellent catalyst precursor, in terms of catalytic activity, for the arylation of 3,4-dihydro-2*H*-pyrane under mild reaction conditions, however without any asymmetric induction.

Introduction

Palladacycles are one of the most important and investigated classes of organometallic compounds. The facility of preparation and versatility for modification of their steric and electronic properties (by simply changing the metalated carbon, donor atom, size of the ring, etc.) combined with their usually high air and thermal stability infer to this class of compounds a variety of applications in a plethora of areas. For example, these compounds have been successfully used in organic synthesis,[1−3] new materials,[4−6] bio-organometallic chemistry,[7] and organometallic catalysis.[8] Among these applications, their use as catalyst precursors in C−C bond formation reactions has recently attracted great interest. In fact, phosphorus- and nitrogen-containing palladacycles are among the most active catalyst precursors to promote the Heck and Suzuki coupling reactions reported do date.[9] In this respect, some of us have recently communicated that sulfur-containing palladacycles, mainly those derived from the orthopalladation of benzylic thioethers, are also exceptional catalyst precursors to promote such C−C bond forming reactions.[10] One interesting aspect of this family of palladacycles is the creation of a stereogenic center

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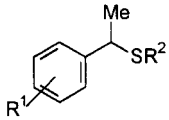
at the sulfur atom during their formation (upon coordination to the metal center). However, in most of the cases this sulfur-stereogenic center is not configurationally stable, undergoing relatively facile pyramidal inversion.[11] It is, however, reasonable to assume that by changing the electronic and steric properties of the sulfur substituents, and using nonracemic thioethers, it will be possible to prepare optically active and configurationally stable sulfur-containing palladacycles. Moreover, the availability of such compounds will make possible the investigation of their properties as catalyst precursors in asymmetric reactions such as the Heck arylation of olefin substrates. We report herein that, indeed, non-racemic and configurationally stable sulfur-containing palladacycles can be prepared from optically active (1-alkylsufanylethyl)benzenes and that these palladacycles promote the arylation of cyclic unsaturated ethers.

Results and Discussion

Synthesis of the Racemic Thioethers. The racemic thioethers **1**−**3** have been prepared in good yields using two different routes. The first involves the simple reaction of the 1-phenylethanol or 1-naphthalen-2-ylethanol with the corresponding thiols in dichloromethane and in the presence of zinc iodide[12] (eq 1). In the second route the hydroxyl group of 1-phenylethanol or 1-naphthyl-2-ethanol was converted into the mesitylates by treatment with mesityl chloride at low temperature and immediately treated with the thiolate salts (eq 1). The racemic thioethers **1**−**3**, thus obtained, were easily purified by simple distillation under reduced pressure or by column chromatography on silica.

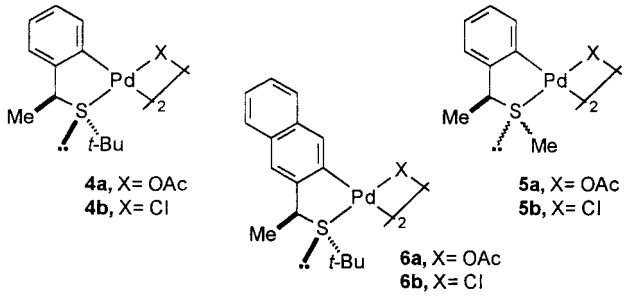


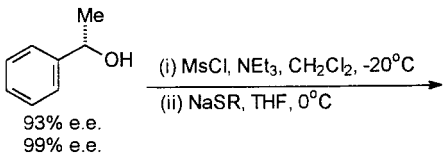
(1)

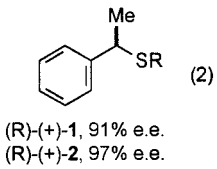
1, R^1 = H, R^2 = *t*-Bu
2, R^1 = H, R^2 = Me
3, R^1 = C_4H_4, R^2 = *t*-Bu

Synthesis of the Non-racemic Thioethers. It is well established that the reaction of (1-chloroethyl)-benzene with nucleophiles occurs with complete inversion of configuration at the chiral carbon center (Walden inversion).[13] However, in these reactions the partial racemization that might occur is due to the instability of chloro starting materials. We have investigated the transformation of (*S*)-(−)-1-phenylethanol into its thioether derivatives, and in order to limit the racemization process, the mesityl ether was prepared in situ at low temperatures (eq 2). Thus, the reaction of (*S*)-(−)-1-phenylethanol (93% ee by GC) with mesityl chloride followed by treatment with sodium *tert*-butyl thiolate affords (*R*)-(+)-(1-*tert*-butylsulfanylethyl)benzene, **1** (91% ee by GC).

Chart 1. Sulfur-Containing Palladacycles 4−6







(2)

(R)-(+)-**1**, 91% e.e.
(R)-(+)-**2**, 97% e.e.

Using a similar procedure, the S-Me analogue (*R*)-(+)-**2** (97% ee by GC) was prepared in 65% overall yield from (*S*)-(−)-1-phenylethanol (99% ee by GC).

Synthesis of the Palladacycles. The preparation of the sulfur-containing palladacycles was accomplished using a similar procedure described earlier.[11a] Thus the reaction of *rac*-**1** with palladium acetate in acetic acid at 90 °C affords the dimeric acetato-bridged palladacycle *rac*-**4a** (Chart 1) in good yield (62%). This air- and water-stable orange compound is slightly soluble in hexanes and highly soluble in polar solvents such as acetone, chloroform, dichloromethane, and acetonitrile. Its IR spectra (Nujol mull) shows the characteristic peaks of the bridged acetato group at 1568 and 1411 cm^{-1}. The presence of a single set of resonances in the ^1H and ^{13}C NMR spectrum, recorded in $CDCl_3$ at room temperature, indicated that *rac*-**4a** was isolated as a single isomer. Moreover the resonance of the methyl protons is at high field (0.85 ppm) in the ^1H spectra, indicating that this group is located in the anisotropic cone of the aromatic ring, as shown in Figure 1. This type of geometry is usually found for acetato-bridged palladacycles; however, a mixture of isomers is generally observed.[14]

To determine the exact geometry of *rac*-**4a** as well as the absolute stereochemistry of the stereogenic centers,

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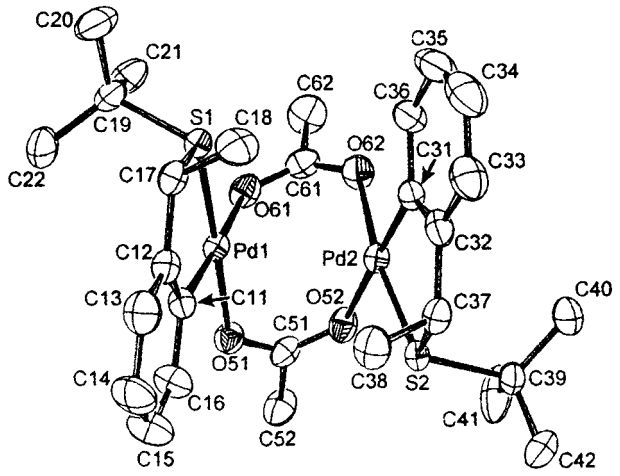

Figure 1. Molecular structure and atomic numbering of $[\{Pd(C_6H_4C(H)(CH_3)SC(CH_3)_3)\}_2(\mu\text{-}O_2CCH_3)_2]$, **4a**. Displacements ellipsoids are at 30% probability; H atoms are omitted for clarity.

Table 1. Crystal Data and Structure Refinement for 4a

chemical formula: $C_{28}H_{40}O_4Pd_2S_2$	$M_r = 717.52$
cryst class: orthorhombic	space group: $P2_12_12_1$
$a = 9.3965(10)$ Å	$T = 303(2)$ K
$b = 17.4956(10)$ Å	$\lambda = 0.71073$ Å
$c = 18.9382(10)$ Å	$D_x = 1.531$ Mg·m^{-3}
$V = 3113.4(4)$ Å^3	$\mu = 1.318$ mm^{-1}
$Z = 4$	$F(000) = 1456$
θ range collected: 2.33−27.48°	no. of reflns collected: 4006
index ranges: $-12 \le h \le 0$, $-22 \le k \le 0$, $-24 \le l \le 0$	no. of reflns unique: 4005 [$R_{int} = 0.0148$]
abs corr: ψ-scan	max & min transm: 0.6702 & 0.6206
no. of params: 356	goodness of fit on F^2: 1.054
R1 [$I > 2\sigma(I)$][a]: 0.0252	wR2 (all data)[a]: 0.0656
ext coeff: 0.00150(13)	absolute structure param: −0.02(4)
max peak in final ΔF map: 0.414 e·Å^{-3}	

[a] Definition of *R* indices: $R1 = \Sigma(F_o - F_c)/\Sigma(F_o)$; $wR2 = [\Sigma\{w(F_o^2 - F_c^2)^2\}/\Sigma\{w(F_o^2)^2\}]^{1/2}$.

an X-ray diffraction analysis was undertaken. An ORTEP drawing of the structure of *rac*-**4a** is shown in Figure 1. Crystallographic data and details of the structure determination are presented in Table 1. Selected bond distances and angles are presented in Table 2. Tables of atomic coordinates, hydrogen coordinates, and anisotropic thermal parameters are supplied as Supporting Information.

The crystal consists of discrete dimeric molecules possessing approximate (noncrystallographic) C_2 symmetry. The palladium−palladium distance is 2.9565(4) Å, which can be regarded as nonbonding since the covalent radius of square-planar Pd(II) is estimated as 1.31 Å.[15] Each palladium center is in a slightly distorted square-planar coordination environment which consists of a sulfur unit, an ortho carbon atom of the aromatic ring, and two oxygen atoms (one of each of the μ-acetate ligands). The angles around the palladium atoms sum to almost exactly 360°, and the deviation from planarity is very small. The Pd−S and Pd−C form the basis for five-membered chelate rings with a bite angle S−Pd−C of 85.31(14)° for Pd1 and 85.48(15)° for Pd2. The five-membered palladacycle is approximately planar; the internal angles sum to 539.4° for Pd1 and 537.5° for Pd2. The maximum deviations from the respective planes are 0.053(2) Å for S1 and 0.119(3) Å for C37.

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Table 2. Selected Bond Lengths (Å) and Angles (deg) for 4a

Pd1−Pd2	2.9565(4)		
Pd1−S1	2.2464(12)	Pd2−S2	2.2467(12)
Pd1−C11	1.971(5)	Pd2−C31	1.968(5)
Pd1−O51	2.083(3)	Pd2−O52	2.145(4)
Pd1−O61	2.131(3)	Pd2−O62	2.085(4)
S1−C17	1.844(5)	S2−C37	1.815(5)
S1−C19	1.854(5)	S2−C39	1.863(4)
O51−C51	1.260(5)	O62−C61	1.258(6)
O52−C51	1.237(5)	O61−C61	1.255(6)
C51−C52	1.525(7)	C61−C62	1.508(7)
C11−Pd1−O51	93.57(17)	C31−Pd2−O52	177.10(18)
C11−Pd1−O61	177.24(15)	C31−Pd2−O62	93.43(18)
O51−Pd1−O61	87.16(14)	O52−Pd2−O62	89.47(15)
C11−Pd1−S1	85.31(14)	C31−Pd2−S2	85.48(15)
O51−Pd1−S1	178.33(10)	O52−Pd2−S2	91.64(11)
O61−Pd1−S1	93.90(10)	O62−Pd2−S2	170.90(10)
C17−S1−Pd1	103.14(16)	C37−S2−Pd2	102.35(17)
C19−S1−Pd1	111.18(18)	C39−S2−Pd2	108.24(18)
C51−O51−Pd1	122.9(3)	C51−O52−Pd2	124.6(3)
C61−O61−Pd1	123.2(3)	C61−O62−Pd2	124.2(3)
C17−S1−C19	103.2(2)	C37−S2−C39	103.7(2)
O52−C51−O51	127.8(4)	O61−C61−O62	126.5(5)
O52−C51−C52	116.3(4)	O61−C61−C62	117.3(5)
O51−C51−C52	115.9(4)	O62−C61−C62	116.2(5)

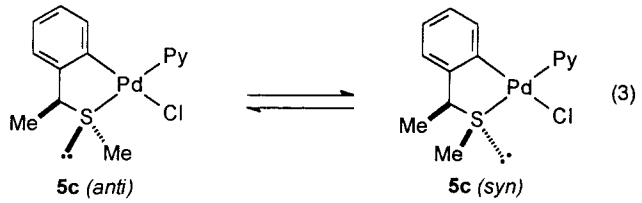
As a result of Pd1 and Pd2 being bridged by two mutually cis-μ-acetate groups, the chelating S,C-bonded thioether ligands are forced into a parallel-type arrangement to each other. This leads to interligand repulsions between the carbon methyl group (C18 or C38) and the phenyl group of the other half of the molecule. As a consequence, the nonbridged side of the molecule is opened considerably and the coordination planes of the palladium centers are tilted at an angle of 35.66(6)° to one another. This configuration puts the S-*t*-Bu groups on the outside of the molecule and CMe groups inside. The *anti* relationship between the S-*t*-Bu and CMe groups gives rise to the C_RS_R (C_SS_S) relative configuration in each palladacycle monomeric unit.

The acetato-bridged palladacycle **4a** was quantitatively transformed in its chloro-bridged dimer **4b** by simple treatment with excess LiCl in acetone. Palladacycle **4b** is insoluble in nonpolar organic solvents and slightly soluble in chloroform, acetone, or dichloromethane. The presence of only one set of signals in its ^{1}H and ^{13}C NMR spectra indicates that this compound is present in solution as a single isomer. The relative stereochemistry C_RS_R (C_SS_S) can be tentatively assigned by analogy with its acetato precursor. Note that this relative configuration is the same predicted by the ^{1}H NMR study (see above).

Using a similar procedure, complexes **5a** and **6a** were prepared in good yields (Chart 1). These complexes were not isolated and transformed in situ to their chloro-bridged dimers **5b** and **6b** by treatment with LiCl. As observed for compound **4b**, the ^{1}H NMR spectra in DMSO indicated that **6b** was isolated as a single isomer. Moreover, by analogy and on steric grounds we can assume the same relative stereochemistry at the C and S stereogenic centers, i.e., C_RS_R (C_SS_S). On the other hand, the ^{1}H NMR spectra show the presence of two

sets of signals, indicating that compound **5b** was isolated as mixture of two isomers in a 3:1 ratio.

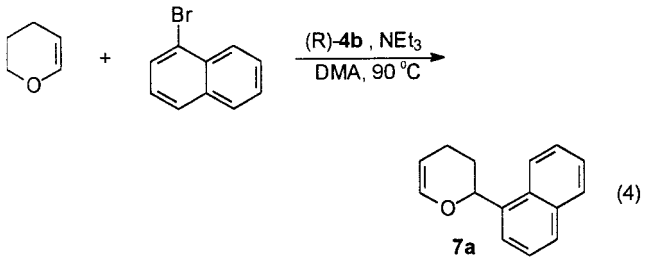
To eliminate the possibility of the presence of *cisoid* and *transoid* isomers due to a chloro bridge, this complex has been transformed quantitatively into its monomeric derivative **5c** (eq 3) by simple treatment with pyridine (Py) in dichloromethane. The ^{1}H NMR spectrum ($CDCl_2CDCl_2$, RT) of monomeric complex **5c** also indicates the presence of two isomers in the same proportion (3:1). These isomers are probably the two diastereoisomers resulting from the different configurations at the sulfur stereogenic center (eq 3). It is reasonable to assume, on steric grounds, that the major isomer possesses an *anti* relationship (SMe and CMe). A variable-temperature ^{1}H NMR investigation of **5c** indicated that it has a fluxional behavior in solution. At room temperature, the SMe resonances of **5c**-*anti* and **5c**-*syn* appear as two sharp singlets at 2.82 and 2.54 ppm. However, these two signals broaden at higher temperatures and coalesce at about 100 °C. This behavior can be attributed to the rapid pyramidal sulfur inversion at higher temperatures, leading to an equilibrium as depicted in eq 4. The calculated free energy of activation for this process, 18 kcal/mol at 373 K (using the Eyring equation),[16] is the same magnitude as usually observed for related sulfur-containing palladacycles.[11]



5c *(anti)* **5c** *(syn)* (3)

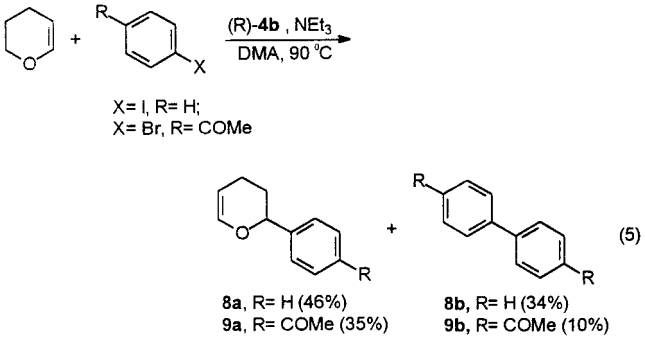
The ^{1}H NMR spectrum of (*R*)-**4b** is unchanged in a large range of temperatures (from −20 to 100 °C), indicating that this palladacycle is configurationally stable at the sulfur atom (in this range of temperature).

Asymmetric Heck Reaction. The catalytic properties of the optically active palladacycle (*R*)-**4b** were tested by the arylation of 3,4-dihydro-2*H*-pyrane (Heck reaction). It is important to note that this type of asymmetric Heck reaction is usually catalyzed by Pd(II)/chiral phosphine catalyst precursors, giving moderate to good asymmetric inductions.[17] The reaction of a large excess of this unsaturated cyclic ether with 1-bromonaphthalene in dimethylacetamide at 90 °C in the presence of triethylamine and 1 mol % of (*R*)-**4b** gave almost exclusively **7a** after 72 h (eq 4). The product was easily isolated from the reaction mixture by dilution with water and extraction with dichloromethane and purified by column chromatography. **7a** was isolated in 89% yield but in essentially in its racemic form. This rather disappointing result suggests that the sulfur-containing palladated moiety is probably not present in catalytic active species for the arylation reaction. Moreover, in these cases the sulfur-containing palladacycles are probably acting as a reservoir of Pd(0) catalytic active species similar to those proposed earlier.[9f]



(4)

The arylation reaction can also be performed with other aryl halides such as iodobenzene and 4-bromoacetophenone using relatively low catalyst concentration (0.25%). However, in these cases a mixture of compounds is obtained after 60−64 h, with the bis-aryl homocoupling compound **8b** or **9b** as the major side product (eq 5).



(5)

The formation of the bis-aryls **8b** and **9b** indicated that this sulfur-containing palladacycle would also be a catalyst precursor for aryl homocoupling reactions. Indeed, using **4b** (0.5%) in similar reaction conditions, 4-iodocetophenone is quantitatively transformed in **9b**. The catalytic properties of **4b** and other sulfur-containing palladacycles in the aryl homocoupling reaction will be published elsewhere.

Experimental Section

General Methods. All catalytic reactions were carried out under an argon or nitrogen atmosphere in oven-dried Schlenk tubes. Elemental analyses were performed by the Analytical Central Service of IQ-UFRGS. The alcohols were prepared according to a known procedure.[18] Solvents were dried with adequate drying agents and distilled under argon prior to use. All the other chemicals were purchased from commercial sources and used without further purification. NMR spectra were recorded on a Varian Inova 300 or Varian VXR-200. Infrared spectra were performed on a Bomem B-102 spectrometer. Optical rotation values were recorded on a Perkin-Elmer 341 polarimeter at 20 °C. Mass spectra were obtained using a GC/MS Shimadzu QP-5050 (EI, 70 eV). Gas chromatography analyses were performed with a Hewlett-Packard-5890 gas chromatograph with a FID and 30 m capillary column with a dimethylpolysiloxane stationary phase.

X-ray Structure Analysis. Compound **4a** crystallized from a slow diffusion of hexane into a dichloromethane solution to form orange blocks. Data from a crystal of dimensions 0.40 × 0.36 × 0.33 mm were collected on an Enraf-Nonius CAD4 diffractometer using ω scans with Mo Kα radiation. Three check reflections were measured every 60 min, and the intensity drift was corrected by a linear treatment. Accurate

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unit cell dimensions were determined using 25 reflections with θ between 10° and 15°. The space group was determined from the unique extinctions. The structure was solved by the Patterson method and refined (full-matrix least-squares on F^2) using the SHELXL97 suite of programs.[19] Scattering factors for neutral atoms were used as stored in the programs. The absolute structure parameter was refined and confirmed the correct hand was chosen. ORTEP-III for Windows[20] was used to generate the molecular view.

Synthesis of Thioethers. Method a. Mesityl chloride (630 mg, 5.5 mmol) was added to a solution of (*S*)-(−)-1-phenylethanol (93% ee, 610 mg, 5.3 mmol) and triethylamine (0.5 mL, 5.0 mmol) in dichloromethane at −20 °C. After 1 h at this temperature, cold water was added and the organic phase extracted. The volatiles were removed under reduced pressure at low temperature (below 10 °C), and the residue was dissolved in THF at −20 °C. A suspension of Na[S-*t*-Bu] (717 mg, 6.4 mmol) in THF (15 mL) was then added at −20 °C, and the resulting white suspension was allowed to attain room temperature under vigorous stirring. After 20 h the volatiles were removed under reduced pressure, water (100 mL) was added, and the organic phase was extracted by dichloromethane (3 × 50 mL). Column chromatography on silica (hexanes/diethyl ether, 5:1) gave (+)-**1** as colorless liquid (490 mg, 50% yield): α_D +235° (*c* 1.0 CH_2Cl_2). CG (Chirasildex CB, 25m): (*R*)-isomer 32 min, (*S*)-isomer 33 min (91% ee). ^{1}H NMR (300 MHz, $CDCl_3$, RT): δ 7.32−7.12 (m, 5H, aromatic), 4.06 (q, 1H, J_{HH} = 7.1 Hz, CH), 1.59 (d, 3H, Me), 1.25 (s, 9H, *t*-Bu). ^{13}C NMR (75 MHz, $CDCl_3$, RT): δ 25.6 (Me), 31.6 (*t*-Bu), 42.7 (CH), 44.0 (C, *t*-Bu), 126.8 (CH, aromatic), 127.3 (CH, aromatic), 128.6 (CH, aromatic), 146.7 (C, aromatic). CG−MS (IE, 70 eV): *m*/*z* (%) 105 (100, M^+ − S-*t*-Bu), 57 (27), 194 (14, M^+), 77 (11), 106 (9), 138 (7).

Thioether (+)-**2** was obtained using the same procedure with the following modifications (starting alcohol 99% ee): After addition of Na[S-Me] in THF at −20 °C, the resulting white suspension was heated at 50 °C for 72 h under vigorous stirring. After workup, distillation at reduced pressure (50−55 °C at 1 mmHg) gave **2** as a pale yellow oil (380 mg, 50% yield): α_D +192° (neat) (97% ee).[13] ^{1}H NMR (300 MHz, $CDCl_3$, RT): δ 7.32−7.19 (m, 5H, aromatic), 3.84 (q, 1H, J_{HH} = 7.1 Hz, CH), 1.87 (d, 3H, SMe), 1.57 (d, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, RT): δ 14.8 (Me), 22.3 (SMe), 45.9 (CH), 127.2 (CH, aromatic), 127.5 (CH, aromatic), 128.7 (CH, aromatic), 143.9 (C, aromatic). CG−MS (IE, 70 eV): *m*/*z* (%) 105 (100, M^+ − S-Me), 77 (19), 152 (19 M^+), 51 (12), 106 (8), 121 (2).

The same procedure was used to obtain thioether (±)-**2** from (±)-1-phenylethanol (940 mg, 49% yield).

Method b. Dried zinc iodide (770 mg, 2.4 mmol) was added to a solution of 1-naphthalen-2-yl-ethanol (800 mg, 4.7 mmol) in dry dichloromethane (30 mL). To the obtained suspension was added 2-methylpropane-2-thiol (540 mg, 6.0 mmol), and the mixture was refluxed for 1 h. The reaction was quenched with water (50 mL), and the reaction products were worked up by extraction with dichloromethane (2 × 30 mL). The combined organic extracts were washed with brine and dried over $MgSO_4$, from which solvent was evaporated at reduced pressure, and a yellow solid was obtained (1 g, 88% yield). ^{1}H NMR (300 MHz, $CDCl_3$, RT): δ 7.84−7.28 (m, 7H, aromatic), 4.25 (q, 1H, J_{HH} = 7.0 Hz, CH), 1.66 (d, 3H, Me), 1.26 (s, 9H, *t*-Bu). ^{13}C NMR (75 MHz, $CDCl_3$, RT): δ 25.4 (Me), 31.7 (*t*-Bu), 42.9 (CH), 44.1 (C, *t*-Bu), 125.3 (CH, aromatic), 125.7 (CH, aromatic), 125.9 (CH, aromatic), 126.2 (CH, aromatic), 127.8 (CH, aromatic), 128.5 (CH, aromatic), 132.7 (C, aromatic), 133.6 (C, aromatic), 144.0 (C, aromatic).

The same procedure was used to obtain thioether (±)-**1** from (±)-1-phenylethanol. After distillation at reduced pressure (83 °C, 1 mmHg) a colorless oil was obtained (5.8 g, 91% yield).

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Synthesis of Palladacycle (−)-4a. To a solution of palladium acetate (295 mg, 1.3 mmol) in acetic acid (15 mL) was added (*R*)-(+)-1-*tert*-butylsulfanylethyl)benzene (470 mg, 1.4 mmol) at room temperature. The solution was stirred at 90 °C for 20 min. The brown solution thus obtained was evaporated to dryness and washed with hexanes (2 × 25 mL). After drying under reduced pressure an orange solid was obtained (186 mg, 52% yield based on Pd): α_D −242° (*c* 0.5, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39 (m, 1H, CH aromatic), 6.87 (m, 2H, CH aromatic), 6.62 (m, 1H, CH aromatic), 3.82 (q, 1H, J_{HH} = 7.3 Hz, CH), 2.12 (s, 3H, Me acetate), 1.48 (s, 9H, *t*-Bu), 0.59 (d, 3H, Me). ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.6 (Me), 24.9 (Me, acetate), 30.5 (Me, *t*-Bu), 49.6 (CH), 51.5 (C), 123.0 (CH, aromatic), 124.7 (CH, aromatic), 125.4 (CH, aromatic), 134.6 (CH, aromatic), 144.5 (C, aromatic), 156.8 (C, aromatic). IR (KBr): ν(cm^{-1}) 1568 and 1582, acetate.

Synthesis of Palladacycle (−)-4b. To a solution of palladium acetate (295 mg, 1.3 mmol) in acetic acid (15 mL) was added (*R*)-(+)-1-*tert*-butylsulfanylethyl)benzene (470 mg, 1.4 mmol, 91% ee) at room temperature. The solution was stirred at 90 °C for 20 min. The brown solution thus obtained was evaporated to dryness and washed with hexanes (1 × 25 mL). The remaining dark solid was suspended in acetone (25 mL), lithium chloride (80 mg, 2.0 mmol) was added, and the reaction mixture stirred at room temperature for 15 min. Evaporation of the volatiles under reduced pressure gave a brown residue that was dissolved in dichloromethane (100 mL), filtered through a plug (4 cm) of alumina (grade I), and concentrated to ca. 3 mL. Addition of hexanes (50 mL) affords a yellow solid, which was collected by filtration, washed with hexanes (3 × 10 mL), and dried under reduced pressure (197 mg, 45% yield based on Pd): α_D −222° (*c* 0.04, DMA). Anal. Calcd for $C_{12}H_{17}$-ClPdS: C 43.00%; H 5.11%. Found: C 42.81%; H 4.96%. ^{1}H NMR (300 MHz, $CDCl_3$ + ϵPy-d_5): δ 7.43 (s(br), 1H, CH aromatic), 6.91 and 6.84 (2m, 3H, CH aromatic), 4.00 (q, 1H, *J* = 7.1 Hz, CH), 1.76 (d, 3H, CMe), 1.44 (s, 9H, *t*-Bu). ^{13}C NMR (75 MHz, $CDCl_3$ + ϵPy-d_5): δ 158.0; 146.1; 136.1; 125.9; 125.4 and 122.6 (C aromatic); 52.2 (C); 51.3 (CH); 31.1 (*t*-Bu); 25.5 (Me).

The same procedure was used for the synthesis of palladacycles **5b** and **6b**.

Palladacycle 5b: 180 mg, 45% yield based on Pd. Anal. Calcd for $C_9H_{11}ClPdS$: C 36.88%; H 3.78%. Found: C 37.01; H 3.67. ^{1}H NMR (300 MHz, $CDCl_3$ + ϵPy-d_5) (two isomers): δ d 7.44 (t, 1H, J_{HH} = 7.4 Hz, CH aromatic), 7.04; 6.92 and 6.83 (3m, 3H, CH aromatic), 4.44 and 4.36 (2q, 1H, CH), 2.78 and 2.49 (2s, 3H, SMe), 1.82 and 1.77 (2 d, *J* = 7.0 and 6.9 Hz, 3H, CMe). ^{13}C NMR (75 MH z, $CDCl_3$ + ϵPy-d_5) (major isomer): δ 152.5, 151.1, 134.6, 124.9, 124.7, and 123.4 (C aromatic); 57.1 (CH), 21.5 and 20.1 (Me).

Palladacycle 6b: 160 mg, 42% yield based on Pd. Anal. Calcd for $C_{16}H_{19}ClPdS$: C 49.88%; H 4.97%. Found: C 49.67, H 5.13. ^{1}H NMR (300 MHz, DMSO): δ 8.14 (s, 1H, CH aromatic); 7.58 (m, 2H, CH aromatic); 7.42 (s, 1H, CH aromatic); 7.27 (m, 2H, CH aromatic); 4.37 (q, 1H, J_{HH} = 6.8 Hz, CH); 1.66 (d, 3H, Me); 1.27 (s, 9H, *t*-Bu). ^{13}C NMR (75 MHz, DMSO): δ 159.0, 148.9, 136.2, 131.7, 131.4, 127.4, 127.3, 125.1, 124.5, and 119.4 (C aromatic); 51.2 (CH); 31.2 (*t*-Bu), and 26.4 (Me).

Typical Experiment for the Heck Reaction. An oven-dried resealable Schlenk flask was evacuated and backfilled with argon, then were added the 1-bromonaphthalene (207.1 mg, 1.0 mmol), 3,4-dihydro-2*H*-pyran (336.5 mg, 4 mmol), NEt_3 (194 μL, 1.4 mmol), dimethylacetamide (4 mL), palladacycle **4b** (1.7 mg in 1 mL of DMA, 5 μmol), and undecane (15.6 mg) as internal standard. The reaction mixture was stirred at 90 °C. After 72 h (90% conversion), the solution was then allowed to cool to room temperature, taken up in ether (20 mL), washed with aqueous NaOH (1 M, 5 mL) and brine (2 × 5 mL), and then dried over $MgSO_4$. After filtration, solvent was evaporated and purified by chromatography (hexanes/CH_2Cl_2, 1:1) to

afford **7a** (203 mg, 81%) as a colorless oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.93−7.34 (m, 7H, CH aromatic), 6.55 (d, 1H, J_{HH} = 6.3 Hz, CH olefinic), 5.49 (d−d, 1H, CH), 4.78 (m, 1H, CH olefinic), 2.21 (m, 2H, CH_2), 1.99 (m, 2H, CH_2). ^{13}C NMR (50 MHz, $CDCl_3$): δ 20.8 (CH_2), 29.7 (CH_2), 74.4 (CH), 100.9 (CH, olefinic), 122.8 (CH, aromatic), 122.9 (CH, aromatic), 123.1 (CH, aromatic), 123.2 (CH, aromatic), 125.4 (CH, aromatic), 125.5 (CH, aromatic), 126.0 (CH, aromatic), 130.3 (C, aromatic), 133.7 (C, aromatic), 137.3 (C, aromatic), 144.5 (CH, olefinic). GC−MS (IE, 70 eV): *m*/*z* (%) 154 (100, $M^+ - C_3H_4O$), 181 (33), 210 (M^+, 17), 127 (8), 101 (5).

The same procedure was used for the **4b** (0.25%)-catalyzed Heck reaction of iodobenzene (2 mmol) and 3,4-dihydro-2*H*-pyran (8 mmol) After 43 h, 95% conversion was obtained. Purification by chromatography (hexanes/ethyl acetate, 10:0.1) gave **8a** (90 mg, 28%) as a colorless oil and biphenyl (58 mg, 37%) as a white solid.

8a: ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.43−7.28 (m, 5H, CH aromatic), 6.61 (d, 1H, J_{HH} = 6.3 Hz, CH olefinic), 4.89 (d−d, 1H, CH), 4.85 (m, 1H, CH olefinic), 2.30 (m, 1H, CH_2), 2.11 (m, 1H, CH_2), 2.11 (m, 2H, CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.6 (CH_2), 30.6 (CH_2), 77.3 (CH), 100.9 (CH, olefinic), 126.2 (CH, aromatic), 127.9 (CH, aromatic), 128.7 (CH, aromatic), 142.3 (C, aromatic), 144.5 (CH, olefinic). GC−MS (IE, 70 eV): *m*/*z* (%) 104 (100, $M^+ - C_3H_4O$), 131 (41), 77 (15), 51 (15), 160 (M^+, 11).

8b: ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.75−7.20 (m, 10H, aromatic). GC−MS (IE, 70 eV): *m*/*z* (%) 154(100, M^+), 76(38), 51(16). Mp: 70−71 °C.

The same procedure was used for the **4b** (0.25%)-catalyzed Heck reaction of *p*-bromoacetophenone (8 mmol) and 3,4-dihydro-2*H*-pyrane. A conversion of 60% was achieved after 72 h. GC yields were obtained using undecane as internal standard.

9a: 50% GC yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.95 and 7.45 (2d, J_{HH} = 8.0 Hz, 4H, aromatic), 6.54 (d, 1H, J_{HH} = 6.3 Hz, CH olefinic), 4.89 (d−d, 1H, CH olefinic), 4.81 (m, 1H, CH), 2.59 (s, 3H, CH_3), 2.17 (m, 2H, CH_2), 2.00 (m, 2H, CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.0 (CH_2), 26.5 (CH_3), 29.7 (CH_2), 100.9 (CH, olefinic), 125.9 (CH, aromatic), 128.5 (CH, aromatic), 135.8 (C, aromatic), 143.8 (CH, olefinic), 196.9 (C═O). GC−MS (IE, 70 eV): *m*/*z* (%) 131 (100, $M^+ - C_4H_7O$), 131 (41), 77 (21), 202 (M^+, 11), 187 (3).

9b: ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.08 (d, 4H, J_{HH} = 8.5 Hz, CH, aromatic), 7.74 (d, 4H, CH, aromatic), 2.67 (s, 6H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 26.9 (CH_3), 127.7 (CH, aromatic), 129.3 (CH, aromatic), 136.8 (C, aromatic), 144.6 (C, aromatic), 197.9 (C═O). GC−MS (IE, 70 eV): *m*/*z* (%) 223 (100, $M^+ - CH_3$), 238 (M^+, 40), 76 (40), 104 (25), 152 (22), 63 (14). Mp: 182−184 °C.

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Supporting Information Available: For the crystal structure of **4a**, complete tables of atomic coordinates, thermal parameters, bond distances and angles, and least-squares planes and atomic deviations therefrom.

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