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Asymmetric Synthesis of Palladacycles by Regioselective Oxidative Cyclization of C_2-Symmetrical, Chiral Alkenes and Determination of the Configuration of All Stereocenters

A. Stephen K. Hashmi,* Frank Naumann, and Michael Bolte

Institut für Organische Chemie der Johann Wolfgang Goethe-Universität,
Marie-Curie-Strasse 11, D-60439 Frankfurt am Main, Germany

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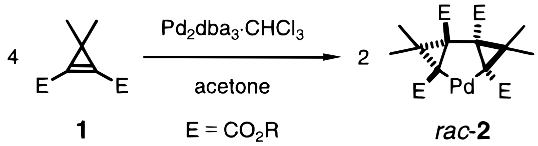
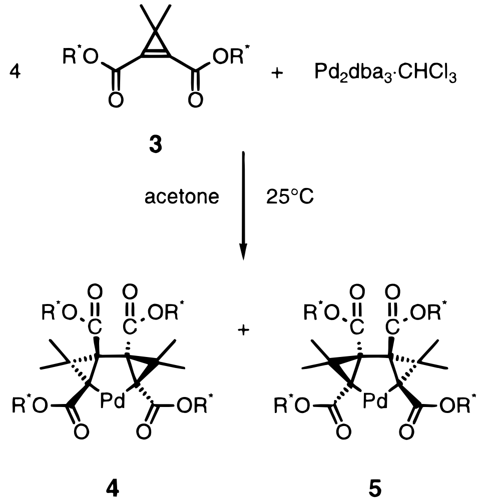
Summary: The reaction of $Pd_2(dba)_3{\cdot}CHCl_3$ with 2 equiv of chiral, C_2-symmetrical cyclopropenes bearing lactate esters at the 1- and 2-positions provided trans-5-palladatricyclo[4.1.0.0^{2,4}]heptanes (PTHs) in high diastereomeric excess. The configuration of all stereocenters in the major diastereomer was determined by X-ray structure analyses of the complexes of the PTH with norbornadiene; the C_2 symmetry of the (+)-DIOP complex of the minor diastereomer proves that this was also a trans isomer.

Enantiomerically pure organotransition-metal compounds are important as chiral building blocks,[1] chiral auxiliaries,[2] and chiral catalysts.[3] Besides resolution methods, in most cases such enantiomerically pure organometallic complexes of the transition metals are prepared by the attachment of ligands that already contain all centers (or elements) of chirality;[4] there exist no examples where new centers of chirality are formed in a stereoselective manner during the formation of the organometallic compound. The feasibility of such a diastereoselective formation of organometallic compounds is demonstrated by diastereoselective transition-metal-catalyzed reactions, in which one can deduce from the products that they proceed through organometallic intermediates possessing newly formed stereocenters.[5] In these reactions usually a facial selection is induced by the stereocenter(s) already present in the substrate. Here we report the first example for the highly diastereoselective formation of chiral organometallic compounds by a regioselection and not a facial selection.

We recently reported the formation and resolution of *trans*-5-palladatricyclo[4.1.0.0^{2,4}]heptanes (PTHs; **2**), which serve as model systems for chiral carbocyclization catalysts, from Pd(0) and cyclopropenes **1**.[6]



We now investigate the synthesis of PTHs from enantiomerically pure, C_2-symmetrical cyclopropenes **3**, which bear two lactic acid esters as chiral units. In all cases high yields were obtained. Due to the sym-



3,4,5:		**4 + 5**	*dr* **4 : 5**
a	R* = (*R*)-CH(Me)CO_2Et	95%	94 : 6
b	R* = (*R*)-CH(Me)CO_2*t* Bu	82%	96 : 4
c	R* = (*S*)-CH(Me)CO_2Me	99%	5 : 95
d	R* = (*S*)-CH(Me)CO_2Et	95%	6 : 94
e	R* = (*S*)-CH(Me)CO_2*i* Pr	70%	3 : 97

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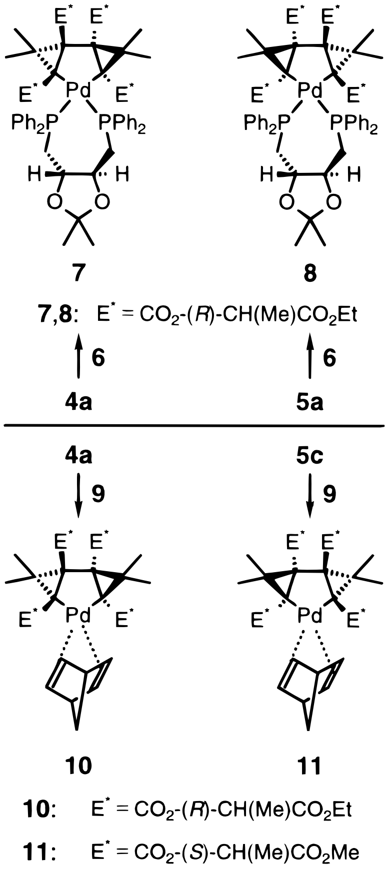
metrical substitution of the cyclopropenes no constitutional isomers can be formed; with **3** the two *trans* diastereomers **4** and **5** are conceivable. Depending on the configuration of the lactate residue in **3**, one of these diastereoisomers was formed preferentially (diastereomeric ratio dr between 94:6 and 97:3). **4** and **5** could be separated by HPLC.[7]

In each case in the NMR spectra only the set of signals one would expect for a C_2-symmetrical *trans*-PTH was visible.[8] We wanted to ensure that there was no accidental isochronism caused by the large distance between the stereocenters in the lactate side chains and the palladacycle. Thus, we coordinated the enantiomerically pure (+)-DIOP ligand **6** to **4a** and **5a**. The C_2-symmetry of the complexes **7** and **8** obtained in this way again confirmed the *trans* arrangement of the two three-membered rings in **4** and **5**, respectively.[9] In the case of an *cis* arrangement one would expect a C_1-symmetrical complex.



With norbornadiene **9** as ligand, crystalline complexes were obtained. The relative configuration of the stereocenters in the side chains and the palladacycle was determined by an X-ray structure analysis of the major diastereomer from each enantiomer of the lactate unit.

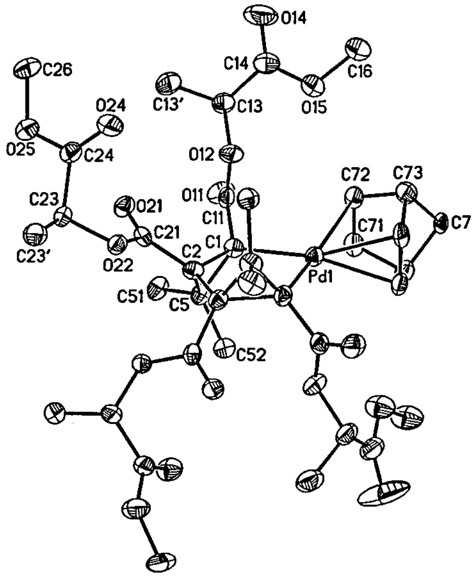


Figure 1. ORTEP plot of **11**.

From **4a** and **9** we synthesized **10**; from **5c** and **9** the olefin complex **11** was formed (the ORTEP plot of **11** is depicted in Figure 1).[10] The absolute configuration was deduced from the known configuration of the lactate and agreed with the absolute configuration determined by the anomalous dispersion effect.[10] In contrast to the PTH−phosphane complexes we investigated previously,[6] with the norbornadiene ligand in **10** and **11** only a small deviation from square-planar coordination at palladium was observed (2 and 0.8°, respectively, between the C−Pd−C plane in the PTH and the plane defined by the centers of the two C═C bonds and the Pd). **10** and **11** are the first alkene complexes of PTHs and serve as model compounds for the coordination of unsaturated substrates in the course of reactions catalyzed by PTHs.[11] The Pd−C bond length of 2.06 Å in the PTH unit of **10** and **11** lies between the values known from other PTH complexes (2.11 Å for phosphane[6,12] and 2.02 Å for acetone ligands[13]). The other bond lengths within the PTH unit of **10** and **11** are quite

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(6) Hashmi, A. S. K.; Naumann, F.; Probst, R.; Bats, J. W. *Angew. Chem.* **1997**, *109*, 127−130; *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 104−106.

(7) The dr values obtained from analytical HPLC and from the amount of each diastereoisomer obtained after preparative HPLC were identical.

(8) Only in the case of the analogous 5-nickelatricyclo[4.1.0.0^{2,4}]-heptanes did Binger also observe the *cis* compound;[12] with PTHs the *cis* isomer is unknown.

(9) Proven by the number of signals in the ^{1}H, ^{13}C, and ^{31}P NMR spectra of the complexes.

(10) Crystal structure analyses of **10** and **11**: Siemens CCD three-circle diffractometer, Mo Kα, 0.710 73 Å, ω scans, Lorentz and polarization correction, empirical absorption correction with SADABS (Sheldrick, G. M. SADABS, a Program for Empirical Absorption Correction of Area Detector Data; Universität Göttingen Göttingen, Germany, 1996), structures were solved by direct methods (Sheldrick, G. M. *Acta Crystallogr., Sect. A* **1990**, *46*, 467−473) and refined with SHELXL 96 (Sheldrick, G. M. SHELXL 96, a Program for the Refinement of Crystal Structures; Universität Göttingen Göttingen, Germany, 1996), by full-matrix least-squares methods against F^2. Hydrogen atoms were placed on ideal positions and refined with fixed isotropic displacement parameters using a riding model. The absolute structure was determined by the method of (Flack, H. D. *Acta Crystallogr., Sect. A* **1983**, *39*, 876−881). **10**: $C_{41}H_{56}O_{16}Pd$, 0.22 × 0.10 × 0.10 mm, monoclinic, space group $C2$; a = 45.4444(7) Å, b = 9.7021(2) Å, c = 9.7201(1) Å, β = 94.730(1)°; V = 4271.06(12) Å^3, Z = 4; $\rho_{\rm calcd}$ = 1.417 g cm^{-3}; μ = 5.04 cm^{-1}, $T_{\rm min}$, $T_{\rm max}$ = 0.906, 1.000; $2\theta_{\rm max}$ = 52.72°; 173 K, 18 393 measured reflections, 7840 independent reflections; 527 parameters refined; R1 = 0.0710, wR2 = 0.0957; Flack parameter −0.02(3), max residual electron density 0.551 e Å^{-3}. **11**: $C_{37}H_{48}O_{16}Pd$, 0.44 × 0.30 × 0.08 mm, tetragonal, space group $P4_32_12$; a, b = 9.5919(1) Å, c = 42.3654(2) Å; V = 3897.81(6) Å^3, Z = 4; $\rho_{\rm calcd}$ = 1.457 g cm^{-3}; μ = 5.48 cm^{-1}, $T_{\rm min}$, $T_{\rm max}$ = 0.796, 1.000; $2\theta_{\rm max}$ = 50.34°; 133 K, 32 406 measured reflections, 3311 independent reflections; 245 parameters refined; R1 = 0.0514, wR2 = 0.1021; Flack parameter −0.02(4), max residual electron density 0.875 e Å^{-3}.

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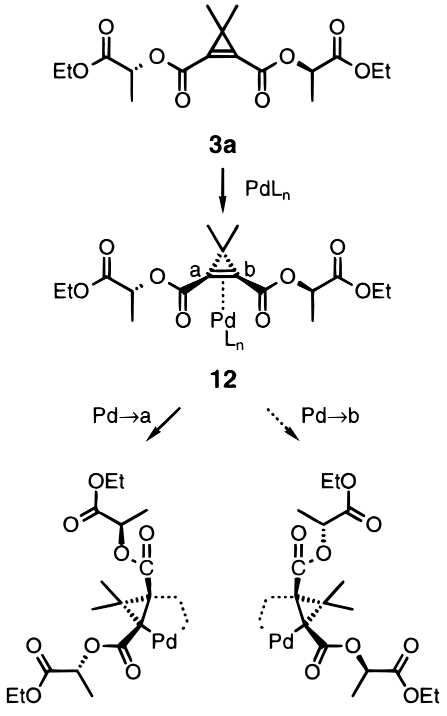
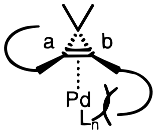
similar to those of PTH structures already reported. The Pd−C bond lengths of 2.26 and 2.27 Å for the π-coordinated **9** resemble those of related compounds.[14]

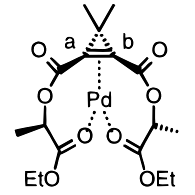
What is the origin of the observed diastereoselectivity? There is no facial selection;[15] due to the C_2 symmetry both faces of the C=C bond are equal (exemplified by **3a**), and the coordination of palladium to each face of the π-bond of the olefin leads to identical complexes **12**. In **12** the carbon atoms of the double bond are no longer symmetry equivalent. The observed diastereoselection results from the regioselectivity of the addition of Pd and carbon during the oxidative cyclization leading to the PTH and is unprecedented in organometallic chemistry. There are two possible causes for the regioselectivity of this addition. Either the lactate side chain prefers a U-shaped conformation (**13**) and thus pushes away the palladium or it actively coordinates to the palladium as shown in **14**.



4a **5a**



13



Pd→a **14**

Since evidence for **13** was not obtained from either molecular modeling or from X-ray structures, we prefer **14**. In **14** each of the lactate units may coordinate to Pd via the carbonyl oxygen of the outer ester moiety, but in one of the rings formed that way the methyl group of the lactate and the CMe$_2$ group of the cyclopropene would be *cis*, while in the other ring they would be *trans*. As the major diastereomer one could expect the product where palladium is directed by the carbonyl group which allows the *trans* orientation in the chelate, which indeed corresponds to the observed major diastereomer. Whether both cyclopropenes cooperate, i.e., the oxidative cyclization passes through a highly ordered transition state, or only the cyclopropene that coordinates first directs the absolute configuration of the newly formed stereocenters and the second cyclopropene just reacts with the known *trans* selectivity (*trans* with respect to the other cyclopropane ring in the PTH) is under investigation.

The observed 1,4-induction opens an easy access to uncharged, enantiomerically pure, and coordinatively unsaturated palladium organic fragments possessing chiral carbon centers in the direct neighborhood of the metal. These compounds offer interesting opportunities as chiral building blocks[1] and as model compounds for chiral catalysts.[3,6]

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Supporting Information Available: Text giving characterization data for **4a**−**e**, **5a**,**c**−**e**, **7**, **8**, **10**, and **11** (6 pages). Ordering information is given on any current masthead page.

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