Stereocontrolled Lactonization Reactions via Palladium-Catalyzed 1,4-Addition to Conjugated Dienes

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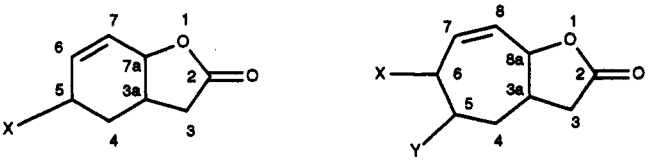
Received May 28, 1993

Stereocontrolled palladium(II)-catalyzed 1,4-chloro- and 1,4-acetoxylactonizations of conjugated cyclic dienes have been developed to give stereodefined fused lactones. The stereochemistry of the 1,4-acetoxylactonization was controlled by the ligand on the metal catalyst, and in this way either a *cis*- or *trans*-acetoxylactonization was obtained. This dual stereoselectivity is explained by a stereocontrolled acetate attack (trans or cis, respectively) on the allyl group in the catalytic (π-allyl)palladium intermediate. To further strengthen the mechanism the intermediate (π-allyl)palladium complex was isolated and fully characterized. A stereospecific synthesis of *cis*- and *trans*-2-[6-(benzyloxy)-2,4-heptadien-1-yl]acetic acid (*cis*- and *trans*-**9**) followed by stereoselective Pd(II)-catalyzed chloro- and acetoxylactonization in acetone/acetic acid resulted in highly functionalized fused lactones with control of the relative stereochemistry at four different carbons.

Introduction

We have recently developed methods for the stereoselective Pd(II)-catalyzed 1,4-oxidation of cyclic and acyclic dienes. Efficient methods for *cis*- or *trans*-1,4-diacetoxylation, *cis*-1,4-chloroacetoxylation, *trans*-1,4-acetoxytrifluoroacetoxylation, *cis*-1,4-dialkoxylation, and more recently, general procedures for *cis*- or *trans*-1,4-diacyloxylation and *cis*-chloroacyloxylation of cyclic conjugated dienes have been developed.[1] These methods are useful in organic synthesis since: (*i*) the stereoselectivity of the Pd(II)-catalyzed 1,4-oxidations is usually high and can be controlled in a predictable way, and (*ii*) further synthetic transformations of chloroacylates allow excellent stereo- and regiospecific control which permits the use of 1,3-dienes as important synthetic building blocks.[2]

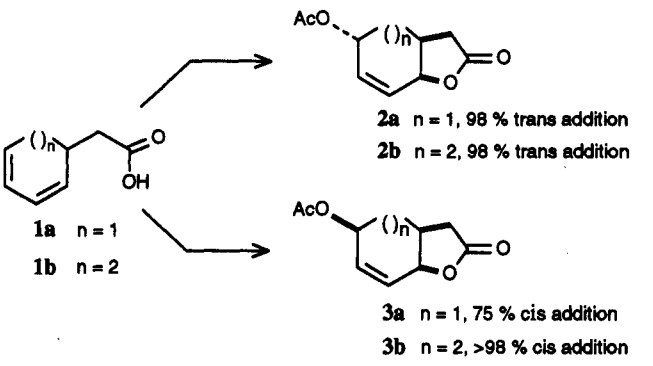
A natural extension of the intermolecular 1,4-oxidation of 1,3-dienes would be the development of intramolecular reactions.[3] In these cases one of the nucleophiles (e.g. a carboxylic acid) is attached to the diene and undergoes an intramolecular *trans*-oxy palladation reaction. In a preliminary report[3a] we described the palladium-catalyzed lactonization of 2-(2,4-cycloalkadien-1-yl)acetic acids to give benzofuranone (**I**) and cyclohepta[*b*]furanone systems (**II**, Y = H) shown in Figure 1. In this paper we give a full account of the 1,4-lactonization, discuss the mechanism, and also demonstrate its synthetic utility in stereoselective organic transformations.



I **II**

Figure 1. The benzofuranone (**I**) and cyclohepta[*b*]furanone systems (**II**).

Scheme I



Results and Discussion

A. Stereoselective Palladium-Catalyzed Lactonization Reactions. Reaction of (2,4-cyclohexadienyl)-acetic acid (**1a**) in acetone/acetic acid (4:1) in the presence of 5 mol% of $Pd(OAc)_2$ and 2 equiv of *p*-benzoquinone afforded lactone **2a** in 88% yield and with >98% overall *trans*-additions (Scheme I). The analogous reaction of (2,4-cycloheptadienyl)acetic acid (**1b**)[3a] gave the lactone **2b** in 72% yield (>98% overall *trans*-addition). These results are in agreement with previous observations in intermolecular additions where the absence of strongly coordinating ligands such as chloride gives an overall 1,4-*trans*-addition.[1a] In order to reverse the stereochemistry toward an overall 1,4-*cis*-addition the corresponding reactions were performed in the presence of LiCl.[1a] This gave a highly stereoselective reaction for the seven-membered ring to give **3b** in 78% yield (>98% *cis*-addition), while the six-membered ring afforded lactone **3a** (69% yield) in a moderate stereoselectivity (overall *cis*-addition/*trans*-addition = 75:25).

The stereochemistry of lactones **2** and **3** was assigned from their ^1H NMR spectra and was confirmed by NOE experiments. For example irradiation of the nonallylic

(1) (a) Bäckvall, J. E.; Byström, S. E.; Nordberg, R. E. *J. Org. Chem.* **1984**, *49*, 4619. (b) Bäckvall, J. E.; Nyström, J. E.; Nordberg, R. E. *J. Am. Chem. Soc.* **1985**, *107*, 3676. (c) Bäckvall, J. E.; Vågberg, J. O.; J., Nordberg, R. E. *Tetrahedron Lett.* **1984**, *25*, 2717. (d) Bäckvall, J. E.; Vågberg, J. O. *J. Org. Chem.* **1988**, *53*, 5695. (e) Bäckvall, J. E.; Granberg, K. L.; Hopkins, R. B. *Acta Chem. Scand.* **1990**, *44*, 492.

(2) (a) Bäckvall, J. E. *New J. Chem.* **1990**, *14*, 447. (b) Bäckvall, J. E. *Bull. Soc. Chim. Fr.* **1987**, 665. (c) Bäckvall, J. E. In *Organic Synthesis: An Interdisciplinary Challenge*; Streith, J., Prinzbach, H., Schill, G., Eds.; Blackwell Scientific Publications: Boston, 1985, p 69.

(3) (a) Bäckvall, J. E.; Vågberg, J. O.; Andersson, P. G. *Tetrahedron Lett.* **1989**, *30*, 137. (b) For a related amidation reaction: Bäckvall, J. E.; Andersson, P. G. *J. Am. Chem. Soc.* **1990**, *112*, 3683. (c) For a related reaction leading to fused tetrahydrofurans and tetrahydropyrans: Bäckvall, J. E.; Andersson, P. G. *J. Am. Chem. Soc.* **1992**, *114*, 6374. (d) For an extension to oxaspirocyclization: Bäckvall, J. E.; Andersson, P. G. *J. Org. Chem.* **1991**, *56*, 5349.

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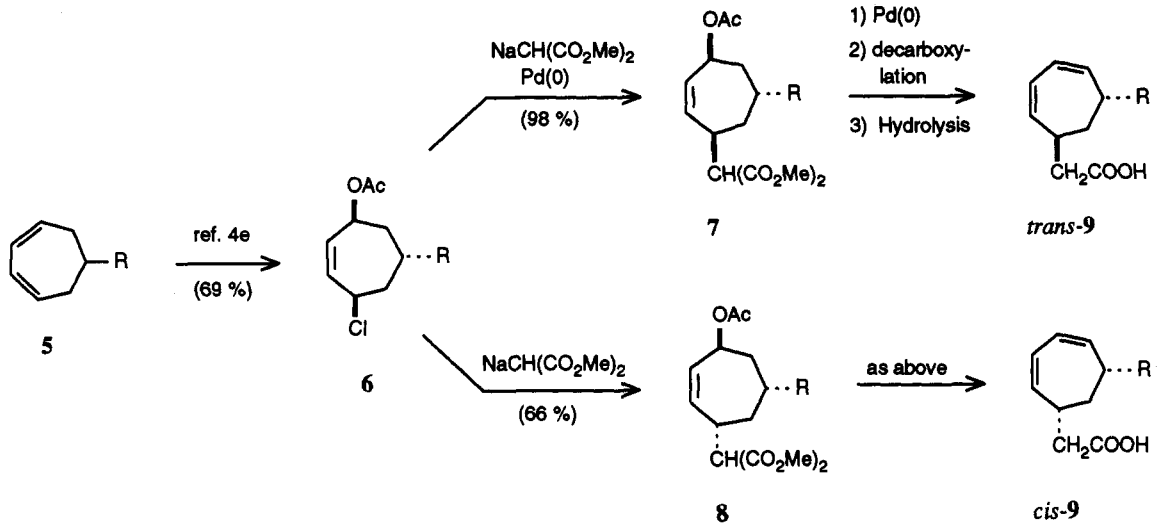
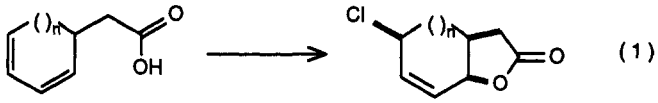
Scheme II. (R = OCH_2Ph)



bridgehead proton in **3b** resulted in a NOE for C*H*OAc (6%) and C*H*OCOCH$_2$ (9%). The corresponding irradiation in **2b** gave a NOE for C*H*OCOCH$_2$ but not for C*H*OAc.

When the palladium-catalyzed lactonization reactions of dienes **1** were performed in the presence of 2 equiv of LiCl, a highly stereo- and regioselective chlorolactonization occurred (eq 1). Thus, reaction of dienes **1a** and **1b**



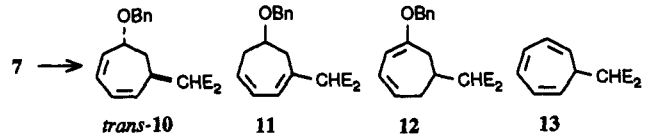
(1)

1a n = 1 **4a** n = 1 85 %

1b n = 2 **4b** n = 2 76 %

afforded chloro lactones **4a** and **4b**, respectively, via a *cis*-1,4-chlorolactonization (>98% *cis*-addition).

It was of interest to study these lactonization reactions on more substituted systems. One way to introduce a CH_2-COOH in a substituted diene, e.g., **5**, would be to employ the chloroacetoxylation approach.[1b,4] Chloroacetoxylation of diene **5** (R = OCH_2Ph) proceeds in a highly diastereoselective manner to give **6**.[4e] Subsequent substitution of the chloride in **6** by dimethyl malonate anion with either retention (Pd(0), 20 °C) or inversion (S_N2, 80 °C) in completely stereospecific reactions[1b,4a] afforded **7** and **8**, respectively. Palladium-catalyzed elimination[5] of acetic acid from **7** and **8** and subsequent decarboxylation and hydrolysis afforded dienes *trans*- and *cis*-**9**, respectively. Dienes of type *cis*-**9** have previously been prepared by a different approach involving (cycloheptadienyl)iron chemistry.[6] However, the latter approach allows only the preparation of the *cis*-isomer, whereas the approach in Scheme II gives access to both stereoisomers.



Time (min)	Product distribution (%)			
6	86	5	8	-
120	< 1	24	60	16

Figure 2. Pd(dba)$_2$/dppe-catalyzed elimination of acetic acid in refluxing toluene + 1 equiv of NEt_3 (E = CO_2Me).

The regioselective Pd(0)-catalyzed elimination of acetic acid from **7** and **8** turned out to be sensitive to the reaction conditions used. The reaction of **7** with Pd(dba)$_2$/dppe (dppe = 1,2-bis(diphenylphosphino)ethane) and triethylamine in refluxing toluene was rapid (6 min) and highly regioselective, and *trans*-**10** was isolated as a mixture in 92% yield, contaminated with 3% of **11** and 3% of **12**. It remains unclear whether the side product **11** originates from a primary reaction or if it is formed via rearrangement of *trans*-**10** (Figure 2). It is important to keep the reaction time at a minimum at these elevated temperatures since *trans*-**10** easily isomerizes to **11** and **12**. Furthermore, *trans*-**10** also undergoes a Pd(0)-catalyzed elimination of benzyl alcohol to give cycloheptatriene **13** on longer reaction time (Figure 2).

The corresponding reaction of **8** was surprisingly slow and was preferably performed at a lower temperature due to extensive formation of side products in refluxing THF. After chromatographic purification, a mixture of *cis*-**10** (71%) and **11** (29%) was obtained. Since formation of **11** from **8** by direct *syn*-β-hydride elimination from an intermediate (σ-allyl)palladium complex is impossible for steric reasons, the product would seem to come from either isomerization of the intermediate (π-allyl)palladium complex by Pd(0) attack[7] or via thermal rearrangements. Alternatively, a base-assisted elimination would explain direct formation of **11** from the intermediate (π-allyl)-palladium complex.

Decarbomethoxylation of *cis*- and *trans*-**10** according

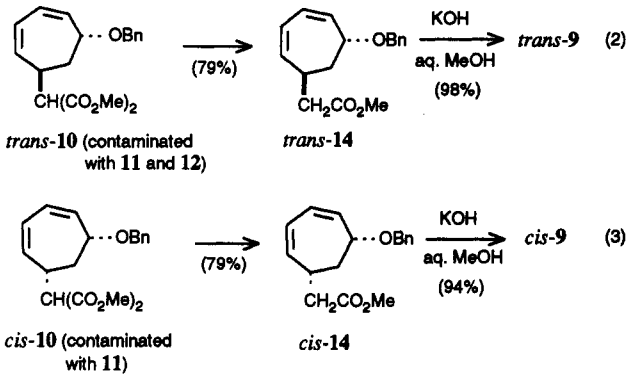
(4) (a) Bäckvall, J. E.; Vågberg, J. O. *Organic Synthesis* **1990**, *69*, 38. (b) Bäckvall, J. E.; Byström, S. E.; Nyström, J. E. *Tetrahedron* **1985**, *41*, 5761. (c) Bäckvall, J. E.; Vågberg, J. O.; Granberg, K. L. *Tetrahedron Lett.* **1989**, *30*, 617. (d) Bäckvall, J. E.; Schink, H. E.; Renko, Z. D. *J. Org. Chem.* **1990**, *55*, 826. (e) Schink, H. E.; Petterson, A. H. E.; Bäckvall, J. E. *J. Org. Chem.* **1992**, *57*, 6025.

(5) (a) Tsuji, J.; Yamakawa, T.; Kaito, M.; Mandai, T. *Tetrahedron Lett.* **1978**, 2075. (b) Trost, B. M.; Verhoeven, T. R.; Fortunal, J. M. *Tetrahedron Lett.* **1979**, 2301. (c) Bäckvall, J. E.; Vågberg, J. O.; Zercher, C.; Genêt, J. P.; Denis, A.; *J. Org. Chem.* **1987**, *52*, 5430.

(6) Pearson, A. J.; Kole, S. L.; Ray, T. *J. Am. Chem. Soc.* **1984**, *106*, 6060.

(7) (a) MacKenzie, P. B.; Whelan, J.; Bosnich, B. *J. Am. Chem. Soc.* **1985**, *107*, 2046. (b) Bäckvall, J. E.; Granberg, K. L.; Heumann, A., *Isr. J. Chem.* **1991**, *31*, 17. (c) Granberg, K. L.; Bäckvall, J. E. *J. Am. Chem. Soc.* **1992**, *114*, 6858.

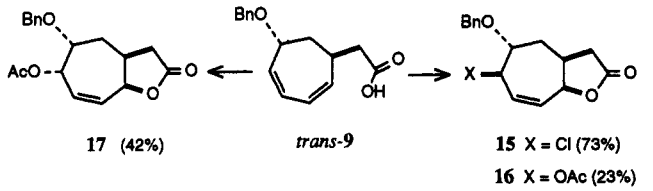
to Keinan's[8] procedure (*p*-aminothiophenol, Cs_2CO_3 in DMF at 85 °C) afforded *cis*- and *trans*-**14**, respectively. The decarboxylated products of contaminants **11** and **12** were readily removed in the workup. The stereochemistry



of methyl esters *cis*- and *trans*-**9** was unambiguously determined by NOE measurements. Simple base hydrolysis (KOH, MeOH) gave the desired carboxylic acids *cis*- and *trans*-**9**, as stereo- and regiochemically pure isomers.

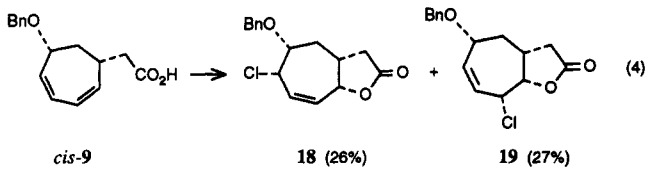
Palladium-catalyzed lactonization reactions of *cis*- and *trans*-**9** proceeded in moderate to good yield. Thus, chlorolactonization of *trans*-**9** in acetone/acetic acid (4:1) with 5 mol% of Li_2PdCl_4 and 2 equiv each of LiCl and *p*-benzoquinone afforded **15** in 73% yield (Scheme III). In

Scheme III



the absence of LiCl and with added LiOAc employing $Pd(OAc)_2$ (5 mol%) as catalyst *trans*-**9** afforded **16** in 23% yield. Reaction of *trans*-**9** in the absence of any lithium salts employing $Pd(OAc)_2$ as the catalyst afforded **17** as the major isomer, which was isolated in 42% yield.

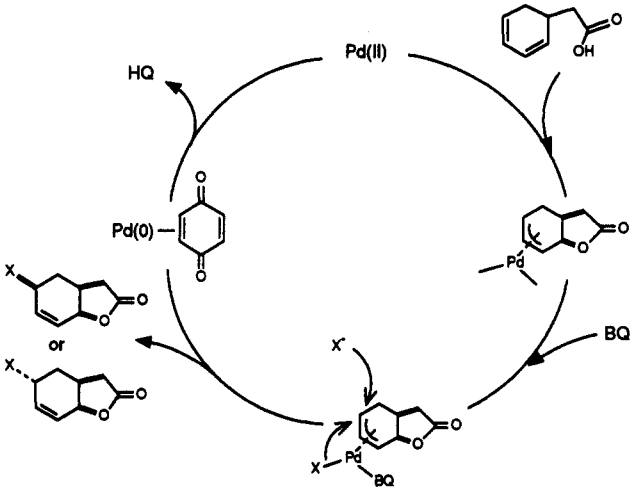
The corresponding chlorolactonization reaction of *cis*-**9** gave a 1:1 mixture between **18** and **19** from 1,2- and 1,4-*cis*-addition, respectively (eq 4). This is one of the few



exceptions to the high 1,4-regioselectivity usually obtained in these palladium-catalyzed oxidations of conjugated dienes. One explanation for the lack of regioselectivity in this particular case is that in the lactonic (π-allyl)palladium intermediate (vide infra, Scheme IV) the 1- and 3-positions of the π-allyl group have similar surroundings. Both carbons vicinal to the π-allyl will have oxygen functions trans to palladium. For this reason the incoming nucleophile cannot distinguish between the 1- and 3-position of the π-allyl.

(8) Keinan, E.; Eren, D. *J. Org. Chem.* **1986**, *50*, 3165.
(9) Paterson, I.; Mansuri, M. M. *Tetrahedron* **1985**, *41*, 3569. (b) Pearson, A. J.; Ray, T. *Tetrahedron Lett.* **1986**, *27*, 3111.

Scheme IV. (HQ = hydroquinone, BQ = *p*-benzoquinone, X = O_2CR, Cl)



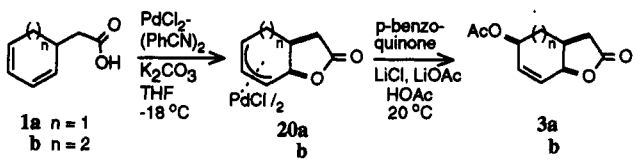
Pearson's methodology[6,9] for stereoselective functionalization of 1,3-cycloheptadiene based on the use of (π-dienyl) iron chemistry gives access only to *cis*-1,6-disubstituted-2,4-cycloheptadienes. The methodology presented in this paper allows synthesis of both the *cis*- and *trans*-isomers, offering a useful control of the relative stereochemistry.

B. Mechanism. The catalytic cycle of these lactonization reactions involves a lactonic (π-allyl)palladium complex formed by *trans*-oxypalladation of the diene (Scheme IV). Coordination of *p*-benzoquinone to palladium in this π-allyl complex induces the attack by the nucleophile.[10] This nucleophilic attack can occur cis or trans to the metal depending on the reaction conditions. In this process a Pd(0)(*p*-benzoquinone) complex is formed, which immediately undergoes an intramolecular redox reaction to give Pd(II) and hydroquinone. Palladium(0)–quinone complexes are known,[11] and we have recently demonstrated that treatment of an isolated Pd(0)(*p*-benzoquinone) complex with acetic acid leads to formation of Pd(II) and hydroquinone.[12] It is now well documented[1a,13] that the role of the lithium chloride in these stereocontrolled catalytic acetoxylation reactions (*i.e.* cis or trans attack by acetate) is to block the coordination of the acetate and hence favor the external nucleophilic attack. In the absence of chloride ions, the ligand on palladium will be acetate and the product may be formed through a cis migration, most likely via a σ-allyl complex.[1a,13,14]

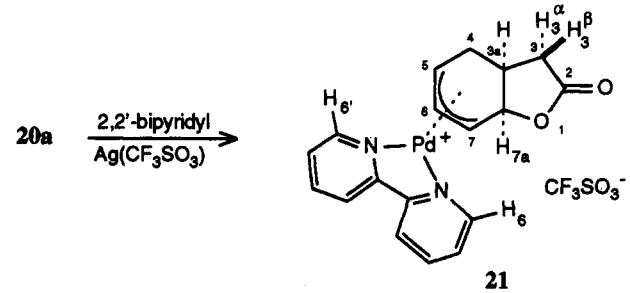
The lactonic (π-allyl)palladium complexes were observed by ^1H NMR spectroscopy *in situ* during the catalytic reaction, and they were also independently prepared and isolated for the simple unsubstituted cases (i.e. **20a** and **20b**). Complexes **20a** and **20b** were obtained as yellow crystalline compounds from the reaction of dienes **1a** and **1b**, respectively, with $PdCl_2(PhCN)_2$. They were fully characterized by spectroscopic methods. Reaction of

(10) Bäckvall, J. E.; Gogoll, A. *Tetrahedron Lett.* **1988**, *29*, 2243.
(11) (a) Minematsu, H.; Takahashi, S.; Hagihara, N. *J. Organometal. Chem.* **1975**, *91*, 389. (b) Hiramatzu, M.; Shiozahi, K.; Fujinami, T.; Sakai, S. *J. Organometal. Chem.* **1983**, *246*, 203. (c) Minematsu, H.; Takahashi, S.; Hagihara, N. *J. Chem. Soc., Chem. Commun.* **1975**, 466.
(12) Grennberg, H.; Gogoll, A.; Bäckvall, J. E. *Organometallics* **1993**, *12*, 1790.
(13) Bäckvall, J. E.; Nordberg, R. E.; Wilhelm, D. *J. Am. Chem. Soc.* **1985**, *107*, 6892.
(14) Grennberg, H.; Langer, V.; Bäckvall, J. E. *J. Chem. Soc. Chem. Commun.* **1991**, 1190.

complexes **20** under the conditions for the catalytic reaction for overall 1,4-*cis* addition (i.e. **1** into **3**) afforded lactones **3** by external acetate attack. These results are fully consistent with the catalytic cycle shown in Scheme IV.



It was of interest to independently establish the configuration of complexes **20**. The vicinal coupling constant of 5.0 and 5.6 Hz, respectively, between the bridgehead protons in **20a** and **20b** is indicative of a *cis*-lactone. The relative stereochemistry between palladium and the oxygen bound to the bridge is however difficult to determine from the NMR spectra of **20a** and **20b**. To obtain this steric information we used a reporter ligand[15] on palladium. The use of reporter ligands has recently been successfully applied to structure determination of (π-allyl)palladium complexes.[15] Complex **20a** was transformed to the bipyridyl complex **21** by treatment with $Ag(SO_3CF_3)$ and bipyridyl. To establish the relative configuration of



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complex **21** ^{1}H NOE difference and 2D NOE (NOESY) experiments were performed. The reporter protons (H-6 and H-6′ of bipyridyl) show strong cross peaks to the outer π-allyl protons and to H-7a in the NOESY experiment. Also the NOE difference experiment gave a significant NOE between the reporter protons and H-3$^\alpha$. There was no observable NOE between the reporter protons and H-3$^\beta$. These results establish the trans relationship between palladium and oxygen.

Concluding Remarks

A number of lactonization reactions of olefins and conjugated dienes have been reported in the literature.[6,16,17] To the best of our knowledge the lactonization reactions described in the present paper constitute the only reported example where the addition step of the lactonization can be directed toward either cis or trans addition. The procedure reported leads to stereodefined lactones that are fused to a six- or seven-membered ring. The synthetic utility of these lactones is enhanced by the fact that the allylic chloride or acetate can be substituted in stereoselective reactions.

Experimental Section

Unless otherwise specified, NMR spectra were obtained for $CDCl_3$ solutions, ^{1}H NMR at 299.3 MHz and ^{13}C NMR at 75.4 MHz and APT, DEPT, and HETCOR techniques were used for ^{13}C NMR assignments. ^{13}C spectra are reported with the middle peak of $CDCl_3$ (77.00 ppm) as internal reference while tetramethylsilane (TMS) was used as reference for ^{1}H NMR spectra. Infrared spectra were performed with a Perkin-Elmer 1600 FT-IR spectrometer. HPLC analysis were done on a Varian instrument. Bis(dibenzylideneacetone)palladium(0) ($Pd(dba)_2$),[18] tetrakis(triphenylphosphine)palladium(0),[1b] and *p*-aminothiophenol[19] were prepared according to literature procedures. GC-MS analysis of compounds **10** and **14** was unreliable because a number of isomeric products are formed under the thermal conditions in the GC. *N*,*N*-Dimethylformamide (DMF) was distilled before use.

2-(2,4-Cyclohexadienyl)acetic Acid (1a). The methyl ester of the acid was prepared according to ref 20 and hydrolyzed employing standard methods. Spectral data are in accordance with those reported in the literature.[17]

2-(2,4-Cycloheptadienyl)acetic Acid (1b). The same procedure as for the preparation of **1a** was used starting from dimethyl (*cis*-4-acetoxycyclohept-2-en-1-yl)malonate.[5c] Spectral data are in accordance with those reported in the literature.[6]

Stereocontrolled Lactonization Reactions. Two different workup procedures are described for **2** and **3**. The workup described for **2b** gives a reasonably pure crude product, whereas the workup described for **2a** gives a crude product containing large amounts of hydroquinone/benzoquinone. In both cases flash chromatography gives a pure product.

Synthesis of 2a. Diene **1a** (0.15 g, 1.09 mmol) was added during 12 h to a stirred solution of $Pd(OAc)_2$ (12.2 mg, 0.0543 mmol) and *p*-benzoquinone (0.235 g, 2.17 mmol) in acetic acid/acetone (2 mL, 1:4).[21] After another 12 h of stirring, the reaction mixture was diluted with brine (2 mL) and extracted with ether (3 × 5 mL). To the combined ethereal fractions was added in ice-cold solution of 2 M NaOH (2 mL) to neutralize the acetic acid, and the phases were briefly shaken. The organic phase was collected, washed with brine (2 mL), and dried ($MgSO_4$). Evaporation of the solvent and chromatography through a silica column using pentane/ether (25:75) as eluent afforded **2a** (0.188 g, 88%) as a colorless, clear oil: ^{1}H NMR δ 6.20 (dd, J = 10.8, 4.8 Hz, 1 H), 6.11 (dd, J = 10.8, 3.6 Hz, 1 H), 5.31 (app q, J = 4.5 Hz, 1 H), 4.86 (dd, J = 6.0, 3.6 Hz, 1 H), 2.90 (m, 1 H), 2.79 (dd, J = 17.4, 8.4 Hz, 1 H), 2.35 (dd, J = 17.4, 4.2 Hz, 1 H), 2.06 (s, 3 H), 1.96–1.77 (m, 2 H); ^{13}C NMR δ 175.8, 170.3, 130.9, 127.4, 74.4, 64.6, 34.5, 30.0, 29.0, 21.0; IR ($CDCl_3$) 2954, 1778, 1735, 1372, 1236, 1176, 974, 929 cm^{-1}; MS *m*/*z* 196 (M^+, 1.2%), 154 (7), 136 (10), 112 (14), 95 (38), 94 (49), 91 (27), 79 (14), 43 (100), 41 (19). Anal. Calcd for $C_{10}H_{12}O_4$: C, 61.22; H, 6.17. Found: C, 61.36; H, 6.11.

2b. Compound **1b** (0.27 g, 1.77 mmol), $Pd(OAc)_2$ (19.9 mg, 0.0887 mmol), and *p*-benzoquinone (0.383 g, 3.54 mmol) were dissolved in acetic acid/acetone (7.2 mL, 1:4) and stirred for 24 h at 40 °C. Brine (3 mL) was added and the excess acetone was removed by a gentle stream of nitrogen. The aqueous phase was extracted with ether (3 × 20 mL). The combined organic phases were cooled on an ice-bath, washed with 1 M NaOH (3 × 3.5 mL), water (2 mL), and brine (3 mL), and dried ($MgSO_4$). Evaporation of the solvent and flash chromatography as above afforded **2b** (0.269 g, 72%) as white crystals (mp 73–74 °C). ^{1}H NMR δ 5.82 (m, 2 H), 5.35 (d, J = 7.8 Hz, 1 H), 5.30 (m, 1 H), 2.97 (m, 1 H),

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(21) Slow addition of the diene **1a** is necessary to minimize Diels–Alder side products between the diene and *p*-benzoquinone. For the cycloheptadiene derivatives this side reaction is considerably slower and in those cases all diene can be added in one portion.

2.75 (dd, J = 17.3, 9.0 Hz, 1 H), 2.21 (dd, J = 17.3, 7.2 Hz, 1 H), 2.10 (m, 1 H), 2.06 (s, 3 H), 1.91 (m, 1 H), 1.68 (m, 1 H), 1.50 (m, 1 H); ^{13}C NMR δ 176.1, 170.1, 129.5, 128.6, 80.2, 71.2, 37.8, 36.3, 28.3, 25.1, 21.1; IR ($CDCl_3$) 2944, 1773, 1733, 1373, 1245, 1177, 1018 cm^{-1}; MS: m/z 210 (M^+, 0.9%), 168 (19), 150 (10), 109 (21), 79 (21), 55 (22), 43 (100). Anal. Calcd for $C_{11}H_{14}O_4$: C, 62.85; H, 6.71. Found: C, 63.04; H, 6.68.

Synthesis of 3a. The same procedure as for **2a** was used (but with added $LiOAc{\cdot}2H_2O$ and LiCl). Diene **1a** (0.15 g, 1.09 mmol), $LiOAc{\cdot}2H_2O$ (0.22 g, 2.17 mmol), LiCl (23 mg, 0.543 mmol), $Pd(OAc)_2$ (12.2 mg, 0.0543 mmol), and p-benzoquinone (0.235 g, 2.17 mmol) were reacted to give **3a** (0.148 g, 0.754 mmol, 69% $cis/trans$ = 75:25) as a colorless, clear oil: ^{1}H NMR δ 6.04 (m, 2 H), 5.30 (m, 1 H), 4.78 (m, 1 H), 2.85 (dd, J = 17.4, 7.2 Hz, 1 H), 2.70 (m, 1 H), 2.43 (dd, J = 17.4, 3.0 Hz, 1 H), 2.13–2.05 (m, 1 H), 2.09 (s, 3 H), 1.53 (m, 1 H); ^{13}C NMR δ 175.6, 170.5, 134.1, 124.9, 74.1, 67.3, 35.9, 31.5, 29.2, 21.1; IR ($CDCl_3$) 2927, 1778, 1735, 1245, 1175, 1024, 987 cm^{-1}; MS m/z 196 (M^+, 1.5%), 154 (9), 136 (10), 95 (39), 94 (51), 91 (26), 43 (100), 41 (24).

3b. Compound **1b** (0.15 g, 0.986 mmol), $LiOAc{\cdot}2H_2O$ (0.20 g, 1.97 mmol), LiCl (8.4 mg, 0.197 mmol), $Pd(OAc)_2$ (11.1 mg, 0.0493 mmol), and p-benzoquinone (0.213 g, 1.97 mmol) were dissolved in acetic acid/acetone (2 mL, 1:4) and stirred for 24 h at 40 °C. The same workup as for **2a** afforded **3b** (0.162 g, 0.771 mmol, 78%) as a colorless, clear oil: ^{1}H NMR δ 5.67 (ddd, J = 11.9, 2.3, 1.8 Hz, 1 H), 5.60 (ddd, J = 11.9, 3.8, 2.3 Hz, 1 H), 5.51 (m, 1 H), 5.33 (dq, J = 7.6, 2.3 Hz, 1 H), 2.80 (m, 1 H), 2.72, dd, J = 17.2, 8.8 Hz, 1 H), 2.28 (dd, J = 17.2, 6.9, Hz, 1 H), 2.07 (s, 3 H), 1.99 (m, 1 H), 1.88 (m, 1 H), 1.77 (m, 2 H); ^{13}C NMR δ 175.8, 170.3, 129.8, 126.5, 80.7, 71.0, 37.0, 35.9, 28.0, 24.8, 21.1; IR (KBr) 1787, 1733, 1373, 1250, 1172, 1034, 975 cm^{-1}. Anal. Calcd for $C_{11}H_{14}O_4$: C, 62.85; H, 6.71. Found: C, 62.81; H, 6.55.

Synthesis of 4a. The same procedure as for **2a** was used (but with added LiCl). Diene **1a** (0.15 g, 1.09 mmol), LiCl (92 mg, 2.17 mmol), $Pd(OAc)_2$ (12.2 mg, 0.0543 mmol), and p-benzoquinone (0.235 g, 2.17 mmol) was reacted to give **4a** (0.154 g, 0.892 mmol, 85%) as a clear colorless oil: ^{1}H NMR δ 6.18 (dm, J = 9.6 Hz, 1 H), 6.00 (dm, J = 9.6 Hz, 1 H), 4.76 (m, 1 H), 4.50 (m, 1 H), 2.83 (dd, J = 17.4, 7.8 Hz, 1 H), 2.65 (m, 1 H), 2.52 (dd, J = 17.4, 3.6 Hz, 1 H), 2.36 (m, 1 H), 1.81 (m, 1 H); ^{13}C NMR δ 175.4, 135.9, 124.4, 73.4, 51.9, 35.6, 33.8, 32.8. Anal. Calcd for $C_8H_9ClO_2$: C, 55.67; H, 5.25. Found: C, 55.78; H, 5.58.

4b. The same procedure as for **3b** was used (but with added LiCl). Diene **1b** (0.15 g, 0.986 mmol), LiCl (84 mg, 1.97 mmol), $Pd(OAc)_2$ (11.1 mg, 0.0493 mmol), and p-benzoquinone (0.213 g, 1.97 mmol) was reacted to give **4b** (0.140 g, 0.750 mmol, 76%) as a clear, colorless oil: ^{1}H NMR δ 5.74 (dm, J = 12.0 Hz, 1 H), 5.63 (dm, J = 12.0 Hz, 1 H), 5.31 (dm, J = 7.8 Hz, 1 H), 4.85 (m, 1 H), 2.91 (m, 1 H), 2.71 (dd, J = 18.0, 8.4 Hz, 1 H), 2.32 (dd, J = 18.0, 9.0 Hz, 1 H), 2.13 (m, 2 H), 1.91 (m, 2 H); ^{13}C NMR δ 175.8, 131.0, 127.2, 79.6, 59.0, 39.1, 35.6, 32.4, 24.8; IR ($CDCl_3$) 2940, 1777, 1338, 1260, 1218, 1018, 927 cm^{-1}; MS m/z 186 (M^+, 1.8%), 151 (100), 95 (49), 79 (77), 67 (41), 55 (57), 53 (38), 41 (53), 39 (78), 27 (43). Anal. Calcd for $C_9H_{11}ClO_2$: C, 57.92; H, 5.94. Found: C, 58.12; H, 6.06.

Synthesis of 7. Sodium hydride (0.24 g, 7.84 mmol) was added to 40 mL of a 0.20 M solution of dimethyl malonate in THF. When the gas evolution had ceased, the solution was cannulated into a mixture of chloroacetate **6** (2.10 g, 7.12 mmol, containing approximately 10% of 4-acetoxy-6-(benzyloxy)-3-chloro-1-cycloheptene), $Pd(OAc)_2$ (80 mg, 0.36 mmol), and PPh_3 (0.47 g, 1.8 mmol). The reaction was quenched after 3.5 h by the addition of saturated $NaHCO_3$ (20 mL) followed by stirring for 30 min. Water (30 mL) was added and the organic phase was collected. The aqueous phase was extracted with ether (3 × 50 mL), and the combined organic phases were dried ($MgSO_4$). Removal of solvent gave an oil from which 2.70 g of **7** (98%, 97% isomerically pure) was obtained as a colorless oil after purification by flash chromatography (hexane/ethyl acetate, 80:20): ^{1}H NMR ($CDCl_3$) δ 7.42–7.24 (m, 5 H), 5.83 (dm, J = 10.8 Hz, 1 H), 5.73 (d, J = 11.0 Hz, 1 H), 5.70 (d, J = 11.0 Hz, 1 H), 4.64 (d, J = 11.9 Hz, 1 H, A-part of an AB system), 4.59 (d, J = 11.9 Hz, 1 H, B-part of an AB-system), 3.89 (m, 1 H), 3.73 (s, 3 H), 3.72 (s, 3 H), 3.48 (m, 1 H), 3.45 (d, J = 6.6 Hz, 1 H), 2.17 (dddm, J = 13.3, 5.5, 1.8 Hz, 1 H), 2.06 (s, 3 H), 1.97 (ddm, J = 13.7, 5.1 Hz, 1 H), 1.81 (ddd, J = 13.4, 10.9, 2.7 Hz, 1 H), 1.67 (ddd, J = 13.7, 10.5, 2.4 Hz, 1 H); ^{13}C NMR δ 170.09, 168.69, 168.64, 136.64, 134.13, 131.66, 128.21, 127.40, 127.32, 72.89, 69.83, 69.04, 56.07, 52.40, 52.34, 36.22, 34.80, 32.44, 21.20; IR (neat) 3031, 2953, 2863, 1735, 1454, 1436, 1370, 1243, 1159, 1091, and 1027 cm^{-1}; MS: m/z (rel inten) 198 (9), 133 (20), 132 (9), 108 (11), 107 (17), 92 (16), 91 (100), 43 (27), 28 (12). Anal. Calcd for $C_{21}H_{26}O_7$: C, 64.60; H, 6.71. Found: C, 64.80; H, 6.67.

Compound 8. Dimethylsodiomalonate (15.7 mmol) was prepared in THF (75 mL) from sodium hydride (0.47 g, 15.7 mmol) and dimethyl malonate (2.18 g, 16.5 mmol). When the gas evolution had ceased, the solvent was removed in vacuo and the remaining salt was dissolved in acetonitrile (75 mL); finally **6** (4-acetoxy-6-(benzyloxy)-3-chloro-1-cycloheptene was added. The solution was refluxed under dry N_2 for 20 h, while continuously monitoring the reaction by HPLC (hexane/ethyl acetate, 90:10). The reaction was quenched with 1 equiv of $NaHCO_3$ followed by stirring for 1 h. Ether (150 mL) was added and the resulting solution was filtered through Celite. Removal of the solvent in vacuo followed by flash chromatography (hexane/ethyl acetate, 80:20) afforded 3.90 g (66%, 98% isomerically pure) of **8** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.37–7.24 (m, 5 H), 5.73 (m, J = 11.5 Hz, 1 H), 5.67 (dm, J = 11.5 Hz, 1 H), 5.58 (dm, J = 9.2 Hz, 1 H), 4.62 (d, J = 11.8 Hz, 1 H, A-part of an AB-system), 4.48 (d, J = 11.8 Hz, 1 H, B-part of an AB-system), 3.87 (m, 1 H), 3.74 (s, 3 H), 3.72 (s, 3 H), 3.53 (d, J = 7.7 Hz, 1 H), 3.02 (m, 1 H), 2.18 (ddd, J = 13.6, 9.3, 4.0 Hz, 1 H), 2.12–2.02 (m, 2 H), 2.05 (s, 3 H), 1.73 (ddd, J = 13.3, 11.1, 9.7 Hz, 1 H); ^{13}C NMR δ 170.05, 168.58 (two C), 138.41, 133.30, 132.148, 128.28, 127.54, 127.45, 74.26, 70.38, 68.30, 56.32, 52.48 (two C), 36.48, 36.42, 32.71, 21.15; IR (neat) 3030, 2953, 2868, 1735, 1454, 1436, 1368, 1240, 1160, 1093, 1026, 738, and 699 cm^{-1}; MS m/z (rel inten) 133 (22), 132 (9), 108 (9), 107 (19), 92 (17), 91 (100), 65 (8), 43 (30). Anal. Calcd for $C_{21}H_{26}O_7$: C, 64.60; H, 6.71. Found: C, 64.55; H, 6.58.

Compound *cis*-9. *cis*-**14** (817 mg, 3.00 mmol) and KOH (3.4 g, 60 mL) were dissolved in a solution of MeOH (5 mL) and H_2O (20 mL). The reaction was complete within 10 min at 50 °C according to TLC. After cooling the reaction mixture, the aqueous solution was washed with ether (2 × 15 mL), followed by acidification of the aqueous phase to pH 1 with concd HCl. The aqueous phase was saturated with NaCl and extracted with ether (4 × 15 mL). Drying of the organic phase over $MgSO_4$ followed by removal of the solvent in vacuo gave an oil which was filtered through a short silica column (eluation with ether). Removal of the solvent in vacuo and high vacuum pumping gave *cis*-**9** (0.73 g, 94%) as a colorless gum: ^{1}H NMR ($CDCl_3$) δ 7.36–7.25 (m, 5 H), 5.93 (dm, J = 11.3 Hz, 1 H), 5.78–5.67 (m, 2 H), 5.62 (m, 1 H), 4.59 (s, 2 H), 4.31 (dm, J = 9.5 Hz, 1 H), 3.03 (m, 1 H), 2.51 (d, 2 H, J = 7.3 Hz), 2.20 (dm, J = 12.8 Hz, 1 H), 2.05 (ddd, J = 12.8, 10.8, 9.7 Hz, 1 H); ^{13}C NMR δ 177.96, 138.24, 136.22 (two C), 135.83, 128.41, 127.66, 124.27, 122.57, 77.27, 70.60, 39.71, 37.25, 34.72; IR (neat) 3150 (broad), 3029, 2924, 1707, 1409, 1162, 1090, 737, 696 cm^{-1}.

Compound *trans*-9. Prepared using the same procedure as for *cis*-**9** in 98% yield as colorless gum: ^{1}H NMR ($CDCl_3$) δ 10.5 (bs, 1 H), 7.39–7.24 (m, 5 H), 6.02 (dd, J = 11.4, 4.2 Hz, 1 H), 5.90 (m, 1 H), 5.85–5.82 (m, 2 H), 4.69 (d, J = 11.9 Hz, 1 H), 4.51 (d, J = 11.9 Hz, 1 H), 4.04 (m, 1 H), 2.94 (bq, 1 H), 2.52 (dd, J = 15.5, 7.1, A-part of an AB-system, 1 H), 2.44 (dd, J = 15.5, 7.1 Hz, B-part of an AB-system, 1 H), 2.17 (ddd, J = 13.8, 6.0, 2.5 Hz, 1 H), 1.82 (ddd, J = 13.8, 9.0, 2.9 Hz, 1 H); ^{13}C NMR δ 178.42, 138.59, 138.18, 134.10, 128.37, 127.69, 127.54, 125.35, 124.42, 74.42, 70.15, 40.33, 37.60, 32.04; IR (neat) 3100 (broad), 3026, 2923, 2860, 2677, 1707, 1410, 1286, 1206, 1163, 1088, 1067, 941, 736, 696 cm^{-1}.

Compound *trans*-10. $Pd(dba)_2$ (8.2 mg, 0.014 mmol), dppe (12.3 mg, 0.031 mmol), and triethylamine (31 mg, 0.31 mmol) were added to a solution of **7** in toluene (5 mL). The resulting solution was evacuated and filled with dry N_2 and heated to reflux on a preheated oil bath. The yellowish solution was cooled on a water bath after vigorous reflux for 6 min. Workup consisted of the addition of 2 M HCl (5 mL) followed by extraction with ether (2 × 20 mL). The organic phase was collected and dried ($MgSO_4$), and the solvent was removed *in vacuo*. Flash chromatography (hexane/ethyl acetate, 90:10) of the residue gave a colorless oil (94 mg, 92%) as a mixture of *trans*-**10** (94%), **11** (3%), and **12** (3%): ^{1}H NMR (*trans*-**10**) ($CDCl_3$) δ 7.40–7.25 (m,

5 H), 6.04–5.83 (m, 4 H), 4.66 (d, J = 12.0 Hz, 1 H, A-part of an AB-system), 4.56 (d, J = 12.0 Hz, 1 H, B-part of an AB-system), 3.89 (bq, 1 H), 3.742 (s, 3 H), 3.732 (s, 3 H), 3.56 (d, J = 6.6 Hz, 1 H), 3.15 (m, 1 H), 2.17 (ddm, J = 14.2, 5.0 Hz, 1 H), 1.79 (ddd, J = 14.2, 10.1, 3.2 Hz, 1 H); IR (neat) 3028, 2953, 2859, 1752, 1735, 1454, 1436, 1270, 1196, 1160, 1089, 1069, 1027, 740, 699 cm^{-1}.

Compound *cis*-10. The same procedure as described for *trans*-**10** was used with a few modifications. $Pd(PPh_3)_4$ (0.49 g, 0.42 mmol) and triethylamine (0.85 g, 8.45 mmol) were added to a solution of **8** (3.30 g, 8.45 mmol) in THF (28 mL) under N_2. The reaction was heated to reflux and was monitored by HPLC. The reaction was stopped after 48 h of reflux. Workup and purification were carried out as above to give a mixture of *cis*-**10** (71%) and **11** (29%) in 56% total yield (1.56 g). This mixture was used in the next step without further purification. ^{1}H NMR (of *cis*-**10** in a mixture with **11**). δ 7.37–7.26 (m, 5 H), 5.98–5.65 (m, 4 H), 4.56 (AB-system, 2 H), 4.29 (m, 1 H), 3.73 (s, 6 H), 3.62 (d, J = 6.8 Hz, 1 H), 3.30 (m, 1 H), 2.23–2.05 (m, 2H).

Compound *trans*-14. *p*-Aminothiophenol (1.25 g, 10.0 mmol) and Cs_2CO_3 (0.49 g, 1.5 mmol) were added to a solution of *trans*-**10** (1.65 g, 5.00 mmol, contaminated with 3% of **11** and 3% of **12**) in DMF (25 mL). TLC indicated complete conversion after heating the mixture to 85 °C for 15 min under N_2. The reaction mixture was cooled to room temp and water was added (10 mL) followed by ether extraction (3 × 50 mL). The combined ethereal layers were washed with 1 M HCl (10 mL) and with brine (10 mL) and finally dried ($MgSO_4$). Evaporation of the solvent gave an oil (1.24 g) which was purified by flash chromatography (hexane/ethyl acetate, 90:10) to give *trans*-**14** (1.01 g, 79%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.32–7.16 (m, 5 H), 5.92 (dd, J = 11.4, 4.3 Hz, 1 H), 5.63 (dm, 1 H), 5.76–5.73 (m, 2 H), 4.56 (d, J = 12.1 Hz, 1 H, A-part of an AB-system), 4.51 (d, J = 12.1 Hz, 1 H, B-part of an AB-system), 3.95 (m, 1 H), 3.59 (s, 3 H), 2.87 (bq, 1 H), 2.41 (dd, J = 14.9, 6.8 Hz, 1 H), 2.32 (dd, J = 14.9, 6.8 Hz, 1 H), 2.08 (dm, J = 13.8, 6.2, 2.6 Hz, 1 H), 1.72 (ddd, J = 13.9, 9.0, 3.0 Hz, 1 H); ^{13}C NMR δ 172.38, 138.51, 138.27, 133.96, 128.14, 127.44, 127.29, 125.07, 124.03, 74.22, 69.83, 51.35, 40.25, 37.20, 32.16; IR (neat) 3024, 2950, 2856, 1737, 1454, 1436, 1272, 1198, 1163, 1089, 1068, 736, 697 cm^{-1}. Anal. Calcd for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 74.75; H, 7.45.

Compound *cis*-14. The same procedure as for *trans*-**14** was used. *cis*-**10** (1.18 g, 3.57 mmol, contaminated with 29% of **11**), *p*-aminothiophenol (0.92 g, 7.4 mmol), and Cs_2CO_3 (0.90 g, 2.8 mmol) were stirred in DMF (11 mL) at 85 °C for 15 min. Workup as for *trans*-**14** followed by flash chromatography afforded 0.544 g (79% yield calculated on a 71% isomerically pure substrate) of *cis*-**14** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.36–7.25 (m, 5 H), 5.92 (dm, J = 10.8 Hz, 1 H), 5.76–5.65 (m, 2 H), 5.58 (m, 1 H), 4.57 (s, 2 H), 4.30 (dm, J = 9.7 Hz, 1 H), 3.68 (s, 3 H), 3.03 (m, 1 H), 2.45 (d, J = 7.4 Hz), 2.17 (dm, J = 12.9 Hz, 1 H), 2.00 (ddd, J = 12.9, 11.1, 9.8 Hz, 1 H); ^{13}C NMR δ 172.78, 138.36, 136.46, 135.97, 128.35, 127.57, 127.52, 124.03, 122.57, 77.33, 70.56, 51.60, 39.89, 37.36, 35.00; IR (neat) 3027, 2950, 2858, 1737, 1453, 1436, 1277, 1194, 1159, 1090, 741, 696 cm^{-1}.

Compound 15. Li_2PdCl_4 (6.6 mg, 0.025 mmol), LiCl (42 mg, 1.00 mmol), *cis*-**9** (130 mg, 0.50 mmol), and *p*-benzoquinone (114 mg, 1.05 mmol) were dissolved in acetone (1.5 mL) and acetic acid (0.30 g, 10 mmol). The reaction was monitored by TLC, and after stirring for 5 days at room temperature only traces of starting material was left. The acetone was removed in vacuo and the black residue was diluted with brine (5 mL) and extracted with CH_2Cl_2 (4 × 10 mL). Washing of the combined organic layers with saturated Na_2CO_3 (3 × 10 mL) and once with 1 M NaOH (8 mL) gave a colorless organic phase which was dried ($MgSO_4$). Removal of the solvent in vacuo gave a yellow solid which was purified by flash chromatography (hexane/ethyl acetate, 60:40) to give 108 mg (73%) of **15** as colorless crystals: mp 109–112 °C; ^{1}H NMR ($CDCl_3$) δ 7.40–7.27 (m, 5 H), 5.78 (ddddd, J = 11.8, 3.8, 2.2, 0.8 Hz, 1 H), 5.68 (ddd, J = 11.8, 1.6, 1.4 Hz, 1 H), 5.39 (ddt, J = 8.0, 2.2, 1.6 Hz, 1 H), 4.65 (m, 1 H), 4.66 (d, J = 11.3 Hz, A-part of an AB-system, 1 H), 4.63 (d, J = 11.3 Hz, B-part of an AB-system, 1 H), 3.88 (m, 1 H), 3.02 (ddddd, J = 10.5, 9.2, 8.0, 7.8, 4.8 Hz, 1 H), 2.75 (dd, J = 17.8, 9.2 Hz, 1 H), 2.24 (dd, J = 17.8, 7.8 Hz, 1 H), 2.09 (ddd, J = 14.5, 10.5, 2.8 Hz, 1 H), 2.04 (dt, J = 14.5, 4.8 Hz, 1 H); ^{13}C NMR δ 175.42, 137.45, 129.28, 128.40, 128.10, 127.89, 127.56, 80.15, 79.01, 72.30, 59.83, 35.84, 32.72, 30.75; IR (KBr) 3028, 2930, 2882, 2854, 1776, 1495, 1453, 1329, 1191, 1171, 1102, 1072, 1049, 1020, 966, 878, 847, 744, 699 cm^{-1}. Anal. Calcd for $C_{16}H_{17}ClO_3$: C, 65.64; H, 5.85. Found: C, 65.41; H, 5.82.

Compound 16 was prepared in essentially the same way as **15** from 227 mg (0.88 mmol) of *trans*-**9** with the use of $Pd(OAc)_2$ (0.05 equiv) as catalyst and added $LiOAc{\cdot}2H_2O$ (4 equiv) but without addition of LiCl. The reaction was heated to 40 °C for 2 days. After workup and purification by HPLC, 63 mg (23%) of **16** was obtained (also 20 mg (21%) of benzyl alcohol was isolated): ^{1}H NMR ($CDCl_3$) δ 7.37–7.26 (m, 5 H), 5.68 (dm, J = 9.4 Hz, 1 H), 5.53–5.44 (m, 2 H), 5.37 (dm, J = 7.2 Hz, 1 H), 4.61 (d, J = 12.0 Hz, A-part of an AB-system, 1 H), 4.52 (d, J = 12.0 Hz, B-part of an AB-system, 1 H), 3.74 (m, 1 H), 3.02 (m, 1 H), 2.83 (dd, J = 17.6, 9.1 Hz, 1 H), 2.19 (dd, J = 17.6, 5.1 Hz, 1 H), 2.05 (s, 3 H), 2.03 (m, 1 H), 2.33 (dt, J = 14.9, 2.9 Hz, 1 H); ^{13}C NMR δ 175.55, 170.20, 137.87, 129.09, 128.34, 127.75, 127.50, 126.91, 80.88, 76.37, 74.12, 71.60 (two C), 36.72, 31.59, 31.35, 20.97); IR (neat) 3031, 2930, 2873, 1780, 1742, 1454, 1435, 1419, 1371, 1331, 1237, 1192, 1166, 1093, 1072, 1036, 960, 912, 876, 813, 737, 700 cm^{-1}.

Compound 17 was prepared as **16** above from 128 mg (0.50 mmol) of *trans*-**9** employing $Pd(OAc)_2$ (0.10 equiv) but without added LiOAc. Purification with HPLC after workup afforded 66 mg (42%) of **17** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.40–7.29 (m, 5 H), 5.86 (ddd, J = 12.4, 2.4, 1.1 Hz, 1 H), 5.70 (dddd, J = 12.3, 4.8, 2.4, 1.2 Hz, 1 H), 5.41 (dtd, J = 7.6, 2.4, 1.6 Hz, 1 H), 5.35 (dddt, J = 5.1, 3.9, 2.7, 1.3 Hz, 1 H), 4.61 (d, J = 11.8 Hz, A-part of an AB-system, 1 H), 4.58 (d, J = 11.8 Hz, B-part of an AB-system, 1 H), 3.96 (m, 1 H), 3.15 (m, 1 H), 2.70 (dd, J = 17.5, 8.6 Hz, 1 H), 2.21 (dd, J = 17.5, 8.8 Hz, 1 H), 2.09 (s, 3 H), 2.03 (ddd, J = 14.9, 6.9, 5.7 Hz, 1 H), 1.67 (ddd, J = 14.9, 10.9, 2.2 Hz, 1 H); ^{13}C NMR δ 175.79, 169.97, 137.62, 130.40, 128.45, 127.93, 127.64, 125.81, 80.72, 73.29, 72.20 (two C), 35.93, 34.07, 30.43, 20.97; IR (neat) 2925, 1777, 1736, 1432, 1238, 1166, 1097, 1026 cm^{-1}. Anal. Calcd for $C_{18}H_{20}O_5$: C, 68.34; H, 6.73; Found: C, 68.88; H, 6.26.

Chlorolactonization of *cis*-9 to 18 and 19. The reaction was performed as described for preparation of **15** but $Pd(OAc)_2$ (0.10 equiv) was employed as catalyst. Workup after 6 days at room temperature gave according to ^{1}H NMR and HPLC a 1:1 mixture of **18** and **19**. These were isolated in 26 and 27% yield, respectively, after preparative HPLC (hexane/ethyl acetate, 70:30).

Compound 18: ^{1}H NMR ($CDCl_3$) δ 7.38–7.29 (m, 5 H), 5.78 (ddd, J = 12,2, 4.7, 2.4 Hz, 1 H), 5.68 (ddd, J = 12.2, 2.3, 1.2 Hz, 1 H), 5.18 (dq, J = 7.7, 2.3 Hz, 1 H), 4.89 (m, 1 H), 4.67 (d, J = 11.9 Hz, A-part of an AB-system, 1 H), 4.59 (d, J = 11.9 Hz, B-part of an AB-system, 1 H), 3.76 (dq, J = 8.7, 3.3 Hz, 1 H), 2.83 (m, 1 H), 2.73 (dd, J = 17.0, 8.7 Hz, 1 H), 2.24 (dd, J = 17.0, 7.0 Hz, 1 H), 2.09 (ddd, J = 14.3, 11.5, 8.8 Hz, 1 H), 2.00 (dddd, J = 14.4, 4.7, 3.0, 1.0 Hz, 1 H); ^{13}C NMR δ 175.12, 137.44, 128.89, 128.50, 127.97, 127.76, 127.33, 79.32, 75.52, 71.34, 61.00, 35.76 (two C), 32.36; IR (neat) 3030, 2937, 2872, 1783, 1453, 1417, 1337, 1303, 1167, 1098, 1069, 1026, 858, 742, 699 cm^{-1}.

Compound 19: ^{1}H NMR ($CDCl_3$) δ 7.39–7.30 (m, 5 H), 6.13 (dt, J = 11.9, 1.9 Hz, 1 H), 5.88 (ddd, J = 11.9, 7.8, 2.5 Hz, 1 H), 4.76 (dd, J = 8.0, 2.5 Hz, 1 H), 4.71 (d, J = 8.8, 2.61 Hz, 1 H), 4.61 (d, J = 12.0 Hz, A-part of an AB-system, 1 H), 4.58 (d, J = 12.0 Hz, B-part of an AB-system, 1 H), 4.09 (dm, J = 10.9 Hz), 2.91 (m, 1 H), 2.70 (dd, J = 17.5, 10.4 Hz, 1 H), 2.66 (dd, J = 17.5, 12.9 Hz, 1 H), 2.49 (m, 1 H), 2.33 (ddt, J = 13.4, 5.4, 2.2 Hz, 1 H); ^{13}C NMR δ 175.79, 140.13, 137.68, 128.53, 127.89, 127.60, 124.38, 80.33, 75.38, 70.42, 57.68, 35.26, 34.64, 32.48; IR (neat) 3031, 2937, 2872, 1783, 1453, 1417, 1337, 1303, 1167, 1098, 1069, 1026, 858, 742, 699 cm^{-1}. Anal. Calcd for $C_{16}H_{17}ClO_3$: C, 65.64; H, 5.85. Found: C, 65.43; H, 5.88.

Complex 20a. A solution of **1a** (160 mg, 1.16 mmol) in THF (14 mL) was added to $PdCl_2(PhCN)_2$ (444 mg, 1.16 mmol) and K_2CO_3 (168 mg, 1.21 mmol) at −18 °C. The mixture was stirred at −18 °C under an atmosphere of nitrogen for 2 h and was then stored in a refrigerator (−20 °C) overnight. The solvent was evaporated in vacuo, and the remaining solids were dissolved in CH_2Cl_2 (80 mL) and washed with H_2O (2 × 7 mL). The aqueous phase was back-extracted with CH_2Cl_2 (2 × 40 mL), and then the combined CH_2Cl_2 phases were evaporated *in vacuo* at below room

temperature (0–5 °C) to ~2 mL. The product was cooled to −20 °C and then **20a** was precipitated out by adding *n*-hexane (10 mL). The solvent was removed and the remaining solid was dried *in vacuo* at 0 °C to give 460 mg (72%) of the pure π-allyl complex **20a** as a pale yellow solid: ^{1}H NMR (400 MHz) δ 5.63 (t, J = 6.4 Hz, 1 H), 5.13 (m, 1 H), 4.91 (br d, J = 5.6 Hz, 1 H), 4.88 (br d, J = 6.8 Hz, 1 H), 3.01 (m, 1 H), 2.54 (dd, J = 17.6, 8 Hz, 1 H), 2.30 (ddd, J = 18.5, 7.5, 2.0 Hz, 1 H), 2.19 (dd, J = 17.6, 8 Hz, 1 H), 1.63 (dt, J = 18.5, 4.7 Hz, 1 H); ^{13}C NMR δ 174.79, 101.84, 78.43, 75.81, 70.04, 34.57, 30.23, 28.45.

Complex 20b. A solution of **1b** (66 mg, 0.434 mmol) in THF (5 mL) was added to $PdCl_2(PhCN)_2$ (166 mg, 0.434 mmol) and K_2CO_3 (63 mg, 0.455 mmol) at −18 °C. The mixture was stirred at −18 °C under an atmosphere of nitrogen for 2 h and was then stored in a refrigerator overnight. The solvent was evaporated *in vacuo*, and the remaining solids were dissolved in CH_2Cl_2 (40 mL) and washed with H_2O (5 mL). The aqueous phase was back-extracted with CH_2Cl_2 (30 mL), and then the combined CH_2Cl_2 phases were evaporated *in vacuo* to yield 155 mg of a yellow precipitate. The solid was rinsed with *n*-hexane (3 × 4 mL), and the remaining material was carefully recrystallized from a CH_2Cl_2/*n*-hexane mixture to give 90 mg (71%) of the π-allyl complex **20b** as a pale yellow crystals: ^{1}H NMR (400 MHz) δ 5.20 (ddd, J = 8.0, 6.0, 2.5 Hz, 1 H), 4.96 (dd, J = 5.0, 3.5 Hz, 1 H), 4.95 (t, J = 8.0 Hz, 1 H), 4.83 (dd, J = 8.0, 3.5 Hz, 1 H), 2.89 (m, 1 H), 2.73 (dd, J = 17.0, 7.6 Hz, 1 H), 2.20 (dd, J = 17.0, 3.7 Hz, 1 H), 2.13–1.92 (m, 2 H), 1.78–1.60 (m, 2 H); ^{13}C NMR δ 174.88, 101.27, 87.52, 79.56, 73.81, 39.35, 36.90, 30.97, 27.00; IR (KBr) 1787, 1157, 958, 930 cm^{-1}.

Complex 21. The bipyridyl complex was prepared according to ref 15, but $Ag(CF_3SO_3)$ was used in place of $Tl(CF_3SO_3)$: ^{1}H NMR (400 MHz, CD_3OD) δ 9.07 (ddd, J = 5.3, 1.6, 0.8 Hz, 2 H, bipy H-6,6′), 8.59 (ddd, J = 8.1, 1.3, 0.8 Hz, 2H, bipy H-3,3′), 8.34 (ddd, J = 8.1, 7.7, 1.6 Hz, 2 H, bipy H-4,4′), 7.82 (ddd, J = 7.7, 5.3, 1.3 Hz, 2 H, bipy H-5,5′), 6.28 (dd, J = 7.3, 6.9 Hz, 1 H, H-6), 5.52 (m, 1 H, H-5), 5.20 (ddd, J = 6.5, 2.0, 0.8 Hz, 1 H, H-7), 5.12 (dd, J = 7.3, 2.0 Hz, 1 H, H-7a), 3.00 (m, 1 H, H-3a), 2.63 (dd, J = 17.5, 8.5 Hz, 1 H, H-3-α), 2.41 (ddd, J = 18.5, 7.5, 2.1 Hz, 1 H, H-4-α), 2.38 (dd, J = 17.5, 8.4 Hz, 1 H, H-3-β), 2.10 (ddd, J = 18.5, 4.5, 4.5 Hz, 1 H, H-4-β).

Acknowledgment. Financial support from the Swedish Board for Technical Development and the Swedish Natural Science Research Council is gratefully acknowledged. We thank Johnson Matthey for a loan of palladium chloride.

Supplementary Material Available: Copies of ^{1}H or ^{13}C NMR spectra of *cis*-**10**, *cis*-**14**, **16**, **18**, **20b**, and **21** (6 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.