CHEMISTRY
A EUROPEAN JOURNAL

Stereocontrol in Alkyne Cyclocarbonylation Reactions Promoted by a Bioxazoline Palladium(II) Complex

Carla Carfagna,*[a] Giuseppe Gatti,[a] Luca Mosca,[a] Paola Paoli,[b] and Annalisa Guerri[b]

Abstract: Insertion of 1,2-disubstituted alkynes into $[Pd(CH_3)(CO)(BIOX)]^+[B\{3,5\text{-}(CF_3)_2C_6H_3\}_4]^-$ (**1**), where BIOX = (4*S*,4′*S*)-(−)-4,4′,5,5′-tetrahydro-4,4′-bis(1-methylethyl)-2,2′-bioxazole, leads to the formation of five-membered palladacycles, which, by reaction with carbon monoxide, produce a mixture of two diastereomeric forms of a palladium complex containing an η^3-allylic γ-lactone ligand. On leaving the mixture in solution, one isomer was converted into the other, reaching a diastereomeric excess of up to 94%. The steric and electronic factors responsible for the epimerization process were investigated by theoretical methods. Cleavage of the η^3-allyl–palladium bond by nucleophiles allowed highly substituted chiral butenolides to be synthesized in good enantiomeric excess.

Keywords: bioxazoline ligands · cyclocarbonylation · density functional calculations · diastereoselectivity · palladium

Introduction

Palladium-catalyzed carbonylation of unsaturated compounds is a powerful methodology which allows direct preparation of linear and cyclic compounds such as acids, esters, lactones, and lactams.[1] In particular, cyclocarbonylation of alkynes in the presence of palladium(II) species represents a well-established pathway for the synthesis of γ-lactones.[2] We have recently demonstrated, through isolation of the reaction intermediates, that the elementary steps involved in this process are the acylpalladation of alkyne, followed by insertion of CO and cyclization to yield a complex in which the lactone moiety is coordinated in an η^3-allylic fashion.[3] Lactone functionality is present in many biologically active compounds and natural products, including insect pheromones, cardenolides, and flavor components.[4] The activity of these substances often depends on their optical purity and absolute configuration. Although, several methodologies for the synthesis of chiral butenolides, obtained with different degrees of enantiomeric purity, have been described,[5] to our knowledge, a synthetic pathway that starts from an alkyne and carbon monoxide and utilizes an asymmetric metal catalyst has never been reported. To explore this possibility we decided to employ a palladium complex that contains a chiral bioxazoline ligand. This type of ligand has been used in several organic asymmetric syntheses catalyzed by transition metals; simple modification of the chiral centers located near to the donor nitrogen atoms allows high enantioselectivities to be achieved in many processes.[6] In previous studies we used the complex $[Pd(CH_3)(CO)(BIOX)]^+[BAr'_4]^-$ (**1**), where BIOX = (4*S*,4′*S*)-(−)-4,4′,5,5′-tetrahydro-4,4′-bis(1-methylethyl)-2,2′-bioxazole and Ar′ = 3,5-$(CF_3)_2C_6H_3$, as catalyst in the isotactic CO/styrene copolymerization reaction; the stereocontrol dictated by the metal center was evidenced in an investigation of the first steps of the copolymerization process.[7]

The purpose of the work described herein was to study, by NMR spectroscopy and DFT calculations, the intermediates deriving from sequential insertions of alkynes and carbon monoxide into complex **1** with the aim of understanding how the presence of the chiral ligand could lead to asymmetric induction in the cyclocarbonylation process. The knowledge acquired can be applied to the catalytic synthesis of enantiomerically pure butenolides.

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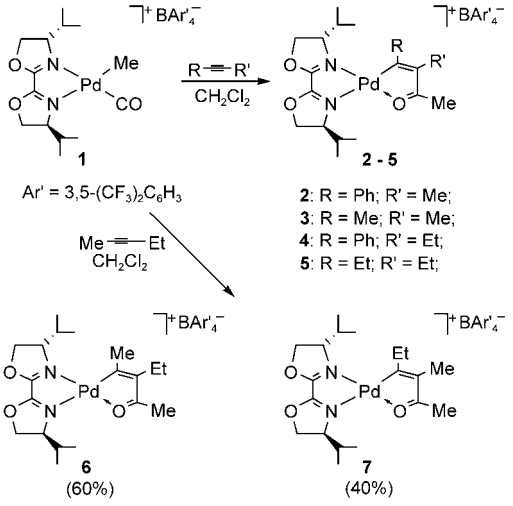
DOI: 10.1002/chem.200400326

Results and Discussion

Alkyne insertions into complex 1: Although the insertion of acetylenes into the palladium–carbon bond is a key step in many catalytic reactions,[1a] there is little information concerning the mechanism of this process.[8] Recently, we[3] and others[8a] reported the synthesis of five-membered palladacycles derived from stoichiometric insertion of alkynes into the palladium–acetyl bond. We found that while the reaction of complex $[Pd(CH_3)(CO)(i\text{PrDAB})]^+[BAr'_4]^-$ (iPrDAB = 1,4-diisopropyl-1,4-diaza-1,3-butadiene) with phenylacetylene produced an homopolymer, with 1,2-disubstituted acetylenes, it was possible to isolate stoichiometric insertion products.[3] An analogous investigation into the reactivity of the chiral complex **1** towards alkynes has been carried out. By using terminal alkynes such as methyl propiolate and 1-hexyne, the complexity of the NMR spectra of the reaction mixtures suggested the formation of multiple insertion products; moreover, with phenylacetylene an homopolymer with a *cis*-transoidal structure was obtained.[9] However, the reactions of 1-phenyl-1-propyne, 2-butyne, 1-phenyl-1-butyne, 3-hexyne, and 2-pentyne with **1** in dichloromethane afforded the five-membered palladacycles **2**–**7** (Scheme 1).



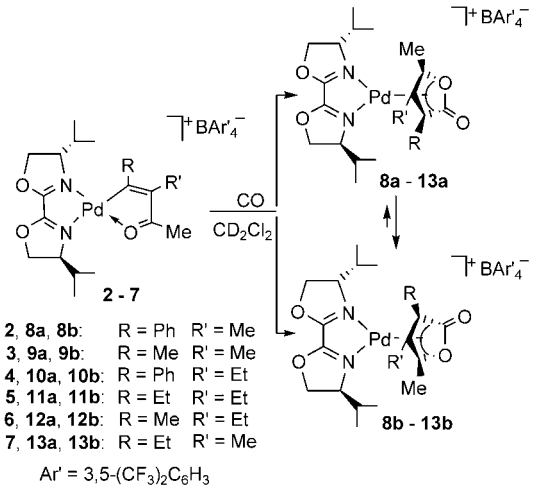
Scheme 1.

The structures of these palladacycles are in agreement with both their ^{1}H and ^{13}C NMR spectra in which the signals of the -C(R)=C(R′)- fragment, together with the resonances of the bioxazoline ligand, can be identified and assigned. Moreover, in all the complexes the methyl resonance at around $\delta_H = 2.30$ ppm and $\delta_C = 26$ ppm provides evidence of the acetyl group. In the ^{13}C NMR spectra, the signals due to the ring carbon atoms were observed in the ranges $\delta =$ 223.3–220.9, 204.1–191.3, and 150.1–141.8 ppm. The resonance at around $\delta = 198$ ppm has been attributed to the olefinic carbon atom linked to the palladium atom, which is strongly deshielded because of conjugation with the electron-withdrawing carbonyl group. For the same reason, the IR spectra of all the compounds show a C=O stretching band at 1570 cm^{-1}, a value lower by ~40 cm^{-1} than that of the analogous alkene-insertion products.[7a,10] The ^{1}H NMR spectra of compounds **2** and **4** also show the different shielding of the two *C*H–N nitrogen ligand signals ($\delta = 2.48$ versus 4.37 and 2.35 versus 4.44 ppm): the protons with signals at around $\delta = 2.4$ ppm are evidently in the shielding cone of the phenyl ring, which has an average conformation perpendicular to the palladium coordination plane.

Note that the insertion reactions of the unsymmetrical alkynes, 1-phenyl-1-propyne and 1-phenyl-1-butyne, are completely regioselective since only complexes **2** and **4**, with the phenyl group in the α position to the palladium atom, were obtained. In contrast, by using 2-pentyne, both regioisomers **6** and **7** were formed (Scheme 1). The slight excess of **6** could be explained by considering that the less bulky methyl group is preferred in the α position to the palladium atom in order to minimize steric repulsions with the ligand. However the regioselective insertion of alkynes bearing a phenyl group cannot be rationalized on the basis of steric factors. With the aim of providing some insight into this matter, molecular orbital calculations on simplified complexes of **6**, **7**, **2**, and its regioisomer **2′** (the latter having the phenyl group in the β position to the palladium atom), in which the BIOX ligand was modeled by L (vide infra), were performed. All the optimized complexes have a very similar molecular geometry around the metal ion, that is, a square-planar arrangement. The phenyl ring is almost perpendicular to the coordination plane in the models of **2′** and **2**; in the latter the CH–N hydrogen atom actually points towards the phenyl group. While the model compounds of **6** and **7** have comparable energies (they differ by ca. 2 kJ mol^{-1}), complex **2** is about 8 kJ mol^{-1} more stable than its corresponding regioisomer **2′**. Thus the selective insertion, which leads only to products in which the phenyl-substituted carbon atom is attached to the metal ion, appears to correlate with the enhanced energy difference. At the moment, from our data we can only suggest that this regioselectivity must be controlled by electronic factors, because, for example, of the ability of the phenyl group to delocalize electron density and/or to interact with the palladium atom during the insertion reaction, thus lowering the activation energy.[11]

Reaction of palladacycles 2–7 with CO: To check whether the reaction with CO resulted in a cyclocarbonylation process, complex **2** was dissolved at −30 °C in CD_2Cl_2 previously saturated with carbon monoxide and the solution was immediately transferred to a precooled NMR probe. Analysis of the ^{1}H and ^{13}C NMR spectra revealed the formation of a mixture of two products. For both species, the NMR and IR data are in agreement with a structure that contains an η^3-allylic γ-lactone moiety.[3] In particular, the two ^{13}C peaks at $\delta = 165$ ppm and the IR stretching bands at around 1800 cm^{-1} demonstrate the presence of the lactone C=O group; the six ^{13}C signals between $\delta = 70$ and 120 ppm provide evidence for the η^3-allyl fragments. The double pattern

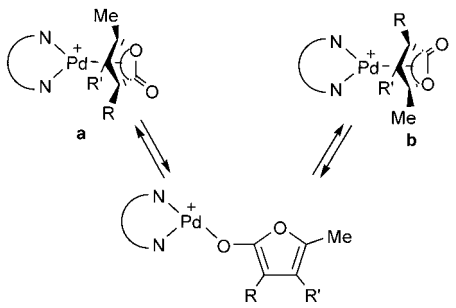
of resonances observed was attributed to the formation of the diastereomers **8a**/**8b** (a ratio of 55:45 was measured from the ^{1}H NMR spectrum), which correspond to the coordination of either one face or the other of the lactone ring to the palladium atom. Analogous behavior was observed for the reactions of **3**–**7** with CO (Scheme 2), with only



Scheme 2.

slight differences in the ratio of the two products **a**/**b** (varying from 56:44 for **11a**/**11b** to 40:60 for **9a**/**9b**). With complexes **6** and **7**, the reaction was carried out by using the mixture of the two palladacycles to produce compounds **12a**/**12b** together with **13a**/**13b**. The tentative assignment of the configuration of complexes **8a**–**13a** and **8b**–**13b**, as depicted in Scheme 2, is based on the calculations reported in the next section.

Note that by allowing the mixtures of **8**–**13** to stand in dichloromethane solution at 20 °C, isomers **a** convert into isomers **b**, finally reaching an equilibrium state that corresponds to a diastereomeric excess (*de*) of between 86 and 94 % depending on the complex.[12] We assume that the epimerization takes place through an intermediate η^1 complex that contains a palladium–oxygen σ bond (Scheme 3). A similar mechanism had been proposed by Trost and Toste to



Scheme 3. Possible intermediate in the epimerization reaction of diastereomers **a**/**b**.

explain the enantioselectivity observed in nucleophilic substitutions of racemic 5-acyloxy-2(5*H*)-furanones catalyzed by a chiral palladium complex.[5b] As far as we know, the present data constitute the first experimental observation of the previously postulated type **a** and **b** intermediates[5b] and of their epimerization.

It appears that the chiral bioxazoline ligand is responsible for the discrimination between the two faces of the lactone, producing an asymmetric induction with fairly good *de*. However the induction is not achieved during the cyclocarbonylation reaction, but rather through the subsequent conversion of **a** into **b**. On the basis of this consideration, we examined some thermodynamic and kinetic aspects of the isomerization process. The equilibrium constants for the epimerization reactions, determined by measuring the steady-state concentrations of the diastereomers at 20 °C, were in the range of 13.3 (for **12a**/**12b**) to 32.3 (for **8a**/**8b** and **10a**/**10b**), which corresponds to a $\Delta G^{\ominus}$ value of between −6.3 and −8.5 kJ mol^{-1}. For complexes **8a**/**8b** we carried out a series of experiments to study the kinetics of the approach to the equilibrium in order to determine the effect of temperature, solvent, and addition of coordinating ligands such as CO or acetonitrile.[13] Starting from the mixture (ratio 55:45) obtained at −30 °C, we monitored the variations of the concentrations of the two species with time by NMR spectroscopy and, as detailed in the Experimental Section, determined the rate constants for the forward reaction (k_f) under different conditions (Table 1).

Experiments (1) and (2) show that the rate constant increases remarkably with temperature. Moreover, comparison of experiments (3) with (1) and (4) indicates that the presence of a coordinating agent such as CO or acetonitrile produces a slight increase in the reaction rate: this effect could be attributed to the fact that these molecules stabilize the σ intermediate shown in Scheme 3, thereby lowering the activation energy. Finally, changing the reaction solvent from dichloromethane to acetone [experiment (5)] did not have a significant effect on the rate constant. These observations can be very useful since a fast epimerization is crucial for an efficient catalytic synthesis of optically active lactones.[5b]

The assignment of the stereochemistry of complexes **8**–**13** by using NMR techniques was not possible. However, as is evident from the data in Table 2, the differences observed between the chemical shifts of the allylic ^{13}C resonances for isomers **b** and **a** show a definite trend: in going from **a** to **b**, a deshielding of C3 and a shielding of C1 are observed. This finding suggests that each complex in the series **8a**–**13a** has the same configuration (and accordingly each complex within the series **8b**–**13b** is the corresponding epimer). This hypothesis is confirmed for compounds **8** and **9** by the theoretical studies reported in the next section.

Computational studies on simplified models of complexes 8 and 9: To understand the factors responsible for the epimerization process, to assign the configurations of compounds **8a**/**8b** and **9a**/**9b**, and to estimate their relative energies, we

Table 1. Rate constants for the forward reaction **8a**→**8b**.

Experiment	1	2	3	4	5
Solvent	CD_2Cl_2 sat. with CO	CD_2Cl_2 sat. with CO	CD_2Cl_2	$CD_2Cl_2+CD_3CN$ (CD_3CN/Pd = 10:1)	$[D_6]$acetone
T [°C]	20	35	20	20	20
k_f [$\times 10^{-3}$ min^{-1}]	17.88	240.0	8.44	13.45	8.28

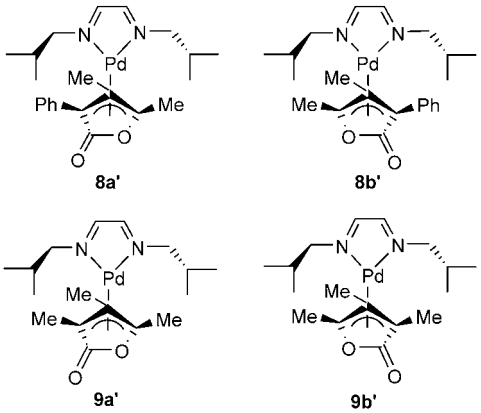
Table 2. ^{13}C chemical shifts for the allylic carbon atoms.[a]

	δ [ppm]		
Compound	C1	C2	C3
8a	79.2	112.4	114.9
8b	74.3	111.7	119.2
$\delta_{8b}-\delta_{8a}$	−4.9	−0.7	+4.3
9a	76.6	113.8	116.3
9b	70.6	113.2	120.3
$\delta_{9b}-\delta_{9a}$	−6.0	−0.6	+4.0
10a	79.4	117.6	112.9
10b	73.9	116.4	118.6
$\delta_{10b}-\delta_{10a}$	−5.5	−1.2	+5.7
11a	82.0	120.5	113.8
11b	75.4	116.5	121.0
$\delta_{11b}-\delta_{11a}$	−6.6	−4.0	+7.2
12a	75.7	119.7	114.9
12b	69.7	116.6	121.0
$\delta_{12b}-\delta_{12a}$	−6.0	−3.1	+6.1
13a	76.6	112.6	121.5
13b	75.7	111.0	122.4
$\delta_{13b}-\delta_{13a}$	−0.9	−1.6	+0.9

[a] For atom labeling refer to Figure 1.

used a combination of different computational approaches. Our starting hypothesis was that the relative disposition of the isopropyl groups with respect to the N–Pd–N plane should be crucial in determining the coordination geometry of the γ-lactone ring. We then focused our attention on the steric interactions between the two isopropyl moieties of the bioxazoline ligand and the substituents on the allylic carbon atoms C1 and C3, considering that, in the metal complexes **8** and **9**, these groups would be almost facing each other. In addition, there is no doubt that repulsive interactions will be more effective in the metal complexes **8a**/**8b** than in **9a**/**9b** given the presence, in the former couple, of the bulky phenyl group. A rough estimation of the relative steric strain of the bioxazoline ligand and the γ-lactone ring was obtained by molecular modeling studies on ad hoc simplified model compounds of the two possible diastereomers of **8**. From these calculations it was possible to deduce that the less crowded complex **8b**, in which the phenyl ring and the nearest isopropyl group are above and below the Pd coordination plane, respectively, is energetically favored over **8a**. Given that the substituents on the allylic carbon atoms C1 and C3 are the same an analogous approach cannot be applied to assign the stereochemistry of the **9a**/**9b** couple.

Thus, to account for the **9a**/**9b** equilibrium ratio observed, electronic effects must be considered. Hence DFT calculations were performed on the four models **8a′**, **8b′**, **9a′**, and **9b′** sketched in Scheme 4. To save computational time, a simplified nitrogen ligand (L), which preserves the steric feature of the bioxazoline, was used.



Scheme 4. Sketches of models **8a′**, **8b′**, **9a′**, and **9b′** used as a basis for the DFT calculations.

The optimized structures are shown in Figure 1, and Table 3 reports the corresponding geometrical parameters together with several experimental bond distances and angles of the analogous compound **14** that contains the α-diimine ligand, 1,4-diisopropyl-1,4-diaza-1,3-butadiene (Figure 2), whose X-ray structure has been described in a previous paper.[3] The results of the calculations show that models **8b′** and **9b′** are more stable than their corresponding isomers, the energy difference being $E_{8b'}-E_{8a'}=-11.7$ kJ mol^{-1} and $E_{9b'}-E_{9a'}=-8.3$ kJ mol^{-1}. Note that such differences are comparable to the order of magnitude of $\Delta G^{\ominus}$ obtained from the value of K_{eq} determined at 20 °C.

To assess the reliability of the optimized model compounds, some geometrical features can be considered. The position of the γ-lactone ring with respect to the coordination plane, described by the tilt angle α, is similar to that in the solid-state structure of **14** (no solid-state structures of Pd–γ-lactone complexes have been found in CSD version 5.24).[14] Moreover, in the model **8b′** and in the structure of **14**, the orientations of the phenyl group with respect to the γ-lactone ring (as evidenced by the dihedral angle β) are comparable (Table 3). Therefore we can assume that the adopted theoretical model adequately describes the steric interactions between the substituents on the palladium ligands. However the bond lengths of the metal coordination sphere were longer than those observed in the crystal structure of **14**. For models **8a′** and **8b′**, we calculated the distances of the hydrogen H^A atom (Figure 1) of the nitrogen ligand from the geometrical center of the phenyl group and from the plane defined by the same ring. These distances, reported in Table 3, were used to evaluate the anisotropic effect of the aromatic ring on H^A by the Haigh–Maillon method:[15] from this estimation the H^A atom should be

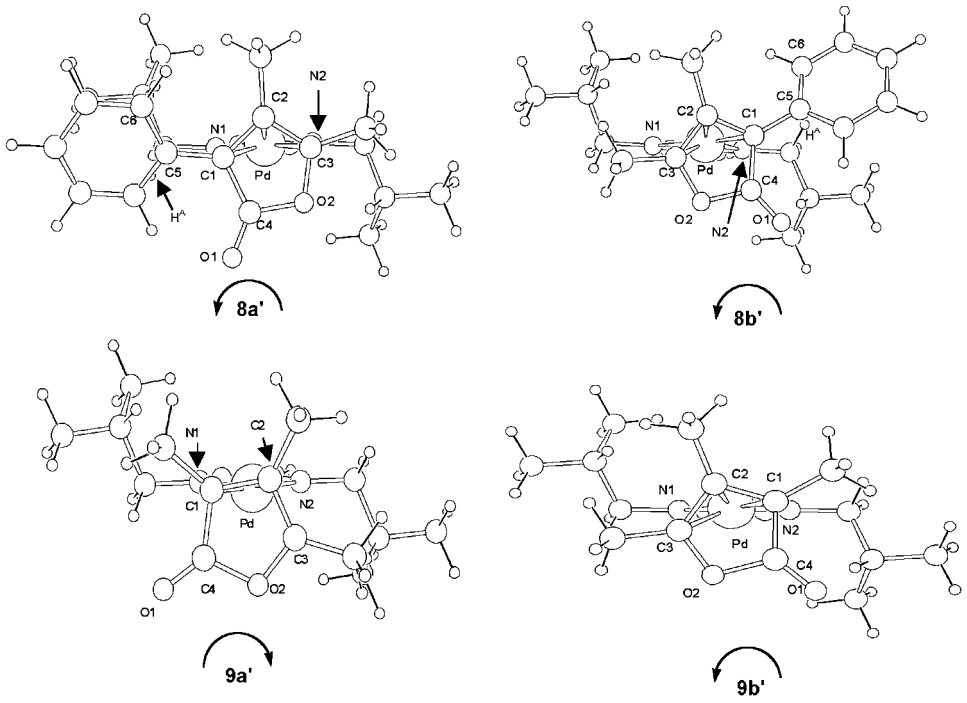


Figure 1. DFT-optimized structures of model compounds **8a′**, **8b′**, **9a′**, and **9b′**. Curled arrows indicate the rotation undergone by the γ-lactone ring during the minimization procedure.

Interestingly, the effect of the optimization procedure on the dihedral angle τ is considerably different in the four models. Indeed, in **8b′** and **9b′** an anticlockwise rotation of the lactone ring (with respect to the starting geometry, where $\tau = 0°$) occurred, resulting in τ values of 18.0 and 19.5°, respectively. The rotation was anticlockwise also in **8a′**, although it was significantly less marked ($\tau = 3.0°$). Note that a twist of 12.2° in the same direction has been observed in the X-ray solid-state structure of the less hindered compound **14**. Finally, in **9a′** a tilting angle of 24.8° in the clockwise direction was observed.

To rationalize the rotation of the γ-lactone produced by the minimization process, additional DFT calculations were performed on the model compounds **I**–**IV** (Scheme 5) that have different steric and electronic features.

Table 3. Most significant geometrical features of the optimized models and comparison with the X-ray structure of **14**.

Geometrical parameter[a]	**8a′**	**8b′**	**9a′**	**9b′**	**14**[b]
Pd–N1 [Å]	2.21	2.20	2.18	2.20	2.107(5)
Pd–N2 [Å]	2.20	2.18	2.21	2.18	2.132(5)
Pd–C1 [Å]	2.33	2.22	2.18	2.21	2.171(6)
Pd–C2 [Å]	2.21	2.21	2.21	2.20	2.152(6)
Pd–C3 [Å]	2.22	2.33	2.47	2.35	2.199(6)
N2–Pd–N1 [°]	76.5	76.8	76.7	79.6	78.6(2)
C1–Pd–C3 [°]	59.7	59.5	57.8	59.2	61.9(2)
τ[c] [°]	3.0	18.0	−24.8	19.5	12.2(3)
α[d] [°]	93.6	91.9	91.3	92.2	96.2(2)
β[e] [°]	−15.2	−47.9			−45(1)
H^A–PhC_g[f] [Å]	3.66	3.29			
H^A–Phpp[g] [Å]	2.74	2.80			

[a] For atom labeling refer to Figure 1. [b] For atom labeling refer to Figure 2. [c] τ is the dihedral angle, defined as N1-N2-C3-C1 in models **8a′** and **9a′** and as N1-N2-C1-C3 in models **8b′**, **9b′**, and in complex **14**. [d] α is the angle between the mean plane described by the γ-lactone ring and the N1-Pd-N2 plane. [e] β is the dihedral angle, defined as C2-C1-C5-C6. [f] The distance between the hydrogen H^A atom and the geometrical center of the phenyl ring. [g] The distance between the hydrogen H^A atom and the plane defined by the aromatic ring.

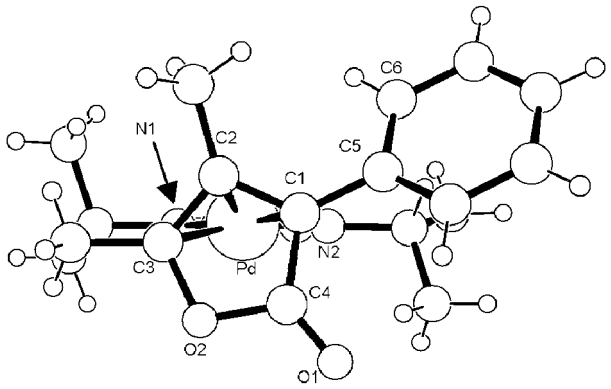
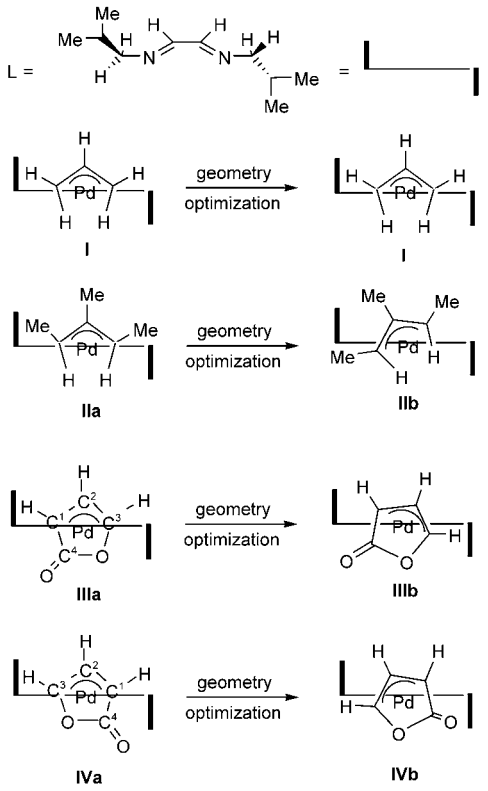


Figure 2. X-ray structure of complex **14**.

0.14 ppm more shielded in model **8b′** than in **8a′**. In fact, in their ^{1}H NMR spectrum (measured at −80 °C in order to prevent the broadening of ligand signals due to fast exchange on the NMR time scale) the chemical shift of the H^A atom is at $\delta = 3.47$ ppm in the more stable isomer and at $\delta = 3.78$ ppm in the less stable one: this is fairly good evidence in favor of the assignment of the configurations for **8a** and **8b**.

The optimization procedure did not generate any twisting of the allyl group in model **I**, as expected on the basis of the π electron distribution of the allyl anion. In fact the four π electrons are spread all over the three carbon atoms (Figure 3). In particular, they are distributed in an *all-in-phase* (second HOMO) and in an *out-of-phase* combination (HOMO), the latter involving the end carbon atoms. As a result, the best interaction between the σ-metal orbital and the second HOMO orbital, as well as the dπ-metal orbital and the HOMO, is reached when there is no twisting of the allyl anion, that is, when it acts as a trihapto ligand. A Walsh diagram for the L-Pd-allyl system obtained with CACAO[16]



Scheme 5.

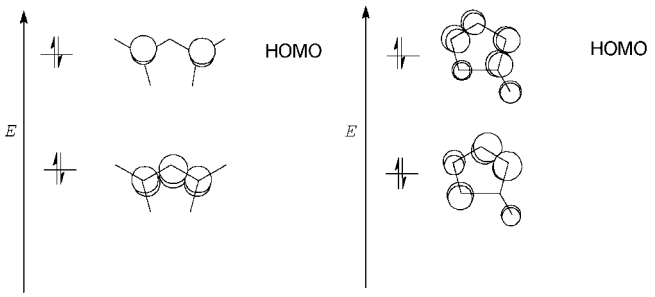


Figure 3. The π molecular orbitals of the allyl anion (left) and the γ-lactone anion (right) as obtained with CACAO.

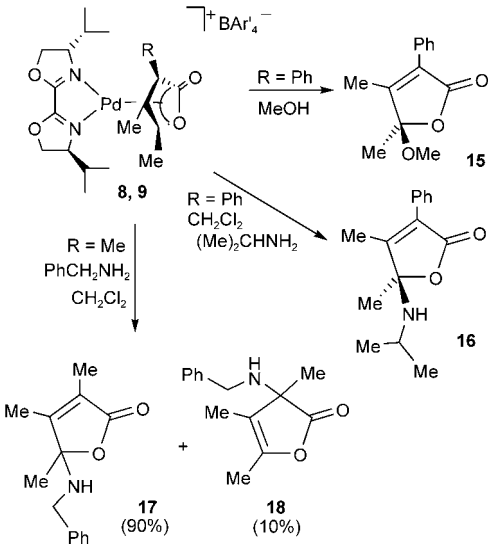
and based on EHMO calculations[17] highlights the existence of an energy barrier to the rotation of the allyl anion and confirms that the energy minimum corresponds to $\tau = 0°$.

In the more crowded model **IIa** (Scheme 5), the allyl group rotates in an anticlockwise direction upon energy minimization ($\tau \approx 6°$). Therefore in this case the intermolecular repulsions must overcome the electronic requirements and drive the rearrangement of the allyl ligand with the result that the methyl groups on the C1 and C3 atoms and the isopropyl groups are no longer facing (model **IIb**). Note that a similar rotation of the allyl moiety has been observed in the crystal structure of several complexes in order to minimize the steric interactions.[18]

In contrast, we can suppose that in **IIIa** and **IVa** (Scheme 5) the orientation of the γ-lactone ligand is mainly driven by electronic effects. As is evident in Figure 3, the -O(C=O)- group significantly changes the π-electron distribution of the allyl system. In fact in the γ-lactone ring the electron density is mostly localized on the C1–C2 bond in the second HOMO. Instead in the HOMO the main contributions arise from the π clouds on C2–C3 and C1–C4. Thus the overlap between the metal and the lactone orbitals is optimized when twisting of the ring takes place (model **IIIb** and **IVb**) as also revealed by the corresponding L-Pd-γ-lactone Walsh diagram which shows an energy minimum when the lactone ring is rotated about 20° out of the L–Pd plane. In particular, in **IIIa** a clockwise rotation is demanded, while in **IVa** the best overlap requires an anticlockwise twisting.

In conclusion, on the basis of these results the higher stability of the model compounds **8b′** and **9b′** can be attributed to the fact that in these isomers steric and electronic effects work in the same direction producing the observed (ca. 19°) anticlockwise rotation of the lactone ring. As a consequence of this twist the coordination of the γ-lactone to the palladium ion is intermediate between two limiting situations: a trihapto- ($\tau = 0°$) and dihapto-bound olefinic system ($\tau \approx 30°$). In **8a′** the two effects, steric and electronic, are working in opposite directions, with the steric contribution prevailing on the electronic one, as seen from the very small anticlockwise rotation observed ($\tau = 3.0°$). Finally, in the less hindered **9a′** complex the γ-lactone rotates in a clockwise direction of about 25°, therefore it behaves almost as a dihapto ligand. In fact, in this case the electronic contribution significantly predominates over the steric one.

Nucleophilic attack on the η^3-allyl lactone moiety and asymmetric synthesis of lactones: It is well known that η^3-allyl palladium complexes undergo nucleophilic attack by carbon, nitrogen, oxygen, or sulfur donor molecules.[19] An appropriate choice of chiral ligand can lead to asymmetric induction in such processes.[20] In particular, bioxazoline[21] and the phosphine-oxazoline[22] mixed ligand have been employed with good results in palladium-catalyzed asymmetric allylic alkylation reactions. We were interested to see whether the reaction of the allylic lactone complexes (after equilibration of the diastereomeric mixture at 20 °C) with nucleophiles resulted in the formation of optically active butenolides. Actually, by dissolving **8** in methanol, compound **15** was formed quantitatively; moreover, the reaction of **8** with isopropylamine in dichloromethane gave the γ-lactone **16** in high yield (Scheme 6). With regards the regioselectivity of the reaction, in both cases the nucleophilic attack takes place exclusively on the η^3-allylic carbon atom next to the oxygen atom, which has the lowest electron density.[5b,23] Nucleophilic addition to this carbon atom is also favored since an η^2-olefinic Pd^0 intermediate with a better π-acceptor olefin is produced. Both compounds **15** and **16** have an *ee* of 90 % [as determined from their ^{1}H NMR spectra with the use of the shift reagent Eu(hfc)$_3$]; this value reflects the diastereomeric excess of the starting palladium complex. By



Scheme 6.

considering an *exo* attack by the nucleophiles, the expected chirality of the major enantiomer is *R*. The reactivity of complex **9** (after equilibration at 20 °C) was tested by using benzylamine as the nucleophilic reagent. The ^{1}H NMR spectrum of the mixture formed shows the presence of two products in a 9:1 ratio with a similar pattern of signals. Compound **17** was the major component and for the minor one we suppose the structure **18**. In this case the attack by the nucleophile seems not to be regioselective, addition taking place at both the C3 (preferred) and C1 atoms of the allyl system. In addition, the presence of two C=O stretching bands at 1742 (strong) and 1774 cm^{-1} (weak) is in agreement with a conjugated (**17**) and a nonconjugated (**18**) carbonyl group.

Conclusions

In summary, we have characterized the intermediates that result from the insertion of alkynes and CO into a methyl carbonyl palladium complex bearing a chiral bioxazoline ligand. We have shown that the resulting products were mixtures of two diastereomeric palladium compounds that contain an η^3-allylic γ-lactone ligand. We then observed an epimerization process that leads to a *de* of up to 94% due to the presence of the chiral ligand, which is responsible for the discrimination between the two possible coordinated faces of the lactone. Theoretical calculations have allowed us to rationalize this finding and to assign the stereochemistry of the products. Finally, through selective nucleophilic attacks on the η^3-allylic lactone complexes, highly substituted chiral butenolides were synthesized with good *ee*. We are planning further investigations in this area with the aim of developing a catalytic system for the asymmetric synthesis of these products starting from alkynes and carbon monoxide.

Experimental Section

All manipulations were carried out under nitrogen by using Schlenk techniques. Solvents were dried by standard methods and freshly distilled under nitrogen. Deuteriated solvents were degassed and stored over 3 Å molecular sieves. Complex $[Pd(CH_3)(CO)(BIOX)]^+[BAr'_4]^-$ (**1**) [BIOX = (4*S*,4′*S*)-(−)-4,4′,5,5′-tetrahydro-4,4′-bis(1-methylethyl)-2,2′-bioxazole; Ar′ = 3,5-$(CF_3)_2C_6H_3$] was synthesized as previously reported in the literature.[7a] 1-Phenyl-1-propyne, 2-butyne, 3-hexyne, 1-phenyl-1-butyne, and 2-pentyne were purchased from Aldrich and used after distillation over calcium hydride. Carbon monoxide (Cp grade 99.99%) was supplied by Air Liquide. Elemental analyses (C, H, N) were carried out with a Fisons Instruments 1108 CHNS-O Elemental Analyzer. Infrared spectra were measured in the range of 4000–600 cm^{-1} on a Nicolet FT-IR Avatar 360 spectrometer. NMR spectra were measured on a Bruker AC200 spectrometer with a multinuclear 5 mm probe head. ^{1}H and ^{13}C NMR chemical shifts are given relative to TMS and were measured by using the residual proton or carbon resonance of the deuteriated solvents. Assignments of ^{13}C NMR spectra were made on the basis of DEPT, HMQC, and HMBC experiments.

In compounds **2**–**13** the counterion $[BAr'_4]^-$ gives a pattern of NMR signals with the following typical chemical shifts: ^{1}H NMR (200.13 MHz, $CDCl_3$, 20 °C): $\delta = 7.71$ (s, 8H; Ar′-H_o), 7.54 ppm (s, 4H; Ar′-H_p); ^{13}C NMR (50.32 MHz, $CDCl_3$, 20 °C): $\delta = 161.7$ (q, ^1J(C,B) = 49.3 Hz, Ar′-C_i), 134.8 (Ar′-C_o), 128.8 (q, ^2J(C,F) = 31.2 Hz, Ar′-C_m), 124.6 (q, ^1J(C,F) = 270.8 Hz, CF_3), 117.5 ppm (Ar′-C_p).

General procedure for the synthesis of complexes 2–5: The appropriate alkyne was added at −30 °C to a solution of **1** in dichloromethane (2 mL). The reaction mixture was warmed to 0 °C over 2 h. After filtration through Celite, the solvent was removed by evaporation and the resulting solid was washed with hexane (4 × 4 mL) to give the yellow compounds **2**–**5**.

$[Pd\{C(Ph)=C(CH_3)C(O)CH_3\}(BIOX)]^+[BAr'_4]^-$ (2): 1-Phenyl-1-propyne: 18.5 μL (0.148 mmol); **1**: 183.0 mg (0.148 mmol). Yield: 194.1 mg (0.143 mmol, 97%) of **2**. IR (Nujol): $\tilde{\nu} = 1638$, 1609 (C=N), 1573 cm^{-1} (C=O); ^{1}H NMR (200.13 MHz, $CDCl_3$, 20 °C): $\delta = 7.42$–7.33 (m, 3H; Ph-H_m, Ph-H_p), 7.28–7.18 (br m, 2H; Ph-H_o), 4.74 (dd, ^2J(H,H) = 9.4, ^3J(H,H) = 10.4 Hz, 1H; CH_2-O), 4.62 (dd, ^2J(H,H) = 9.4, ^3J(H,H) = 7.4 Hz, 1H; CH_2-O), 4.45 (dd, ^2J(H,H) = 9.6, ^3J(H,H) = 4.0 Hz, 1H; CH_2-O), 4.37 (ddd, ^3J(H,H) = 10.4, 7.4, 3.1 Hz, 1H; CH-N), 4.30 (dd, ^2J(H,H) = 9.6, ^3J(H,H) = 9.3 Hz, 1H; CH_2-O), 2.48 (ddd, ^3J(H,H) = 9.3, 4.0, 3.1 Hz, 1H; CH-N), 2.34 (s, 3H; C(O)(CH_3)), 2.32–2.16, 1.40–1.24 (m, 1H each, CH-$(CH_3)_2$), 1.68 (s, 3H; C(Ph)=C(CH_3)), 1.00, 0.99, 0.57, 0.34 ppm (d, ^3J(H,H) = 6.9 Hz, 3H each, CH(CH_3)$_2$); ^{13}C NMR (50.32 MHz, $CDCl_3$, 20 °C): $\delta = 223.1$ (*C*(O)), 191.3 (Pd*C*(Ph)=C(CH_3)), 159.7, 158.7 (*C*=N), 143.6 (PdC(Ph)=*C*(CH_3)), 142.3 (Ph-C_i), 129.0, 124.9 (Ph-C_m, Ph-C_o), 128.8 (Ph-C_p), 74.6, 72.4 (*C*H$_2$O), 69.5, 65.2 (*C*HN), 30.3, 29.6 (*C*H-$(CH_3)_2$), 26.4 (C(O)(*C*H$_3$)), 18.1, 17.6 15.9, 13.2 (CH(*C*H$_3$)$_2$), 14.4 ppm (C(Ph)=C(*C*H$_3$)); elemental analysis calcd (%) for $C_{55}H_{43}BF_{24}N_2O_3Pd$ (1353.1): C 48.82, H 3.20, N 2.07; found: C 49.10, H 3.00, N 2.15.

$[Pd\{C(CH_3)=C(CH_3)C(O)CH_3\}(BIOX)]^+[BAr'_4]^-$ (3): 2-Butyne: 11.0 μL (0.141 mmol); **1**: 97.6 mg (0.079 mmol). Yield: 89.3 mg (0.069 mmol, 88%) of **3**. IR (Nujol): $\tilde{\nu} = 1638$, 1611 (C=N), 1572 cm^{-1} (C=O); ^{1}H NMR (200.13 MHz, $CDCl_3$, 20 °C): $\delta = 4.79$ (dd, ^2J(H,H) = 10.0, ^3J(H,H) = 4.1 Hz, 1H; CH_2-O), 4.73 (dd, ^2J(H,H) = 10.0, ^3J(H,H) = 9.2 Hz, 1H; CH_2-O), 4.65 (dd, ^2J(H,H) = 10.0, ^3J(H,H) = 10.0 Hz, 1H; CH_2-O), 4.59 (dd, ^2J(H,H) = 10.0, ^3J(H,H) = 7.4 Hz, 1H; CH_2-O), 4.34 (ddd, ^3J(H,H) = 10.0, 7.4, 4.4 Hz, 1H; CH-N), 4.26 (ddd, ^3J(H,H) = 9.2, 4.1, 3.1 Hz, 1H; CH-N), 2.22 (s, 3H; C(O)(CH_3)), 2.30–2.14, 2.08–1.92 (m, 1H each, CH-$(CH_3)_2$), 1.91 (q, ^5J(H,H) = 1.0 Hz, 3H; C(CH_3)=C(CH$_3$)), 1.74 (q, ^5J(H,H) = 1.0 Hz, 3H; C(CH$_3$)=C(CH_3)), 0.94 (d, ^3J(H,H) = 6.9 Hz, 3H; CH(CH_3)$_2$), 0.93 (d, ^3J(H,H) = 6.9 Hz, 6H; CH(CH_3)$_2$), 0.80 ppm (d, ^3J(H,H) = 6.9 Hz, 3H; CH(CH_3)$_2$); ^{13}C NMR (50.32 MHz, CD_2Cl_2, −30 °C): $\delta = 221.1$ (*C*(O)), 197.9 (Pd*C*(CH$_3$)=C(CH$_3$)), 160.4, 158.5 (*C*=N), 143.3 (PdC(CH$_3$)=*C*(CH$_3$)), 74.7, 73.1 (*C*H$_2$O), 69.3, 66.9 (*C*HN), 30.2, 30.1 (*C*H(CH$_3$)$_2$), 26.5 (C(O)(*C*H$_3$)), 25.9 (PdC(*C*H$_3$)=C(CH$_3$)), 18.2, 18.1, 15.5, 13.5 (CH(*C*H$_3$)$_2$), 13.0 ppm (PdC(CH$_3$)=C(*C*H$_3$)); elemental analysis

calcd (%) for $C_{50}H_{41}BF_{24}N_2O_3Pd$ (1291.1): C 46.52, H 3.20, N 2.17; found: C 46.15, H 3.15, N 2.03.

$[Pd\{C(Ph)=C(CH_2CH_3)C(O)CH_3\}(BIOX)]^+[BAr'_4]^-$ (4): 1-Phenyl-1-butyne: 5.2 μL (36.6 μmol); **1**: 45.4 mg (36.7 μmol). Yield: 45.7 mg (33.4 μmol, 91%) of **4**. IR (Nujol): $\tilde{\nu}$ = 1639, 1610 (C=N), 1568 cm^{-1} (C=O); ^1H NMR (200.13 MHz, CD_2Cl_2, −30°C): δ = 7.43–7.33 (m, 3H; Ph-H_m, Ph-H_p), 7.20–7.12 (br m, 2H; Ph-H_o), 4.80 (dd, ^2J(H,H) = 9.4, ^3J(H,H) = 10.4 Hz, 1H; CH_2-O), 4.69 (dd, ^2J(H,H) = 9.4, ^3J(H,H) = 7.4 Hz, 1H; CH_2-O), 4.51 (dd, ^2J(H,H) = 9.6, ^3J(H,H) = 4.0 Hz, 1H; CH_2-O), 4.42 (ddd, ^3J(H,H) = 10.4, 7.4, 3.3 Hz, 1H; CH-N), 4.38 (dd, ^2J(H,H) = 9.6, ^3J(H,H) = 9.4 Hz, 1H; CH_2-O), 2.42–2.24 (m, 2H; CH-N and CH(CH_3)$_2$), 2.39 (s, 3H; C(O)(CH_3)), 1.40–1.24 (m, 1H; CH(CH_3)$_2$), 2.06 (dq, ^2J(H,H) = 14.5 Hz, ^3J(H,H) = 7.5 Hz, 1H; C(Ph)=C(CH_2CH$_3$)), 1.93 (dq, ^2J(H,H) = 14.5 Hz, ^3J(H,H) = 7.5 Hz, 1H; C(Ph)=C(CH_2CH$_3$)), 0.99, 0.97, 0.57, 0.34 (d, ^3J(H,H) = 6.9 Hz, 3H each, CH(CH_3)$_2$), 0.90 ppm (t, ^3J(H,H) = 7.5 Hz, 3H; C(Ph)=C(CH$_2$CH_3)); ^{13}C NMR (50.32 MHz, CD_2Cl_2, −30°C): δ = 223.3 (*C*(O)), 192.4 (Pd*C*(Ph)=C(CH$_2$CH$_3$)), 159.6, 158.5 (*C*=N), 150.1 (PdC(Ph)=*C*(CH$_2$CH$_3$)), 142.4 (Ph-C_i), 129.1, 128.3, 125.2, 124.0 (Ph-C_m, Ph-C_o), 128.9 (Ph-C_p), 74.5, 72.8 (*C*H$_2$O), 69.1, 64.9 (*C*HN), 30.0, 29.6 (*C*H(CH_3)$_2$), 26.3 (C(O)(*C*H$_3$)), 22.0 (C(Ph)=C(*C*H$_2$CH$_3$)), 18.2, 17.6 15.5, 13.1 (CH(*C*H$_3$)$_2$), 14.5 ppm (C(Ph)=C(CH$_2$*C*H$_3$)); elemental analysis calcd (%) for $C_{56}H_{45}BF_{24}N_2O_3Pd$ (1367.2): C 49.20, H 3.32, N 2.05; found: C 48.85, H 3.20, N 1.99.

$[Pd\{C(CH_2CH_3)=C(CH_2CH_3)C(O)CH_3\}(BIOX)]^+[BAr'_4]^-$ (5): 3-Hexyne: 15.5 μL (136.6 μmol); **1**: 84.3 mg (68.1 μmol). Yield: 66.7 mg (50.5 μmol, 75%) of **5**. IR (Nujol): $\tilde{\nu}$ = 1634, 1612 (C=N), 1565 cm^{-1} (C=O); ^1H NMR (200.13 MHz, CD_2Cl_2, −30°C): δ = 4.91–4.65 (m, 4H; CH_2-O), 4.47–4.36, 4.13–4.05 (m, 1H each, CH-N), 2.29 (s, 3H; C(O)(CH_3)), 2.28–1.90 (m, 2H; CH(CH_3)$_2$), 2.17 (q, ^3J(H,H) = 7.5 Hz, 2H; PdC(CH$_2$CH$_3$)=C(CH_2CH$_3$)), 2.07–1.86 (m, 2H; PdC(CH_2CH$_3$)=C(CH$_2$CH$_3$)), 1.14 (t, ^3J(H,H) = 7.5 Hz, 3H; PdC(CH$_2$CH_3)=C(CH$_2$CH$_3$)), 0.99 (t, ^3J(H,H) = 7.5 Hz, 3H; PdC(CH$_2$CH$_3$)=C(CH$_2$CH_3)), 0.94 (d, ^3J(H,H) = 6.9 Hz, 9H; CH(CH_3)$_2$), 0.80 ppm (d, ^3J(H,H) = 6.9 Hz, 3H; CH(CH_3)$_2$); ^{13}C NMR (50.32 MHz, CD_2Cl_2, −30°C): δ = 221.7 (*C*(O)), 204.1 (Pd*C*(CH$_2$CH$_3$)=C(CH$_2$CH$_3$)), 160.4, 158.1 (*C*=N), 148.4 (PdC(CH$_2$CH$_3$)=*C*(CH$_2$CH$_3$)), 74.3, 72.8 (*C*H$_2$O), 69.1, 66.5 (*C*HN), 30.5, 29.8 (*C*H(CH_3)$_2$), 30.0 (PdC(*C*H$_2$CH$_3$)=C(CH$_2$CH$_3$)), 25.8 (C(O)(*C*H$_3$)), 20.7 (PdC(CH$_2$CH$_3$)=C(*C*H$_2$CH$_3$)), 18.1, 17.9, 15.3, 13.4 (CH(*C*H$_3$)$_2$), 14.5 (PdC(CH$_2$CH$_3$)=C(CH$_2$*C*H$_3$)), 12.6 ppm (PdC(CH$_2$*C*H$_3$)=C(CH$_2$CH$_3$)); elemental analysis calcd (%) for $C_{52}H_{45}BF_{24}N_2O_3Pd$ (1319.1): C 47.35, H 3.44, N 2.12; found: C 46.97, H 3.30, N 2.01.

$[Pd\{C(CH_3)=C(CH_2CH_3)C(O)CH_3\}(BIOX)]^+[BAr'_4]^-$ (6) and $[Pd\{C(CH_2CH_3)=C(CH_3)C(O)CH_3\}(BIOX)]^+[BAr'_4]^-$ (7): 2-Pentyne (14 μL, 0.147 mmol) was added to a solution of **1** (89.0 mg, 0.072 mmol) in dichloromethane (2 mL) at −30°C. The reaction mixture was warmed to 0°C over 2 h. After filtration through Celite, the solvent was evaporated and the resulting solid was washed with hexane to give 92.7 mg (0.071 mmol, 98%) of a yellow powder, which was a 60:40 mixture of the two regioisomers **6**/**7**. IR (Nujol): $\tilde{\nu}$ = 1632, 1611 (C=N), 1567 cm^{-1} (C=O). Complex **6**: ^1H NMR (200.13 MHz, CD_2Cl_2, −30°C): δ = 4.89–4.63 (m, 4H; CH_2-O), 4.45–4.35, 4.37–4.28 (m, 1H each, CH-N), 2.26 (s, 3H; C(O)(CH_3)), 2.36–2.18, 2.12–1.94 (m, 1H each, CH(CH_3)$_2$), 2.16 (q, ^3J(H,H) = 7.5 Hz, 2H; PdC(CH$_3$)=C(CH_2CH$_3$)), 0.96 (t, ^3J(H,H) = 7.5 Hz, 3H; PdC(CH$_3$)=C(CH$_2$CH_3)), 0.94 (d, ^3J(H,H) = 6.9 Hz, 3H; CH(CH_3)$_2$), 0.92 (d, ^3J(H,H) = 6.9 Hz, 6H; CH(CH_3)$_2$), 0.80 ppm (d, ^3J(H,H) = 6.9 Hz, 3H; CH(CH_3)$_2$); ^{13}C NMR (50.32 MHz, CD_2Cl_2, −30°C): δ = 220.9 (*C*(O)), 198.5 (Pd*C*(CH$_3$)=C(CH$_2$CH$_3$)), 160.5, 158.2 (*C*=N), 149.8 (PdC(CH$_3$)=*C*(CH$_2$CH$_3$)), 74.4, 72.9 (*C*H$_2$O), 69.1, 66.8 (*C*HN), 30.0, 29.9 (*C*H(CH_3)$_2$), 25.7 (C(O)(*C*H$_3$)), 25.3 (PdC(*C*H$_3$)=C(CH$_2$CH$_3$)), 20.8 (PdC(CH$_3$)=C(*C*H$_2$CH$_3$)), 18.0, 17.9, 15.3, 13.3 (CH(*C*H$_3$)$_2$), 13.6 ppm (PdC(CH$_3$)=C(CH$_2$*C*H$_3$)). Complex **7**: ^1H NMR (200.13 MHz, CD_2Cl_2, −30°C): δ = 4.91–4.65 (m, 4H; CH_2-O), 4.46–4.36, 4.15–4.07 (m, 1H each, CH-N), 2.24 (s, 3H; C(O)(CH_3)), 2.28–2.10, 2.12–1.94 (m, 1H each, CH(CH_3)$_2$), 2.06–1.86 (m, 2H; PdC(CH_2CH$_3$)=C(CH$_3$)), 1.08 (t, ^3J(H,H) = 7.5 Hz, 3H; PdC(CH$_2$CH_3)=C(CH$_3$)), 0.94 (d, ^3J(H,H) = 6.9 Hz, 3H; CH(CH_3)$_2$), 0.92 (d, ^3J(H,H) = 6.9 Hz, 6H; CH(CH_3)$_2$), 0.80 ppm (d, ^3J(H,H) = 6.9 Hz, 3H; CH(CH_3)$_2$); ^{13}C NMR (50.32 MHz, CD_2Cl_2, −30°C): δ = 221.8 (*C*(O)), 203.1 (Pd*C*(CH$_2$CH$_3$)=C(CH$_3$)), 160.3, 158.2 (*C*=N), 141.8 (PdC(CH$_2$CH$_3$)=*C*(CH$_3$)), 74.4, 72.9 (*C*H$_2$O), 69.1, 66.5 (*C*HN), 30.4 (PdC(*C*H$_2$CH$_3$)=C(CH$_3$)), 30.0, 29.9 (*C*H(CH$_3$)$_2$), 26.3 (C(O)(*C*H$_3$)), 18.0, 17.9, 15.2, 13.4 (CH(*C*H$_3$)$_2$), 12.5 (PdC(CH$_2$CH$_3$)=C-(*C*H$_3$)), 11.5 ppm (PdC(CH$_2$*C*H$_3$)=C(CH$_3$)); elemental analysis calcd (%) for $C_{51}H_{43}BF_{24}N_2O_3Pd$ (1305.1): C 46.94, H 3.32, N 2.15; found: C 46.50, H 3.06, N 2.31.

General procedure for the synthesis of complexes 8–11: In an NMR tube complexes **2**–**5** were dissolved at −30°C in CD_2Cl_2 (0.5 mL) previously saturated with CO. The solution was immediately transferred to the NMR probe, previously cooled to −30°C; the ^1H and ^{13}C NMR spectra showed the formation of two diastereomers **a**/**b** in a ratio dependent on the starting complex. The mixture was then allowed to stand at 20°C until the equilibrium ratio was reached (incidentally the same ratio was obtained on measuring the spectra again at −30°C). The solvent was removed by evaporation and the resulting solid was washed with hexane (4×4 mL) to give compounds **8**–**11**. The assignment of the NMR signals to diastereomers **a** was confirmed by subtraction of the spectra of diastereomers **b** from those of the initial mixtures.

$[Pd\{\eta^3\text{-}C(Ph)C(CH_3)C(CH_3)OC(O)\}(BIOX)]^+[BAr'_4]^-$ (8a and 8b): Complex **2** (60.0 mg, 0.044 mmol) was dissolved at −30°C in CD_2Cl_2 (0.5 mL) saturated with CO. Initial ratio **8a**/**8b**: 55:45 (calculated from the integration of the C(Ph)C(CH_3) peaks in the ^1H NMR spectrum). Final equilibrium ratio (after 4 h at 20°C): 3:97. Yield: 57.3 mg (0.041 mmol, 94%). IR (initial mixture) (CD_2Cl_2): ν = 1803, 1786 (C=O), 1640, 1610 cm^{-1} (C=N); IR (powder) (Nujol): $\tilde{\nu}$ = 1806 (C=O), 1641, 1610 cm^{-1} (C=N). Complex **8a**: ^1H NMR (200.13 MHz, CD_2Cl_2, −30°C): δ = 7.79–7.74 (m, 2H; Ph-H_o), 7.46–7.35 (m, 3H; Ph-H_m, Ph-H_p), 4.75–4.39 (br m, 4H; CH_2-O), 4.25–3.75 (br m, 2H; CH-N), 2.20–2.00 (br m, 1H; CH(CH_3)$_2$), 2.54 (s, 3H; C(Ph)C(CH_3)), 1.65 (s, 3H; C(CH_3)O), 1.00–0.70, 0.45–0.15 ppm (br m, 12H; CH(CH_3)$_2$ and 1H; CH(CH_3)$_2$)); ^{13}C NMR (50.32 MHz, CD_2Cl_2, −30°C): δ = 165.5 (O*C*(O)), 160.4, 159.2 (*C*=N), 130.8 (Ph-C_p), 129.9, 128.6 (Ph-C_m, Ph-C_o), 129.2 (Ph-C_i), 114.9 (C(Ph)C(CH$_3$)*C*(CH$_3$)), 112.4 (C(Ph)*C*(CH$_3$)C(CH$_3$)), 79.2 (*C*(Ph)C-(CH$_3$)C(CH$_3$)), 74.1 (*C*H$_2$O), 68.6 (*C*HN), 31.4, 28.5 (*C*H(CH_3)$_2$), 18.8, 18.1, 14.7, 14.1 (CH(*C*H$_3$)$_2$), 14.9 (C(CH$_3$)C(*C*H$_3$)O), 13.0 ppm (C-(*C*H$_3$)C(CH$_3$)O). Complex **8b**: ^1H NMR (200.13 MHz, CD_2Cl_2, −30°C): δ = 7.79–7.74 (m, 2H; Ph-H_o), 7.45–7.33 (m, 3H; Ph-H_m, Ph-H_p), 4.76 (dd, ^2J(H,H) = 9.8, ^3J(H,H) = 9.8 Hz, 1H; CH_2-O), 4.69 (dd, ^2J(H,H) = 9.8, ^3J(H,H) = 6.8 Hz, 1H; CH_2-O), 4.57 (dd, ^2J(H,H) = 9.8, ^3J(H,H) = 10.7 Hz, 1H; CH_2-O), 4.45 (dd, ^2J(H,H) = 9.8, ^3J(H,H) = 7.8 Hz, 1H; CH_2-O), 4.21 (ddd, ^3J(H,H) = 9.8, 6.8, 3.8 Hz, 1H; CH-N), 3.48 (ddd, ^3J(H,H) = 10.7, 7.8, 3.5 Hz, 1H; CH-N), 2.34 (s, 3H; C(Ph)C(CH_3)), 180–1.62 (m, 1H; CH(CH_3)$_2$), 1.71 (s, 3H; C(CH_3)O), 1.20–1.02 (m, 1H; CH(CH_3)$_2$), 0.86, 0.70, 0.53, 0.28 ppm (d, ^3J(H,H) = 7.0 Hz, 3H each, CH(CH_3)$_2$); ^{13}C NMR (50.32 MHz, CD_2Cl_2, −30°C): δ = 164.4 (O*C*(O)), 160.2, 159.9 (*C*=N), 130.3 (Ph-C_p), 129.6, 129.3 (Ph-C_m, Ph-C_o), 119.2 (C(Ph)C(CH$_3$)*C*(CH$_3$)), 111.7 (C(Ph)*C*(CH$_3$)C(CH$_3$)), 74.7 (*C*H$_2$O), 74.3 (*C*(Ph)C(CH$_3$)C(CH$_3$)), 68.1, 68.0 (*C*HN), 31.0, 29.2 (*C*H(CH_3)$_2$), 18.4, 18.1, 14.6, 14.1 (CH-(*C*H$_3$)$_2$), 15.4 (C(CH$_3$)C(*C*H$_3$)O), 12.4 ppm (C(*C*H$_3$)C(CH$_3$)O); elemental analysis calcd (%) for $C_{56}H_{43}BF_{24}N_2O_4Pd$ (1381.2): C 48.70, H 3.14, N 2.03; found: C 48.45, H 3.06, N 1.94.

Determination of the rate constants k_f and k_r for the epimerization reaction 8a⇌8b: Complex **2** (88.5 mg, 0.065 mmol) was dissolved at −30°C in CH_2Cl_2 (2 mL) previously saturated with CO; the solvent was then removed by evaporation in vacuo to yield a 55:45 mixture of **8a**/**8b** as a yellow powder (87.2 mg, 0.063 mmol), which was employed in experiments 1–5. 1) A sample (15.6 mg) was dissolved in an NMR tube at 20°C in CD_2Cl_2 (0.5 mL) previously saturated with CO and immediately transferred to the NMR probe maintained at the same temperature: the concentrations of **8a** and **8b** were monitored every 20 minutes for up to 4 h (final ratio 3:97; $K_{eq} = k_f/k_r = 32.3$). The value of $k_f + k_r$ (18.43×10^{-3} min^{-1}) was determined from the angular coefficient of $\ln[([\mathbf{8a}]_0 - [\mathbf{8a}]_{eq})/([\mathbf{8a}]_t - [\mathbf{8a}]_{eq})]$ versus time; therefore $k_f = 17.88 \times 10^{-3}$ min^{-1} and $k_r = 0.55 \times 10^{-3}$ min^{-1}. 2) A sample (13.0 mg) was dissolved in an NMR tube at 35°C in CD_2Cl_2 (0.5 mL) previously saturated with CO and immediately transferred to the NMR probe maintained at the same temperature: the concentrations of **8a** and **8b** were monitored every 5 minutes for up to 1 h (final ratio 3:97). The value of $k_f + k_r$ was

determined as described in the previous experiment: $k_f = 240.0 \times 10^{-3}\ min^{-1}$ and $k_r = 7.4 \times 10^{-3}\ min^{-1}$. 3) A sample (16.1 mg) was dissolved in CD_2Cl_2 (0.5 mL) under nitrogen at 20 °C and immediately transferred to the NMR probe maintained at the same temperature. The concentrations of **8a** and **8b** were monitored every 20 minutes for up to 8 h (final ratio 3:97): $k_f = 8.44 \times 10^{-3}\ min^{-1}$ and $k_r = 0.26 \times 10^{-3}\ min^{-1}$. 4) A sample (14.9 mg) was dissolved in CD_2Cl_2 (0.5 mL) under nitrogen at 20 °C, then CD_3CN (5.7 μL) was added and the sample was immediately transferred to the NMR probe maintained at the same temperature. The concentrations of **8a** and **8b** were monitored every 20 min for up to 6 h (final ratio 3:97): $k_f = 13.45 \times 10^{-3}\ min^{-1}$ and $k_r = 0.42 \times 10^{-3}\ min^{-1}$. 5) A sample (12.8 mg) was dissolved in [D$_6$]acetone (0.7 mL) under nitrogen at 20 °C and the sample was immediately transferred to the NMR probe maintained at the same temperature. The concentrations of **8a** and **8b** were monitored every 20 minutes for up to 8 h (final ratio 3:97): $k_f = 8.28 \times 10^{-3}\ min^{-1}$ and $k_r = 0.26 \times 10^{-3}\ min^{-1}$.

[Pd{η³-C(CH$_3$)C(CH$_3$)C(CH$_3$)OC(O)}(BIOX)]$^+$[BAr′$_4$]$^-$ (9a and 9b): Complex **3** (83.5 mg, 0.065 mmol) was dissolved at −30 °C in CD_2Cl_2 (0.5 mL) saturated with CO. Initial ratio of **9a**/**9b**: 40:60 [calculated from the integration of the C(CH$_3$)C(CH$_3$)C(CH$_3$)O peaks in the ^{1}H NMR spectrum]. Final equilibrium ratio (after 4 h at 20 °C): 5:95. Yield: 78.6 mg (0.060 mmol, 92 %). IR (initial mixture) (CD_2Cl_2): $\tilde{\nu}$ = 1795 (C=O), 1639, 1610 cm^{-1} (C=N); IR (powder) (Nujol): $\tilde{\nu}$ = 1789 (C=O), 1642, 1611 cm^{-1} (C=N). Complex **9a**: ^{1}H NMR (200.13 MHz, CD_2Cl_2, 20 °C): δ = 4.75–4.54 (m, 4H; CH_2-O), 4.21–4.08 (m, 2H; C*H*-N), 2.21 (s, 3H; C-(CH$_3$)C(CH_3)C(CH$_3$)O), 2.05–1.85 (br m, 2H; C*H*(CH$_3$)$_2$), 1.59 (s, 3H; C-(CH$_3$)C(CH$_3$)C(CH_3)O), 1.53 (s, 3H; C(CH_3)C(CH$_3$)C(CH$_3$)O), 0.89, 0.77 ppm (d, ^3J(H,H) = 7.0 Hz, 6H each, CH(CH_3)$_2$); ^{13}C NMR (50.32 MHz, CD_2Cl_2, −44 °C): δ = 166.8 (O*C*(O)), 160.1 (*C*=N), 116.3 (C-(CH$_3$)C(CH$_3$)*C*(CH$_3$)O), 113.8 (C(CH$_3$)*C*(CH$_3$)C(CH$_3$)O), 76.6 (*C*-(CH$_3$)C(CH$_3$)C(CH$_3$)O), 74.1 (*C*H$_2$O), 69.1 (*C*HN), 31.4, 30.0 (*C*H-(CH$_3$)$_2$), 18.5, 13.9 (CH(*C*H$_3$)$_2$), 14.9 (C(CH$_3$)C(CH$_3$)C(*C*H$_3$)O), 12.2 (C-(CH$_3$)C(*C*H$_3$)C(CH$_3$)O), 10.9 ppm (C(*C*H$_3$)C(CH$_3$)C(CH$_3$)O). Complex **9b**: ^{1}H NMR (200.13 MHz, CD_2Cl_2, 20 °C): δ = 4.72 (dd, ^2J(H,H) = 9.7 Hz, ^3J(H,H) = 9.7 Hz, 2H; CH_2-O), 4.66 (dd, ^2J(H,H) = 9.7 Hz, ^3J-(H,H) = 7.0 Hz, 2H; CH_2-O), 4.13 (ddd, ^3J(H,H) = 9.7 Hz, 7.0 Hz, 3.8 Hz, 2H; C*H*-N), 2.21 (s, 3H; C(CH$_3$)C(CH_3)C(CH$_3$)O), 193–1.75 (m, 2H; C*H*(CH$_3$)$_2$), 1.65 (s, 3H; C(CH$_3$)C(CH$_3$)C(CH_3)O), 1.49 (s, 3H; C-(CH_3)C(CH$_3$)C(CH$_3$)O), 0.88, 0.76 ppm (d, ^3J(H,H) = 7.0 Hz, 6H each, CH(CH_3)$_2$); ^{13}C NMR (50.32 MHz, CD_2Cl_2, −44 °C): δ = 166.2 (O*C*(O)), 160.1, 160.0 (*C*=N), 120.3 (C(CH$_3$)C(CH$_3$)*C*(CH$_3$)O), 113.2 (C(CH$_3$)*C*-(CH$_3$)C(CH$_3$)O), 74.7, 74.3 (*C*H$_2$O), 70.6 (*C*(CH$_3$)C(CH$_3$)C(CH$_3$)O), 68.9, 67.8 (*C*HN), 30.8, 30.2 (*C*H(CH$_3$)$_2$), 18.5, 18.3, 14.5, 14.1 (CH-(*C*H$_3$)$_2$), 15.2 (C(CH$_3$)C(CH$_3$)C(*C*H$_3$)O), 11.8 (C(CH$_3$)C(*C*H$_3$)C(CH$_3$)O), 9.9 ppm (C(*C*H$_3$)C(CH$_3$)C(CH$_3$)O); elemental analysis calcd (%) for $C_{51}H_{41}BF_{24}N_2O_4Pd$ (1319.1): C 46.44, H 3.13, N 2.12; found: C 46.68, H 3.22, N 2.19.

[Pd{η³-C(Ph)C(CH$_2$CH$_3$)C(CH$_3$)OC(O)}(BIOX)]$^+$[BAr′$_4$]$^-$ (10a and 10b): Complex **4** (41.0 mg, 0.030 mmol) was dissolved at −30 °C in CD_2Cl_2 (0.5 mL) saturated with CO. Initial ratio of **10a**/**10b:** 45:55 [calculated from the integration of the C(Ph)C(CH$_2$CH$_3$)C(CH_3) peaks in the ^{1}H NMR spectrum]. Final equilibrium ratio (after 7 h at 20 °C): 3:97. Yield: 37.7 mg (0.027 mmol, 90 %). IR (powder) (Nujol): $\tilde{\nu}$ = 1805 (C=O), 1641, 1610 cm^{-1} (C=N). Complex **10a**: ^{1}H NMR (200.13 MHz, CD_2Cl_2, −30 °C): δ = 7.86–7.77 (m, 2H; Ph-H_o), 7.56–7.42 (m, 3H; Ph-H_m, Ph-H_p), 4.85–4.45 (br m, 4H; CH_2-O), 4.18–3.98 (br m, 2H; C*H*-N), 3.01 (dq, ^2J-(H,H) = 14.8, ^3J(H,H) = 7.6 Hz, 1H; C(Ph)=C(CH_2CH$_3$)), 2.83 (dq, ^2J-(H,H) = 14.8, ^3J(H,H) = 7.6 Hz, 1H; C(Ph)=C(CH_2CH$_3$)), 1.95–1.75 (br m, 1H; C*H*(CH$_3$)$_2$), 1.75 (s, 3H; C(CH_3)O), 1.40 (t, ^3J(H,H) = 7.6 Hz, 3H; C(Ph)C(CH$_2$CH_3)), 1.02–0.58, 0.43–0.33 ppm (br m, 12H; CH(CH_3)$_2$ and 1H; C*H*(CH$_3$)$_2$)); ^{13}C NMR (50.32 MHz, CD_2Cl_2, −30 °C): δ = 165.4 (O*C*(O)), 159.9 (*C*=N), 130.4 (Ph-C_p), 129.7, 128.4 (Ph-C_m, Ph-C_o), 128.7 (Ph-C_i), 117.6 (C(Ph)*C*(CH$_2$CH$_3$)C(CH$_3$)), 112.1 (C(Ph)C(CH$_2$CH$_3$)*C*-(CH$_3$)), 79.4 (*C*(Ph)C(CH$_2$CH$_3$)C(CH$_3$)), 73.8 (*C*H$_2$O), 68.5 (*C*HN), 30.7, 29.4 (*C*H(CH$_3$)$_2$), 20.8 (C(*C*H$_2$CH$_3$)C(CH$_3$)O), 18.5, 18.0, 14.2, 13.8 (CH-(*C*H$_3$)$_2$), 15.1 (C(CH$_2$CH$_3$)C(*C*H$_3$)O), 13.3 ppm (C(CH$_2$*C*H$_3$)C(CH$_3$)O). Complex **10b**: ^{1}H NMR (200.13 MHz, CD_2Cl_2, −30 °C): δ = 7.86–7.77 (m, 2H; Ph-H_o), 7.56–7.42 (m, 3H; Ph-H_m, Ph-H_p), 4.85–4.45 (br m, 4H; CH_2-O), 4.42–4.22, 3.72–3.57 (br m, 1H each, C*H*-N), 2.98 (dq, ^2J(H,H) = 14.4, ^3J(H,H) = 7.5 Hz, 1H; C(Ph)=C(CH_2CH$_3$)), 2.58 (dq, ^2J(H,H) = 14.4, ^3J(H,H) = 7.5 Hz, 1H; C(Ph)=C(CH_2CH$_3$)), 1.95–1.75 (br m, 1H; C*H*-(CH$_3$)$_2$), 1.83 (s, 3H; C(CH_3)O), 1.13 (t, ^3J(H,H) = 7.5 Hz, 3H; C(Ph)C-(CH$_2$CH_3)), 1.02–0.58, 0.43–0.33 ppm (br m, 12H; CH(CH_3)$_2$ and 1H; C*H*(CH$_3$)$_2$)); ^{13}C NMR (50.32 MHz, CD_2Cl_2, −30 °C): δ = 164.5 (O*C*(O)), 159.9 (*C*=N), 130.1 (Ph-C_p), 129.4, 129.1 (Ph-C_m, Ph-C_o), 127.6 (Ph-C_i), 116.4 (C(Ph)*C*(CH$_2$CH$_3$)C(CH$_3$)), 118.6 (C(Ph)C(CH$_2$CH$_3$)*C*(CH$_3$)), 73.9 (*C*(Ph)C(CH$_2$CH$_3$)C(CH$_3$)), 74.4 (*C*H$_2$O), 67.9 (*C*HN), 30.7, 29.0 (*C*H-(CH$_3$)$_2$), 20.8 (C(*C*H$_2$CH$_3$)C(CH$_3$)O), 18.3, 18.1, 14.2, 13.8 (CH(*C*H$_3$)$_2$), 15.1 (C(CH$_2$CH$_3$)C(*C*H$_3$)O), 13.9 ppm (C(CH$_2$*C*H$_3$)C(CH$_3$)O); elemental analysis calcd (%) for $C_{57}H_{45}BF_{24}N_2O_4Pd$ (1395.2): C 49.07, H 3.25, N 2.01; found: C 48.61, H 3.13, N 2.16.

[Pd{η³-C(CH$_2$CH$_3$)C(CH$_2$CH$_3$)C(CH$_3$)OC(O)}(BIOX)]$^+$[BAr′$_4$]$^-$ (11a and 11b): Complex **5** (58.0 mg, 0.044 mmol) was dissolved at −30 °C in CD_2Cl_2 (0.5 mL) saturated with CO. Initial ratio of **11a**/**11b**: 56:44 (calculated from the integration of the C(CH$_2$CH$_3$)C(CH$_2$CH$_3$)C(CH_3)O peaks in the ^{1}H NMR spectrum). Final equilibrium ratio (after 8 h at 20 °C): 6:94. Yield: 55.2 mg (0.041 mmol, 93 %). IR (powder) (Nujol): $\tilde{\nu}$ = 1790 (C=O), 1643, 1610 cm^{-1} (C=N). Complex **11a**: ^{1}H NMR (200.13 MHz, CD_2Cl_2, 20 °C): δ = 4.80–4.70 (m, 4H; CH_2-O), 4.30–4.18 (m, 2H; C*H*-N), 2.64 (q, ^3J(H,H) = 7.5 Hz, 2H; C(CH$_2$CH$_3$)C-(CH_2CH$_3$)C(CH$_3$)), 2.31 (dq, ^2J(H,H) = 13.8, ^3J(H,H) = 7.5 Hz, 1H; C-(CH$_2$CH$_3$)C(CH_2CH$_3$)C(CH$_3$)), 2.15 (dq, ^2J(H,H) = 13.8, ^3J(H,H) = 7.5 Hz, 1H; C(CH$_2$CH$_3$)C(CH_2CH$_3$)C(CH$_3$)), 2.27 (q, ^3J(H,H) = 7.5 Hz, 2H; C(CH_2CH$_3$)C(CH$_2$CH$_3$)C(CH$_3$)), 2.10–1.90 (br m, 2H; C*H*(CH$_3$)$_2$), 1.71 (s, 3H; C(CH$_2$CH$_3$)C(CH$_2$CH$_3$)C(CH_3)O), 1.34 (t, ^3J(H,H) = 7.5 Hz, 3H; C(CH$_2$CH$_3$)C(CH$_2$CH_3)C(CH$_3$)O), 1.31 (t, ^3J(H,H) = 7.5 Hz, 3H; C-(CH$_2$CH_3)C(CH$_2$CH$_3$)C(CH$_3$)O), 0.98, 0.86 ppm (d, ^3J(H,H) = 7.0 Hz, 12H; CH(CH_3)$_2$); ^{13}C NMR (50.32 MHz, CD_2Cl_2, −30 °C): δ = 166.0 (O*C*(O)), 159.9 (*C*=N), 120.5 (C(CH$_2$CH$_3$)*C*(CH$_2$CH$_3$)C(CH$_3$)O), 113.8 (C(CH$_2$CH$_3$)C(CH$_2$CH$_3$)*C*(CH$_3$)O), 82.0 (*C*(CH$_2$CH$_3$)C(CH$_2$CH$_3$)C-(CH$_3$)O), 74.3, 73.8 (*C*H$_2$O), 69.0, 67.7 (*C*HN), 30.5, 29.9 (*C*H(CH$_3$)$_2$), 19.7 (C(*C*H$_2$CH$_3$)C(CH$_2$CH$_3$)C(CH$_3$)O), 19.3 (C(CH$_2$CH$_3$)C(*C*H$_2$CH$_3$)C-(CH$_3$)O), 18.3, 14.3 (CH(*C*H$_3$)$_2$), 15.1 (C(CH$_2$CH$_3$)C(CH$_2$CH$_3$)C(*C*H$_3$)O), 13.8 (C(CH$_2$CH$_3$)C(CH$_2$*C*H$_3$)C(CH$_3$)O), 12.8 ppm (C(CH$_2$*C*H$_3$)C-(CH$_2$CH$_3$)C(CH$_3$)O). Complex **11b**: ^{1}H NMR (200.13 MHz, CD_2Cl_2, 20 °C): δ = 4.80–4.70 (m, 4H; CH_2-O), 4.30–4.18 (m, 2H; C*H*-N), 2.75 (dq, ^2J(H,H) = 14.7 Hz, ^3J(H,H) = 7.5 Hz, 1H; C(CH$_2$CH$_3$)C(CH_2CH$_3$)C-(CH$_3$)), 2.54 (dq, ^2J(H,H) = 14.7 Hz, ^3J(H,H) = 7.6 Hz, 1H; C(CH$_2$CH$_3$)C-(CH_2CH$_3$)C(CH$_3$)), 2.16 (q, ^3J(H,H) = 7.6 Hz, 2H; C(CH_2CH$_3$)C-(CH$_2$CH$_3$)C(CH$_3$)), 2.10–1.90 (br m, 2H; C*H*(CH$_3$)$_2$), 1.76 (s, 3H; C-(CH$_2$CH$_3$)C(CH$_2$CH$_3$)C(CH_3)O), 1.33 (t, ^3J(H,H) = 7.5 Hz, 3H; C-(CH$_2$CH$_3$)C(CH$_2$CH_3)C(CH$_3$)O), 1.29 (t, ^3J(H,H) = 7.6 Hz, 3H; C-(CH$_2$CH_3)C(CH$_2$CH$_3$)C(CH$_3$)O), 0.98, 0.86 ppm (d, ^3J(H,H) = 7.0 Hz, 12H; CH(CH_3)$_2$); ^{13}C NMR (50.32 MHz, CD_2Cl_2, −30 °C): δ = 165.5 (O*C*(O)), 159.9 (*C*=N), 121.0 (C(CH$_2$CH$_3$)C(CH$_2$CH$_3$)*C*(CH$_3$)O), 116.5 (C(CH$_2$CH$_3$)*C*(CH$_2$CH$_3$)C(CH$_3$)O), 75.4 (*C*(CH$_2$CH$_3$)C(CH$_2$CH$_3$)C-(CH$_3$)O), 73.8 (*C*H$_2$O), 69.0 (*C*HN), 29.9 (*C*H(CH$_3$)$_2$), 19.7 (C-(*C*H$_2$CH$_3$)C(CH$_2$CH$_3$)C(CH$_3$)O), 18.4 (C(CH$_2$CH$_3$)C(*C*H$_2$CH$_3$)C-(CH$_3$)O), 18.3, 14.3 (CH(*C*H$_3$)$_2$), 14.9 (C(CH$_2$CH$_3$)C(CH$_2$CH$_3$)C(*C*H$_3$)O), 14.0 (C(CH$_2$CH$_3$)C(CH$_2$*C*H$_3$)C(CH$_3$)O), 12.9 ppm (C(CH$_2$*C*H$_3$)C-(CH$_2$CH$_3$)C(CH$_3$)O); elemental analysis calcd (%) for $C_{53}H_{45}BF_{24}N_2O_4Pd$ (1347.1): C 47.25, H 3.37, N 2.08; found: C 46.90, H 3.12, N 2.29.

[Pd{η³-C(CH$_3$)C(CH$_2$CH$_3$)C(CH$_3$)OC(O)}(BIOX)]$^+$[BAr′$_4$]$^-$ (12a and 12b) and [Pd{η³-C(CH$_2$CH$_3$)C(CH$_3$)C(CH$_3$)OC(O)}(BIOX)]$^+$[BAr′$_4$]$^-$ (13a and 13b): The 60:40 mixture of complexes **6** and **7** (93.0 mg sample, 0.071 mmol) was dissolved in an NMR tube at −30 °C in CD_2Cl_2 (0.5 mL) previously saturated with CO. The solution was immediately transferred to the NMR probe previously cooled to −30 °C; the ^{1}H and ^{13}C NMR spectra showed the formation of the four compounds **12a**, **12b**, **13a**, and **13b** in a ratio of 26:34:17:23, respectively (**12a**/**12b** = 42:58; **13a**/**13b** = 44:56); the ratios are calculated from the integration of methyl peaks in the ^{1}H NMR spectrum. The mixture was then allowed to stand for 8 h at 20 °C in order to attain an equilibrium; an equilibrium ratio of 4:56:2:38 (**12a**/**12b** = 7:93; **13a**/**13b** = 5:95) was obtained which did not change with time. The solvent was removed by evaporation and the resulting solid was washed with hexane (4 × 4 mL) to give a mixture of compounds **12** and **13**. Yield: 88.0 mg (0.066 mmol, 93 %). The NMR signals arising from **12a** and **13a** were assigned by subtracting the NMR spectra of **12b**

and **13b** from those of the initial mixture; the signals due to the bioxazoline ligand have not been reported since each of the compounds has a similar pattern which is in the same region as that of compounds **9**. IR (powder) (Nujol): $\nu = 1805$, 1790 (C=O), 1643, 1610 cm^{-1} (C=N). Complex **12a**: ^1H NMR (200.13 MHz, CD_2Cl_2, 20 °C): $\delta = 2.70$–2.58 (m, 2H; $C(CH_3)C(CH_2CH_3)C(CH_3)O$), 1.71 (s, 3H; $C(CH_3)C(CH_2CH_3)C(CH_3)O$), 1.65 (s, 3H; $C(CH_3)C(CH_2CH_3)C(CH_3)O$), 1.30 ppm (t, $^3J(H,H) = 7.6$ Hz, 3H; $C(CH_2)C(CH_2CH_3)C(CH_3)O$); ^{13}C NMR (50.32 MHz, CD_2Cl_2, −30 °C): $\delta = 165.2$ ($OC(O)$), 119.7 ($C(CH_3)C(CH_2CH_3)C(CH_3)O$), 114.9 ($C(CH_3)C(CH_2CH_3)C(CH_3)O$), 75.7 ($C(CH_3)C(CH_2CH_3)C(CH_3)O$), 19.9 ($C(CH_3)C(CH_2CH_3)C(CH_3)O$), 14.9 ($C(CH_3)C(CH_2CH_3)C(CH_3)O$), 13.7 ($C(CH_3)C(CH_2CH_3)C(CH_3)O$), 10.4 ppm ($C(CH_3)C(CH_2CH_3)C(CH_3)O$). Complex **12b**: ^1H NMR (200.13 MHz, CD_2Cl_2, 20 °C): $\delta = 2.75$ (dq, $^2J(H,H) = 14.6$ Hz, $^3J(H,H) = 7.6$ Hz, 1H; $C(CH_3)C(CH_2CH_3)C(CH_3)O$), 2.54 (dq, $^2J(H,H) = 14.6$, $^3J(H,H) = 7.6$ Hz, 1H; $C(CH_3)C(CH_2CH_3)C(CH_3)O$), 1.76 (s, 3H; $C(CH_3)C(CH_2CH_3)C(CH_3)O$), 1.61 (s, 3H; $C(CH_3)C(CH_2CH_3)C(CH_3)O$), 1.29 ppm (t, $^3J(H,H) = 7.6$ Hz, 3H; $C(CH_2)C(CH_2CH_3)C(CH_3)O$); ^{13}C NMR (50.32 MHz, CD_2Cl_2, −30 °C): $\delta = 165.2$ ($OC(O)$), 121.0 ($C(CH_3)C(CH_2CH_3)C(CH_3)O$), 116.6 ($C(CH_3)C(CH_2CH_3)C(CH_3)O$), 69.7 ($C(CH_3)C(CH_2CH_3)C(CH_3)O$), 19.7 ($C(CH_3)C(CH_2CH_3)C(CH_3)O$), 14.7 ($C(CH_3)C(CH_2CH_3)C(CH_3)O$), 13.1 ($C(CH_3)C(CH_2CH_3)C(CH_3)O$), 9.5 ppm ($C(CH_3)C(CH_2CH_3)C(CH_3)O$). Complex **13a**: ^1H NMR (200.13 MHz, CD_2Cl_2, 20 °C): $\delta = 2.32$ (s, 3H; $C(CH_2CH_3)C(CH_3)C(CH_3)O$), 2.28 (q, $^3J(H,H) = 7.6$ Hz, 2H; $C(CH_2CH_3)C(CH_3)C(CH_3)O$), 1.70 (s, 3H; $C(CH_2CH_3)C(CH_3)C(CH_3)O$), 1.26 ppm (t, $^3J(H,H) = 7.6$ Hz, 3H; $C(CH_2CH_3)C(CH_2)C(CH_3)O$); ^{13}C NMR (50.32 MHz, CD_2Cl_2, −30 °C): $\delta = 164.9$ ($OC(O)$), 121.5 ($C(CH_2CH_3)C(CH_3)C(CH_3)O$), 112.6 ($C(CH_2CH_3)C(CH_3)C(CH_3)O$), 76.6 ($C(CH_2CH_3)C(CH_3)C(CH_3)O$), 18.8 ($C(CH_2CH_3)C(CH_3)C(CH_3)O$), 14.7 ($C(CH_2CH_3)C(CH_3)C(CH_3)O$), 13.0 ($C(CH_2CH_3)C(CH_3)C(CH_3)O$), 11.7 ppm ($C(CH_2CH_3)C(CH_3)C(CH_3)O$). Complex **13b**: ^1H NMR (200.13 MHz, CD_2Cl_2, 20 °C): $\delta = 2.32$ (s, 3H; $C(CH_2CH_3)C(CH_3)C(CH_3)O$), 2.17 (dq, $^2J(H,H) = 15.0$ Hz, $^3J(H,H) = 7.6$ Hz, 1H; $C(CH_2CH_3)C(CH_3)C(CH_3)O$), 2.15 (dq, $^2J(H,H) = 15.0$ Hz, $^3J(H,H) = 7.6$ Hz, 1H; $C(CH_2CH_3)C(CH_3)C(CH_3)O$), 1.76 (s, 3H; $C(CH_2CH_3)C(CH_3)C(CH_3)O$), 1.25 ppm (t, $^3J(H,H) = 7.6$ Hz, 3H; $C(CH_2CH_3)C(CH_2)C(CH_3)O$). ^{13}C NMR (50.32 MHz, CD_2Cl_2, −30 °C): $\delta =$ 164.9 ($OC(O)$), 122.4 ($C(CH_2CH_3)C(CH_3)C(CH_3)O$), 111.0 ($C(CH_2CH_3)C(CH_3)C(CH_3)O$), 75.7 ($C(CH_2CH_3)C(CH_3)C(CH_3)O$), 18.8 ($C(CH_2CH_3)C(CH_3)C(CH_3)O$), 14.9 ($C(CH_2CH_3)C(CH_3)C(CH_3)O$), 12.0 ($C(CH_2CH_3)C(CH_3)C(CH_3)O$), 11.9 ppm ($C(CH_2CH_3)C(CH_3)C(CH_3)O$); elemental analysis calcd (%) for $C_{52}H_{43}BF_{24}N_2O_4Pd$ (1333.1): C 46.85, H 3.25, N 2.10; found: C 46.51, H 3.03, N 2.37.

Reaction of complex 8 with MeOH: Complex **8** (43.7 mg, 0.032 mmol) was dissolved in methanol (2 mL); a black palladium precipitate was formed immediately. The reaction mixture was stirred for 1 h at 20 °C and then concentrated under reduced pressure. The residue was purified by column chromatography on silica gel using a mixture of hexane/ethyl acetate = 6:4 as eluent to give compound **15** (6.4 mg, 0.029 mmol, 91 %) as a yellow solid. Its IR and ^1H and ^{13}C NMR spectra are in agreement with those reported in the literature;[3] elemental analysis calcd (%) for $C_{13}H_{14}O_3$ (218.3): C 71.54, H 6.47; found: C 71.18, H 6.70.

Reaction of complex 8 with isopropylamine: Complex **8** (27.5 mg, 0.020 mmol) was dissolved in dichloromethane (1 mL) and then isopropylamine (6.0 μL, 0.070 mmol) was added. The solution was allowed to stand at 20 °C for 24 h (a black palladium precipitate was formed) and then concentrated under reduced pressure. The residue was purified by column chromatography on silica gel using a mixture of hexane/ethyl acetate = 6:4 as eluent to give compound **16** (4.5 mg, 0.018 mmol, 90 %) as a white solid. IR (film): $\nu = 3346$ (N-H), 1740 cm^{-1} (C=O); ^1H NMR (200.13 MHz, $CDCl_3$, 20 °C): $\delta = 7.54$–7.35 (m, 5H; Ph-*H*), 2.85 (sept, $^3J(H,H) = 6.3$ Hz, 1H; $CH(CH_3)_2$), 2.13 (s, 3H; $C(Ph)=C(CH_3)$), 1.65 (s, 3H; $C(NH)-C(CH_3)$), 1.26 (br s, 1H; N*H*), 1.13, 1.05 ppm (d, $^3J(H,H) = 6.3$, 3H each, $CH(CH_3)_2$); ^{13}C NMR (50.32 MHz, $CDCl_3$, 20 °C): $\delta =$ 170.7, 160.1, 130.2, 129.0, 128.7, 128.5, 128.4, 99.6, 43.7, 25.7, 25.3, 25.1, 12.6 ppm; elemental analysis calcd (%) for $C_{15}H_{19}NO_2$ (245.3): C 73.44, H 7.81, N 5.71; found: C 73.12, H 7.70, N 5.59.

Reaction of complex 9 with benzylamine: Complex **9** (28.0 mg, 0.021 mmol) was dissolved in dichloromethane (1 mL) and then benzylamine (5.0 μL, 0.046 mmol) was added. The solution was allowed to stand at 20 °C for 24 h (a black palladium precipitate was formed) and then concentrated under reduced pressure. The residue was purified by column chromatography on silica gel using a mixture of hexane/ethyl acetate = 6:4 as eluent to give a 9:1 mixture of compounds **17** and **18** (3.8 mg, 0.017 mmol, 81 %) as a white solid. IR (film): $\nu = 3336$ (N-H), 1774, 1742 cm^{-1} (C=O). Compound **17**: ^1H NMR (200.13 MHz, $CDCl_3$, 20 °C): $\delta = 7.37$–7.22 (m, 5H; Ph-*H*), 3.74, 3.41 (d, $^2J(H,H) = 12.8$ Hz, 1H each, NH-CH_2-Ph), 1.92, 1.85 (q, $^5J(H,H) = 1.1$ Hz, 3H each, $C(CH_3)=C(CH_3)$), 1.60 (s, 3H; $C(NH)-C(CH_3)$), 1.27 ppm (br s, 1H; N*H*); ^{13}C NMR (50.32 MHz, $CDCl_3$, 20 °C): $\delta = 177.4$, 158.3, 138.1, 128.5, 128.3, 127.9, 127.4, 99.3, 45.9, 24.6, 11.2, 8.8 ppm. Compound **18**: ^1H NMR (200.13 MHz, $CDCl_3$, 20 °C): $\delta = 7.37$–7.22 (m, 5H; Ph-*H*), 4.33, 4.01 (d, $^2J(H,H) = 14.1$ Hz, 1H each, NH-CH_2-Ph), 2.01, 1.87 (q, $^5J(H,H) = 1.1$ Hz, 3H each, $C(CH_3)=C(CH_3)$), 1.81 (s, 3H; $C(NH)-C(CH_3)$), 1.27 (br s, 1H; N*H*) ppm; elemental analysis calcd (%) for $C_{14}H_{17}NO_2$ (231.3): C 72.70, H 7.41, N 6.06; found: C 72.96, H 7.80, N 5.94.

Computational details: The Gaussian 98 (revision A.7)[24] package implemented on a 44P IBM computer and the package of programs for Molecular Orbital Analysis CACAO (PC Beta-Version 5.0) was used. All the species studied[25] were fully optimized using the density functional theory (DFT) method by means of Becke's three-parameter hybrid method using the LYP correlation functional.[26] The effective core potential of Hay and Wadt[27] was used for the palladium atom. The 6-31G* basis set was used for the remaining atomic species.[28] Molecular modeling studies were performed by using the MSI software program Insight-II.[29]

Acknowledgements

This work was supported by the Ministero dell'Istruzione, dell'Università e della Ricerca (MIUR-Rome), PRIN N° 2003039774. We thank Dr. C. Mealli, ICCOM-CNR, Florence, for helpful discussions and Mrs. Anna Rita Pierleoni for technical assistance.

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Received: April 2, 2004
Revised: January 19, 2005
Published online: March 22, 2005