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PAPER

Carbonylation of styrenes catalyzed by bioxazoline Pd(II) complexes: mechanism of enantioselectivity†

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Preliminary studies of the elementary steps involved in the reaction of a chiral methyl carbonyl bioxazoline Pd(II) complex with aromatic olefins and CO have allowed development of a new enantioselective catalytic carbonylation process, leading to γ-ketoester derivatives with high yield and good enantiomeric excess. The intermediate palladacycle complexes have been isolated and characterized by NMR spectroscopy and X-ray diffraction. Factors that govern the stereoselectivity of the olefin carbonylation process are discussed.

Introduction

Insertions of unsaturated molecules into palladium-carbon bonds represent the fundamental steps in many catalytic processes.[1] In particular, in the last ten years insertion reactions of olefins into Pd-acyl bonds and of carbon monoxide into Pd-alkyl bonds have been extensively studied, since they correspond to the elementary steps involved in several metal-catalyzed processes including alkoxycarbonylation[1] of alkenes and synthesis of polyketones.[2] The starting compound is generally represented by a monocationic palladium(II) complex containing a chelating ligand and an acyl moiety.[3] Concerning the olefin, in many cases ethylene[4] has been used and, among α-olefins, styrene[5] and propylene[6] insertions have been reported. Moreover, while several examples with cyclic olefin have been described,[7] insertions of acyclic 1,2-substituted olefins are rare.[6,8] In this field, our research group has studied copolymerization reactions of α-olefins with carbon monoxide and identified the elementary process steps. In particular, using precatalysts of general formula [Pd(Me)(MeCN)(N-N)][X] (X = PF_6^-, $B[(CF_3)_2C_6H_3]_4^-$), we have developed catalytic systems for the synthesis, under mild conditions, of copolymers vinylarene/CO having a syndiotactic microstructure when N-N = diazabutadienes,[9] isotactic if N-N = bioxazolines[10] and stereoblock-isotactic when N-N = aryl α-diimine *ortho*-disubstituted ligands.[11] In all cases, the first organometallic intermediates deriving from stoichiometric insertion of the comonomers in methyl carbonyl palladium complexes, which proved to be the real catalytic species,[9,10b,11a] have been isolated and characterized. Analogous studies carried out with 1,2-substituted olefins and with Pd complexes bearing achiral α-diimine ligands have allowed some important aspects concerning the regio- and stereochemistry of the insertion process to be highlighted.[12] With the aim of creating a new way to selectively synthesize highly substituted chiral carbonyl compounds, we have now turned our attention to the study of the reactivity of an optically active bioxazoline palladium complex [Pd(Me)(CO)(BIOX)][BAr'_4^-] **1** (Scheme 1) with aromatic olefins (namely *cis*-β-methylstyrene, *trans*-β-methylstyrene, styrene) and carbon monoxide. The resulting intermediate complexes have been shown to be interesting model compounds for the design of catalytic olefin carbonylation reactions. These investigations have been undertaken also to evaluate how steric and electronic properties of the alkenes and the geometry of the ligand can influence the stereochemistry of the synthesized products.

Results and discussion

Olefin insertion reactions and synthesis of the palladacycle complexes 2–4

Insertion of the 1,2-substituted olefins into the acylpalladium bond was achieved by reaction of the methyl carbonyl Pd complex **1** with a 10 : 1 excess of *trans*-β-methylstyrene (tbms) or *cis*-β-methylstyrene (cbms) in dichloromethane at 0 °C.

Using an analogous methodology, the styrene insertion was previously described by us as an intermediate of the copolymerization process.[10b] The reactions were monitored by ^{1}H NMR, following the disappearance of the Pd-CH_3 signal of the starting compound together with the increase of an acetyl peak at around 2.4 ppm. After complete consumption of complex **1**, the solvent was evaporated, and the resulting solids were washed with hexane

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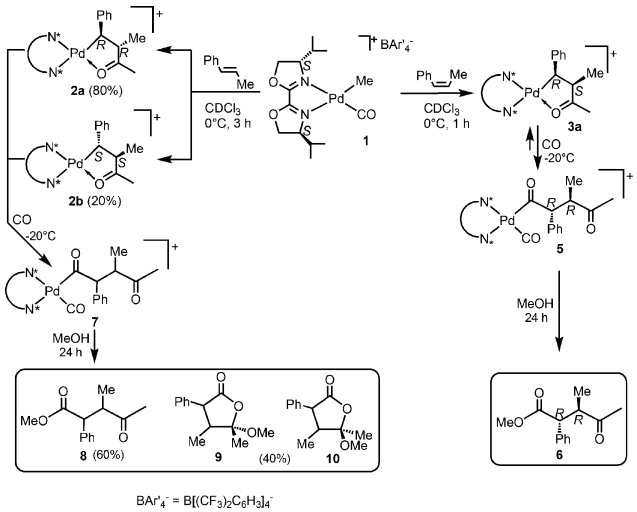
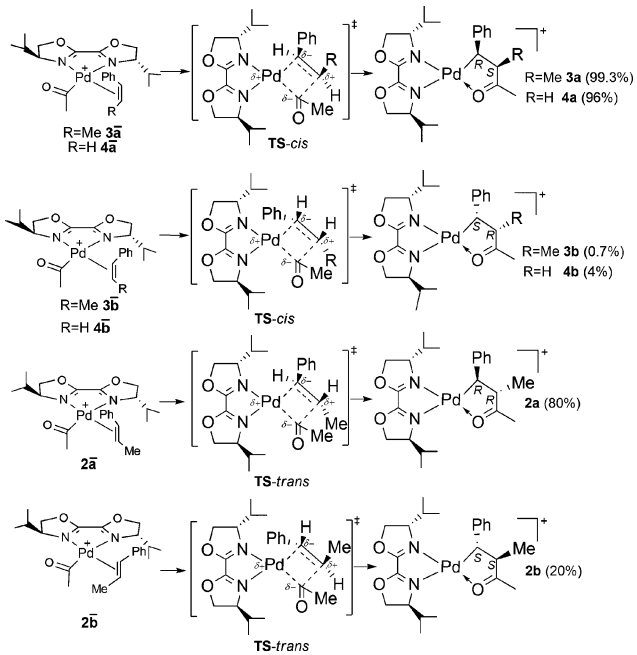


Scheme 1

obtaining in high yield products **2–4**, which revealed a structure containing a 5-membered palladacycle (Scheme 1 and 2).



Scheme 2 Proposed reaction path for olefin insertion.

The individuation of the spin system C*H*(Ph)-C*H*$_2$ or C*H*(Ph)-C*H*(CH$_3$) and of an acetyl fragment in the ^{1}H and ^{13}C-NMR spectra confirms the olefin insertion. The coordination of the acetyl oxygen atom to the metal was proved by the presence of a very deshielded carbonyl signal (at more than 238 ppm) together with an IR stretching band at around 1600 cm^{-1}.[3] Interestingly, almost exclusive formation of the five-membered palladacycle complex **3a** was observed with *cis*-β-methylstyrene, while a 4 : 1 mixture of two diastereomeric complexes **2a** and **2b** was obtained with *trans*-β-methylstyrene (Scheme 1 and 2).

The regio- and stereochemistry of complexes **2** and **3** were determined by means of NOE measurements: the experimental data prove that the process is regioselective and in the palladacycles the *cis* or *trans* relation between the phenyl group and the adjacent methyl is the same as the starting olefin. The observation of NOE contacts, in **2a** and **3a**, between the C*H*(Ph) resonances and the C*H*(CH$_3$)$_2$ signals of the bioxazoline isopropyl group reveals that these two protons are on the same side with respect to the Pd coordination plane, resulting in an *R* configuration of the *C*H(Ph) carbons. Considering the similarity of the ^{1}H NMR patterns of **2b** with **2a** and the values of the vicinal coupling constant C*H*(Ph)-C*H*(CH$_3$), we can reasonably assume that compound **2b** is the *trans SS* diastereoisomer (Scheme 1). Regarding the insertion of styrene in complex **1**, NOE experiments, carried out on the resulting cyclopalladate product **4**, indicated that also in this case the regiochemistry is of 2,1 type and that one diastereoisomeric species **4a**, with an *R* configuration of the new –CHPh– stereogenic center, is generated.[10b] However a closer investigation has revealed also the presence of a small amount (4%) of the diastereoisomer **4b**, having an *S* configuration, as shown in Scheme 2, this percentage was determined from the intensity of the signal of C*H*Ph at δ 3.85.

Crystal structure of compounds 2a and 3a

Isomorphous crystals of compounds **2a** and **3a** are triclinic, space group *P*1 (*Z* = 1). Also, the two metal complexes are roughly superimposable (Fig. 1) except for the relative arrangement of the hydrogen and the methyl group bound to C(15), which makes the absolute configuration of this stereocenter opposite for the complexes **2a** and **3a**, being *R* and *S* respectively.

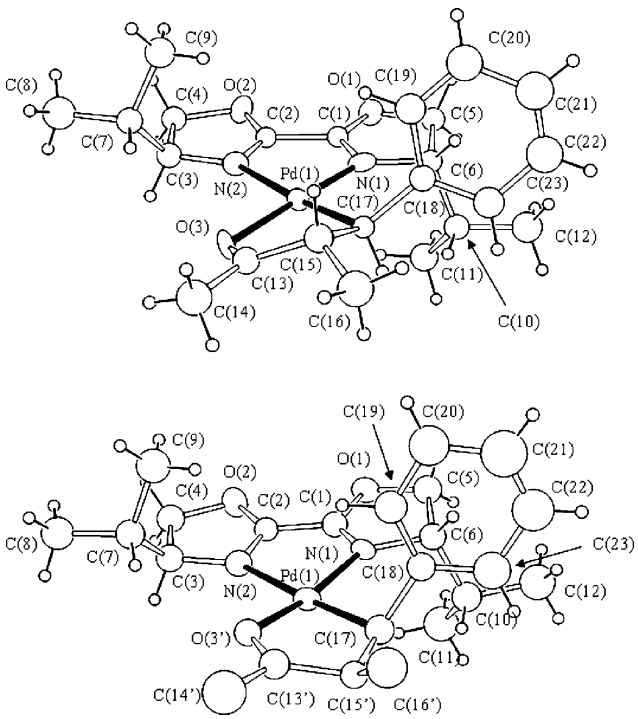


Fig. 1 ORTEP3 views of the complex cation of **2a** (above) and **3a′** (below). The **3a″** drawing has not been shown due to the close similarity with **3a′**. All atoms are drawn at 50% probability, except hydrogens to which have been assigned arbitrary thermal parameters.

As a consequence of the disorder affecting the atoms O(3), C(13), C(14), C(15), and C(16) in **3a**, two cationic species (indicated with ′ and ″ in the following) are present in the crystal lattice

Table 1 Selected bond lengths (Å) and angles (°) for complex cations **2a** and **3a**

2a		**3a**	
Pd(1)–N(1)	2.05(1)	Pd(1)–N(1)	2.06(1)
Pd(1)–N(2)	2.19(1)	Pd(1)–N(2)	2.17(1)
Pd(1)–O(3)	2.069(9)	Pd(1)–O(3′)[a]	1.95(2)
		Pd(1)–O(3″)	2.15(2)
Pd(1)–C(17)	2.04(1)	Pd(1)–C(17)	2.05(2)
N(1)–Pd(1)–N(2)	78.0(5)	N(1)–Pd(1)–N(2)	77.2(5)
N(1)–Pd(1)–O(3)	175.9(6)	N(1)–Pd(1)–O(3′)	168.9(8)
		N(1)–Pd(1)–O(3″)	170.9(7)
N(1)–Pd(1)–C(17)	99.6(5)	N(1)–Pd(1)–C(17)	99.9(7)
N(2)–Pd(1)–O(3)	99.8(4)	N(2)–Pd(1)–O(3′)	102.0(7)
		N(2)–Pd(1)–O(3″)	97.2(7)
N(2)–Pd(1)–C(17)	175.2(5)	N(2)–Pd(1)–C(17)	176.9(8)
O(3)–Pd(1)–C(17)	82.8(5)	O(3′)–Pd(1)–C(17)	80.6(8)
		O(3″)–Pd(1)–C(17)	85.8(8)

[a] Due to disorder in the crystal lattice of **3a**, two positions, labelled with ′ and ″, were assigned to atoms O(3), C(13), C(14), C(15) and C(16).

of this compound, which only slightly differ in the conformation of the acetyl palladacycle ring (*vide infra*). However, it must be mentioned here that despite this disorder the *S* stereochemistry of the carbon atom C(15) has been undoubtedly established (see Experimental section for further details).

Given that the bioxazoline (BIOX) ligand has a *SS* configuration and the stereochemistry of C(17) is *R* in both **2a** and **3a** complexes, the latter are diastereoisomers, with the adjacent methyl and phenyl groups *trans* disposed in **2a** and *cis* oriented in **3a**. Bond distances and angles of BIOX, which lies almost in a plane except for the iso-propyl groups (the highest deviation being the one of N(1) and C(5) in **2a** and **3a**, respectively), are within the expected range. In both the complex cations, the conformation of the *iso*-propyl groupings of the BIOX ligand with respect to the C(3)–C(7) and C(6)–C(10) bonds is *gauche* (≈–60°) with the less bulky ^{i}Pr hydrogen atom facing in all cases the 5-membered acetyl palladacycle.

Concerning the metal coordination environment, in both complexes, the palladium ion is tetra-coordinated in a square planar geometry, the greatest displacement of the metal ion from the mean plane defined by the four donors is 0.1013(4) Å in complex **3a′**. The palladium-donor atom distances (Table 1) are in agreement with those found in analogous complexes retrieved in the Cambridge Structural Database (CSD), V. 5.31,[13] with the Pd(1)–N(1) distance shorter than the Pd(1)–N(2) one in both complexes as a result of the larger *trans* effect due to the (Ph)C moiety compared to the O-donor group. The moiety O(3)–C(13)–C(15)–C(17) is not planar as proved by the torsion about C(13)–C(15) (τ_1 = –25(2), 13(5) and –33(4)° for **2a**, **3a′** and **3a″**, respectively).

The orientation of the phenyl ring as defined by the value of the dihedral angle τ_2 (τ_2 = C(15)–C(17)–C(18)–C(19)) is in all cases comparable within 3σ (τ_2 = –65(2)°in **2a**, τ_2 = –80(3)° in **3a′** and τ_2 = –62(3)° in **3a″**). Moreover the relative orientation of the phenyl and methyl groups, *trans* in **2a** and *cis* in **3a**, can be quantified by the value of the dihedral angle τ_3 (τ_3 = C(16)–C(15)–C(17)–C(18)): –78(2)° in **2a**, –19(4) and 22(4)° in **3a′** and **3a″**, respectively. Thus, while in **2a** the conformation about τ_3 can be classified as -*syn*-clinal, in **3a** is ±*syn*-periplanar.[14] In this respect, it is noteworthy that in the analogous complex (*trans*-[Pd(CH(Ph)CH(Me)C(O)Me(^{i}Pr$_2$dab)]$^+$[BAr′$_4$]$^-$ (where ^{i}Pr$_2$dab = 1,4-diisopropyl-1,4-diazabuta-1,3-diene and Ar′ = 3,5-(CF$_3$)$_2$C$_6$H$_3$), which features the same palladacycle, the value of τ_3 corresponds to a –*anti*-periplanar conformation, while in the (*cis*-[Pd(CH(Ph)CH(Me)C(O)Me(^{i}Pr$_2$dab)]$^+$[BAr′$_4$]$^-$ complex a –*syn*-clinal conformation was found.[12] More comparable τ_1 and τ_2 values are observed within each *trans* and *cis* couple of metal complexes. Finally, there are no significant intermolecular interactions in the crystal lattice.

Table 2 Free energy differences (kcal mol^{-1}) and molar fractions of reaction species

		Molar fractions x_a			
Species	$G°_b - G°_a$[a]	Calc.	Obs.	$G°_{\bar{b}} - G°_{\bar{a}}$[a]	$G^{\ddagger}_b - G^{\ddagger}_a$[b]
2	1.81	0.95	0.80	–0.74	0.82
3	1.24	0.89	0.993	–0.32	2.93
4	2.10	0.97	0.96	–0.33	1.88

[a] Calculated from DFT electronic energies including the Gibbs energy correction at 298 K. LANL2DZ basis set for the palladium ion. [b] Calculated with eqn (1), using the observed molar fractions.

Selectivity of the olefin insertion

Concerning substituents configuration of the obtained palladacycles and the regio- and stereoselectivity of their formation, the above reported experimental finding can be rationalized as follows.

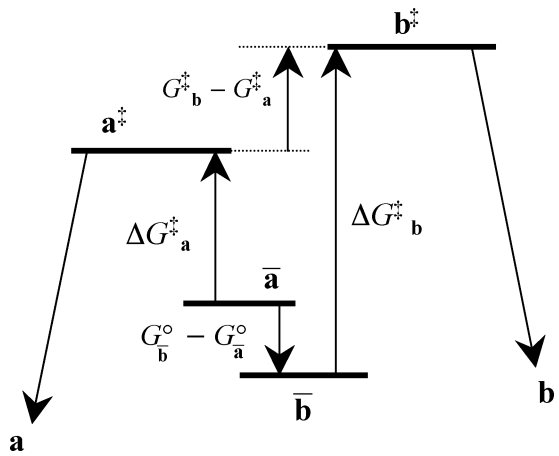
i. The conservation of the *trans* or *cis* geometry of substituents in compounds **2** and **3** can be explained with a concerted *syn* addition of the Pd-acetyl fragment to the olefin double bond, through a four-membered transition state (Scheme 2), in agreement with a generally accepted mechanism.[12]

ii. The high regioselectively observed in the insertion of styrene, tbms and cbms into the chiral bioxazoline complex **1** can be attributed to the steric effect of the phenyl group, which directs the acetyl group to bind to the less hindered carbon of the alkene.[5a,6,15]

iii. Concerning stereoselectivity, it is evident that in each case the molar fractions of isomers of **a** type (80 to 99%) are much larger than those of isomers **b** (Scheme 2). This fact could be attributed in first order approximation to the larger thermodynamic stability of palladacycles **a** over **b**. Actually, free energy differences $G°_b - G°_a$ estimated by density functional calculations (see computational details in the Experimental section) and reported in Table 2, are qualitatively in agreement with this suggestion. It appears that these values are largely due to the unfavourable steric interaction between phenyl and isopropyl groups in isomers **b**, while in isomers **a** these two groups are always far apart. Nevertheless, small but significant discrepancies between thermodynamically calculated and observed molar fractions (see Table 2) still remain to be explained, so that a consideration of the reaction path illustrated in Scheme 2 is necessary.

A simplistic hypothesis could be that stereoselectivity is controlled by the relative stability of the intermediates **ā** and **b̄** in which the *Re* or *Si* face of the olefin is coordinated respectively. However, a DFT estimate of the differences in the free energy of these intermediates $G°_{\bar{b}} - G°_{\bar{a}}$ revealed that they do not correlate at all with the observed concentrations of the final reaction products: for example, intermediate **2ā** is less stable than **2b̄** while leading to predominant product **2a**. Apparently, in any of the examined cases the less stable intermediates are more reactive, and this

suggests that the transition states for the conversion of **ā** forms must have a considerably lower energy than the transition states for the conversion of forms **b̄** The difference between these two energy values could be simply estimated in the following way. The reaction mechanism is assumed to be a rapid interconversion of intermediates **ā** and **b̄** followed by their change to products **a** and **b** *via* the respective transition states **a**‡ and **b**‡ (Scheme 3).



Scheme 3

According to this Curtin–Hammett-type scheme, the ratio between molar fractions x_b and x_a is given by [eqn (1)]:

$$G^{\ddagger}_{b} - G^{\ddagger}_{a} = -RT \ln \frac{x_b}{x_a} \quad (1)$$

This relationship shows that the relative amounts of products **a** and **b** do not depend on the energy difference between the intermediates ground states $G^{\circ}_{\bar{b}} - G^{\circ}_{\bar{a}}$, but only on the free energy difference between the transition states $G^{\ddagger}_{b} - G^{\ddagger}_{a}$. It is just this energy difference that governs the stereoselectivity of the process. The calculated values, reported in Table 2, show that the energy of the transition state for the production of **b**-type stereoisomers is in any case higher than for **a**-type isomers, in a range of about 1–3 kcal mol^{-1}, the upper value corresponding to high stereoselectivity. Now, there is one last question concerning the structure-selectivity relationship. Apparently, the free energy differences of the transition states depend mainly on the presence of steric interactions between the Ph of the olefin and the ^{i}Pr group of the bioxazoline ligand and the methyl of olefin and the formed acetyl group. Indeed, considering a TS as depicted in Scheme 2, in the case of the mono-substituted olefin styrene, the Ph-^{i}Pr interaction destabilizes species **4b**‡ relative to **4a**‡ by 1.88 kcal mol^{-1} (Table 2). On the other hand, for the di-substituted olefins, it turns out that the steric effects depend on configuration of substituents. In the case of the *trans* isomer, the Ph-^{i}Pr interaction destabilizes the species **2b**‡, while the Me-Acetyl interaction destabilizes the species **2a**‡, resulting in a net difference of 1.88–1.05 = 0.82 kcal mol^{-1}, corresponding to a modest stereoselectivity. In the case of the *cis* isomer the sum of the two interactions Ph-^{i}Pr + Me-Acyl = 1.88 + 1.05 = 2.93 kcal mol^{-1} destabilizes the species **3b**‡, resulting in very high selectivity. In summary, the above proposed mechanism suggests that the ultimate source of stereoselectivity is the steric interaction of the catalytic site with the olefin substituents in the transition states.

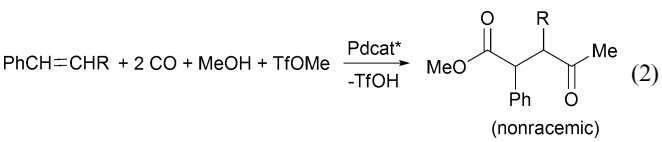
Similar conclusions were reached recently to rationalize the different reactivity observed in the polymerization of (*E*)- and (*Z*)-2-butene isomers with (α-diimine)Ni(II) complexes, known as "Brookhart catalysts".[16]

Reaction of complexes 2 and 3 with CO and methanolysis of the resulting products

With the aim of checking whether the **2** and **3** complexes can be intermediates for the synthesis of highly substituted chiral carbonyl compounds, their reactivity with carbon monoxide was investigated. Bubbling CO in a $CDCl_3$ solution of **3a** or **2** resulted in the formation of complex **5** or **7**, respectively; the open chain structure of the latter is evidenced by three *C*O chemical shifts observed in the ^{13}C NMR spectra: one at around 170 ppm, due to the *C*O coordinated to Pd, and the other two at more than 200 ppm due to the acyl *C*O of the chain. This assignment is further confirmed by the presence in the IR spectrum of three bands, one of which (2130 cm^{-1}) is typical of a CO ligand bonded to a metal center. With regard to the stereochemistry, the number of signals observed in the ^{13}C NMR spectrum of compound **5** indicates the presence of just one diastereoisomer and the successive methanolysis provides the 2,3-disubstituted γ-ketoester **6** in only one diastereomeric form; for the two chiral centres an *RR* configuration is predicted, corresponding to a retention of configuration with respect to complex **3a** and **5**. Instead, in the case of the mixture of palladacycle complexes **2a** and **2b**, after reaction with CO, compound **7** is obtained as a mixture of two diastereoisomers (**7a,7b**) (Scheme 1). Unfortunately, due to free carbon monoxide in solution, the ^{1}H NMR signals of **7** are broad and the less abundant diastereoisomer **7b** (corresponding to CO insertion in **2b**) is not clearly detectable; the presence of a shoulder in the terminal –COC*H*$_3$ signal is however an evidence of the formation of this diastereoisomer. Methanolysis of complex **7** leads mainly to the formation of γ-ketoester **8** (60%) together with the two epimeric lactones **9** and **10** (40%). The concomitant formation of compounds **9** and **10**, probably due to steric reasons, should take place through a non-stereoselective nucleophilic attack of methanol on the terminal acetyl carbon of the acylpalladium complex **7**, with consequent cyclization and formation of highly substituted chiral lactones.[17] Also, the palladacycle deriving from styrene reacts with CO to give the open chain structure complex having, nearly exclusively, an *SSR* configuration as its precursor **4**.[10b]

Catalytic synthesis of γ-ketoesters 6,8,11

On the basis of the acquired knowledge on the stoichiometric reactive sequences above described, we have devised a new enantioselective synthesis of γ-ketoesters, according to eqn (2):



(2)

For the realization of catalytic alkoxycarbonylation reactions of the aromatic olefins, we used enantiopure Pd(II) complex [Pd(OTf)$_2$(BIOX)] as catalyst, methanol as reagent and solvent,

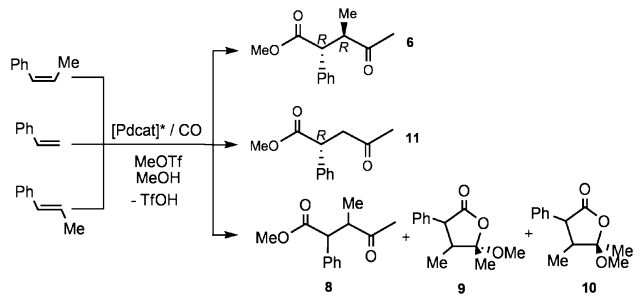
Table 3 Catalytic synthesis of γ-ketoesters[a]

Entry	Catalyst	Olefin	T/°C	Yield[b] (%)	TON	ee[d] (%)
1	[Pd(OTf)$_2$(BIOX)]	*c*bms	18	87	174	85
2	[Pd(OTf)$_2$(BIOX)]	*c*bms	0	74	148	83
3	[Pd(OTf)$_2$(BzBOX)]	*c*bms	18	94	188	87
4	[Pd(Me)(OTf)(BIOX)]	*c*bms	20	72	144	85
5	[Pd(OTf)$_2$(BIOX)]	styrene	18	88	176	90
6	[Pd(OTf)$_2$(BIOX)]	styrene	50	55	110	10
7	[Pd(OTf)$_2$(BIOX)]	*t*bms	18	68[c]	136	—

[a] Reaction conditions: *n* Pd = 0.045 mmol, olefin = 9 mmol, (olefin/Pd cat = 200/1), MeOTf V = 0.38 mL (9 mmol); solvent MeOH V = 2 mL; TFE V = 30 μL (0.3 mmol); P_{CO} = 3 atm. [b] Isolated yield, based on starting olefin. [c] Total yield. [d] Evaluated by ^{1}H NMR with shift reagent.

and MeOTf as methylation agent. Small amounts of TFE (TFE = 2,2,2-trifluoroethanol) were added to stabilize the active species.[18] The reaction was conducted in autoclave for 5 days under very mild conditions (T = 18 °C, P_{CO} = 3 atm); products were easily purified from the reaction mixture since no by-products were formed.

The nature and the composition of obtained compounds reflected closely what was observed for the stoichiometric model reactions. In fact, with *cis*-β-methylstyrene and with styrene the process resulted to be perfectly chemo- and regioselective leading to the exclusive formation of the disubstituted β-ketoesters **6** and **11** respectively, in good yield; while, in the case of *trans*-β-methylstyrene the reaction was less selective, producing the linear γ-ketoester **8** (41%) together with the two epimeric lactones **9** and **10** (27% total yield) (Scheme 4, Table 3).



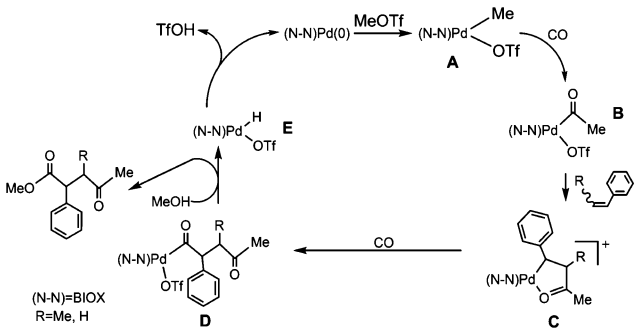
Scheme 4

Regarding the enantioselectivity, with styrene an *ee* of 90% was achieved (entry 5). This value is in agreement with the *de* (92%) found for the intermediate palladacycle complex **4** (Scheme 2). Instead in the case of *cis*-β-methylstyrene the *ee* value (85%), obtained in the catalytic reaction (entry 1, 3, 4), turned out to be lower than the *de* value (98.6%) of the intermediate palladacycle complex **3**, isolated in the stoichiometric reaction. This discrepancy suggests that a counterion effect is present; evidently the olefin enantioface discrimination is partially influenced also by the nature of the counterion and hence by the interactions between the anion and the catalyst metal centre.[19]

The best temperature for the process resulted to be *ca.* 20 °C; when running the reaction at 0 °C a slight decrease in productivity was observed (entry 2 *vs.* 1). Moreover, at a temperature of 50 °C a sharp decline in yields and a complete loss of enantioselectivity was registered (entry 6 *vs.* 5), probably due to a quicker decomposition of the catalyst and/or to a fast process of β-hydrogen elimination involving the intermediate five-membered palladacycle complex. Accordingly, products deriving from β-hydrogen elimination were detected in the stoichiometric reactions run at 40–50 °C.

In order to evaluate whether a different steric arrangement on the metal centre could have an effect, we performed a reaction with *cis*-β-methylstyrene using the catalyst [Pd(OTf)$_2$(BzBOX)] were BzBOX = (*S*)-4,4′-bis(phenylmethyl)-4,4′,5,5′-tetrahydro-2,2′-bioxazole and a slight increase in yield and *ee* was observed (entry 3 *vs.* 1). The use of the preformed complex [Pd(Me)(OTf)(BIOX)] resulted in a decrease in productivity (entry 4) while the *ee* (85%) was the same as found in entry 1 with catalyst [Pd(OTf)$_2$(BIOX)].

Regarding the catalytic cycle, we presume that, starting from a catalyst of the type [Pd(Me)(OTf)(BIOX)], the olefin and CO insertions should proceed easily, similarly to the stoichiometric reactions, producing the palladacycle **C** and then the open-chain acyl palladium complex complex **D** (Scheme 5). Alcoholysis of the latter is expected to generate, besides the γ-ketoester, also a palladium hydride species that evolves to give a Pd(0) complex, which will be reoxidized by methyl triflate restoring catalyst **A**.



Scheme 5

Although 1,4-dicarbonyl compounds and in particular γ-ketoesters are useful building blocks in organic synthesis and in the production of pharmaceutical compounds,[20] to our knowledge a direct catalytic synthesis of chiral γ-ketoesters, promoted by metal complexes, is unprecedented. Indeed, so far the synthesis of γ-ketoesters was achieved only through several steps, using a variety of different reaction pathways[5a,21] and only in very few particular cases the obtained products are optically active.[22]

Experimental

General

All manipulations were carried out under a nitrogen atmosphere by using Schlenk techniques. Solvents were dried by

standard methods and freshly distilled under nitrogen. *cis*-β-Methylstyrene (TCI Europe), styrene (Aldrich) and *trans*-β-methylstyrene (Aldrich) were distilled before use. Carbon monoxide (Cp grade 99.99%) was supplied by Air Liquide. CP grade chemicals were used as received unless otherwise stated. Chloroform-*d* and methylene chloride-d_2 were degassed and stored over 3 Å molecular sieves.

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 was synthesized as previously reported by us.[10b] Catalysts $[Pd(OTf)_2(BIOX)]$ and $[Pd(OTf)_2(BzBOX)]$ were BzBOX = (*S*)-4,4′-Bis(phenylmethyl)-4,4′,5,5′-tetrahydro-2,2′-bioxazole were prepared by a two step procedure, based on the synthesis of the corresponding neutral dichloride derivatives followed by the usual dehalogenation using silver trifluoromethane sulfonate.[19,23] Compounds $[PdCl_2(BIOX)]$,[24] $[PdCl_2(BzBOX)]$[21] and $NaBAr'_4$ (Ar′ = 3,5-$(CF_3)_2C_6H_3$)[25] were synthesized according to the literature. Complex [Pd(Me)(OTf)(BIOX)] was obtained from [Pd(Me)(Cl)(BIOX)][10b] by adding silver trifluoromethane sulfonate.

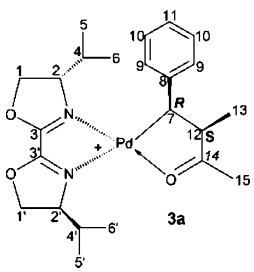
Elemental analyses (C, H, N) were carried out with a Fisons Instruments 1108 CHNS-O Elemental Analyser. Infrared spectra were measured in the range 4000–600 cm^{-1} on a Nicolet FT-IR Avatar 360 spectrometer. NMR spectra were measured in CD_2Cl_2 or $CDCl_3$ on a Bruker Advance 200 spectrometer with a multinuclear 5 mm probehead. ^1H and ^{13}C NMR chemical shifts are relative to TMS and were measured using the residual proton or carbon resonance of the deuterated solvents. The assignment of the ^1H and ^{13}C resonances was performed by using the ^1H-COSY, ^{13}C-DEPT, $^1H^{13}C$-HSQC, $^1H^{13}C$-HMBC and ^1H-NOESY experiments.

Synthesis and characterization of complexes 2, 3, 5, 7

In compounds **2, 3, 5, 7** the counterion $[BAr'_4]^-$ tetrakis[3,5-bis(trifluoromethyl)phenyl]borate(1−) gives a pattern of NMR signals with the following typical chemical shifts:

^1H NMR ($CDCl_3$, 293 K): δ 7.71 (8H, s, Ar′-H_o), 7.54 (4H, s, Ar′-H_p). ^{13}C NMR ($CDCl_3$, 293 K): δ 161.7 (q, ^1J(C,B) = 49.3 Hz, Ar′-C_i), 134.8 (s, 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 (s, Ar′-C_p).

cis-(*R*,*S*)-[Pd(CH(Ph)CH(CH_3)C(O)CH_3)(BIOX)]$^+$[BAr′$_4$]$^-$ (3a)



cis-β-Methylstyrene (125.83 μL, 0.97 mmol) was added to a dichloromethane solution (3 mL) of compound **1** (120 mg, 0.097 mmol) cooled to −25 °C. The solution was warmed to 0 °C and allowed reaction of until the starting Pd complex completely disappeared (1 h). Then the solution was filtered through Celite and the solvent was evaporated in vacuum. The resulting solid was washed with hexane (2 × 3 ml) and dried under vacuum to yield almost exclusively the palladacycle **3a**(*RS*) together a trace (0.7%) of the diastereoisomer **3b**(*SR*) (Scheme 2) as yellow powder (114 mg, 0.0844 mmol, 94%).

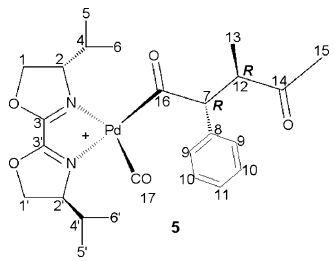
IR (liquid, $CDCl_3$): 1618 (CO-CH_3), 1640, 1612 (C═N) cm^{-1}

3a: ^1H NMR ($CDCl_3$, 293 K): δ 7.33 (3H, m, H10), 7.19 (3H, m, H11) 7.03–6.99 (2H, m, H9), 4.71–4.42 (4H, m, H1 and H1′), 4.21–4.13, 3.77–3.69 (1H each, m, H2 and H2′), 4.16 (1H, d, J = 6.8 Hz, H7), 3.15 (1H, dq, J = 6.8 and 7.2 Hz, H12), 2.41 (3H, s, H15), 2.20–2.04 (2H, m, H4 and H4′), 1.12 (3H, d, J = 7.2 Hz, H13), 0.96, 0.94, 0.92, 0.85 (3H each, d, J = 7.0, H5–H6 and H5′-H6′). $^{13}C\{^1H\}$NMR (CDCl3, 253 K): δ 238.6 (s, C14), 159.7, 157.5 (C3 and C3′), 141.2 (C8), 129.9 (C9), 126.9 (C10), 126.9 (C11), 74.5, 72.9 (C1 and C1′), 69.6, 66.2 (C2 and C2′), 59.4 (C12), 47.0 (C7), 30.9, 30.1 (C4 and C4′), 28.3 (C15), 18.5, 18.3, 16.4, 13.6 (C5–C6 and C5′-C6′), 14.6 (C13).

3b compound is present only in trace 0,7%, this percentage was determined from the intensity of the signal of H12 at δ 2.95.

Anal. calcd for $C_{55}H_{45}F_{24}N_2O_3BPd$ (1355.16): C, 48.75; H, 3.35; N, 2.07%. Found: C, 48.45; H, 2.90; N, 2.18%.

(*R*,*R*)-[Pd(C(O)CH(Ph)CH(CH_3)C(O)CH_3)(CO)(BIOX)]$^+$ [BAr′$_4$]$^-$ (5)

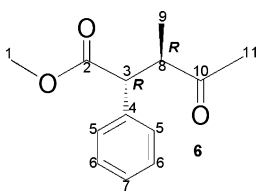


Bubbling of CO at −30 °C for 3 min into a $CDCl_3$ solution (0.6 ml) of **3** (50 mg, 0.037 mmol) resulted in the formation of the open chain complexes **5**. This complex was stable only in solution and for a few hours, which precludes elemental analysis.

IR (liquid, $CDCl_3$): 2127 (C≡O), 1750, 1713 (C═O), 1636, 1611 (C═N) cm^{-1}.

^1H NMR ($CDCl_3$, 293 K): δ 7.45–7.38 (3H, m, H10 and H11), 7.27–7.19 (2H, m, H9), 4.69–4.43 (4H, m br, H1 and H1′), 4.47 (1H, d, J = 6.9 Hz, H7), 4.28–4.13 (2H, m br, H2 and H2′), 3.25 (1H, dq, J = 6.9 and 7.1 Hz, H12), 2.07 (3H, s, H15), 1.94–1.78 (2 H, m br, H4 and H4′), 1.31 (3H, d, J = 7.1 Hz, H13), 0.85, 0.78 (6H each, d, J = 6.8 Hz, H5–H6 and H5′–H6′). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 253 K): δ 210.3 (C16), 207.0 (C14), 171.3 (C17), 161.5, 158.7 (C3 and C3′), 131.5 (C8), 130.5, 130.2, 130.1 (C9–C10 and C11), 74.4, 73.7 (C1 and C1′), 69.1, 68.1 (C2 and C2′), 68.9 (C7), 50.0 (C12), 30.9, 29.3 (C4 and C4′), 30.3 (C15), 18.3 15.7, 13.4 (C5–C6 and C5′-C6′), 15.4 (s, C13).

Stoichiometric methoxycarbonylation of complex 3a leading to the synthesis of compound 6

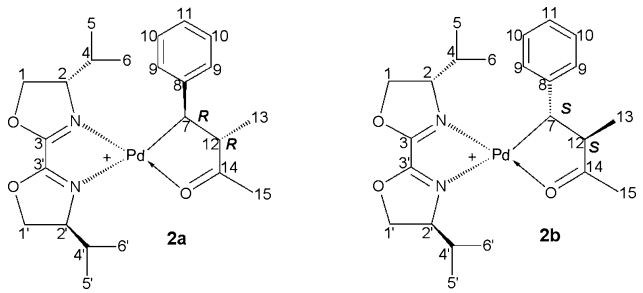


Complex **3a** (90 mg, 0.066 mmol) was dissolved in a mixture of dichloromethane (4 mL) and methanol (1 ml) and CO was bubbled, at −30 °C for 5 min. The reaction was stirred for 24 h at 4 °C, then the solvents were evaporated in vacuum. The residue was purified by column chromatography on silica gel with hexane/ethyl acetate = 6/4 as eluent, giving compound **6** as yellow oil (15.01 mg, 0.064 mmol, 97%).

(2*R*,3*R*)-Methyl 3-methyl-4-oxo-2-phenylpentanoate (6). ^{1}H NMR ($CDCl_3$, 293 K): δ 7.46–7.27 (5H, m, H5–H6 and H7), 3.87 (1H, d, J = 10.9, H3), 3.68 (3H, s, H1), 3.34 (1H, dq, J = 6.8 and 10.9 Hz, H8), 2.02 (3H, s, H11), 1.29 (3H, d, J = 6.8 Hz, H9). ^{13}C{^{1}H} NMR ($CDCl_3$, 293 K): δ 210.5 (s, C10), 173.1 (s, C2), 136.9 (s, C4), 128.7, 128.3 (s, C5 and C6), 127.7 (s, C7), 54.1 (s, C1), 52.1 (s, C3), 50.0 (s, C8), 30.0 (s, C11), 15.8 (s, C9).

Anal. calcd for $C_{13}H_{16}O_3$ (220.11): C, 70.89; H, 7.32%. Found: C, 70.88; H, 7.31%.

trans-(*R*,*R*)-[Pd(CH(Ph)CH(CH$_3$)C(O)CH$_3$)(BIOX)]$^+$[BAr′$_4$]$^-$ (2a) and _trans_-(*S*,*S*)-[Pd(CH(Ph)CH(CH$_3$)C(O)CH$_3$)(BIOX)]$^+$ [BAr′$_4$]$^-$ (2b)



trans-β-Methylstyrene (125.83 μL, 0.97 mmol) was added to a dichloromethane solution (3 mL) of compound **1** (120 mg, 0.097 mmol) cooled to −25 °C. The solution was warmed to 0 °C and allowed reaction until the starting Pd complex completely disappeared (3 h). Then the solution was filtered through Celite and the solvent was evaporated in vacuum. The resulting solid was washed with hexane (2 × 3 ml) and dried under vacuum. A 120 mg (0.088 mmol, 91%) sample of compound **2** was collected as a yellow solid which was shown to be a diastereoisomeric mixture of **2a**/**2b** (4/1 ratio).

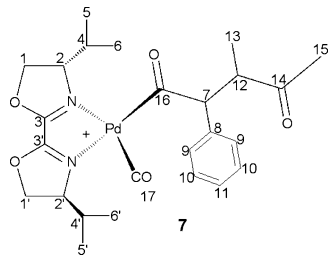
IR (liquid, $CDCl_3$): 1612 (CO–CH_3), 1636, 1612 (C═N) cm^{-1}.

2a: ^{1}H NMR (CDCl3, 293 K): δ 7.45–7.42 (2H, m, H9), 7.33–7.29 (1H, m, H11), 7.24–7.20 (2H, m, H10), 4.68 (1H, dd, J = 5.6 and J = 6.4 Hz, H1′), 4.53 (1H, dd, J = 4.8 and J = 5.6 Hz, H1′), 4.44 (1H, dd, J = 4.8 and J = 9.6 Hz, H1), 4.21 (1H, dd, J = 10.0 and J = 9.6 Hz, H1), 4.28–4.23 (1H, m, H2′) 2.15–2.10 (1H, m, H2), 3.68 (1H, d, J = 7.6 Hz, H7), 2.99 (1H, dq, J = 7.6 and 7.2 Hz, H12), 2.36 (3H, s, H15), 2.10–2.02 (1H, m, H4), 1.69–1.61 (1H, m, H4′), 1.17 (1H, d, J = 7.2 Hz, H13), 0.71, 0.62 (3H each, d, J = 7.0 Hz, H5 and H6), 0.94, 0.93, (3H each, d, J = 7.0 Hz, H5′ and H6′). ^{13}C{^{1}H}NMR ($CDCl_3$, 253 K): δ 238.1 (C14), 157.92 (C3), 159.2 (C3′), 145.1 (C8), 129.2, (C10), 127.9 (C9), 127.3 (C11), 74.3, 72.3 (C1 and C1′), 69.9, 64.8 (C2 and C2′), 62.9 (C12), 48.7 (C7), 30.6, 29.4 (C4 and C4′), 27.5 (C15), 18.0, 17.5, 16.2, 13.3 (C5–C6 and C5′-C6′), 14.4 (C13).

2b: ^{1}H-NMR ($CDCl_3$, 293 K): δ 4.20 (1H, d, J = 7.2 Hz, H7), 2.88 (1H, dq, J = 7.2 Hz, H12), 2.34 (3H, s, H15), 1.22 (1H, d, J = 7.2 Hz, H13).

Elemental analysis of the **2a** and **2b** mixture: anal. calcd for $C_{55}H_{45}F_{24}N_2O_3BPd$ (1355.16): C, 48.75; H, 3.35; N, 2.07%. Found: C, 48.48; H, 2.91; N, 2.13%.

(*R*,*S*)(*S*,*R*)-[Pd(C(O)CH(Ph)CH(CH$_3$)C(O)CH$_3$)(CO)(BIOX)]$^+$ [BAr′$_4$]$^-$ (7)

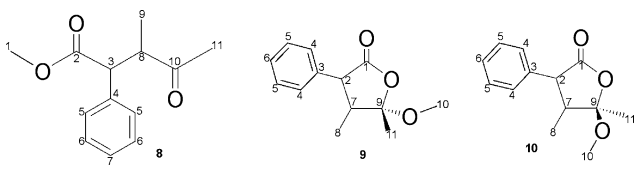


Bubbling of CO at −30 °C for 3 min into a $CDCl_3$ solution (0.6 ml) of **2a** and **2b** (50 mg, 0.037 mmol) resulted in the formation of the open chain complex **7** as a mixture of two diastereoisomers (**7a, 7b**). These complexes are stable only in solution and for a few hours, which precludes elemental analysis.

IR (liquid, $CDCl_3$): 2130 (C≡O), 1757, 1716 (C═O), 1639, 1610 (C═N) cm^{-1}.

^{1}H NMR ($CDCl_3$, 293 K): δ 7.48–7.25 (5H, m br, H9–H10 and H11), 4.78–4.10 (6H, m br, H1–H1′ and H2–H2′), 4.47 (1H, d, J = 10.5 Hz, H7), 3,44 (1H, dq, J = 10.5 and 7.2 Hz, H12), 2.28 (3H, s, H15), 1.86–1.68 (2H, m br, H4 and H4′), 0.90 (3H, d, J = 7.2 Hz, H13), 0.86, 0.77 (6H each, 2d, J = 6.7 Hz, H5–H6 and H5′–H6′). ^{13}C{^{1}H} NMR ($CDCl_3$, 253 K): δ 212.4, (C16), 209.1 (C14), 171.2 (C17), 161.2, 159.0 (C3 and C3′), 131.2 (C8), 130.6 (C9), 130.2 (C10), 129.9 (C11), 74.3, 74.1 (C1 and C1′), 70.0 (C7), 69.1, 68.0 (C2 and C2′), 49.4 (C12), 30.9, 29.1 (C4 and C4′), 29.5 (C15), 18.2 15.8, 13.5 (C5–C6 and C5′-C6′), 15.6 (C13).

Stoichiometric methoxycarbonylation of complexes 2a/2b leding to the synthesis of compounds 8, 9 and 10



The **2a**/**2b** mixture (100 mg, 0.073 mmol) was dissolved in a solution of dichloromethane (4 mL) and methanol (0.5 ml) and CO was bubbled, at −20 °C for 5 min. The reaction was stirred for 24 h at 4° C, formation of a black Pd precipitate was observed then solvents were evaporated in vacuum. The residue was purified by column chromatography on silica gel with hexane/ethyl acetate = 6/4 as eluent, giving a yellow oil containing a mixture of **8** (60%), **9** and **10** (40%) (16.99 mg, 0.072 mmol, 98%).

(2*RS*,3*SR*) Methyl 3-methyl-4-oxo-2-phenylpentanoate (8). ^{1}H NMR ($CDCl_3$, 293 K): δ 7.39–7.18 (5H, m, H5–H6 and H7), 3.80 (1H, d, J = 11.2 Hz, H3), 3.61 (3H, s, H1), 3.29 (1H, dq, J = 7.4 and 11.2 Hz, H8), 2.30 (3H, s, H11), 0.88 (3H, d, J = 7.4 Hz, H9).

^{13}C{^{1}H} NMR ($CDCl_3$, 293 K): δ 210.5 (C10), 173.1 (C2), 136.9 (C4), 128.7, 128.3 (C5 and C6), 127.7 (C7), 54.1 (C1), 52.1 (C3), 50.0 (C8), 30.0 (C11), 15.8 (C9).

5-Methoxy-4,5-dimethyl-3-phenyldihydrofuran-2(3H)-one (9). ^{1}H NMR ($CDCl_3$, 293 K): δ 7.39–7.18 (5H, m, H4–H5 and H6), 3.67 (1H, d, J = 12.1 Hz, H2), 3.44 (3H, s, H10), 2.43 (1H, dq, J = 6.8 and 12.1 Hz, H7), 1.64 (3H, s, H11), 1.07 (3H, d, J = 6.8 Hz, H8).

^{13}C{^{1}H} NMR ($CDCl_3$, 293 K): δ 174.4 (C1), 135.2 (C3), 128.5, 128.1 (C4 and C5), 127.8 (C6), 118.12 (C9), 54.6 (C2), 49.8 (C10), 37.9 (C7), 20.1 (C11), 14.3 (C8).

5-Methoxy-4,5-dimethyl-3-phenyldihydrofuran-2(3H)-one (10). ^{1}H NMR ($CDCl_3$, 293 K): δ 7.39–7.18 (5H, m, H4–H5 and H6), 3.51 (3H, s, H10), 3.44 (1H, d, J = 11.8 Hz, H2), 2.64 (1H, dq, J = 7.0 and 11.8 Hz, H7), 1.55 (3H, s, H11), 1.10 (3H, d, J = 7.0 Hz, H8).

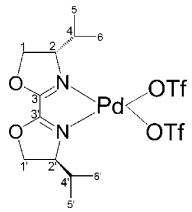
^{13}C{^{1}H} NMR ($CDCl_3$, 293 K): δ 175.2 (C1), 136.2 (C3), 128.3, 128.0 (C4 and C5), 127.6 (C6), 117.64 (C9), 54.3 (C2), 49.6 (C10), 37.7 (C7), 20.4 (C11), 15.1 (C8).

Elemental analysis of the **8, 9** and **10** mixture: anal. calcd for $C_{13}H_{16}O_3$ (220.11): C, 70.89; H, 7.32%. Found: C, 70.85; H, 7.34%.

(2*R*)-Methyl-4-oxo-2-phenylpentanoate (11)

The experimental data of this compound turned out to be the same as those reported in the literature.[5a]

Synthesis of the catalyst [Pd(OTf)$_2$(BIOX)]



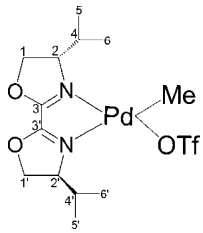
To a flame dried 10 mL round bottom flask equipped with a stir bar under a nitrogen atmosphere, were added [PdCl$_2$(BIOX)] (100 mg, 0.25 mmol) and 5 mL of CH_2Cl_2. The orange solution was stirred for 5 min and 13 mg of silver trifluoromethane sulfonate (0.50 mmol, 2.00 equiv.) was added in the exclusion of light. The cloudy orange solution was stirred for 4 h and the precipitate AgCl was removed by filtering the solution through Celite rinsing with CH_2Cl_2 (2 × 5 mL). The solvent was removed *in vacuo* to yield an yellow–orange solid in 96% yield (150.96 mg, 0.24 mmol).

^{1}H NMR (200 MHz, CD_2Cl_2, 293 K): δ (ppm) 4.65–4.42 (4H, m, H1 and H1′), 4.11–4.08, 3.72–3.58 (1H each, m, H2 and H2′), 2.34 (2H, m, H4 and H4′), 0.96, 0.94, 0.92, 0.85 (3H each, J = 7.2, d, H5–H6 and H5′-H6′). ^{13}C{^{1}H}NMR (CD_2Cl_2, 293 K): δ (ppm)157.2 (s, C3 and C3′), 74.3, 72.6 (s, C1 and C1′), 69.3, 66.7 (s, C2 and C2′), 30.5, 29.9 (s, C4 and C4′), 18.5, 18.3, 16.4, 13.6 (s, C5–C6 and C5–C6′).

^{19}F NMR (94.14 MHz, CD_2Cl_2): δ (ppm) = –78.46.

Anal. calcd for $C_{14}H_{20}F_6N_2O_8PdS_2$ (628.86): C 26.74, H 3.21, N 4.45%. Found: C 26.42, H 2.87, N 4.82%.

Synthesis of the catalyst [Pd(Me)(OTf)(BIOX)]



To a flame-dried 10 mL round bottom flask equipped with a stir bar under a nitrogen atmosphere, were added [Pd(Me)(Cl)(BIOX)] (100 mg, 0.25 mmol) and 5 mL of CH_2Cl_2. The orange solution was stirred for 5 min and 13 mg of silver trifluoromethane sulfonate (0.50 mmol, 2.00 equiv.) was added in the exclusion of light. The cloudy orange solution was stirred for 4 h and the precipitate AgCl was removed by filtering the solution through Celite rinsing with CH_2Cl_2 (2 × 5 mL). The solvent was removed *in vacuo* to yield an yellow–orange solid in 96% yield (150.96 mg, 0.24 mmol).

^{1}H NMR (200 MHz, CD_2Cl_2, 293 K): δ (ppm) 4.63–4.40 (4H, m, H1 and H1′), 4.18–4.12, 3.81–3.64 (1H each, m, H2 and H2′), 2.42 (2H, m, H4 and H4′), 1.12 (3H, s, Pd-Me), 0.98, 0.96, 0.94, 0.88 (3H each, J = 7.2, d, H5–H6 and H5′-H6′). 13C{1H}NMR (CD_2Cl_2, 293 K): δ (ppm) 157.2 (s, C3 and C3′), 74.3, 72.6 (s, C1 and C1′), 69.3, 66.7 (s, C2 and C2′), 30.5, 29.9 (s, C4 and C4′), 18.5, 18.3, 16.4, 13.6 (s, C5–C6 and C5′–C6′), 8.2 (s, Pd-Me). ^{19}F NMR (94.14 MHz, CD_2Cl_2): δ (ppm) = –78.35.

Anal. calcd for $C_{14}H_{23}F_3N_2O5PdS$ (494.83): C 33.98, H 4.68, N 5.66%. Found: C 33.53, H 4.65, N 5.22%.

Catalytic carbonylation procedure

Typically, a MeOH solution (2 mL) of the selected olefin (*cis*-β-methylstyrene, styrene or *trans*-β-methylstyrene) (9 mmol) was introduced by suction into an autoclave, previously evacuated by a vacuum pump, containing 0.045 mmol of the chosen catalyst, MeOTf (9 mmol, 1.47 g, 1.01 mL) and TFE (30 μL, 0.3 mmol). The autoclave was pressurized with CO to 3 atm. After 5 days, the reaction was stopped and the pressure was released. The formation of a black precipitate of palladium metal was observed, diethyl ether was added and the mixture was filtered off through Celite. The solution was evaporated and the residue was purified by column chromatography (SiO_2, hexane/ethyl acetate = 9/1, v/v) to give the corresponding γ-ketoesters. Isolated yields are given in Table 1.

The optical purity of γ-ketoesters **6** and **11**, resulting from cbms or styrene respectively, was determined by ^{1}H NMR using as shift reagent europium tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorate]. An excess of the latter (three equivalents) was added to a chloroform-d_1 solution of compound **6** or **11** producing a splitting of the –COMe signals.

^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ 2.22 (92.5%), δ 2.02 (7.5%) (s, 3H) in the case of compound **6**. ^{1}H NMR (200 MHz, CDCl3, 25 °C, TMS): δ 2.22 (95%), δ 2.02 (5%) (s, 3H) in the case of compound **11**.

Crystallographic data collection and refinement

Crystals of **2a** and **3a** were obtained by slow diffusion of hexane into a dichloromethane solution of compounds **2** and **3**.

Crystallographic data for **2a** and **3a** were collected on a Siemens SMART diffractometer equipped with a rotating anode and controlled with the SMART software.[26] The radiation used was Cu-Kα (λ = 1.5418 Å) and intensity data were acquired at 200 K. Five settings of ω were used and narrow data "frames" were collected for 0.3° increments in ω. A total of 3000 frames of data were stored providing a sphere of data.[27] Data reduction was performed with the SAINT 4.0 program.[28] Structures were then solved using the SIR97 program,[29] and then refined using the SHELX97 program.[30] Absorption corrections to all data were applied (SADABS).[31] In both cases the correct enantiomer was identified by means of the Flack parameter.[32] In this respect it must be noticed that in spite of the disorder affecting the atoms O(3), C(13), C(15) as well as the methyl carbon atoms C(14) and C(16) in **3a**, the stereochemistry of the carbon atom C(15) has been clearly established. For each disordered atom two positions were introduced, each one with an occupancy factor of 0.5. As often found for this species,[33] in both structures the fluorine atoms of the counter ion are disordered. During the refinement it was decided for every CF_3 group (with just one exception), to introduce and refine anisotropically the three highest density peaks. In the last CF_3 group a two sets of fluorine atoms were introduced with an occupancy factor of 0.5, these atoms were isotropically refined. Anisotropic thermal parameters were used for all the atoms but carbon and hydrogen atoms because of the otherwise poor observed reflections/parameters ratio. All the hydrogen atoms were introduced in calculated position and refined with a temperature factor depending on the one of the atom to which the hydrogen atom is bound. In complex **3a**, the hydrogen atoms bound to C(14), C(15), C(16) and C(17) were not introduced because of the above-mentioned disorder. Geometrical calculations were performed by PARST97[34] and molecular plots were produced by the ORTEP3 program.[35] Crystal data and structure refinement parameters are listed in Table 4.

Table 4 Crystal data and structure refinement details for **2a** and **3a**

	2a	**3a**
Empirical formula	$C_{55}H_{45}BF_{24}N_2O_3Pd$	$C_{55}H_{45}BF_{24}N_2O_3Pd$
M_r/g mol^{-1}	1355.14	1355.14
T/K	200	200
λ/Å	1.54184	1.54184
Crystal system	Triclinic	Triclinic
Space group	$P\bar{1}$	$P\bar{1}$
a/Å	10.231(1)	10.193(1)
b/Å	11.168(1)	11.051(1)
c/Å	13.729(1)	13.743(1)
α (°)	72.340(2)	72.314(3)
β (°)	75.249(2)	78.093(3)
γ (°)	80.614(2)	81.707(3)
V/Å^3	1439.2(2)	1437.6(2)
Z	1	1
D_c/g cm^{-3}	1.564	1.565
μ(Cu-K α)/mm^{-1}	3.712	3.716
Reflections collected	5458	6533
Unique reflections	4376	4821
R_{int}	0.0364	0.0386
Data/restraints/param	4376/3/500	4821/3/512
R_1 ($I > 2\sigma(I)$)	0.0734	0.0829
wR_2 (all data)	0.1912	0.2172
GOF on F^2	1.034	0.0829
Flack's parameter	0.05(1)	0.06(1)

Computational details

The Gaussian 03 (Revision C.02)[36] package was used. All the species were fully optimized by using the density functional method (DFT) by means of Becke's three-parameter hybrid method using the LYP correlation functional.[37] Two sets of calculations were performed on each modelled species by using two different effective core potentials for the palladium ion: the Hay and Wadt[38] potential and the Stuttgart/Dresden ECPs.[39] Neither the relative energy trends or the geometrical parameters were significantly affected by the two different potential schemes, as a consequence only data from the Hay and Wadt ECP were reported. The 6-31G* basis set[40] was used for all the other atomic species. In all cases the reliability of the stationary points (minima on the potential energy hypersurface) was assessed by evaluating the vibrational frequencies. Starting geometries for the **2ā** – **4ā** and **2b̄** – **4b̄** olefin adducts, as well as of their corresponding insertion products, were based on the available X-ray diffraction data of metal complexes featuring analogous molecular fragments (Cambridge Structural Database, version 5.31, November 2009).[13]

Conclusions

In short, the result of the present investigation is twofold. A carbonylation process of styrenes, catalyzed by an optically active bioxazoline palladium complex has been studied by isolating the reaction intermediates and determining their structure in solution by NMR spectroscopy and, for two cases, in the solid state by X-ray crystallography. The stereoselectivity of the reaction has been rationalized on the basis of a simple model of Curtin–Hammett type. According to this model, the degree of stereoselectivity appears to be proportional to the difference in the free energy of the two possible transition states $G^{\ddagger}_{b}$ and $G^{\ddagger}_{a}$, which correspond to the insertion of either the *Si* or the *Re* olefin face respectively. In conclusion, the ultimate source of stereoselectivity is the steric interaction of the catalytic site with the olefin substituents in the transition states.

Moreover, on the practical application side, the investigated reaction scheme allowed a new simple way to selectively synthesize, in one pot and in mild conditions, highly substituted chiral γ-ketoesters with a good enantiomeric excess.

The optimization of the process, the extension to variously substituted olefin as well as the use of other nucleophiles instead of the simple alcohol are currently in progress.

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